



## Clinical trial results:

### A Randomized, Open Label, Phase 2 Study Of the Selective Inhibitor of Nuclear Export (SINE) Selinexor (KPT-330) Versus Specified Physician's Choice in Patients 60 Years Old With Relapsed or Refractory Acute Myeloid Leukemia (AML) Who are Ineligible for Intensive Chemotherapy and/or Transplantation

#### Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2014-000920-26          |
| Trial protocol           | DE ES NL GB DK BE HU IT |
| Global end of trial date | 08 January 2018         |

#### Results information

|                                |                   |
|--------------------------------|-------------------|
| Result version number          | v1 (current)      |
| This version publication date  | 25 September 2021 |
| First version publication date | 25 September 2021 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | KCP-330-008 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02088541 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Karyopharm Therapeutics, Inc.  |
| Sponsor organisation address | 85 Wells Avenue, Newton, MA, United States, 02459  |
| Public contact               | Clinical Trial Information Desk, Karyopharm Therapeutics, Inc.,<br>clinicaltrials@karyopharm.com |
| Scientific contact           | Clinical Trial Information Desk, Karyopharm Therapeutics, Inc.,<br>clinicaltrials@karyopharm.com |

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 08 January 2018 |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 08 January 2018 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The main purpose of this study was to determine overall survival of selinexor as compared to physicians choice in subjects greater than or equal to ( $\geq$ ) 60 years old with relapsed/refractory AML that requires treatment and were ineligible for intensive chemotherapy and/or transplantation.

Protection of trial subjects:

This study was monitored by Argint International KFT and BCN Clinical Research SL in Europe and Israel and the Sponsor in North America in accordance with Sponsor's procedures, which meet the ICH Harmonised Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations, and with the ethical principles outlined in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 28 May 2014 |
| 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 | Netherlands: 18    |
| Country: Number of subjects enrolled | Poland: 7          |
| Country: Number of subjects enrolled | Spain: 42          |
| Country: Number of subjects enrolled | United Kingdom: 13 |
| Country: Number of subjects enrolled | Belgium: 16        |
| Country: Number of subjects enrolled | Denmark: 5         |
| Country: Number of subjects enrolled | France: 14         |
| Country: Number of subjects enrolled | Germany: 44        |
| Country: Number of subjects enrolled | Canada: 7          |
| Country: Number of subjects enrolled | Israel: 5          |
| Country: Number of subjects enrolled | Italy: 3           |
| Country: Number of subjects enrolled | United States: 143 |
| Worldwide total number of subjects   | 317                |
| EEA total number of subjects         | 162                |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 20  |
| From 65 to 84 years                       | 286 |
| 85 years and over                         | 11  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 317 subjects were enrolled at 95 sites between March 2014 (first subject enrolled) and 08 Jan 2018 (last subject completed study).

### Pre-assignment

Screening details:

Subjects who met the eligibility criteria were randomized into 5 treatment groups: Selinexor Approximately 55mg/m<sup>2</sup> (60 to 120 mg based on body surface area); Selinexor 60 mg (PV<5)(Equivalent to 35 mg/m<sup>2</sup>); Selinexor 60 mg (PV ≥5)(Equivalent to 35 mg/m<sup>2</sup>); Physician's Choice 1 (PV<5) and Physician's Choice 2 (PV≥5).

### Period 1

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

### Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes  |
| <b>Arm title</b>             | Selinexor Approximately 55 mg/m <sup>2</sup> (60 to 120 mg based on BSA) |

Arm description:

Subjects under protocol versions (PV) less than (<) 5.0 (those who had one prior line of acute myeloid leukemia [AML] therapy), received oral selinexor tablets at a dose of approximately 55 mg/m<sup>2</sup> (milligrams per square meter) (60 to 120 mg based on BSA) twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Selinexor    |
| Investigational medicinal product code |              |
| Other name                             | KPT-330      |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Subjects received Selinexor tablets, orally, at a dose of approximately 55 mg/m<sup>2</sup> (60 to 120 mg based on BSA) twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|                  |  |
|------------------|--|
| <b>Arm title</b> | Selinexor 60 mg (PV<5) (Equivalent to 35 mg/m <sup>2</sup> ) |
|------------------|--|

Arm description:

Subjects under PV < 5.0 (those who had one prior line of AML therapy), receive oral selinexor tablets at a fixed dose of 60 mg (equivalent to 35 mg/m<sup>2</sup>), based on BSA, twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Selinexor    |
| Investigational medicinal product code |              |
| Other name                             | KPT-330      |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Subjects received Selinexor tablets, orally, at a dose of 60 mg (equivalent to 35 mg/m<sup>2</sup>), based on BSA, twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|                  |   |
|------------------|---|
| <b>Arm title</b> | Selinexor 60 mg (PV ≥5) (Equivalent to 35 mg/m <sup>2</sup> ) |
|------------------|---|

Arm description:

Subjects under PV  $\geq 5$  (PV 5: those who had at least one prior line of AML therapy, PV 5.1: who had at least two prior line of AML therapy), receive oral selinexor tablets at a dose of 60 mg (equivalent to 35 mg/m<sup>2</sup>) twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Selinexor    |
| Investigational medicinal product code |              |
| Other name                             | KPT-330      |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Subjects received Selinexor tablets, orally, at a dose of 60 mg (equivalent to 35 mg/m<sup>2</sup>), based on BSA, twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|                  |                              |
|------------------|------------------------------|
| <b>Arm title</b> | Physician's Choice 1 (PV <5) |
|------------------|------------------------------|

Arm description:

Subjects under PV < 5.0 (those who had one prior line of AML therapy) received Best Supportive Care (BSC) which included blood product transfusions, antimicrobials, growth factors as needed, and hydroxyurea.

|  |                   |
|--|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Hydroxyurea       |
| Investigational medicinal product code |                   |
| Other name                             | Hydroxycarbamide  |
| Pharmaceutical forms                   | Capsule           |
| Routes of administration               | Oral use          |

Dosage and administration details:

Subjects under PV < 5.0 received Best Supportive Care (BSC) which included blood product transfusions, antimicrobials, growth factors as needed, and hydroxyurea.

|                  |                                     |
|------------------|-------------------------------------|
| <b>Arm title</b> | Physician's Choice 2 (PV $\geq 5$ ) |
|------------------|-------------------------------------|

Arm description:

Subjects under PV  $\geq 5$  (PV 5: those who had at least one prior line of AML therapy, PV 5.1: who had at least two prior line of AML therapy), received BSC along with subcutaneous injection of arabinoside cytosine (Ara-C), 20 mg, twice daily, for 10 days, repeated at 28 to 42 day intervals.

|  |  |
|--|--|
| Arm type                               | Active comparator                      |
| Investigational medicinal product name | Ara-C                                  |
| Investigational medicinal product code |  |
| Other name                             | Cytosine arabinoside                   |
| Pharmaceutical forms                   | Concentrate for solution for injection |
| Routes of administration               | Subcutaneous use                       |

Dosage and administration details:

Subcutaneous injection of arabinoside cytosine (Ara-C), 20 mg, twice daily, for 10 days, repeated at 28 to 42 day intervals.

| Number of subjects in period 1 | Selinexor<br>Approximately 55<br>mg/m <sup>2</sup> (60 to 120<br>mg based on BSA) | Selinexor 60 mg<br>(PV<5) (Equivalent<br>to 35 mg/m <sup>2</sup> ) | Selinexor 60 mg (PV<br>$\geq 5$ ) (Equivalent to<br>35 mg/m <sup>2</sup> ) |
|--------------------------------|---|--|--|
| Started                        | 71  | 27   | 118  |
| Completed                      | 0   | 0  | 0  |
| Not completed                  | 71  | 27   | 118  |
| Consent withdrawn by subject   | 3   | 2  | 9  |
| Physician decision             | 2   | 1  | 2  |

|   |    |    |    |
|---|----|----|----|
| Disease progression                             | 7  | 1  | 2  |
| Study terminated by Sponsor                     | 1  | 1  | 12 |
| Adverse event, non-fatal                        | 3  | -  | 3  |
| Death   | 51 | 21 | 85 |
| Other   | 2  | 1  | 3  |
| Subject treated with PC2 counted under this arm | -  | -  | 1  |
| Lost to follow-up                               | 2  | -  | 1  |

| <b>Number of subjects in period 1</b>           | Physician's Choice 1<br>(PV <5) | Physician's Choice 2<br>(PV ≥5) |
|---|---------------------------------|---------------------------------|
| Started   | 44                              | 57                              |
| Completed                                       | 0                               | 0                               |
| Not completed                                   | 44                              | 57                              |
| Consent withdrawn by subject                    | 7                               | 10                              |
| Physician decision                              | -                               | 2                               |
| Disease progression                             | 3                               | 1                               |
| Study terminated by Sponsor                     | 2                               | 6                               |
| Adverse event, non-fatal                        | 3                               | -                               |
| Death   | 28                              | 37                              |
| Other   | 1                               | 1                               |
| Subject treated with PC2 counted under this arm | -                               | -                               |
| Lost to follow-up                               | -                               | -                               |

## Baseline characteristics

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Selinexor Approximately 55 mg/m <sup>2</sup> (60 to 120 mg based on BSA) |
|-----------------------|--|

Reporting group description:

Subjects under protocol versions (PV) less than (<) 5.0 (those who had one prior line of acute myeloid leukemia [AML] therapy), received oral selinexor tablets at a dose of approximately 55 mg/m<sup>2</sup> (milligrams per square meter) (60 to 120 mg based on BSA) twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|                       |  |
|-----------------------|--|
| Reporting group title | Selinexor 60 mg (PV<5) (Equivalent to 35 mg/m <sup>2</sup> ) |
|-----------------------|--|

Reporting group description:

Subjects under PV < 5.0 (those who had one prior line of AML therapy), receive oral selinexor tablets at a fixed dose of 60 mg (equivalent to 35 mg/m<sup>2</sup>), based on BSA, twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|                       |  |
|-----------------------|--|
| Reporting group title | Selinexor 60 mg (PV ≥ 5) (Equivalent to 35 mg/m <sup>2</sup> ) |
|-----------------------|--|

Reporting group description:

Subjects under PV ≥ 5 (PV 5: those who had at least one prior line of AML therapy, PV 5.1: who had at least two prior line of AML therapy), receive oral selinexor tablets at a dose of 60 mg (equivalent to 35 mg/m<sup>2</sup>) twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Physician's Choice 1 (PV <5) |
|-----------------------|------------------------------|

Reporting group description:

Subjects under PV < 5.0 (those who had one prior line of AML therapy) received Best Supportive Care (BSC) which included blood product transfusions, antimicrobials, growth factors as needed, and hydroxyurea.

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | Physician's Choice 2 (PV ≥ 5) |
|-----------------------|-------------------------------|

Reporting group description:

Subjects under PV ≥ 5 (PV 5: those who had at least one prior line of AML therapy, PV 5.1: who had at least two prior line of AML therapy), received BSC along with subcutaneous injection of arabinoside cytosine (Ara-C), 20 mg, twice daily, for 10 days, repeated at 28 to 42 day intervals.

| Reporting group values                | Selinexor Approximately 55 mg/m <sup>2</sup> (60 to 120 mg based on BSA) | Selinexor 60 mg (PV<5) (Equivalent to 35 mg/m <sup>2</sup> ) | Selinexor 60 mg (PV ≥ 5) (Equivalent to 35 mg/m <sup>2</sup> ) |
|---------------------------------------|--|--|--|
| Number of subjects                    | 71   | 27   | 118  |
| Age categorical<br>Units: Subjects    |  |  |  |
| 18-64 years                           | 8  | 0  | 6  |
| 65-84 years                           | 60   | 27   | 107  |
| ≥ 85 years                            | 3  | 0  | 5  |
| Gender categorical<br>Units: Subjects |  |  |  |
| Female                                | 26   | 11   | 46   |
| Male                                  | 45   | 16   | 72   |

| Reporting group values             | Physician's Choice 1 (PV <5) | Physician's Choice 2 (PV ≥ 5) | Total |
|------------------------------------|------------------------------|-------------------------------|-------|
| Number of subjects                 | 44                           | 57                            | 317   |
| Age categorical<br>Units: Subjects |                              |                               |       |
| 18-64 years                        | 3                            | 3                             | 20    |
| 65-84 years                        | 40                           | 52                            | 286   |
| ≥ 85 years                         | 1                            | 2                             | 11    |

|                    |    |    |     |
|--------------------|----|----|-----|
| Gender categorical |    |    |     |
| Units: Subjects    |    |    |     |
| Female             | 22 | 16 | 121 |
| Male               | 22 | 41 | 196 |



## End points

### End points reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Selinexor Approximately 55 mg/m <sup>2</sup> (60 to 120 mg based on BSA) |
|-----------------------|--|

#### Reporting group description:

Subjects under protocol versions (PV) less than (<) 5.0 (those who had one prior line of acute myeloid leukemia [AML] therapy), received oral selinexor tablets at a dose of approximately 55 mg/m<sup>2</sup> (milligrams per square meter) (60 to 120 mg based on BSA) twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|                       |  |
|-----------------------|--|
| Reporting group title | Selinexor 60 mg (PV<5) (Equivalent to 35 mg/m <sup>2</sup> ) |
|-----------------------|--|

#### Reporting group description:

Subjects under PV < 5.0 (those who had one prior line of AML therapy), receive oral selinexor tablets at a fixed dose of 60 mg (equivalent to 35 mg/m<sup>2</sup>), based on BSA, twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|                       |  |
|-----------------------|--|
| Reporting group title | Selinexor 60 mg (PV ≥ 5) (Equivalent to 35 mg/m <sup>2</sup> ) |
|-----------------------|--|

#### Reporting group description:

Subjects under PV ≥ 5 (PV 5: those who had at least one prior line of AML therapy, PV 5.1: who had at least two prior line of AML therapy), receive oral selinexor tablets at a dose of 60 mg (equivalent to 35 mg/m<sup>2</sup>) twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Physician's Choice 1 (PV <5) |
|-----------------------|------------------------------|

#### Reporting group description:

Subjects under PV < 5.0 (those who had one prior line of AML therapy) received Best Supportive Care (BSC) which included blood product transfusions, antimicrobials, growth factors as needed, and hydroxyurea.

|                       |                               |
|-----------------------|-------------------------------|
| Reporting group title | Physician's Choice 2 (PV ≥ 5) |
|-----------------------|-------------------------------|

#### Reporting group description:

Subjects under PV ≥ 5 (PV 5: those who had at least one prior line of AML therapy, PV 5.1: who had at least two prior line of AML therapy), received BSC along with subcutaneous injection of arabinoside cytosine (Ara-C), 20 mg, twice daily, for 10 days, repeated at 28 to 42 day intervals.

### Primary: Overall Survival

|                 |                                 |
|-----------------|---------------------------------|
| End point title | Overall Survival <sup>[1]</sup> |
|-----------------|---------------------------------|

#### End point description:

Overall survival was defined as the time (in days) from the date of randomization to the date of death due to any cause. Subjects last known to be alive were censored at date of last contact. Intent-to-treat (ITT) population included all subjects who were randomized to study treatment under PV ≥ 5.0, regardless of whether or not they received study treatment. One subjects was randomized to receive selinexor 60 mg (PV ≥ 5) but was treated with physician's choice 2. Hence, this subjects was counted under selinexor 60 mg (PV ≥ 5).

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

#### End point timeframe:

Baseline until disease progression or discontinuation from the study, or death, whichever occurred first (up to a maximum of approximately 104 weeks)

#### Notes:

[1] - 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: As pre-specified in the protocol, data was assessed and reported of the Selinexor 60 mg (PV ≥ 5) and Physician's Choice 2 (PV ≥ 5) arm only for this endpoint.

|                                  |  |                                     |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| <b>End point values</b>          | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> ) | Physician's Choice 2 (PV $\geq 5$ ) |  |  |
| Subject group type               | Reporting group  | Reporting group                     |  |  |
| Number of subjects analysed      | 118  | 57                                  |  |  |
| Units: Days                      |  |                                     |  |  |
| median (confidence interval 95%) | 94.0 (78.0 to 158.0)   | 170.0 (111.0 to 220.0)              |  |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> )                                       |
| Comparison groups                       | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> ) v Physician's Choice 2 (PV $\geq 5$ ) |
| Number of subjects included in analysis | 175  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | = 0.4221   |
| Method                                  | Logrank  |
| Parameter estimate                      | Hazard ratio (HR)  |
| Point estimate                          | 1.18   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.79   |
| upper limit                             | 1.75   |

## Primary: Percentage of Subjects With Overall Survival of at Least 3 Months (OS3.0)

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Overall Survival of at Least 3 Months (OS3.0) <sup>[2]</sup> |
|-----------------|--|

### End point description:

Overall survival was defined as the time (in days) from the date of randomization to the date of death due to any cause. Subjects last known to be alive were censored at date of last contact. Analysis was performed using Kaplan-Meier method. ITT population included all subjects who were randomized to study treatment under PV  $\geq 5.0$ , regardless of whether or not they received study treatment. One subjects was randomized to receive selinexor 60 mg (PV $\geq 5$ ) but was treated with physician's choice 2. Hence, this subjects was counted under selinexor 60 mg (PV $\geq 5$ ).

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

### End point timeframe:

From randomization (Day 1) up to 3 months

### Notes:

[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: As pre-specified in the protocol, data was assessed and reported of the Selinexor 60 mg (PV  $\geq 5$ ) and Physician's Choice 2 (PV  $\geq 5$ ) arm only for this endpoint.

|                                  |  |                                     |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| <b>End point values</b>          | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> ) | Physician's Choice 2 (PV $\geq 5$ ) |  |  |
| Subject group type               | Reporting group  | Reporting group                     |  |  |
| Number of subjects analysed      | 118  | 57                                  |  |  |
| Units: percent                   |  |                                     |  |  |
| number (confidence interval 95%) | 53.49 (43.54 to 62.44)   | 70.73 (55.60 to 81.52)              |  |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> )                                       |
| Comparison groups                       | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> ) v Physician's Choice 2 (PV $\geq 5$ ) |
| Number of subjects included in analysis | 175  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | = 0.9464   |
| Method                                  | Logrank  |

## Secondary: Percentage of Subjects With Complete Remission Rate (CRR) for Those Who Achieved Complete Remission (CR)

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With Complete Remission Rate (CRR) for Those Who Achieved Complete Remission (CR) <sup>[3]</sup> |
|-----------------|---|

End point description:

CRR was analyzed using International Working Group (IWG) 2003 criteria, as the difference in the proportions of subjects with IWG results of CR. CR per IWG 2003 criteria was defined as morphologic presence of < 5 percentage (%) myeloblasts in bone marrow, the absence of circulating blasts, hematologic recovery (as evidenced by a peripheral blood absolute neutrophil count (ANC) > 1000 cells/microliter (mcL) and platelet count > 100,000/mcL, with no need for red blood cell (RBC) transfusions), and the absence of extramedullary disease. ITT population included all subjects who were randomized to study treatment under PV $\geq 5.0$ , regardless of whether or not they received study treatment. One subjects was randomized to receive selinexor 60 mg (PV $\geq 5$ ) but was treated with physician's choice 2. Hence, this subjects was counted under selinexor 60 mg (PV $\geq 5$ ).

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

End point timeframe:

Baseline until disease progression or discontinuation from the study, or death, whichever occurred first (up to a maximum of approximately 104 weeks)

Notes:

[3] - 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: As pre-specified in the protocol, data was assessed and reported of the Selinexor 60 mg (PV  $\geq 5$ ) and Physician's Choice 2 (PV  $\geq 5$ ) arm only for this endpoint.

|                                  |  |                                     |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| <b>End point values</b>          | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> ) | Physician's Choice 2 (PV $\geq 5$ ) |  |  |
| Subject group type               | Reporting group  | Reporting group                     |  |  |
| Number of subjects analysed      | 118  | 57                                  |  |  |
| Units: percentage of subject     |  |                                     |  |  |
| number (confidence interval 95%) | 5.1 (1.9 to  | 0.0 (0.0 to 6.3)                    |  |  |

**Statistical analyses**

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> )                                       |
| Comparison groups                       | Physician's Choice 2 (PV $\geq 5$ ) v Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> ) |
| Number of subjects included in analysis | 175  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | = 0.0986   |
| Method                                  | Cochran-Mantel-Haenszel  |

**Secondary: Median Disease-Free Survival (DFS) for Subjects Who Achieved Complete Remission (CR)**

|                 |   |
|-----------------|---|
| End point title | Median Disease-Free Survival (DFS) for Subjects Who Achieved Complete Remission (CR) <sup>[4]</sup> |
|-----------------|---|

## End point description:

DFS for CRR based on IWG criteria, was calculated from the first date of response of CR to the date of progression or recurrence, or date of death if progression or recurrence did not occur. Subjects who discontinued prior to disease progression or recurrence or did not progress as of the time of the analysis were censored at the time of last radiologic assessment. CR per IWG 2003 criteria was defined as morphologic presence of < 5 % myeloblasts in bone marrow, the absence of circulating blasts, hematologic recovery (as evidenced by a peripheral blood ANC > 1000 cells/mcL and platelet count > 100,000/mcL, with no need for RBC transfusions), and the absence of extramedullary disease. ITT population. Here, "99999" indicates that upper limits of 95% CI was not estimable due to less number of subject. This endpoint was only defined for CR subjects. For Physician Choice 2, there was zero CR subjects.

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

## End point timeframe:

Baseline until disease progression or discontinuation from the study, or death, whichever occurred first (up to a maximum of approximately 104 weeks)

## Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As pre-specified in the protocol, data was assessed and reported of the Selinexor 60 mg (PV  $\geq 5$ ) and Physician's Choice 2 (PV  $\geq 5$ ) arm only for this endpoint.

|                                  |  |                                     |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| <b>End point values</b>          | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> ) | Physician's Choice 2 (PV $\geq 5$ ) |  |  |
| Subject group type               | Reporting group  | Reporting group                     |  |  |
| Number of subjects analysed      | 6  | 0 <sup>[5]</sup>                    |  |  |
| Units: Days                      |  |                                     |  |  |
| median (confidence interval 95%) | 121 (49.0 to 99999)  | ( to )                              |  |  |

## Notes:

[5] - No subjects in this group achieved CR.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Modified Complete Remission Rate (mCRR) for Those Who Achieved Complete Remission (CR) or Complete Remission With Incomplete Hematologic Recovery (Cri)

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Modified Complete Remission Rate (mCRR) for Those Who Achieved Complete Remission (CR) or Complete Remission With Incomplete Hematologic Recovery (Cri) <sup>[6]</sup> |
|-----------------|--|

End point description:

mCRR was defined as the point estimate of the percentage of subjects who had CR, CRi, or CRp. Responses defined as per IWG 2003 response criteria: Morphologic CR: < 5% myeloblasts in bone marrow, the absence of circulating blasts, hematologic recovery (as evidenced by a peripheral blood ANC > 1000 cells/mcL and platelet count > 100,000/mcL, with no need for RBC transfusions), and the absence of extramedullary disease. Morphologic CRp: All criteria for CR except for residual neutropenia (<1x10<sup>9</sup>/L) or thrombocytopenia (<100 x10<sup>9</sup>/L), Cri (< 5% bone marrow blasts with residual neutropenia [ANC < 1000 cells/mcL] or thrombocytopenia [platelets < 100,000/mcL]), normal maturation of all cellular components in the bone marrow, no extramedullary disease and transfusion independent. ITT population included all subjects who were randomized to study treatment under PV>=5.0, regardless of whether or not they received study treatment.

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

End point timeframe:

Baseline until disease progression or discontinuation from the study, or death, whichever occurred first (up to a maximum of approximately 104 weeks)

Notes:

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

Justification: As pre-specified in the protocol, data was assessed and reported of the Selinexor 60 mg (PV >=5) and Physician's Choice 2 (PV >=5) arm only for this endpoint.

| End point values                 | Selinexor 60 mg (PV >=5) (Equivalent to 35 mg/m <sup>2</sup> ) | Physician's Choice 2 (PV >=5) |  |  |
|----------------------------------|--|-------------------------------|--|--|
| Subject group type               | Reporting group  | Reporting group               |  |  |
| Number of subjects analysed      | 118  | 57                            |  |  |
| Units: percentage of subjects    |  |                               |  |  |
| number (confidence interval 95%) | 11.9 (6.6 to 19.1)   | 3.5 (0.4 to 12.1)             |  |  |

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title              | Selinexor 60 mg (PV >=5) (Equivalent to 35 mg/m <sup>2</sup> )                                 |
| Comparison groups                       | Selinexor 60 mg (PV >=5) (Equivalent to 35 mg/m <sup>2</sup> ) v Physician's Choice 2 (PV >=5) |
| Number of subjects included in analysis | 175  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | superiority  |
| P-value                                 | = 0.0844   |
| Method                                  | Cochran-Mantel-Haenszel  |

## Secondary: Median Disease-Free Survival (DFS) for Subjects Who Achieved Complete Remission or CR With Incomplete Hematologic Recovery (CRi) or Complete Remission With Incomplete Platelet Recovery (CRp)

|                 |   |
|-----------------|---|
| End point title | Median Disease-Free Survival (DFS) for Subjects Who Achieved Complete Remission or CR With Incomplete Hematologic Recovery (CRi) or Complete Remission With Incomplete Platelet Recovery (CRp) <sup>[7]</sup> |
|-----------------|---|

### End point description:

DFS: the duration from start of the complete response achieved until disease progression or death from any cause. Responses defined by IWG 2003 Response Criteria: morphologic CR: <5% myeloblasts in bone marrow, the absence of circulating blasts, hematologic recovery (as evidenced by a peripheral blood ANC > 1000 cells/mcL and PC > 100,000/mcL, with no need for RBC transfusions), and the absence of extramedullary disease. Morphologic CRp: All criteria for CR except for residual neutropenia (<1x10<sup>9</sup>/L) or thrombocytopenia (<100 x10<sup>9</sup>/L), Cri < 5% bone marrow blasts with residual neutropenia [ANC < 1000 cells/mcL] or thrombocytopenia [platelets < 100,000/mcL], normal maturation of all cellular components in the bone marrow, no extramedullary disease and transfusion independent. ITT Population. Number of subjects analysed signifies those subjects evaluable for this endpoint. Here, "99 and 99999" indicates that upper and lower limits of 95% CI was not estimable due to less number of subjects.

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

### End point timeframe:

Baseline until disease progression or discontinuation from the study, or death, whichever occurred first (up to a maximum of approximately 104 weeks)

### Notes:

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

Justification: As pre-specified in the protocol, data was assessed and reported of the Selinexor 60 mg (PV ≥ 5) and Physician's Choice 2 (PV ≥ 5) arm only for this endpoint.

| End point values                 | Selinexor 60 mg (PV ≥ 5) (Equivalent to 35 mg/m <sup>2</sup> ) | Physician's Choice 2 (PV ≥ 5) |  |  |
|----------------------------------|--|-------------------------------|--|--|
| Subject group type               | Reporting group  | Reporting group               |  |  |
| Number of subjects analysed      | 14   | 2                             |  |  |
| Units: Days                      |  |                               |  |  |
| median (confidence interval 95%) | 175.0 (61.0 to 288.0)  | 106.0 (99 to 99999)           |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Overall Response Rate (ORR)

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Overall Response Rate (ORR) <sup>[8]</sup> |
|-----------------|--|

### End point description:

Overall response rate was defined as the point estimate of the percentage of subjects who achieved CR (disappearance of all target and non-target lesions), partial response (PR) (≥ 30 % decrease in sum of longest diameters of target lesions taking as reference baseline sum longest diameters associated to non-progressive disease response for non-target lesions). CRi; < 5% BM blasts with residual neutropenia [ANC < 1000 cells/mcL] or thrombocytopenia [platelets < 100,000/mcL]. CRp; All criteria for CR except for residual neutropenia (<1x10<sup>9</sup>/L) or thrombocytopenia (<100 x10<sup>9</sup>/L) and morphologic leukemia-free state (MLFS); morphologic BM blast clearance to <5% in a marrow sample in which ≤ 200 cells enumerated or cellularity is ≥ 10%, in absence of blasts with Auer rods, no hematologic recovery required. ITT population included all subjects who were randomized to study treatment under PV ≥ 5.0, regardless of whether or not they received study treatment.

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

End point timeframe:

Baseline until disease progression or discontinuation from the study, or death, whichever occurred first (up to a maximum of approximately 104 weeks)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As pre-specified in the protocol, data was assessed and reported of the Selinexor 60 mg (PV  $\geq 5$ ) and Physician's Choice 2 (PV  $\geq 5$ ) arm only for this endpoint.

| End point values                 | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> ) | Physician's Choice 2 (PV $\geq 5$ ) |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| Subject group type               | Reporting group  | Reporting group                     |  |  |
| Number of subjects analysed      | 118  | 57                                  |  |  |
| Units: percentage of subjects    |  |                                     |  |  |
| number (confidence interval 95%) | 13.6 (8.0 to 21.1)   | 8.8 (2.9 to 19.3)                   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Response (DOR)

|                 |   |
|-----------------|---|
| End point title | Duration of Response (DOR) <sup>[9]</sup> |
|-----------------|---|

End point description:

DOR was calculated from date of response of CR, CRi, CRp, MLFS, or PR to date of progression or recurrence based on IWG criteria. CR:  $<5\%$  myeloblasts in bone marrow, absence of circulating blasts, hematologic recovery (peripheral blood ANC  $>1000$  cells/mcL, platelet count  $>100,000$ /mcL, no need for RBC transfusions), absence of extramedullary disease. PR: No circulating blasts, neutrophil count  $\geq 1.0 \times 10^9/L$ , platelet count  $\geq 100 \times 10^9/L$ ,  $\geq 50\%$  reduction in bone marrow blast to 6% to 25%, or blasts less than or equal to ( $\leq$ ) 5% if Auer rods are present. Number of subjects analysed signifies those subjects evaluable for this endpoint. Here, "99999" indicates that upper and lower limits of 95% CI was not estimable due to less number of subjects.

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

End point timeframe:

Baseline until disease progression or discontinuation from the study, or death, whichever occurred first (up to a maximum of approximately 104 weeks)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As pre-specified in the protocol, data was assessed and reported of the Selinexor 60 mg (PV  $\geq 5$ ) and Physician's Choice 2 (PV  $\geq 5$ ) arm only for this endpoint.

| End point values                 | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> ) | Physician's Choice 2 (PV $\geq 5$ ) |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| Subject group type               | Reporting group  | Reporting group                     |  |  |
| Number of subjects analysed      | 16   | 5                                   |  |  |
| Units: Days                      |  |                                     |  |  |
| median (confidence interval 95%) | 204.0 (117.0 to 334.0)   | 148.0 (85.0 to 99999)               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Disease Control Rate (DCR)

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Disease Control Rate (DCR) <sup>[10]</sup> |
|-----------------|--|

End point description:

DCR: Point estimate of % of subjects with CR, CRi, CRp, MLFS, PR, or SD for  $\leq 4$  weeks. CR:  $< 5\%$  myeloblasts in bone marrow (BM), absence of circulating blasts, hematologic recovery (peripheral blood ANC  $> 1000$  cells/mcL and platelet count  $> 100,000$ /mcL, no need of RBC transfusions), absence of extramedullary disease. PR: No circulating blasts, Neutrophil count  $\geq 1.0 \times 10^9/L$ , Platelet count  $\geq 100 \times 10^9/L$ ,  $\geq 50\%$  reduction in BM blast to 6% to 25%, or blasts  $\leq 5\%$  if Auer rods are present. CRp: All criteria for CR except for residual neutropenia ( $< 1 \times 10^9/L$ ) or thrombocytopenia ( $< 100 \times 10^9/L$ ), CRi:  $< 5\%$  BM blasts with residual neutropenia [ANC  $< 1000$  cells/mcL] or thrombocytopenia [platelets  $< 100,000$ /mcL]. MLFS: morphologic BM blast clearance to  $< 5\%$  in a marrow sample in which  $\leq 200$  cells enumerated or cellularity is  $\geq 10\%$ , in absence of blasts with Auer rods, no hematologic recovery required, SD: failure to achieve a response but not meeting criteria for disease progression over period of  $> 4$  weeks.

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

End point timeframe:

Up to 4 weeks from the date of randomization to the date of progression or recurrence based on IWG criteria

Notes:

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

Justification: As pre-specified in the protocol, data was assessed and reported of the Selinexor 60 mg (PV  $\geq 5$ ) and Physician's Choice 2 (PV  $\geq 5$ ) arm only for this endpoint.

| End point values                 | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> ) | Physician's Choice 2 (PV $\geq 5$ ) |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| Subject group type               | Reporting group  | Reporting group                     |  |  |
| Number of subjects analysed      | 118  | 57                                  |  |  |
| Units: percentage of subjects    |  |                                     |  |  |
| number (confidence interval 95%) | 50.8 (41.5 to 60.2)  | 40.4 (27.6 to 54.2)                 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Disease Control Rate

|                 |  |
|-----------------|--|
| End point title | Duration of Disease Control Rate <sup>[11]</sup> |
|-----------------|--|

End point description:

Duration of DCR calculated for all subjects with DCR. CR:  $< 5\%$  myeloblasts in BM, absence of circulating blasts, hematologic recovery (peripheral blood ANC  $> 1000$  cells/mcL and platelet count  $>$



100,000/mcL, no need for RBC transfusions), absence of extra medullary disease. PR: No circulating blasts, Neutrophil count  $\geq 1.0 \times 10^9/L$ , Platelet count  $\geq 100 \times 10^9/L$ ,  $\geq 50$  % reduction in BM blast to 6% to 25%, or blasts  $\leq 5\%$  if Auer rods are present. CRp: All criteria for CR except for residual neutropenia ( $< 1 \times 10^9/L$ ), CRi;  $< 5\%$  BM blasts with residual neutropenia [ANC  $< 1000$  cells/mcL]. MLFS; morphologic BM blast clearance to  $< 5\%$  in a marrow sample in which  $\leq 200$  cells enumerated/cellularity is  $\geq 10\%$ , in absence of blasts with Auer rods, no hematologic recovery required and SD; failure to achieve a response but not meeting criteria for disease progression over period of  $> 4$  weeks. Here, "number of subjects analysed" signifies those subjects evaluable for this endpoint.

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

End point timeframe:

Up to 4 weeks from the date of randomization to the date of progression or recurrence based on IWG criteria

Notes:

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

Justification: As pre-specified in the protocol, data was assessed and reported of the Selinexor 60 mg (PV  $\geq 5$ ) and Physician's Choice 2 (PV  $\geq 5$ ) arm only for this endpoint.

|                                  |  |                                     |  |  |
|----------------------------------|--|-------------------------------------|--|--|
| <b>End point values</b>          | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> ) | Physician's Choice 2 (PV $\geq 5$ ) |  |  |
| Subject group type               | Reporting group  | Reporting group                     |  |  |
| Number of subjects analysed      | 60   | 23                                  |  |  |
| Units: Days                      |  |                                     |  |  |
| median (confidence interval 95%) | 187 (125 to 261)   | 233 (155 to 263)                    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Quality of Life (QoL) and Patient-Reported Outcomes (Functional Assessment of Cancer Therapy -Leukemia [FACT-Leu])

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Quality of Life (QoL) and Patient-Reported Outcomes (Functional Assessment of Cancer Therapy -Leukemia [FACT-Leu]) <sup>[12]</sup> |
|-----------------|--|

End point description:

QoL was assessed by FACT-Leu. FACT-Leu combines General version of the FACT-G with a leukemia-specific sub-scale (17 items). Sub-scales for the FACT-G are Physical Well-Being (7 items), Social/Family Well-Being (7 items), Emotional Well-Being (6 items) & Functional Well-Being (7 items). TOI (total of 31 items) was primary measurement of interest, comprising Physical and Functional sub-scales plus the leukemia - specific sub-scale. Each item was rated on a 5-point Likert scale. Range from 0=(Not at all) to 4=(Very much); TOI had a score ranging from 0-124. Higher scores indicated improvement in well being. QoL was performed at baseline (prior to first dose of study treatment), Day 1 of each cycle on or after second, and at final visit. Here, "number of subjects analysed" signifies those subjects evaluable for this endpoint and "number analysed" signifies those subjects evaluable for specified categories. Here, "99999" indicates SD was not estimated due to single and no subject.

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

End point timeframe:

Baseline, Day 1 of each treatment cycle (a maximum of 20 cycles: 28 days per cycle) up to 30 days after last dose of study drug (final visit)

Notes:

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

Justification: Per protocol, only descriptive analyses was planned for this endpoint.

| End point values                     | Selinexor 60 mg (PV $\geq 5$ ) (Equivalent to 35 mg/m <sup>2</sup> ) | Physician's Choice 2 (PV $\geq 5$ ) |  |  |
|--------------------------------------|--|-------------------------------------|--|--|
| Subject group type                   | Reporting group  | Reporting group                     |  |  |
| Number of subjects analysed          | 71   | 34                                  |  |  |
| Units: Unit on a scale               |  |                                     |  |  |
| arithmetic mean (standard deviation) |  |                                     |  |  |
| Baseline (n=65, 29)                  | 70.5 ( $\pm$ 15.20)  | 75.4 ( $\pm$ 14.74)                 |  |  |
| C2D1 (n=59, 25)                      | 0.5 ( $\pm$ 16.50)   | -1.9 ( $\pm$ 15.18)                 |  |  |
| C3D1 (n=39, 16)                      | -1.9 ( $\pm$ 16.88)  | -5.4 ( $\pm$ 22.25)                 |  |  |
| C4D1 (n=26, 7)                       | -1.2 ( $\pm$ 15.70)  | -7.4 ( $\pm$ 25.41)                 |  |  |
| C5D1 (n=20, 7)                       | -2.4 ( $\pm$ 16.84)  | 1.9 ( $\pm$ 8.40)                   |  |  |
| C6D1 (n=19, 6)                       | -3.4 ( $\pm$ 15.66)  | -4.7 ( $\pm$ 13.20)                 |  |  |
| C7D1 (n=15, 5)                       | -5.0 ( $\pm$ 17.21)  | -11.8 ( $\pm$ 27.43)                |  |  |
| C8D1 (n=15, 5)                       | -3.9 ( $\pm$ 15.78)  | -10.6 ( $\pm$ 7.83)                 |  |  |
| C9D1 (n=11, 4)                       | -2.7 ( $\pm$ 7.47)   | -8.0 ( $\pm$ 8.49)                  |  |  |
| C10D1 (n=9, 3)                       | 2.4 ( $\pm$ 13.19)   | -10.7 ( $\pm$ 12.70)                |  |  |
| C11D1 (n=7, 2)                       | -0.1 ( $\pm$ 8.65)   | -10.0 ( $\pm$ 9.90)                 |  |  |
| C12D1 (n=6, 2)                       | -3.7 ( $\pm$ 11.69)  | -7.0 ( $\pm$ 16.97)                 |  |  |
| C13D1 (n=4, 1)                       | -3.3 ( $\pm$ 6.40)   | -9.0 ( $\pm$ 99999)                 |  |  |
| C14D1 (n=3, 1)                       | -4.0 ( $\pm$ 3.46)   | -15.0 ( $\pm$ 99999)                |  |  |
| C15D1 (n=2, 1)                       | 1.5 ( $\pm$ 3.54)  | -10.0 ( $\pm$ 99999)                |  |  |
| C16D1 (n=0, 1)                       | 99999 ( $\pm$ 99999)   | -15.0 ( $\pm$ 99999)                |  |  |
| C17D1 (n=1, 1)                       | -15.0 ( $\pm$ 99999)   | -7.0 ( $\pm$ 99999)                 |  |  |
| C18D1 (n=1, 0)                       | -1.0 ( $\pm$ 99999)  | 99999 ( $\pm$ 99999)                |  |  |
| C19D1 (n=1, 0)                       | -12.0 ( $\pm$ 99999)   | 99999 ( $\pm$ 99999)                |  |  |
| C20D1 (n=1, 0)                       | -14.0 ( $\pm$ 99999)   | 99999 ( $\pm$ 99999)                |  |  |
| Final visit (n=25, 12)               | 2.5 ( $\pm$ 17.71)   | -1.7 ( $\pm$ 20.46)                 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in European Quality of Life-5 Dimension (EQ-5D) Health Questionnaire Visual Analogue Scale (VAS)

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in European Quality of Life-5 Dimension (EQ-5D) Health Questionnaire Visual Analogue Scale (VAS) <sup>[13]</sup> |
|-----------------|---|

End point description:

EQ-5D descriptive system comprises of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: 1=no problems, 2=slight

problems, 3=moderate problems, 4=severe problems, and 5=extreme problems. EQ-5D-5L is a standardized instrument that measures health-related quality of life for men with prostate cancer. EQ-5D consists of EQ-5D descriptive system and EQ VAS. EQ-5D-5-VAS records subject's self-rated health on a vertical VAS that allows them to indicate their health state that can range from 0 (worst imaginable) to 100 (best imaginable), higher scores indicating a better health state. PP Population. Here, "number of subjects analysed" signifies those subjects evaluable for this endpoint and "number analysed" signifies those subjects evaluable for specified categories. Here, "99999" indicates standard deviation was not estimated due to single and no subject at that time point.

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

End point timeframe:

Baseline, Day 1 of each treatment cycle (a maximum of 20 cycles: 28 days per cycle) up to 30 days after last dose of study drug (final visit)

Notes:

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

Justification: As pre-specified in the protocol, data was assessed and reported of the Selinexor 60 mg (PV >=5) and Physician's Choice 2 (PV >=5) arm only for this endpoint.

| End point values                     | Selinexor 60 mg (PV >=5) (Equivalent to 35 mg/m <sup>2</sup> ) | Physician's Choice 2 (PV >=5) |  |  |
|--------------------------------------|--|-------------------------------|--|--|
| Subject group type                   | Reporting group  | Reporting group               |  |  |
| Number of subjects analysed          | 71   | 34                            |  |  |
| Units: Unit on a scale               |  |                               |  |  |
| arithmetic mean (standard deviation) |  |                               |  |  |
| Baseline (n=59, 30)                  | 67.9 (± 19.51)   | 63.5 (± 21.10)                |  |  |
| C2D1 (n=51, 25)                      | -7.5 (± 23.45)   | 0.8 (± 15.82)                 |  |  |
| C3D1 (n=35, 17)                      | -13.3 (± 25.04)  | -5.2 (± 23.54)                |  |  |
| C4D1 (n=23, 9)                       | -6.1 (± 20.80)   | -5.0 (± 11.46)                |  |  |
| C5D1 (n=18, 10)                      | -0.9 (± 20.83)   | -2.0 (± 15.31)                |  |  |
| C6D1 (n=17, 7)                       | -11.2 (± 25.90)  | -1.4 (± 24.10)                |  |  |
| C7D1 (n=14, 5)                       | -3.7 (± 23.91)   | 4.0 (± 10.84)                 |  |  |
| C8D1 (n=13, 5)                       | 0.1 (± 16.77)  | 5.0 (± 9.35)                  |  |  |
| C9D1 (n=9, 4)                        | 4.6 (± 13.25)  | 5.0 (± 10.80)                 |  |  |
| C10D1 (n=7, 4)                       | 0.7 (± 18.58)  | 6.3 (± 15.48)                 |  |  |
| C11D1 (n=6, 2)                       | 0.8 (± 18.55)  | -5.0 (± 21.21)                |  |  |
| C12D1 (n=6, 2)                       | 3.3 (± 16.63)  | -5.0 (± 28.28)                |  |  |
| C13D1 (n=3, 1)                       | 6.7 (± 20.21)  | 10.0 (± 99999)                |  |  |
| C14D1 (n=3, 1)                       | 6.7 (± 25.66)  | 15.0 (± 99999)                |  |  |
| C15D1 (n=2, 1)                       | 3.5 (± 30.41)  | -10.0 (± 99999)               |  |  |
| C16D1 (n=0, 1)                       | 99999 (± 99999)  | 20 (± 99999)                  |  |  |
| C17D1 (n=1, 1)                       | 25.0 (± 99999)   | -5.0 (± 99999)                |  |  |
| C18D1 (n=1, 0)                       | 25.0 (± 99999)   | 99999 (± 99999)               |  |  |
| C19D1 (n=1, 0)                       | 30.0 (± 99999)   | 99999 (± 99999)               |  |  |
| C20D1 (n=1, 0)                       | 35.0 (± 99999)   | 99999 (± 99999)               |  |  |

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From start of study drug administration to 30 days after last dose of study drug (approximately 48 months)

Adverse event reporting additional description:

Same event may appear as both an adverse event (AE) and a serious adverse event (SAE). However, what is presented are distinct events. An event may be categorized as serious in one subject and as non-serious in another subjects, or one subject may have experienced both a serious and non-serious event during the study.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 20.1   |

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Selinexor Approximately 55 mg/m <sup>2</sup> (60 to 120 mg Based on BSA) |
|-----------------------|--|

Reporting group description:

Subjects under PV <5.0 (those who had one prior line of AML therapy), received oral selinexor tablets at a dose of approximately 55 mg/m<sup>2</sup> (60 to 120 mg based on BSA) twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|                       |   |
|-----------------------|---|
| Reporting group title | Selinexor 60mg (PV<5) (Equivalent to 35 mg/m <sup>2</sup> ) |
|-----------------------|---|

Reporting group description:

Subjects under PV <5.0 (those who had one prior line of AML therapy), received oral selinexor tablets at a fixed dose of 60 mg (equivalent to 35 mg/m<sup>2</sup>), based on BSA, twice weekly, on Day 1 and 3 of each week of 4-week cycle (28 days per cycle).

|                       |  |
|-----------------------|--|
| Reporting group title | Selinexor 60mg (PV ≥5) (Equivalent to 35 mg/m <sup>2</sup> ) |
|-----------------------|--|

Reporting group description:

Subjects under PV ≥5 (PV 5: those who had at least one prior line of AML therapy, PV 5.1: who had at least two prior line of AML therapy), received oral selinexor tablets at a dose of 60 mg (equivalent to 35 mg/m<sup>2</sup>) twice weekly, on Day 1 and 3 of each week of 4- week cycle (28 days per cycle).

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Physician's Choice 1 (PV <5) |
|-----------------------|------------------------------|

Reporting group description:

Subjects under PV < 5.0 (those who had one prior line of AML therapy) received Best Supportive Care (BSC) which included blood product transfusions, antimicrobials, growth factors as needed, and hydroxyurea.

|                       |                              |
|-----------------------|------------------------------|
| Reporting group title | Physician's Choice 2 (PV ≥5) |
|-----------------------|------------------------------|

Reporting group description:

Subjects under PV ≥ 5 (PV 5: those who had at least one prior line of AML therapy, PV 5.1: who had at least two prior line of AML therapy), received BSC along with subcutaneous injection of arabinoside cytosine (Ara-C), 20 mg, twice daily, for 10 days, repeated at 28 to 42 day intervals.

| Serious adverse events                            | Selinexor Approximately 55 mg/m <sup>2</sup> (60 to 120 mg Based on BSA) | Selinexor 60mg (PV<5) (Equivalent to 35 mg/m <sup>2</sup> ) | Selinexor 60mg (PV ≥5) (Equivalent to 35 mg/m <sup>2</sup> ) |
|---|--|---|--|
| Total subjects affected by serious adverse events |  |   |  |
| subjects affected / exposed                       | 58 / 71 (81.69%)   | 15 / 27 (55.56%)  | 89 / 115 (77.39%)  |
| number of deaths (all causes)                     | 51   | 21  | 85   |
| number of deaths resulting from adverse events    | 24   | 3   | 28   |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |                 |
| Cerebellar tumour   |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0           |
| Basal cell carcinoma  |                |                |                 |
| alternative assessment type: Systematic                             |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0           |
| Squamous cell carcinoma   |                |                |                 |
| alternative assessment type: Systematic                             |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0           |
| Vascular disorders  |                |                |                 |
| Hypotension   |                |                |                 |
| alternative assessment type: Systematic                             |                |                |                 |
| subjects affected / exposed   | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 4 / 115 (3.48%) |
| occurrences causally related to treatment / all                     | 1 / 1          | 0 / 0          | 1 / 4           |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0           |
| Aortic aneurysm   |                |                |                 |
| alternative assessment type: Systematic                             |                |                |                 |
| subjects affected / exposed   | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (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           |
| Haematoma   |                |                |                 |
| alternative assessment type: Systematic                             |                |                |                 |
| subjects affected / exposed   | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0           |
| Peripheral ischaemia  |                |                |                 |
| alternative assessment type: Systematic                             |                |                |                 |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed                          | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Thrombophlebitis                                     |                |                |                 |
| alternative assessment type: Systematic              |                |                |                 |
| subjects affected / exposed                          | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Venous thrombosis                                    |                |                |                 |
| alternative assessment type: Systematic              |                |                |                 |
| subjects affected / exposed                          | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| 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 disorders and administration site conditions |                |                |                 |
| General physical health deterioration                |                |                |                 |
| alternative assessment type: Systematic              |                |                |                 |
| subjects affected / exposed                          | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all           | 1 / 1          | 0 / 0          | 0 / 2           |
| Fatigue  |                |                |                 |
| alternative assessment type: Systematic              |                |                |                 |
| subjects affected / exposed                          | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 8 / 115 (6.96%) |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          | 7 / 8           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 2 / 2           |
| Pyrexia  |                |                |                 |
| alternative assessment type: Systematic              |                |                |                 |
| subjects affected / exposed                          | 4 / 71 (5.63%) | 1 / 27 (3.70%) | 7 / 115 (6.09%) |
| occurrences causally related to treatment / all      | 2 / 4          | 0 / 1          | 1 / 7           |
| deaths causally related to treatment / all           | 0 / 1          | 0 / 0          | 0 / 1           |
| Condition aggravated                                 |                |                |                 |
| alternative assessment type: Systematic              |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all  | 0 / 0          | 0 / 0          | 0 / 0           |
| Multiple organ dysfunction syndrome<br>alternative assessment type:<br>Systematic                             |                |                |                 |
| subjects affected / exposed   | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (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           |
| Asthenia<br>alternative assessment type:<br>Systematic  |                |                |                 |
| subjects affected / exposed   | 3 / 71 (4.23%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences causally related to treatment / all   | 3 / 3          | 0 / 0          | 2 / 2           |
| deaths causally related to treatment / all  | 0 / 0          | 0 / 0          | 0 / 0           |
| Malaise<br>alternative assessment type:<br>Systematic   |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| 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<br>alternative assessment type:<br>Systematic  |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all  | 0 / 0          | 0 / 0          | 0 / 0           |
| Social circumstances<br>Social stay hospitalisation<br>alternative assessment type:<br>Systematic             |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (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           |
| Reproductive system and breast disorders<br>Vaginal haemorrhage<br>alternative assessment type:<br>Systematic |                |                |                 |



|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                |                |                 |
| Respiratory failure                             |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 2          | 0 / 0          | 0 / 1           |
| Acute respiratory failure                       |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (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           |
| Haemoptysis                                     |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| 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                                |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1           |
| Pneumonia aspiration                            |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0           |
| Dyspnoea  |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 2 / 71 (2.82%) | 1 / 27 (3.70%) | 3 / 115 (2.61%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 1          | 1 / 3           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Epistaxis                                       |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Cough   |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Pulmonary embolism                              |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| 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 mass                                  |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Psychiatric disorders                           |                |                |                 |
| Confusional state                               |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 4 / 71 (5.63%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences causally related to treatment / all | 3 / 4          | 0 / 0          | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Mental status changes                           |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Hallucination                                   |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Organic brain syndrome                          |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Investigations                                  |                |                |                 |
| Weight decreased                                |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Blood alkaline phosphatase increased            |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (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           |
| C-reactive protein increased                    |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| 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 change                        |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Enterococcus test positive                      |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| 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                            |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Vitamin B12 decreased                           |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| 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  |                |                |                 |
| Fall  |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1           |
| Subdural haematoma                              |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1           |
| Subdural haemorrhage                            |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (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           |
| Subarachnoid haemorrhage<br>alternative assessment type:<br>Systematic                 |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all  | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0           |
| Femur fracture<br>alternative assessment type:<br>Systematic                           |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all  | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0           |
| Cardiac disorders<br>Atrial fibrillation<br>alternative assessment type:<br>Systematic |                |                |                 |
| subjects affected / exposed  | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all  | 0 / 2          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all   | 0 / 1          | 0 / 0          | 0 / 3           |
| Cardiac failure<br>alternative assessment type:<br>Systematic                          |                |                |                 |
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences causally related to treatment / all  | 1 / 1          | 0 / 0          | 1 / 3           |
| deaths causally related to treatment / all   | 0 / 1          | 0 / 0          | 0 / 0           |
| Cardiac failure congestive<br>alternative assessment type:<br>Systematic               |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all  | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 1           |
| Cardio-respiratory arrest<br>alternative assessment type:<br>Systematic                |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Ventricular fibrillation                        |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1           |
| Acute coronary syndrome                         |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (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           |
| Bradycardia                                     |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Sinus bradycardia                               |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (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           |
| Tachyarrhythmia                                 |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Nervous system disorders                        |                |                |                 |
| Cerebral haemorrhage                            |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences causally related to treatment / all                                | 0 / 1          | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all                                     | 0 / 1          | 0 / 0          | 0 / 1           |
| Cerebrovascular accident<br>alternative assessment type:<br>Systematic         |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all                                | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all                                     | 0 / 0          | 0 / 0          | 0 / 1           |
| Dizziness<br>alternative assessment type:<br>Systematic                        |                |                |                 |
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences causally related to treatment / all                                | 1 / 1          | 0 / 0          | 2 / 2           |
| deaths causally related to treatment / all                                     | 1 / 1          | 0 / 0          | 0 / 0           |
| Embolic stroke<br>alternative assessment type:<br>Systematic                   |                |                |                 |
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (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           |
| Haemorrhage intracranial<br>alternative assessment type:<br>Systematic         |                |                |                 |
| subjects affected / exposed  | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all                                | 1 / 2          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all                                     | 0 / 0          | 0 / 0          | 0 / 1           |
| Haemorrhagic cerebral infarction<br>alternative assessment type:<br>Systematic |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all                                | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all                                     | 0 / 0          | 0 / 0          | 0 / 1           |
| Loss of consciousness<br>alternative assessment type:<br>Systematic            |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all                                | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all                                     | 0 / 0          | 0 / 0          | 0 / 1           |

|  |                |                |                 |  |
|--|----------------|----------------|-----------------|--|
| Syncope  |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |
| subjects affected / exposed                        | 2 / 71 (2.82%) | 1 / 27 (3.70%) | 3 / 115 (2.61%) |  |
| occurrences causally related to<br>treatment / all | 1 / 2          | 1 / 1          | 1 / 3           |  |
| deaths causally related to<br>treatment / all      | 1 / 1          | 0 / 0          | 0 / 0           |  |
| Ataxia   |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Cerebral infarction                                |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Encephalopathy                                     |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Headache   |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Ischaemic stroke                                   |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Presyncope   |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |



|   |                  |                 |                   |
|---|------------------|-----------------|-------------------|
| subjects affected / exposed                     | 1 / 71 (1.41%)   | 0 / 27 (0.00%)  | 0 / 115 (0.00%)   |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0           | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0           | 0 / 0             |
| Blood and lymphatic system disorders            |                  |                 |                   |
| Febrile neutropenia                             |                  |                 |                   |
| alternative assessment type: Systematic         |                  |                 |                   |
| subjects affected / exposed                     | 16 / 71 (22.54%) | 4 / 27 (14.81%) | 20 / 115 (17.39%) |
| occurrences causally related to treatment / all | 8 / 16           | 4 / 4           | 11 / 20           |
| deaths causally related to treatment / all      | 1 / 2            | 1 / 1           | 2 / 4             |
| Anaemia   |                  |                 |                   |
| alternative assessment type: Systematic         |                  |                 |                   |
| subjects affected / exposed                     | 2 / 71 (2.82%)   | 0 / 27 (0.00%)  | 2 / 115 (1.74%)   |
| occurrences causally related to treatment / all | 1 / 2            | 0 / 0           | 2 / 2             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0           | 0 / 0             |
| Thrombocytopenia                                |                  |                 |                   |
| alternative assessment type: Systematic         |                  |                 |                   |
| subjects affected / exposed                     | 1 / 71 (1.41%)   | 1 / 27 (3.70%)  | 1 / 115 (0.87%)   |
| occurrences causally related to treatment / all | 1 / 1            | 1 / 1           | 1 / 1             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0           | 0 / 0             |
| Neutropenia                                     |                  |                 |                   |
| alternative assessment type: Systematic         |                  |                 |                   |
| subjects affected / exposed                     | 1 / 71 (1.41%)   | 0 / 27 (0.00%)  | 1 / 115 (0.87%)   |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0           | 1 / 1             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0           | 0 / 0             |
| Leukostasis syndrome                            |                  |                 |                   |
| alternative assessment type: Systematic         |                  |                 |                   |
| subjects affected / exposed                     | 0 / 71 (0.00%)   | 0 / 27 (0.00%)  | 0 / 115 (0.00%)   |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0           | 0 / 0             |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0           | 0 / 0             |
| Splenic infarction                              |                  |                 |                   |
| alternative assessment type: Systematic         |                  |                 |                   |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Ear and labyrinth disorders                     |                |                |                 |
| Vertigo   |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Eye disorders                                   |                |                |                 |
| Cataract  |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 3 / 3           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Gastrointestinal disorders                      |                |                |                 |
| Diarrhoea                                       |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 3 / 71 (4.23%) | 1 / 27 (3.70%) | 6 / 115 (5.22%) |
| occurrences causally related to treatment / all | 3 / 3          | 1 / 1          | 4 / 6           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1           |
| Vomiting  |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 4 / 71 (5.63%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences causally related to treatment / all | 3 / 4          | 0 / 0          | 3 / 3           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Gastrointestinal haemorrhage                    |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Abdominal pain upper                            |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Constipation                                    |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (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           |
| Diverticular perforation                        |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Large intestinal haemorrhage                    |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Mouth ulceration                                |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Nausea  |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 3           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Tooth loss                                      |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| Hepatobiliary disorders                            |                |                |                 |
| Cholecystitis acute                                |                |                |                 |
| alternative assessment type:<br>Systematic         |                |                |                 |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 2           |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Hyperbilirubinaemia                                |                |                |                 |
| alternative assessment type:<br>Systematic         |                |                |                 |
| subjects affected / exposed                        | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to<br>treatment / all | 1 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Renal and urinary disorders                        |                |                |                 |
| Acute kidney injury                                |                |                |                 |
| alternative assessment type:<br>Systematic         |                |                |                 |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 1           |
| Oliguria   |                |                |                 |
| alternative assessment type:<br>Systematic         |                |                |                 |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 1           |
| Renal failure                                      |                |                |                 |
| alternative assessment type:<br>Systematic         |                |                |                 |
| subjects affected / exposed                        | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Musculoskeletal and connective tissue disorders    |                |                |                 |
| Bone pain  |                |                |                 |
| alternative assessment type:<br>Systematic         |                |                |                 |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Muscular weakness                                  |                |                |                 |

|  |                  |                 |                  |
|--|------------------|-----------------|------------------|
| alternative assessment type:<br>Systematic         |                  |                 |                  |
| subjects affected / exposed                        | 0 / 71 (0.00%)   | 0 / 27 (0.00%)  | 1 / 115 (0.87%)  |
| occurrences causally related to<br>treatment / all | 0 / 0            | 0 / 0           | 1 / 1            |
| deaths causally related to<br>treatment / all      | 0 / 0            | 0 / 0           | 0 / 0            |
| Infections and infestations                        |                  |                 |                  |
| Pneumonia  |                  |                 |                  |
| alternative assessment type:<br>Systematic         |                  |                 |                  |
| subjects affected / exposed                        | 10 / 71 (14.08%) | 4 / 27 (14.81%) | 10 / 115 (8.70%) |
| occurrences causally related to<br>treatment / all | 3 / 10           | 3 / 4           | 3 / 10           |
| deaths causally related to<br>treatment / all      | 2 / 5            | 1 / 1           | 1 / 5            |
| Lung infection                                     |                  |                 |                  |
| alternative assessment type:<br>Systematic         |                  |                 |                  |
| subjects affected / exposed                        | 3 / 71 (4.23%)   | 1 / 27 (3.70%)  | 1 / 115 (0.87%)  |
| occurrences causally related to<br>treatment / all | 0 / 3            | 0 / 1           | 1 / 1            |
| deaths causally related to<br>treatment / all      | 0 / 2            | 0 / 1           | 0 / 0            |
| Sepsis   |                  |                 |                  |
| alternative assessment type:<br>Systematic         |                  |                 |                  |
| subjects affected / exposed                        | 8 / 71 (11.27%)  | 1 / 27 (3.70%)  | 3 / 115 (2.61%)  |
| occurrences causally related to<br>treatment / all | 4 / 8            | 0 / 1           | 1 / 3            |
| deaths causally related to<br>treatment / all      | 1 / 3            | 0 / 0           | 0 / 1            |
| Septic shock                                       |                  |                 |                  |
| alternative assessment type:<br>Systematic         |                  |                 |                  |
| subjects affected / exposed                        | 1 / 71 (1.41%)   | 0 / 27 (0.00%)  | 3 / 115 (2.61%)  |
| occurrences causally related to<br>treatment / all | 0 / 1            | 0 / 0           | 2 / 3            |
| deaths causally related to<br>treatment / all      | 0 / 1            | 0 / 0           | 2 / 3            |
| Escherichia sepsis                                 |                  |                 |                  |
| alternative assessment type:<br>Systematic         |                  |                 |                  |
| subjects affected / exposed                        | 1 / 71 (1.41%)   | 0 / 27 (0.00%)  | 0 / 115 (0.00%)  |
| occurrences causally related to<br>treatment / all | 1 / 1            | 0 / 0           | 0 / 0            |
| deaths causally related to<br>treatment / all      | 1 / 1            | 0 / 0           | 0 / 0            |
| Pneumonia fungal                                   |                  |                 |                  |
| alternative assessment type:<br>Systematic         |                  |                 |                  |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0           |
| Klebsiella sepsis                               |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (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           |
| Sinusitis                                       |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0           |
| Urinary tract infection                         |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1           |
| Urosepsis                                       |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Cellulitis                                      |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Device related infection                        |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| 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                                       |                |                |                 |  |
| alternative assessment type:                    |                |                |                 |  |
| Systematic                                      |                |                |                 |  |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| 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 respiratory tract infection               |                |                |                 |  |
| alternative assessment type:                    |                |                |                 |  |
| Systematic                                      |                |                |                 |  |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Aspergillus infection                           |                |                |                 |  |
| alternative assessment type:                    |                |                |                 |  |
| Systematic                                      |                |                |                 |  |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Biliary sepsis                                  |                |                |                 |  |
| alternative assessment type:                    |                |                |                 |  |
| Systematic                                      |                |                |                 |  |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Biliary tract infection                         |                |                |                 |  |
| alternative assessment type:                    |                |                |                 |  |
| Systematic                                      |                |                |                 |  |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Clostridium difficile infection                 |                |                |                 |  |
| alternative assessment type:                    |                |                |                 |  |
| Systematic                                      |                |                |                 |  |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (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           |  |
| Diverticulitis                                  |                |                |                 |  |
| alternative assessment type:                    |                |                |                 |  |
| Systematic                                      |                |                |                 |  |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Fungal infection                                |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Laryngitis                                      |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Necrotising fasciitis                           |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Neutropenic sepsis                              |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Penile infection                                |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Arthritis bacterial                             |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |



|  |                |                |                 |  |
|--|----------------|----------------|-----------------|--|
| Perirectal abscess                                 |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Pneumocystis jirovecii pneumonia                   |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |
| subjects affected / exposed                        | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 1 / 1          | 0 / 0          | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Sialoadenitis                                      |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Skin infection                                     |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Soft tissue infection                              |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |
| subjects affected / exposed                        | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1          | 0 / 0          | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Tonsillitis  |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |  |
| Upper respiratory tract infection                  |                |                |                 |  |
| alternative assessment type:<br>Systematic         |                |                |                 |  |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (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           |
| Vaginal abscess                                 |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Vulval cellulitis                               |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| 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                                     |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 5 / 71 (7.04%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences causally related to treatment / all | 5 / 5          | 0 / 0          | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Decreased appetite                              |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 6 / 115 (5.22%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 6 / 6           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Hyperglycaemia                                  |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 5 / 71 (7.04%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all | 2 / 5          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Hyponatraemia                                   |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 3 / 71 (4.23%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3          | 1 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Fluid overload                                  |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Hypercreatininaemia                             |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Failure to thrive                               |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Hyperkalaemia                                   |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (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           |
| Hypophagia                                      |                |                |                 |
| alternative assessment type: Systematic         |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |

| <b>Serious adverse events</b>                     | Physician's Choice 1<br>(PV <5) | Physician's Choice 2<br>(PV >=5) |  |
|---|---------------------------------|----------------------------------|--|
| Total subjects affected by serious adverse events |                                 |                                  |  |
| subjects affected / exposed                       | 25 / 39 (64.10%)                | 30 / 45 (66.67%)                 |  |
| number of deaths (all causes)                     | 28                              | 38                               |  |
| number of deaths resulting from                   | 7                               | 9                                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| adverse events  |                |                |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |  |
| Cerebellar tumour   |                |                |  |
| subjects affected / exposed   | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 1          | 0 / 0          |  |
| Basal cell carcinoma  |                |                |  |
| alternative assessment type: Systematic                             |                |                |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Squamous cell carcinoma   |                |                |  |
| alternative assessment type: Systematic                             |                |                |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Vascular disorders  |                |                |  |
| Hypotension   |                |                |  |
| alternative assessment type: Systematic                             |                |                |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Aortic aneurysm   |                |                |  |
| alternative assessment type: Systematic                             |                |                |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Haematoma   |                |                |  |
| alternative assessment type: Systematic                             |                |                |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Peripheral ischaemia  |                |                |  |
| alternative assessment type: Systematic                             |                |                |  |

|  |                |                |  |
|--|----------------|----------------|--|
| subjects affected / exposed                          | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Thrombophlebitis                                     |                |                |  |
| alternative assessment type: Systematic              |                |                |  |
| subjects affected / exposed                          | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Venous thrombosis                                    |                |                |  |
| alternative assessment type: Systematic              |                |                |  |
| subjects affected / exposed                          | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| General disorders and administration site conditions |                |                |  |
| General physical health deterioration                |                |                |  |
| alternative assessment type: Systematic              |                |                |  |
| subjects affected / exposed                          | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Fatigue  |                |                |  |
| alternative assessment type: Systematic              |                |                |  |
| subjects affected / exposed                          | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Pyrexia  |                |                |  |
| alternative assessment type: Systematic              |                |                |  |
| subjects affected / exposed                          | 2 / 39 (5.13%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all      | 0 / 2          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Condition aggravated                                 |                |                |  |
| alternative assessment type: Systematic              |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed   | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all   | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all  | 0 / 0          | 1 / 1          |  |
| Multiple organ dysfunction syndrome<br>alternative assessment type:<br>Systematic                             |                |                |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all  | 0 / 0          | 0 / 0          |  |
| Asthenia<br>alternative assessment type:<br>Systematic  |                |                |  |
| subjects affected / exposed   | 2 / 39 (5.13%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all   | 2 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all  | 0 / 0          | 0 / 0          |  |
| Malaise<br>alternative assessment type:<br>Systematic   |                |                |  |
| subjects affected / exposed   | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all   | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all  | 0 / 0          | 0 / 0          |  |
| Pain<br>alternative assessment type:<br>Systematic  |                |                |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all  | 0 / 0          | 0 / 0          |  |
| Social circumstances<br>Social stay hospitalisation<br>alternative assessment type:<br>Systematic             |                |                |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all  | 0 / 0          | 0 / 0          |  |
| Reproductive system and breast disorders<br>Vaginal haemorrhage<br>alternative assessment type:<br>Systematic |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders |                |                |  |
| Respiratory failure                             |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Acute respiratory failure                       |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Haemoptysis                                     |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| Pleural effusion                                |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia aspiration                            |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Dyspnoea  |                |                |  |
| alternative assessment type: Systematic         |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Epistaxis                                       |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 2 / 45 (4.44%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 4          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cough   |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pulmonary embolism                              |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pulmonary mass                                  |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Psychiatric disorders                           |                |                |  |
| Confusional state                               |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Mental status changes                           |                |                |  |
| alternative assessment type: Systematic         |                |                |  |



|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hallucination                                   |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Organic brain syndrome                          |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Investigations                                  |                |                |  |
| Weight decreased                                |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Blood alkaline phosphatase increased            |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| C-reactive protein increased                    |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Electrocardiogram change                        |                |                |  |
| alternative assessment type: Systematic         |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Enterococcus test positive                      |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Troponin T increased                            |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Vitamin B12 decreased                           |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Injury, poisoning and procedural complications  |                |                |  |
| Fall  |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Subdural haematoma                              |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Subdural haemorrhage                            |                |                |  |
| alternative assessment type: Systematic         |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Subarachnoid haemorrhage                        |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Femur fracture                                  |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac disorders                               |                |                |  |
| Atrial fibrillation                             |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| Cardiac failure                                 |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac failure congestive                      |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardio-respiratory arrest                       |                |                |  |
| alternative assessment type: Systematic         |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| Ventricular fibrillation                        |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Acute coronary syndrome                         |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bradycardia                                     |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Sinus bradycardia                               |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Tachyarrhythmia                                 |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Nervous system disorders                        |                |                |  |
| Cerebral haemorrhage                            |                |                |  |
| alternative assessment type: Systematic         |                |                |  |

|   |                |                |  |  |
|---|----------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |  |
| Cerebrovascular accident                        |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Dizziness                                       |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Embolic stroke                                  |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Haemorrhage intracranial                        |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Haemorrhagic cerebral infarction                |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Loss of consciousness                           |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |

|   |                |                |  |  |
|---|----------------|----------------|--|--|
| Syncope   |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Ataxia  |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Cerebral infarction                             |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Encephalopathy                                  |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Headache  |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Ischaemic stroke                                |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Presyncope                                      |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |

|   |                 |                  |  |
|---|-----------------|------------------|--|
| subjects affected / exposed                     | 0 / 39 (0.00%)  | 0 / 45 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Blood and lymphatic system disorders            |                 |                  |  |
| Febrile neutropenia                             |                 |                  |  |
| alternative assessment type: Systematic         |                 |                  |  |
| subjects affected / exposed                     | 8 / 39 (20.51%) | 16 / 45 (35.56%) |  |
| occurrences causally related to treatment / all | 5 / 8           | 9 / 16           |  |
| deaths causally related to treatment / all      | 0 / 0           | 2 / 2            |  |
| Anaemia   |                 |                  |  |
| alternative assessment type: Systematic         |                 |                  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%)  | 3 / 45 (6.67%)   |  |
| occurrences causally related to treatment / all | 0 / 0           | 2 / 3            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Thrombocytopenia                                |                 |                  |  |
| alternative assessment type: Systematic         |                 |                  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%)  | 0 / 45 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Neutropenia                                     |                 |                  |  |
| alternative assessment type: Systematic         |                 |                  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%)  | 0 / 45 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Leukostasis syndrome                            |                 |                  |  |
| alternative assessment type: Systematic         |                 |                  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%)  | 1 / 45 (2.22%)   |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            |  |
| Splenic infarction                              |                 |                  |  |
| alternative assessment type: Systematic         |                 |                  |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Ear and labyrinth disorders                     |                |                |  |
| Vertigo   |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Eye disorders                                   |                |                |  |
| Cataract  |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                      |                |                |  |
| Diarrhoea                                       |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Vomiting  |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal haemorrhage                    |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Abdominal pain upper                            |                |                |  |
| alternative assessment type: Systematic         |                |                |  |



|   |                |                |  |  |
|---|----------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Constipation                                    |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Diverticular perforation                        |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Large intestinal haemorrhage                    |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Mouth ulceration                                |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Nausea  |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Tooth loss                                      |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |

|  |                |                |  |
|--|----------------|----------------|--|
| Hepatobiliary disorders                            |                |                |  |
| Cholecystitis acute                                |                |                |  |
| alternative assessment type:<br>Systematic         |                |                |  |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          |  |
| Hyperbilirubinaemia                                |                |                |  |
| alternative assessment type:<br>Systematic         |                |                |  |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          |  |
| Renal and urinary disorders                        |                |                |  |
| Acute kidney injury                                |                |                |  |
| alternative assessment type:<br>Systematic         |                |                |  |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          |  |
| Oliguria   |                |                |  |
| alternative assessment type:<br>Systematic         |                |                |  |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          |  |
| Renal failure                                      |                |                |  |
| alternative assessment type:<br>Systematic         |                |                |  |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders    |                |                |  |
| Bone pain  |                |                |  |
| alternative assessment type:<br>Systematic         |                |                |  |
| subjects affected / exposed                        | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to<br>treatment / all      | 0 / 0          | 0 / 0          |  |
| Muscular weakness                                  |                |                |  |

|  |                 |                |  |
|--|-----------------|----------------|--|
| alternative assessment type:<br>Systematic         |                 |                |  |
| subjects affected / exposed                        | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to<br>treatment / all      | 0 / 0           | 0 / 0          |  |
| Infections and infestations                        |                 |                |  |
| Pneumonia  |                 |                |  |
| alternative assessment type:<br>Systematic         |                 |                |  |
| subjects affected / exposed                        | 4 / 39 (10.26%) | 3 / 45 (6.67%) |  |
| occurrences causally related to<br>treatment / all | 2 / 4           | 1 / 3          |  |
| deaths causally related to<br>treatment / all      | 0 / 1           | 1 / 1          |  |
| Lung infection                                     |                 |                |  |
| alternative assessment type:<br>Systematic         |                 |                |  |
| subjects affected / exposed                        | 3 / 39 (7.69%)  | 0 / 45 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 1 / 3           | 0 / 0          |  |
| deaths causally related to<br>treatment / all      | 0 / 2           | 0 / 0          |  |
| Sepsis   |                 |                |  |
| alternative assessment type:<br>Systematic         |                 |                |  |
| subjects affected / exposed                        | 3 / 39 (7.69%)  | 1 / 45 (2.22%) |  |
| occurrences causally related to<br>treatment / all | 0 / 3           | 0 / 1          |  |
| deaths causally related to<br>treatment / all      | 0 / 1           | 0 / 0          |  |
| Septic shock                                       |                 |                |  |
| alternative assessment type:<br>Systematic         |                 |                |  |
| subjects affected / exposed                        | 1 / 39 (2.56%)  | 0 / 45 (0.00%) |  |
| occurrences causally related to<br>treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to<br>treatment / all      | 0 / 1           | 0 / 0          |  |
| Escherichia sepsis                                 |                 |                |  |
| alternative assessment type:<br>Systematic         |                 |                |  |
| subjects affected / exposed                        | 1 / 39 (2.56%)  | 1 / 45 (2.22%) |  |
| occurrences causally related to<br>treatment / all | 1 / 1           | 1 / 1          |  |
| deaths causally related to<br>treatment / all      | 1 / 1           | 0 / 0          |  |
| Pneumonia fungal                                   |                 |                |  |
| alternative assessment type:<br>Systematic         |                 |                |  |

|   |                |                |  |  |
|---|----------------|----------------|--|--|
| subjects affected / exposed                     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |  |
| Klebsiella sepsis                               |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Sinusitis                                       |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Urinary tract infection                         |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Urosepsis                                       |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |  |
| Cellulitis                                      |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Device related infection                        |                |                |  |  |
| alternative assessment type: Systematic         |                |                |  |  |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 1 / 45 (2.22%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |

|   |                |                |  |  |
|---|----------------|----------------|--|--|
| Infection                                       |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 2 / 45 (4.44%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Lower respiratory tract infection               |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Aspergillus infection                           |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Biliary sepsis                                  |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Biliary tract infection                         |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Clostridium difficile infection                 |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |  |
| Diverticulitis                                  |                |                |  |  |
| alternative assessment type:                    |                |                |  |  |
| Systematic                                      |                |                |  |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Fungal infection                                |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Laryngitis                                      |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Necrotising fasciitis                           |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Neutropenic sepsis                              |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Penile infection                                |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Arthritis bacterial                             |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

|   |                |                |  |  |
|---|----------------|----------------|--|--|
| Perirectal abscess<br>alternative assessment type:<br>Systematic                |                |                |  |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                              | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0          | 0 / 0          |  |  |
| Pneumocystis jirovecii pneumonia<br>alternative assessment type:<br>Systematic  |                |                |  |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                              | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0          | 0 / 0          |  |  |
| Sialoadenitis<br>alternative assessment type:<br>Systematic                     |                |                |  |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                              | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0          | 0 / 0          |  |  |
| Skin infection<br>alternative assessment type:<br>Systematic                    |                |                |  |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                              | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0          | 0 / 0          |  |  |
| Soft tissue infection<br>alternative assessment type:<br>Systematic             |                |                |  |  |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                              | 0 / 0          | 0 / 0          |  |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0          | 0 / 0          |  |  |
| Tonsillitis<br>alternative assessment type:<br>Systematic                       |                |                |  |  |
| subjects affected / exposed   | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |  |
| occurrences causally related to<br>treatment / all                              | 1 / 1          | 0 / 0          |  |  |
| deaths causally related to<br>treatment / all                                   | 0 / 0          | 0 / 0          |  |  |
| Upper respiratory tract infection<br>alternative assessment type:<br>Systematic |                |                |  |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Vaginal abscess                                 |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Vulval cellulitis                               |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Metabolism and nutrition disorders              |                |                |  |
| Dehydration                                     |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Decreased appetite                              |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hyperglycaemia                                  |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hyponatraemia                                   |                |                |  |
| alternative assessment type: Systematic         |                |                |  |



|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Fluid overload                                  |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hypercreatininaemia                             |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Failure to thrive                               |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hyperkalaemia                                   |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hypophagia                                      |                |                |  |
| alternative assessment type: Systematic         |                |                |  |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>   | Selinexor<br>Approximately 55<br>mg/m <sup>2</sup> (60 to 120<br>mg Based on BSA) | Selinexor 60mg<br>(PV<5) (Equivalent<br>to 35 mg/m <sup>2</sup> ) | Selinexor 60mg (PV<br>≥5) (Equivalent to<br>35 mg/m <sup>2</sup> ) |
|---|---|---|--|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed | 71 / 71 (100.00%)   | 27 / 27 (100.00%)   | 113 / 115 (98.26%)   |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps)                  |   |   |  |
| Acute Myeloid Leukaemia<br>subjects affected / exposed                                  | 1 / 71 (1.41%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%)  |
| occurrences (all)   | 1   | 0   | 0  |
| Basal Cell Carcinoma<br>subjects affected / exposed                                     | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%)  |
| occurrences (all)   | 0   | 0   | 0  |
| Chloroma<br>subjects affected / exposed   | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%)  |
| occurrences (all)   | 0   | 0   | 0  |
| Leukaemic Infiltration<br>subjects affected / exposed                                   | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%)  |
| occurrences (all)   | 0   | 0   | 0  |
| Uterine Leiomyoma<br>subjects affected / exposed  | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 1 / 115 (0.87%)  |
| occurrences (all)   | 0   | 0   | 1  |
| Vascular disorders  |   |   |  |
| Hypotension<br>subjects affected / exposed  | 6 / 71 (8.45%)  | 1 / 27 (3.70%)  | 11 / 115 (9.57%)   |
| occurrences (all)   | 6   | 1   | 11   |
| Haematoma<br>subjects affected / exposed  | 0 / 71 (0.00%)  | 2 / 27 (7.41%)  | 5 / 115 (4.35%)  |
| occurrences (all)   | 0   | 2   | 5  |
| Hypertension<br>subjects affected / exposed   | 4 / 71 (5.63%)  | 2 / 27 (7.41%)  | 2 / 115 (1.74%)  |
| occurrences (all)   | 4   | 2   | 2  |
| Pallor<br>subjects affected / exposed   | 1 / 71 (1.41%)  | 0 / 27 (0.00%)  | 3 / 115 (2.61%)  |
| occurrences (all)   | 1   | 0   | 3  |
| Haemorrhage<br>subjects affected / exposed  | 1 / 71 (1.41%)  | 0 / 27 (0.00%)  | 2 / 115 (1.74%)  |
| occurrences (all)   | 1   | 0   | 2  |

|                              |                |                |                 |
|------------------------------|----------------|----------------|-----------------|
| Phlebitis                    |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |
| Thrombophlebitis             |                |                |                 |
| subjects affected / exposed  | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 2              | 0              | 0               |
| Orthostatic Hypotension      |                |                |                 |
| subjects affected / exposed  | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 2              | 0              | 1               |
| Deep Vein Thrombosis         |                |                |                 |
| subjects affected / exposed  | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 2              | 0              | 0               |
| Flushing                     |                |                |                 |
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 1              | 0              | 1               |
| Circulatory Collapse         |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |
| Embolism                     |                |                |                 |
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 1              | 0              | 0               |
| Hot Flush                    |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 0              | 0               |
| Intermittent Claudication    |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |
| Lymphoedema                  |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 1              | 0               |
| Poor Peripheral Circulation  |                |                |                 |
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 1              | 0              | 0               |
| Thrombophlebitis Superficial |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 0              | 0               |

|   |                        |                        |                         |
|---|------------------------|------------------------|-------------------------|
| Venous Thrombosis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0    | 1 / 115 (0.87%)<br>1    |
| General disorders and administration<br>site conditions   |                        |                        |                         |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)   | 33 / 71 (46.48%)<br>33 | 13 / 27 (48.15%)<br>13 | 50 / 115 (43.48%)<br>50 |
| Pyrexia<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)           | 8 / 71 (11.27%)<br>8   | 5 / 27 (18.52%)<br>5   | 28 / 115 (24.35%)<br>28 |
| Oedema peripheral<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all) | 17 / 71 (23.94%)<br>17 | 5 / 27 (18.52%)<br>5   | 21 / 115 (18.26%)<br>21 |
| Asthenia<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)          | 17 / 71 (23.94%)<br>17 | 6 / 27 (22.22%)<br>6   | 22 / 115 (19.13%)<br>22 |
| Malaise<br>subjects affected / exposed<br>occurrences (all)   | 2 / 71 (2.82%)<br>2    | 1 / 27 (3.70%)<br>1    | 8 / 115 (6.96%)<br>8    |
| Oedema<br>subjects affected / exposed<br>occurrences (all)  | 2 / 71 (2.82%)<br>2    | 0 / 27 (0.00%)<br>0    | 5 / 115 (4.35%)<br>5    |
| Chills<br>subjects affected / exposed<br>occurrences (all)  | 1 / 71 (1.41%)<br>1    | 1 / 27 (3.70%)<br>1    | 5 / 115 (4.35%)<br>5    |
| Mucosal Inflammation<br>subjects affected / exposed<br>occurrences (all)  | 3 / 71 (4.23%)<br>3    | 0 / 27 (0.00%)<br>0    | 1 / 115 (0.87%)<br>1    |
| Pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0    | 7 / 115 (6.09%)<br>7    |
| Gait Disturbance  |                        |                        |                         |

|                                       |                |                |                 |
|---------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed           | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                     | 2              | 0              | 2               |
| General Physical Health Deterioration |                |                |                 |
| subjects affected / exposed           | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                     | 1              | 0              | 2               |
| Injection Site Bruising               |                |                |                 |
| subjects affected / exposed           | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0               |
| Non-Cardiac Chest Pain                |                |                |                 |
| subjects affected / exposed           | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                     | 1              | 0              | 2               |
| Ulcer                                 |                |                |                 |
| subjects affected / exposed           | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                     | 2              | 0              | 1               |
| Catheter Site Haemorrhage             |                |                |                 |
| subjects affected / exposed           | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0               |
| Face Oedema                           |                |                |                 |
| subjects affected / exposed           | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0               |
| Generalised Oedema                    |                |                |                 |
| subjects affected / exposed           | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0               |
| Secretion Discharge                   |                |                |                 |
| subjects affected / exposed           | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                     | 0              | 0              | 2               |
| Catheter Site Haematoma               |                |                |                 |
| subjects affected / exposed           | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                     | 0              | 0              | 1               |
| Chest Pain                            |                |                |                 |
| subjects affected / exposed           | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                     | 0              | 0              | 1               |
| Drug Intolerance                      |                |                |                 |
| subjects affected / exposed           | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                     | 0              | 0              | 1               |
| Extravasation                         |                |                |                 |

|                               |                |                |                 |
|-------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed   | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)             | 1              | 0              | 0               |
| Feeling Cold                  |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)             | 0              | 0              | 1               |
| Granuloma                     |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)             | 0              | 0              | 0               |
| Hernia                        |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)             | 0              | 0              | 1               |
| Impaired Healing              |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)             | 0              | 1              | 0               |
| Infusion Site Haemorrhage     |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)             | 0              | 1              | 0               |
| Injection Site Discolouration |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)             | 0              | 0              | 0               |
| Injection Site Pain           |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)             | 0              | 0              | 0               |
| Mucosal Dryness               |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)             | 0              | 0              | 0               |
| Nodule                        |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)             | 0              | 0              | 0               |
| Peripheral Swelling           |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)             | 0              | 0              | 0               |
| Swelling                      |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)             | 0              | 0              | 1               |
| Decreased appetite            |                |                |                 |

|   |                        |                        |                         |
|---|------------------------|------------------------|-------------------------|
| subjects affected / exposed<br>occurrences (all)  | 41 / 71 (57.75%)<br>41 | 12 / 27 (44.44%)<br>12 | 61 / 115 (53.04%)<br>61 |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0    | 1 / 115 (0.87%)<br>1    |
| Reproductive system and breast disorders<br>Breast Pain<br>subjects affected / exposed<br>occurrences (all)     | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0    | 0 / 115 (0.00%)<br>0    |
| Breast Swelling<br>subjects affected / exposed<br>occurrences (all)   | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0    | 1 / 115 (0.87%)<br>1    |
| Gynaecomastia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0    | 0 / 115 (0.00%)<br>0    |
| Nipple Pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0    | 1 / 115 (0.87%)<br>1    |
| Oedema Genital<br>subjects affected / exposed<br>occurrences (all)  | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0    | 1 / 115 (0.87%)<br>1    |
| Ovarian Cyst<br>subjects affected / exposed<br>occurrences (all)  | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0    | 1 / 115 (0.87%)<br>1    |
| Testicular Oedema<br>subjects affected / exposed<br>occurrences (all)   | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0    | 0 / 115 (0.00%)<br>0    |
| Vaginal Haemorrhage<br>subjects affected / exposed<br>occurrences (all)   | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0    | 1 / 115 (0.87%)<br>1    |
| Respiratory, thoracic and mediastinal disorders<br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all) | 14 / 71 (19.72%)<br>14 | 5 / 27 (18.52%)<br>5   | 24 / 115 (20.87%)<br>24 |
| Epistaxis   |                        |                        |                         |

|                             |                  |                 |                   |
|-----------------------------|------------------|-----------------|-------------------|
| subjects affected / exposed | 13 / 71 (18.31%) | 3 / 27 (11.11%) | 25 / 115 (21.74%) |
| occurrences (all)           | 13               | 3               | 25                |
| Cough                       |                  |                 |                   |
| subjects affected / exposed | 12 / 71 (16.90%) | 3 / 27 (11.11%) | 15 / 115 (13.04%) |
| occurrences (all)           | 12               | 3               | 15                |
| Oropharyngeal Pain          |                  |                 |                   |
| subjects affected / exposed | 3 / 71 (4.23%)   | 2 / 27 (7.41%)  | 3 / 115 (2.61%)   |
| occurrences (all)           | 3                | 2               | 3                 |
| Productive Cough            |                  |                 |                   |
| subjects affected / exposed | 4 / 71 (5.63%)   | 0 / 27 (0.00%)  | 3 / 115 (2.61%)   |
| occurrences (all)           | 4                | 0               | 3                 |
| Haemoptysis                 |                  |                 |                   |
| subjects affected / exposed | 2 / 71 (2.82%)   | 0 / 27 (0.00%)  | 2 / 115 (1.74%)   |
| occurrences (all)           | 2                | 0               | 2                 |
| Dyspnoea Exertional         |                  |                 |                   |
| subjects affected / exposed | 1 / 71 (1.41%)   | 0 / 27 (0.00%)  | 4 / 115 (3.48%)   |
| occurrences (all)           | 1                | 0               | 4                 |
| Nasal Congestion            |                  |                 |                   |
| subjects affected / exposed | 1 / 71 (1.41%)   | 1 / 27 (3.70%)  | 4 / 115 (3.48%)   |
| occurrences (all)           | 1                | 1               | 4                 |
| Pleural Effusion            |                  |                 |                   |
| subjects affected / exposed | 1 / 71 (1.41%)   | 2 / 27 (7.41%)  | 2 / 115 (1.74%)   |
| occurrences (all)           | 1                | 2               | 2                 |
| Hypoxia                     |                  |                 |                   |
| subjects affected / exposed | 2 / 71 (2.82%)   | 0 / 27 (0.00%)  | 1 / 115 (0.87%)   |
| occurrences (all)           | 2                | 0               | 1                 |
| Rhinorrhoea                 |                  |                 |                   |
| subjects affected / exposed | 1 / 71 (1.41%)   | 0 / 27 (0.00%)  | 2 / 115 (1.74%)   |
| occurrences (all)           | 1                | 0               | 2                 |
| Wheezing                    |                  |                 |                   |
| subjects affected / exposed | 0 / 71 (0.00%)   | 0 / 27 (0.00%)  | 2 / 115 (1.74%)   |
| occurrences (all)           | 0                | 0               | 2                 |
| Atelectasis                 |                  |                 |                   |
| subjects affected / exposed | 2 / 71 (2.82%)   | 0 / 27 (0.00%)  | 0 / 115 (0.00%)   |
| occurrences (all)           | 2                | 0               | 0                 |
| Hiccups                     |                  |                 |                   |



|                                       |                |                |                 |
|---------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed           | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                     | 1              | 0              | 2               |
| Pleuritic Pain                        |                |                |                 |
| subjects affected / exposed           | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                     | 0              | 0              | 1               |
| Respiratory Failure                   |                |                |                 |
| subjects affected / exposed           | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                     | 0              | 0              | 2               |
| Pulmonary Oedema                      |                |                |                 |
| subjects affected / exposed           | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0               |
| Sinus Congestion                      |                |                |                 |
| subjects affected / exposed           | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                     | 1              | 0              | 1               |
| Sinus Pain                            |                |                |                 |
| subjects affected / exposed           | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                     | 1              | 0              | 1               |
| Upper-Airway Cough Syndrome           |                |                |                 |
| subjects affected / exposed           | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0               |
| Chronic Obstructive Pulmonary Disease |                |                |                 |
| subjects affected / exposed           | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0               |
| Dysphonia                             |                |                |                 |
| subjects affected / exposed           | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0               |
| Laryngeal Pain                        |                |                |                 |
| subjects affected / exposed           | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0               |
| Lung Consolidation                    |                |                |                 |
| subjects affected / exposed           | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0               |
| Lung Infiltration                     |                |                |                 |
| subjects affected / exposed           | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0               |

|                              |                |                |                 |
|------------------------------|----------------|----------------|-----------------|
| Nasal Dryness                |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |
| Nasal Inflammation           |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 1              | 0               |
| Paranasal Sinus Discomfort   |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |
| Pharyngeal Inflammation      |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 1              | 0               |
| Pneumonitis                  |                |                |                 |
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 1              | 0              | 0               |
| Pulmonary Mass               |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 0              | 0               |
| Rales                        |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 0              | 0               |
| Respiratory Tract Congestion |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 0              | 0               |
| Rhinitis Allergic            |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |
| Rhonchi                      |                |                |                 |
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 1              | 0              | 0               |
| Sinus Disorder               |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 0              | 0               |
| Tachypnoea                   |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |

|   |                        |                      |                      |
|---|------------------------|----------------------|----------------------|
| Tonsillar Erythema<br>subjects affected / exposed<br>occurrences (all)    | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0  | 0 / 115 (0.00%)<br>0 |
| Tonsillar Hypertrophy<br>subjects affected / exposed<br>occurrences (all) | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0  | 0 / 115 (0.00%)<br>0 |
| Psychiatric disorders   |                        |                      |                      |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)              | 10 / 71 (14.08%)<br>10 | 4 / 27 (14.81%)<br>4 | 7 / 115 (6.09%)<br>7 |
| Confusional State<br>subjects affected / exposed<br>occurrences (all)     | 5 / 71 (7.04%)<br>5    | 2 / 27 (7.41%)<br>2  | 8 / 115 (6.96%)<br>8 |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)               | 2 / 71 (2.82%)<br>2    | 2 / 27 (7.41%)<br>2  | 4 / 115 (3.48%)<br>4 |
| Depression<br>subjects affected / exposed<br>occurrences (all)            | 2 / 71 (2.82%)<br>2    | 2 / 27 (7.41%)<br>2  | 2 / 115 (1.74%)<br>2 |
| Agitation<br>subjects affected / exposed<br>occurrences (all)             | 6 / 71 (8.45%)<br>6    | 0 / 27 (0.00%)<br>0  | 0 / 115 (0.00%)<br>0 |
| Restlessness<br>subjects affected / exposed<br>occurrences (all)          | 0 / 71 (0.00%)<br>0    | 2 / 27 (7.41%)<br>2  | 0 / 115 (0.00%)<br>0 |
| Abnormal Dreams<br>subjects affected / exposed<br>occurrences (all)       | 1 / 71 (1.41%)<br>1    | 0 / 27 (0.00%)<br>0  | 0 / 115 (0.00%)<br>0 |
| Bulimia Nervosa<br>subjects affected / exposed<br>occurrences (all)       | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0  | 1 / 115 (0.87%)<br>1 |
| Delirium<br>subjects affected / exposed<br>occurrences (all)              | 0 / 71 (0.00%)<br>0    | 0 / 27 (0.00%)<br>0  | 1 / 115 (0.87%)<br>1 |
| Disorientation  |                        |                      |                      |

|                                      |                  |                 |                   |
|--------------------------------------|------------------|-----------------|-------------------|
| subjects affected / exposed          | 0 / 71 (0.00%)   | 0 / 27 (0.00%)  | 1 / 115 (0.87%)   |
| occurrences (all)                    | 0                | 0               | 1                 |
| Flat Affect                          |                  |                 |                   |
| subjects affected / exposed          | 0 / 71 (0.00%)   | 0 / 27 (0.00%)  | 1 / 115 (0.87%)   |
| occurrences (all)                    | 0                | 0               | 1                 |
| Hallucination, Visual                |                  |                 |                   |
| subjects affected / exposed          | 0 / 71 (0.00%)   | 0 / 27 (0.00%)  | 0 / 115 (0.00%)   |
| occurrences (all)                    | 0                | 0               | 0                 |
| Irritability                         |                  |                 |                   |
| subjects affected / exposed          | 1 / 71 (1.41%)   | 0 / 27 (0.00%)  | 0 / 115 (0.00%)   |
| occurrences (all)                    | 1                | 0               | 0                 |
| Listless                             |                  |                 |                   |
| subjects affected / exposed          | 1 / 71 (1.41%)   | 0 / 27 (0.00%)  | 0 / 115 (0.00%)   |
| occurrences (all)                    | 1                | 0               | 0                 |
| Mental Disorder                      |                  |                 |                   |
| subjects affected / exposed          | 1 / 71 (1.41%)   | 0 / 27 (0.00%)  | 0 / 115 (0.00%)   |
| occurrences (all)                    | 1                | 0               | 0                 |
| Mental Status Changes                |                  |                 |                   |
| subjects affected / exposed          | 0 / 71 (0.00%)   | 0 / 27 (0.00%)  | 1 / 115 (0.87%)   |
| occurrences (all)                    | 0                | 0               | 1                 |
| Nervousness                          |                  |                 |                   |
| subjects affected / exposed          | 0 / 71 (0.00%)   | 0 / 27 (0.00%)  | 1 / 115 (0.87%)   |
| occurrences (all)                    | 0                | 0               | 1                 |
| Psychomotor Retardation              |                  |                 |                   |
| subjects affected / exposed          | 1 / 71 (1.41%)   | 0 / 27 (0.00%)  | 0 / 115 (0.00%)   |
| occurrences (all)                    | 1                | 0               | 0                 |
| Investigations                       |                  |                 |                   |
| Weight Decreased                     |                  |                 |                   |
| subjects affected / exposed          | 15 / 71 (21.13%) | 4 / 27 (14.81%) | 20 / 115 (17.39%) |
| occurrences (all)                    | 15               | 4               | 20                |
| Alanine Aminotransferase Increased   |                  |                 |                   |
| subjects affected / exposed          | 2 / 71 (2.82%)   | 2 / 27 (7.41%)  | 5 / 115 (4.35%)   |
| occurrences (all)                    | 2                | 2               | 5                 |
| Aspartate Aminotransferase Increased |                  |                 |                   |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 5 / 115 (4.35%) |
| occurrences (all)                               | 2              | 0              | 5               |
| International Normalised Ratio Increased        |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 2 / 27 (7.41%) | 4 / 115 (3.48%) |
| occurrences (all)                               | 1              | 2              | 4               |
| Weight Increased                                |                |                |                 |
| subjects affected / exposed                     | 2 / 71 (2.82%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)                               | 2              | 1              | 0               |
| Blood Lactate Dehydrogenase Increased           |                |                |                 |
| subjects affected / exposed                     | 5 / 71 (7.04%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                               | 5              | 0              | 1               |
| Blood Alkaline Phosphatase Increased            |                |                |                 |
| subjects affected / exposed                     | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                               | 2              | 0              | 2               |
| C-Reactive Protein Increased                    |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 1 / 27 (3.70%) | 2 / 115 (1.74%) |
| occurrences (all)                               | 1              | 1              | 2               |
| Blood Uric Acid Increased                       |                |                |                 |
| subjects affected / exposed                     | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                               | 2              | 0              | 2               |
| Electrocardiogram Qt Prolonged                  |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                               | 1              | 0              | 2               |
| Activated Partial Thromboplastin Time Prolonged |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                               | 1              | 0              | 2               |
| Blood Creatine Phosphokinase Increased          |                |                |                 |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                               | 1              | 0              | 1               |
| Blood Thyroid Stimulating Hormone Increased     |                |                |                 |
| subjects affected / exposed                     | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                               | 2              | 0              | 0               |
| General Physical Condition Abnormal             |                |                |                 |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed            | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0               |
| Blood Creatine Phosphokinase Decreased |                |                |                 |
| subjects affected / exposed            | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                      | 2              | 0              | 0               |
| Blood Pressure Decreased               |                |                |                 |
| subjects affected / exposed            | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                      | 0              | 0              | 1               |
| Blood Urea Increased                   |                |                |                 |
| subjects affected / exposed            | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                      | 0              | 0              | 1               |
| Cardiac Murmur                         |                |                |                 |
| subjects affected / exposed            | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                      | 0              | 0              | 2               |
| Ejection Fraction Decreased            |                |                |                 |
| subjects affected / exposed            | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                      | 1              | 0              | 1               |
| Electrocardiogram Change               |                |                |                 |
| subjects affected / exposed            | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                      | 1              | 0              | 1               |
| Hypophonesis                           |                |                |                 |
| subjects affected / exposed            | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                      | 0              | 0              | 2               |
| Oxygen Saturation Decreased            |                |                |                 |
| subjects affected / exposed            | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                      | 0              | 0              | 2               |
| Transaminases Increased                |                |                |                 |
| subjects affected / exposed            | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                      | 1              | 0              | 0               |
| Alpha 1 Foetoprotein Increased         |                |                |                 |
| subjects affected / exposed            | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0               |
| Astrovirus Test Positive               |                |                |                 |
| subjects affected / exposed            | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0               |

|                                      |                |                |                 |
|--------------------------------------|----------------|----------------|-----------------|
| Bilirubin Urine                      |                |                |                 |
| subjects affected / exposed          | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0               |
| Blast Cell Count Increased           |                |                |                 |
| subjects affected / exposed          | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0               |
| Bleeding Time Prolonged              |                |                |                 |
| subjects affected / exposed          | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0               |
| Blood Alkaline Phosphatase Decreased |                |                |                 |
| subjects affected / exposed          | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                    | 0              | 0              | 1               |
| Blood Lactic Acid Increased          |                |                |                 |
| subjects affected / exposed          | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0               |
| Blood Test Abnormal                  |                |                |                 |
| subjects affected / exposed          | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                    | 0              | 0              | 1               |
| Body Temperature Increased           |                |                |                 |
| subjects affected / exposed          | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0               |
| Gamma-Glutamyltransferase Increased  |                |                |                 |
| subjects affected / exposed          | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                    | 0              | 0              | 0               |
| Glomerular Filtration Rate Decreased |                |                |                 |
| subjects affected / exposed          | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                    | 0              | 0              | 1               |
| Liver Function Test Increased        |                |                |                 |
| subjects affected / exposed          | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0               |
| Prothrombin Time Prolonged           |                |                |                 |
| subjects affected / exposed          | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                    | 1              | 0              | 0               |
| White Blood Cell Count               |                |                |                 |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed                    | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0               |
| White Blood Cell Count Increased               |                |                |                 |
| subjects affected / exposed                    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0               |
| Injury, poisoning and procedural complications |                |                |                 |
| Contusion                                      |                |                |                 |
| subjects affected / exposed                    | 5 / 71 (7.04%) | 2 / 27 (7.41%) | 5 / 115 (4.35%) |
| occurrences (all)                              | 5              | 2              | 5               |
| Fall   |                |                |                 |
| subjects affected / exposed                    | 6 / 71 (8.45%) | 2 / 27 (7.41%) | 9 / 115 (7.83%) |
| occurrences (all)                              | 6              | 2              | 9               |
| Infusion Related Reaction                      |                |                |                 |
| subjects affected / exposed                    | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0               |
| Laceration                                     |                |                |                 |
| subjects affected / exposed                    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                              | 0              | 0              | 2               |
| Procedural Pain                                |                |                |                 |
| subjects affected / exposed                    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                              | 0              | 0              | 1               |
| Skin Abrasion                                  |                |                |                 |
| subjects affected / exposed                    | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                              | 1              | 0              | 1               |
| Transfusion Reaction                           |                |                |                 |
| subjects affected / exposed                    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                              | 0              | 0              | 1               |
| Allergic Transfusion Reaction                  |                |                |                 |
| subjects affected / exposed                    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0               |
| Animal Bite                                    |                |                |                 |
| subjects affected / exposed                    | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0               |
| Head Injury                                    |                |                |                 |



|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Joint Injury                |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Overdose                    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Periorbital Haematoma       |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Post Procedural Contusion   |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Post Procedural Haemorrhage |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Sunburn                     |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Tooth Fracture              |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Wound                       |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Cardiac disorders           |                |                |                 |
| Tachycardia                 |                |                |                 |
| subjects affected / exposed | 5 / 71 (7.04%) | 1 / 27 (3.70%) | 4 / 115 (3.48%) |
| occurrences (all)           | 5              | 1              | 4               |
| Sinus Tachycardia           |                |                |                 |
| subjects affected / exposed | 4 / 71 (5.63%) | 1 / 27 (3.70%) | 2 / 115 (1.74%) |
| occurrences (all)           | 4              | 1              | 2               |
| Atrial Fibrillation         |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |

|                                |                |                |                 |
|--------------------------------|----------------|----------------|-----------------|
| Bradycardia                    |                |                |                 |
| subjects affected / exposed    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)              | 0              | 0              | 1               |
| Acute Left Ventricular Failure |                |                |                 |
| subjects affected / exposed    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)              | 0              | 0              | 0               |
| Angina Pectoris                |                |                |                 |
| subjects affected / exposed    | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)              | 0              | 1              | 0               |
| Arrhythmia                     |                |                |                 |
| subjects affected / exposed    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)              | 0              | 0              | 0               |
| Bundle Branch Block Right      |                |                |                 |
| subjects affected / exposed    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)              | 0              | 0              | 0               |
| Cardiac Failure                |                |                |                 |
| subjects affected / exposed    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)              | 0              | 0              | 1               |
| Cardiac Flutter                |                |                |                 |
| subjects affected / exposed    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)              | 0              | 0              | 0               |
| Extrasystoles                  |                |                |                 |
| subjects affected / exposed    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)              | 0              | 0              | 0               |
| Palpitations                   |                |                |                 |
| subjects affected / exposed    | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)              | 1              | 0              | 0               |
| Sinus Bradycardia              |                |                |                 |
| subjects affected / exposed    | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)              | 0              | 1              | 0               |
| Supraventricular Tachycardia   |                |                |                 |
| subjects affected / exposed    | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)              | 1              | 0              | 0               |
| Tachycardia Paroxysmal         |                |                |                 |
| subjects affected / exposed    | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)              | 0              | 0              | 0               |

|                             |                  |                 |                   |
|-----------------------------|------------------|-----------------|-------------------|
| Nervous system disorders    |                  |                 |                   |
| Dysgeusia                   |                  |                 |                   |
| subjects affected / exposed | 7 / 71 (9.86%)   | 3 / 27 (11.11%) | 12 / 115 (10.43%) |
| occurrences (all)           | 7                | 3               | 12                |
| Headache                    |                  |                 |                   |
| subjects affected / exposed | 5 / 71 (7.04%)   | 3 / 27 (11.11%) | 3 / 115 (2.61%)   |
| occurrences (all)           | 5                | 3               | 3                 |
| Syncope                     |                  |                 |                   |
| subjects affected / exposed | 3 / 71 (4.23%)   | 1 / 27 (3.70%)  | 5 / 115 (4.35%)   |
| occurrences (all)           | 3                | 1               | 5                 |
| Dizziness                   |                  |                 |                   |
| subjects affected / exposed | 12 / 71 (16.90%) | 2 / 27 (7.41%)  | 18 / 115 (15.65%) |
| occurrences (all)           | 12               | 2               | 18                |
| Presyncope                  |                  |                 |                   |
| subjects affected / exposed | 1 / 71 (1.41%)   | 3 / 27 (11.11%) | 3 / 115 (2.61%)   |
| occurrences (all)           | 1                | 3               | 3                 |
| Somnolence                  |                  |                 |                   |
| subjects affected / exposed | 4 / 71 (5.63%)   | 0 / 27 (0.00%)  | 2 / 115 (1.74%)   |
| occurrences (all)           | 4                | 0               | 2                 |
| Ageusia                     |                  |                 |                   |
| subjects affected / exposed | 1 / 71 (1.41%)   | 1 / 27 (3.70%)  | 2 / 115 (1.74%)   |
| occurrences (all)           | 1                | 1               | 2                 |
| Balance Disorder            |                  |                 |                   |
| subjects affected / exposed | 2 / 71 (2.82%)   | 1 / 27 (3.70%)  | 1 / 115 (0.87%)   |
| occurrences (all)           | 2                | 1               | 1                 |
| Memory Impairment           |                  |                 |                   |
| subjects affected / exposed | 3 / 71 (4.23%)   | 0 / 27 (0.00%)  | 1 / 115 (0.87%)   |
| occurrences (all)           | 3                | 0               | 1                 |
| Ataxia                      |                  |                 |                   |
| subjects affected / exposed | 1 / 71 (1.41%)   | 1 / 27 (3.70%)  | 1 / 115 (0.87%)   |
| occurrences (all)           | 1                | 1               | 1                 |
| Lethargy                    |                  |                 |                   |
| subjects affected / exposed | 1 / 71 (1.41%)   | 0 / 27 (0.00%)  | 1 / 115 (0.87%)   |
| occurrences (all)           | 1                | 0               | 1                 |
| Polyneuropathy              |                  |                 |                   |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 1              | 0              | 1               |
| Tremor                      |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)           | 0              | 0              | 2               |
| Aphasia                     |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 1              | 0              | 1               |
| Cognitive Disorder          |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Dysarthria                  |                |                |                 |
| subjects affected / exposed | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 2              | 0              | 0               |
| Neuropathy Peripheral       |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)           | 0              | 0              | 2               |
| Paraesthesia                |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 2 / 27 (7.41%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 2              | 0               |
| Speech Disorder             |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 1              | 0               |
| Aphonia                     |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Cogwheel Rigidity           |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Coordination Abnormal       |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Drooling                    |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Dysaesthesia                |                |                |                 |

|                               |                |                |                 |
|-------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)             | 0              | 0              | 1               |
| Encephalopathy                |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)             | 0              | 0              | 0               |
| Haemorrhage Intracranial      |                |                |                 |
| subjects affected / exposed   | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)             | 1              | 0              | 0               |
| Hemianopia                    |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)             | 0              | 0              | 1               |
| Hemianopia Homonymous         |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)             | 0              | 0              | 1               |
| Hypersomnia                   |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)             | 0              | 0              | 1               |
| Hypoaesthesia                 |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)             | 0              | 0              | 0               |
| Hyposmia                      |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)             | 0              | 0              | 1               |
| Migraine                      |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)             | 0              | 0              | 1               |
| Parosmia                      |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)             | 0              | 1              | 0               |
| Peripheral Sensory Neuropathy |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)             | 0              | 0              | 1               |
| Sensory Loss                  |                |                |                 |
| subjects affected / exposed   | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)             | 0              | 0              | 0               |
| Synaesthesia                  |                |                |                 |

|  |                     |                     |                      |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 71 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 1 / 115 (0.87%)<br>1 |
| Blood and lymphatic system disorders             |                     |                     |                      |
| Thrombocytopenia                                 |                     |                     |                      |
| subjects affected / exposed                      | 29 / 71 (40.85%)    | 7 / 27 (25.93%)     | 38 / 115 (33.04%)    |
| occurrences (all)                                | 29                  | 7                   | 38                   |
| Anaemia  |                     |                     |                      |
| subjects affected / exposed                      | 20 / 71 (28.17%)    | 7 / 27 (25.93%)     | 29 / 115 (25.22%)    |
| occurrences (all)                                | 20                  | 7                   | 29                   |
| Neutropenia                                      |                     |                     |                      |
| subjects affected / exposed                      | 6 / 71 (8.45%)      | 5 / 27 (18.52%)     | 17 / 115 (14.78%)    |
| occurrences (all)                                | 6                   | 5                   | 17                   |
| Leukopenia                                       |                     |                     |                      |
| subjects affected / exposed                      | 2 / 71 (2.82%)      | 3 / 27 (11.11%)     | 10 / 115 (8.70%)     |
| occurrences (all)                                | 2                   | 3                   | 10                   |
| Febrile neutropenia                              |                     |                     |                      |
| subjects affected / exposed                      | 9 / 71 (12.68%)     | 2 / 27 (7.41%)      | 7 / 115 (6.09%)      |
| occurrences (all)                                | 9                   | 2                   | 7                    |
| Leukocytosis                                     |                     |                     |                      |
| subjects affected / exposed                      | 6 / 71 (8.45%)      | 2 / 27 (7.41%)      | 6 / 115 (5.22%)      |
| occurrences (all)                                | 6                   | 2                   | 6                    |
| Lymphopenia                                      |                     |                     |                      |
| subjects affected / exposed                      | 0 / 71 (0.00%)      | 0 / 27 (0.00%)      | 2 / 115 (1.74%)      |
| occurrences (all)                                | 0                   | 0                   | 2                    |
| Pancytopenia                                     |                     |                     |                      |
| subjects affected / exposed                      | 1 / 71 (1.41%)      | 0 / 27 (0.00%)      | 2 / 115 (1.74%)      |
| occurrences (all)                                | 1                   | 0                   | 2                    |
| Coagulopathy                                     |                     |                     |                      |
| subjects affected / exposed                      | 0 / 71 (0.00%)      | 1 / 27 (3.70%)      | 2 / 115 (1.74%)      |
| occurrences (all)                                | 0                   | 1                   | 2                    |
| Lymphadenopathy                                  |                     |                     |                      |
| subjects affected / exposed                      | 0 / 71 (0.00%)      | 0 / 27 (0.00%)      | 1 / 115 (0.87%)      |
| occurrences (all)                                | 0                   | 0                   | 1                    |
| Increased Tendency To Bruise                     |                     |                     |                      |
| subjects affected / exposed                      | 1 / 71 (1.41%)      | 0 / 27 (0.00%)      | 0 / 115 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                    |

|                              |                |                |                 |
|------------------------------|----------------|----------------|-----------------|
| Polycythaemia                |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 1              | 0               |
| Splenomegaly                 |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 0              | 0               |
| Thrombocytosis               |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 0              | 0               |
| Ear and labyrinth disorders  |                |                |                 |
| Deafness                     |                |                |                 |
| subjects affected / exposed  | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)            | 2              | 0              | 2               |
| Ear Discomfort               |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 2 / 27 (7.41%) | 2 / 115 (1.74%) |
| occurrences (all)            | 0              | 2              | 2               |
| Vertigo                      |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences (all)            | 0              | 0              | 3               |
| Ear Pain                     |                |                |                 |
| subjects affected / exposed  | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 2              | 0              | 1               |
| Tinnitus                     |                |                |                 |
| subjects affected / exposed  | 3 / 71 (4.23%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 3              | 0              | 0               |
| Ear Congestion               |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |
| Eustachian Tube Dysfunction  |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |
| Excessive Cerumen Production |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |
| Hypoacusis                   |                |                |                 |

|  |                     |                     |                      |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 71 (1.41%)<br>1 | 0 / 27 (0.00%)<br>0 | 0 / 115 (0.00%)<br>0 |
| Eye disorders                                    |                     |                     |                      |
| Vision blurred                                   |                     |                     |                      |
| alternative assessment type:<br>Systematic       |                     |                     |                      |
| subjects affected / exposed                      | 8 / 71 (11.27%)     | 1 / 27 (3.70%)      | 9 / 115 (7.83%)      |
| occurrences (all)                                | 8                   | 1                   | 9                    |
| Visual Impairment                                |                     |                     |                      |
| subjects affected / exposed                      | 4 / 71 (5.63%)      | 0 / 27 (0.00%)      | 2 / 115 (1.74%)      |
| occurrences (all)                                | 4                   | 0                   | 2                    |
| Cataract   |                     |                     |                      |
| subjects affected / exposed                      | 0 / 71 (0.00%)      | 1 / 27 (3.70%)      | 3 / 115 (2.61%)      |
| occurrences (all)                                | 0                   | 1                   | 3                    |
| Dry Eye  |                     |                     |                      |
| subjects affected / exposed                      | 1 / 71 (1.41%)      | 1 / 27 (3.70%)      | 1 / 115 (0.87%)      |
| occurrences (all)                                | 1                   | 1                   | 1                    |
| Visual Acuity Reduced                            |                     |                     |                      |
| subjects affected / exposed                      | 1 / 71 (1.41%)      | 0 / 27 (0.00%)      | 2 / 115 (1.74%)      |
| occurrences (all)                                | 1                   | 0                   | 2                    |
| Conjunctival Haemorrhage                         |                     |                     |                      |
| subjects affected / exposed                      | 0 / 71 (0.00%)      | 0 / 27 (0.00%)      | 1 / 115 (0.87%)      |
| occurrences (all)                                | 0                   | 0                   | 1                    |
| Eye Pain   |                     |                     |                      |
| subjects affected / exposed                      | 1 / 71 (1.41%)      | 0 / 27 (0.00%)      | 2 / 115 (1.74%)      |
| occurrences (all)                                | 1                   | 0                   | 2                    |
| Lacrimation Increased                            |                     |                     |                      |
| subjects affected / exposed                      | 1 / 71 (1.41%)      | 1 / 27 (3.70%)      | 1 / 115 (0.87%)      |
| occurrences (all)                                | 1                   | 1                   | 1                    |
| Eye Haemorrhage                                  |                     |                     |                      |
| subjects affected / exposed                      | 1 / 71 (1.41%)      | 0 / 27 (0.00%)      | 0 / 115 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                    |
| Eyelid Oedema                                    |                     |                     |                      |
| subjects affected / exposed                      | 0 / 71 (0.00%)      | 0 / 27 (0.00%)      | 2 / 115 (1.74%)      |
| occurrences (all)                                | 0                   | 0                   | 2                    |
| Ocular Hyperaemia                                |                     |                     |                      |



|  |                  |                  |                   |
|--|------------------|------------------|-------------------|
| subjects affected / exposed                | 0 / 71 (0.00%)   | 0 / 27 (0.00%)   | 1 / 115 (0.87%)   |
| occurrences (all)                          | 0                | 0                | 1                 |
| Periorbital Oedema                         |                  |                  |                   |
| subjects affected / exposed                | 1 / 71 (1.41%)   | 1 / 27 (3.70%)   | 0 / 115 (0.00%)   |
| occurrences (all)                          | 1                | 1                | 0                 |
| Photopsia                                  |                  |                  |                   |
| subjects affected / exposed                | 2 / 71 (2.82%)   | 0 / 27 (0.00%)   | 0 / 115 (0.00%)   |
| occurrences (all)                          | 2                | 0                | 0                 |
| Retinal Haemorrhage                        |                  |                  |                   |
| subjects affected / exposed                | 0 / 71 (0.00%)   | 0 / 27 (0.00%)   | 1 / 115 (0.87%)   |
| occurrences (all)                          | 0                | 0                | 1                 |
| Diplopia                                   |                  |                  |                   |
| subjects affected / exposed                | 0 / 71 (0.00%)   | 0 / 27 (0.00%)   | 1 / 115 (0.87%)   |
| occurrences (all)                          | 0                | 0                | 1                 |
| Eye Inflammation                           |                  |                  |                   |
| subjects affected / exposed                | 0 / 71 (0.00%)   | 0 / 27 (0.00%)   | 0 / 115 (0.00%)   |
| occurrences (all)                          | 0                | 0                | 0                 |
| Eye Swelling                               |                  |                  |                   |
| subjects affected / exposed                | 0 / 71 (0.00%)   | 0 / 27 (0.00%)   | 0 / 115 (0.00%)   |
| occurrences (all)                          | 0                | 0                | 0                 |
| Eyelid Ptosis                              |                  |                  |                   |
| subjects affected / exposed                | 1 / 71 (1.41%)   | 0 / 27 (0.00%)   | 0 / 115 (0.00%)   |
| occurrences (all)                          | 1                | 0                | 0                 |
| Vitreous Floaters                          |                  |                  |                   |
| subjects affected / exposed                | 0 / 71 (0.00%)   | 0 / 27 (0.00%)   | 1 / 115 (0.87%)   |
| occurrences (all)                          | 0                | 0                | 1                 |
| Vitreous Haemorrhage                       |                  |                  |                   |
| subjects affected / exposed                | 1 / 71 (1.41%)   | 0 / 27 (0.00%)   | 0 / 115 (0.00%)   |
| occurrences (all)                          | 1                | 0                | 0                 |
| Gastrointestinal disorders                 |                  |                  |                   |
| Nausea                                     |                  |                  |                   |
| alternative assessment type:<br>Systematic |                  |                  |                   |
| subjects affected / exposed                | 41 / 71 (57.75%) | 16 / 27 (59.26%) | 68 / 115 (59.13%) |
| occurrences (all)                          | 41               | 16               | 68                |
| Diarrhoea                                  |                  |                  |                   |
| alternative assessment type:<br>Systematic |                  |                  |                   |

|  |                  |                  |                   |
|--|------------------|------------------|-------------------|
| subjects affected / exposed                | 17 / 71 (23.94%) | 13 / 27 (48.15%) | 41 / 115 (35.65%) |
| occurrences (all)                          | 17               | 13               | 41                |
| Constipation                               |                  |                  |                   |
| alternative assessment type:<br>Systematic |                  |                  |                   |
| subjects affected / exposed                | 20 / 71 (28.17%) | 8 / 27 (29.63%)  | 25 / 115 (21.74%) |
| occurrences (all)                          | 20               | 8                | 25                |
| Vomiting                                   |                  |                  |                   |
| alternative assessment type:<br>Systematic |                  |                  |                   |
| subjects affected / exposed                | 19 / 71 (26.76%) | 10 / 27 (37.04%) | 30 / 115 (26.09%) |
| occurrences (all)                          | 19               | 10               | 30                |
| Stomatitis                                 |                  |                  |                   |
| alternative assessment type:<br>Systematic |                  |                  |                   |
| subjects affected / exposed                | 8 / 71 (11.27%)  | 0 / 27 (0.00%)   | 8 / 115 (6.96%)   |
| occurrences (all)                          | 8                | 0                | 8                 |
| Abdominal pain                             |                  |                  |                   |
| alternative assessment type:<br>Systematic |                  |                  |                   |
| subjects affected / exposed                | 1 / 71 (1.41%)   | 0 / 27 (0.00%)   | 12 / 115 (10.43%) |
| occurrences (all)                          | 1                | 0                | 12                |
| Abdominal Pain Upper                       |                  |                  |                   |
| subjects affected / exposed                | 1 / 71 (1.41%)   | 1 / 27 (3.70%)   | 6 / 115 (5.22%)   |
| occurrences (all)                          | 1                | 1                | 6                 |
| Dyspepsia                                  |                  |                  |                   |
| subjects affected / exposed                | 3 / 71 (4.23%)   | 2 / 27 (7.41%)   | 3 / 115 (2.61%)   |
| occurrences (all)                          | 3                | 2                | 3                 |
| Gingival Bleeding                          |                  |                  |                   |
| subjects affected / exposed                | 0 / 71 (0.00%)   | 0 / 27 (0.00%)   | 7 / 115 (6.09%)   |
| occurrences (all)                          | 0                | 0                | 7                 |
| Haemorrhoids                               |                  |                  |                   |
| subjects affected / exposed                | 1 / 71 (1.41%)   | 0 / 27 (0.00%)   | 3 / 115 (2.61%)   |
| occurrences (all)                          | 1                | 0                | 3                 |
| Aphthous Ulcer                             |                  |                  |                   |
| subjects affected / exposed                | 1 / 71 (1.41%)   | 1 / 27 (3.70%)   | 1 / 115 (0.87%)   |
| occurrences (all)                          | 1                | 1                | 1                 |
| Mouth Haemorrhage                          |                  |                  |                   |

|                                  |                |                |                 |
|----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed      | 1 / 71 (1.41%) | 1 / 27 (3.70%) | 4 / 115 (3.48%) |
| occurrences (all)                | 1              | 1              | 4               |
| Abdominal Discomfort             |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences (all)                | 0              | 1              | 1               |
| Gingival Pain                    |                |                |                 |
| subjects affected / exposed      | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences (all)                | 1              | 0              | 3               |
| Odynophagia                      |                |                |                 |
| subjects affected / exposed      | 1 / 71 (1.41%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)                | 1              | 1              | 0               |
| Toothache                        |                |                |                 |
| subjects affected / exposed      | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences (all)                | 2              | 0              | 3               |
| Dry Mouth                        |                |                |                 |
| subjects affected / exposed      | 2 / 71 (2.82%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences (all)                | 2              | 1              | 1               |
| Gastrooesophageal Reflux Disease |                |                |                 |
| subjects affected / exposed      | 3 / 71 (4.23%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                | 3              | 0              | 2               |
| Dysphagia                        |                |                |                 |
| subjects affected / exposed      | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                | 2              | 0              | 1               |
| Flatulence                       |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences (all)                | 0              | 0              | 3               |
| Melaena                          |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                | 0              | 0              | 1               |
| Abdominal Pain Lower             |                |                |                 |
| subjects affected / exposed      | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                | 1              | 0              | 0               |
| Anal Fissure                     |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)                | 0              | 1              | 0               |
| Angina Bullosa Haemorrhagica     |                |                |                 |

|                              |                |                |                 |
|------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 0              | 0               |
| Enterocolitis                |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 1              | 1               |
| Eructation                   |                |                |                 |
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 1              | 0              | 1               |
| Gastritis                    |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |
| Gastrointestinal Haemorrhage |                |                |                 |
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 1              | 0              | 1               |
| Mouth Ulceration             |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |
| Oral Disorder                |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)            | 0              | 0              | 2               |
| Oral Mucosa Haematoma        |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 1              | 0               |
| Oral Mucosal Blistering      |                |                |                 |
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 1              | 0              | 1               |
| Abdominal Tenderness         |                |                |                 |
| subjects affected / exposed  | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)            | 1              | 0              | 0               |
| Anal Incontinence            |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)            | 0              | 0              | 1               |
| Breath Odour                 |                |                |                 |
| subjects affected / exposed  | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)            | 0              | 1              | 0               |
| Diverticulum                 |                |                |                 |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Faeces Soft                 |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 1              | 0               |
| Gastrointestinal Pain       |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Gingival Hypertrophy        |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Glossitis                   |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Ileus                       |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Inguinal Hernia             |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Lip Blister                 |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Lip Dry                     |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Lip Oedema                  |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Lip Pain                    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Lip Swelling                |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Lip Ulceration              |                |                |                 |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Mouth Swelling              |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 1              | 0               |
| Oesophagitis                |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Oral Dysaesthesia           |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Palatal Disorder            |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Perianal Erythema           |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Proctalgia                  |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Rectal Fissure              |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Rectal Haemorrhage          |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Retching                    |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Salivary Hypersecretion     |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Tongue Haematoma            |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Tongue Ulceration           |                |                |                 |

|  |                 |                 |                  |
|--|-----------------|-----------------|------------------|
| subjects affected / exposed            | 1 / 71 (1.41%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%)  |
| occurrences (all)                      | 1               | 0               | 0                |
| Tooth Loss                             |                 |                 |                  |
| subjects affected / exposed            | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 1 / 115 (0.87%)  |
| occurrences (all)                      | 0               | 0               | 1                |
| Trichoglossia                          |                 |                 |                  |
| subjects affected / exposed            | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0                |
| Oral Contusion                         |                 |                 |                  |
| subjects affected / exposed            | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0                |
| Oral Pain                              |                 |                 |                  |
| subjects affected / exposed            | 1 / 71 (1.41%)  | 0 / 27 (0.00%)  | 1 / 115 (0.87%)  |
| occurrences (all)                      | 1               | 0               | 1                |
| Hepatobiliary disorders                |                 |                 |                  |
| Hyperbilirubinaemia                    |                 |                 |                  |
| subjects affected / exposed            | 2 / 71 (2.82%)  | 0 / 27 (0.00%)  | 5 / 115 (4.35%)  |
| occurrences (all)                      | 2               | 0               | 5                |
| Cholelithiasis                         |                 |                 |                  |
| subjects affected / exposed            | 1 / 71 (1.41%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%)  |
| occurrences (all)                      | 1               | 0               | 0                |
| Hepatomegaly                           |                 |                 |                  |
| subjects affected / exposed            | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0                |
| Jaundice                               |                 |                 |                  |
| subjects affected / exposed            | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 1 / 115 (0.87%)  |
| occurrences (all)                      | 0               | 0               | 1                |
| Ocular Icterus                         |                 |                 |                  |
| subjects affected / exposed            | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 1 / 115 (0.87%)  |
| occurrences (all)                      | 0               | 0               | 1                |
| Skin and subcutaneous tissue disorders |                 |                 |                  |
| Night sweats                           |                 |                 |                  |
| subjects affected / exposed            | 8 / 71 (11.27%) | 3 / 27 (11.11%) | 10 / 115 (8.70%) |
| occurrences (all)                      | 8               | 3               | 10               |
| Petechiae                              |                 |                 |                  |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 4 / 71 (5.63%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences (all)           | 4              | 0              | 3               |
| Hyperhidrosis               |                |                |                 |
| subjects affected / exposed | 6 / 71 (8.45%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences (all)           | 6              | 0              | 3               |
| Rash                        |                |                |                 |
| subjects affected / exposed | 2 / 71 (2.82%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences (all)           | 2              | 1              | 1               |
| Rash Maculo-Papular         |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences (all)           | 1              | 0              | 3               |
| Ecchymosis                  |                |                |                 |
| subjects affected / exposed | 3 / 71 (4.23%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 3              | 0              | 1               |
| Pruritus                    |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 1 / 27 (3.70%) | 2 / 115 (1.74%) |
| occurrences (all)           | 1              | 1              | 2               |
| Skin Lesion                 |                |                |                 |
| subjects affected / exposed | 3 / 71 (4.23%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 3              | 0              | 1               |
| Skin Ulcer                  |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 1 / 27 (3.70%) | 2 / 115 (1.74%) |
| occurrences (all)           | 1              | 1              | 2               |
| Alopecia                    |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)           | 1              | 0              | 2               |
| Decubitus Ulcer             |                |                |                 |
| subjects affected / exposed | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 2              | 0              | 0               |
| Erythema                    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)           | 0              | 0              | 2               |
| Cold Sweat                  |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Dermatitis                  |                |                |                 |



|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 1              | 0              | 1               |
| Purpura                     |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Skin Mass                   |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Swelling Face               |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 1              | 0              | 1               |
| Dermal Cyst                 |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Dermatitis Acneiform        |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Dermatitis Bullous          |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 1              | 0               |
| Dry Skin                    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Facial Wasting              |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Macule                      |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Miliaria                    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Nail Disorder               |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Photosensitivity Reaction   |                |                |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 1 / 115 (0.87%) |
| occurrences (all)           | 0               | 0               | 1               |
| Rash Erythematous           |                 |                 |                 |
| subjects affected / exposed | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Rash Pruritic               |                 |                 |                 |
| subjects affected / exposed | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Skin Discolouration         |                 |                 |                 |
| subjects affected / exposed | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 1 / 115 (0.87%) |
| occurrences (all)           | 0               | 0               | 1               |
| Skin Hyperpigmentation      |                 |                 |                 |
| subjects affected / exposed | 1 / 71 (1.41%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Skin Induration             |                 |                 |                 |
| subjects affected / exposed | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Skin Maceration             |                 |                 |                 |
| subjects affected / exposed | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Urticaria                   |                 |                 |                 |
| subjects affected / exposed | 0 / 71 (0.00%)  | 0 / 27 (0.00%)  | 0 / 115 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Renal and urinary disorders |                 |                 |                 |
| Acute Kidney Injury         |                 |                 |                 |
| subjects affected / exposed | 8 / 71 (11.27%) | 2 / 27 (7.41%)  | 3 / 115 (2.61%) |
| occurrences (all)           | 8               | 2               | 3               |
| Haematuria                  |                 |                 |                 |
| subjects affected / exposed | 3 / 71 (4.23%)  | 3 / 27 (11.11%) | 1 / 115 (0.87%) |
| occurrences (all)           | 3               | 3               | 1               |
| Pollakiuria                 |                 |                 |                 |
| subjects affected / exposed | 2 / 71 (2.82%)  | 0 / 27 (0.00%)  | 3 / 115 (2.61%) |
| occurrences (all)           | 2               | 0               | 3               |
| Proteinuria                 |                 |                 |                 |
| subjects affected / exposed | 3 / 71 (4.23%)  | 1 / 27 (3.70%)  | 1 / 115 (0.87%) |
| occurrences (all)           | 3               | 1               | 1               |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| Dysuria                     |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 1 / 27 (3.70%) | 2 / 115 (1.74%) |
| occurrences (all)           | 1              | 1              | 2               |
| Renal Failure               |                |                |                 |
| subjects affected / exposed | 2 / 71 (2.82%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences (all)           | 2              | 1              | 1               |
| Urinary Incontinence        |                |                |                 |
| subjects affected / exposed | 2 / 71 (2.82%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences (all)           | 2              | 1              | 1               |
| Urinary Retention           |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 2 / 115 (1.74%) |
| occurrences (all)           | 0              | 1              | 2               |
| Bladder Dilatation          |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 1              | 0              | 1               |
| Chronic Kidney Disease      |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Micturition Urgency         |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Bladder Pain                |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 1              | 0               |
| Chromaturia                 |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Incontinence                |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Nocturia                    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Polyuria                    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |

|   |                     |                     |                      |
|---|---------------------|---------------------|----------------------|
| Urethral Caruncle<br>subjects affected / exposed<br>occurrences (all)         | 0 / 71 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 1 / 115 (0.87%)<br>1 |
| Urethral Haemorrhage<br>subjects affected / exposed<br>occurrences (all)      | 1 / 71 (1.41%)<br>1 | 0 / 27 (0.00%)<br>0 | 0 / 115 (0.00%)<br>0 |
| Urge Incontinence<br>subjects affected / exposed<br>occurrences (all)         | 0 / 71 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 1 / 115 (0.87%)<br>1 |
| Urinary Tract Obstruction<br>subjects affected / exposed<br>occurrences (all) | 0 / 71 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 0 / 115 (0.00%)<br>0 |
| Urinary Tract Pain<br>subjects affected / exposed<br>occurrences (all)        | 0 / 71 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1 | 0 / 115 (0.00%)<br>0 |
| Endocrine disorders   |                     |                     |                      |
| Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)            | 0 / 71 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1 | 4 / 115 (3.48%)<br>4 |
| Cushingoid<br>subjects affected / exposed<br>occurrences (all)                | 0 / 71 (0.00%)<br>0 | 0 / 27 (0.00%)<br>0 | 1 / 115 (0.87%)<br>1 |
| Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)           | 0 / 71 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1 | 0 / 115 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders                               |                     |                     |                      |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                | 5 / 71 (7.04%)<br>5 | 0 / 27 (0.00%)<br>0 | 6 / 115 (5.22%)<br>6 |
| Back Pain<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 71 (0.00%)<br>0 | 1 / 27 (3.70%)<br>1 | 6 / 115 (5.22%)<br>6 |
| Muscular Weakness<br>subjects affected / exposed<br>occurrences (all)         | 5 / 71 (7.04%)<br>5 | 0 / 27 (0.00%)<br>0 | 4 / 115 (3.48%)<br>4 |
| Pain In Extremity   |                     |                     |                      |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 4 / 71 (5.63%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences (all)           | 4              | 0              | 3               |
| Muscle Spasms               |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 2 / 27 (7.41%) | 2 / 115 (1.74%) |
| occurrences (all)           | 1              | 2              | 2               |
| Bone Pain                   |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 5 / 115 (4.35%) |
| occurrences (all)           | 0              | 0              | 5               |
| Musculoskeletal Pain        |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)           | 1              | 0              | 2               |
| Myalgia                     |                |                |                 |
| subjects affected / exposed | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 2              | 0              | 1               |
| Neck Pain                   |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)           | 0              | 0              | 2               |
| Arthritis                   |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 1              | 1               |
| Flank Pain                  |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Hypercreatinaemia           |                |                |                 |
| subjects affected / exposed | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 2              | 0              | 0               |
| Joint Swelling              |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)           | 0              | 0              | 2               |
| Musculoskeletal Chest Pain  |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Pain In Jaw                 |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Bursitis                    |                |                |                 |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Groin Pain                  |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Ligament Pain               |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Limb Discomfort             |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Limb Mass                   |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Muscle Mass                 |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Muscle Tightness            |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Muscle Twitching            |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Osteitis                    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Osteoarthritis              |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Spinal Osteoarthritis       |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Torticollis                 |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Infections and infestations |                |                |                 |

|                                   |                |                |                 |
|-----------------------------------|----------------|----------------|-----------------|
| Urinary Tract Infection           |                |                |                 |
| subjects affected / exposed       | 6 / 71 (8.45%) | 2 / 27 (7.41%) | 9 / 115 (7.83%) |
| occurrences (all)                 | 6              | 2              | 9               |
| Oral Herpes                       |                |                |                 |
| subjects affected / exposed       | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences (all)                 | 2              | 0              | 3               |
| Nasopharyngitis                   |                |                |                 |
| subjects affected / exposed       | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 5 / 115 (4.35%) |
| occurrences (all)                 | 1              | 0              | 5               |
| Oral Candidiasis                  |                |                |                 |
| subjects affected / exposed       | 4 / 71 (5.63%) | 0 / 27 (0.00%) | 4 / 115 (3.48%) |
| occurrences (all)                 | 4              | 0              | 4               |
| Pneumonia                         |                |                |                 |
| subjects affected / exposed       | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 4 / 115 (3.48%) |
| occurrences (all)                 | 1              | 0              | 4               |
| Cellulitis                        |                |                |                 |
| subjects affected / exposed       | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                 | 2              | 0              | 2               |
| Lung Infection                    |                |                |                 |
| subjects affected / exposed       | 2 / 71 (2.82%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences (all)                 | 2              | 1              | 1               |
| Sinusitis                         |                |                |                 |
| subjects affected / exposed       | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 2 / 115 (1.74%) |
| occurrences (all)                 | 0              | 1              | 2               |
| Upper Respiratory Tract Infection |                |                |                 |
| subjects affected / exposed       | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                 | 1              | 0              | 2               |
| Device Related Infection          |                |                |                 |
| subjects affected / exposed       | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                 | 1              | 0              | 2               |
| Periodontitis                     |                |                |                 |
| subjects affected / exposed       | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                 | 0              | 0              | 2               |
| Pneumonia Fungal                  |                |                |                 |
| subjects affected / exposed       | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                 | 1              | 0              | 0               |

|                                 |                |                |                 |
|---------------------------------|----------------|----------------|-----------------|
| Sepsis                          |                |                |                 |
| subjects affected / exposed     | 1 / 71 (1.41%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences (all)               | 1              | 1              | 1               |
| Candida Infection               |                |                |                 |
| subjects affected / exposed     | 3 / 71 (4.23%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)               | 3              | 0              | 0               |
| Folliculitis                    |                |                |                 |
| subjects affected / exposed     | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 2 / 115 (1.74%) |
| occurrences (all)               | 0              | 1              | 2               |
| Oesophageal Candidiasis         |                |                |                 |
| subjects affected / exposed     | 0 / 71 (0.00%) | 2 / 27 (7.41%) | 0 / 115 (0.00%) |
| occurrences (all)               | 0              | 2              | 0               |
| Skin Infection                  |                |                |                 |
| subjects affected / exposed     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)               | 1              | 0              | 1               |
| Staphylococcal Infection        |                |                |                 |
| subjects affected / exposed     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)               | 0              | 0              | 1               |
| Clostridium Difficile Colitis   |                |                |                 |
| subjects affected / exposed     | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences (all)               | 0              | 1              | 1               |
| Clostridium Difficile Infection |                |                |                 |
| subjects affected / exposed     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)               | 1              | 0              | 0               |
| Conjunctivitis                  |                |                |                 |
| subjects affected / exposed     | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences (all)               | 0              | 1              | 1               |
| Ear Infection                   |                |                |                 |
| subjects affected / exposed     | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)               | 1              | 0              | 1               |
| Fungal Infection                |                |                |                 |
| subjects affected / exposed     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)               | 0              | 0              | 2               |
| Herpes Dermatitis               |                |                |                 |
| subjects affected / exposed     | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)               | 0              | 0              | 1               |



|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| Infection                   |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Lip Infection               |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 1              | 1               |
| Nasal Herpes                |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 1              | 0              | 1               |
| Pharyngitis                 |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Pseudomonas Infection       |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Rash Pustular               |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 1              | 0               |
| Rhinovirus Infection        |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Soft Tissue Infection       |                |                |                 |
| subjects affected / exposed | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 2              | 0              | 0               |
| Abscess Limb                |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Acute Sinusitis             |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Anal Abscess                |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Aspergillus Infection       |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| Asymptomatic Bacteriuria    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Bacterial Infection         |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 1              | 0               |
| Bacteriuria                 |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 1              | 0               |
| Bronchitis                  |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Catheter Site Cellulitis    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Clostridium Colitis         |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Dermo-Hypodermatitis        |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Diverticulitis              |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Emphyema                    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Encephalitis                |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Enterobiasis                |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Enterococcal Infection      |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |

|                                   |                |                |                 |
|-----------------------------------|----------------|----------------|-----------------|
| Furuncle                          |                |                |                 |
| subjects affected / exposed       | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0               |
| Genital Herpes                    |                |                |                 |
| subjects affected / exposed       | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                 | 0              | 0              | 1               |
| Gingivitis                        |                |                |                 |
| subjects affected / exposed       | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                 | 1              | 0              | 0               |
| Groin Infection                   |                |                |                 |
| subjects affected / exposed       | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                 | 1              | 0              | 0               |
| Herpes Simplex                    |                |                |                 |
| subjects affected / exposed       | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0               |
| Herpes Zoster                     |                |                |                 |
| subjects affected / exposed       | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0               |
| Infected Dermal Cyst              |                |                |                 |
| subjects affected / exposed       | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                 | 0              | 0              | 1               |
| Influenza                         |                |                |                 |
| subjects affected / exposed       | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0               |
| Lower Respiratory Tract Infection |                |                |                 |
| subjects affected / exposed       | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0               |
| Lymph Gland Infection             |                |                |                 |
| subjects affected / exposed       | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                 | 1              | 0              | 0               |
| Meningitis                        |                |                |                 |
| subjects affected / exposed       | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                 | 0              | 0              | 1               |
| Metapneumovirus Infection         |                |                |                 |
| subjects affected / exposed       | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0               |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| Mucosal Infection           |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Oesophageal Infection       |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Ophthalmic Herpes Simplex   |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Oral Fungal Infection       |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Oral Infection              |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Osteomyelitis               |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Parotitis                   |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Pneumonia Klebsiella        |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Proteus Infection           |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 0              | 0              | 0               |
| Pseudomembranous Colitis    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Respiratory Tract Infection |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Rhinitis                    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |

|                                  |                |                |                 |
|----------------------------------|----------------|----------------|-----------------|
| Septic Shock                     |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                | 0              | 0              | 1               |
| Sialoadenitis                    |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                | 0              | 0              | 1               |
| Staphylococcal Bacteraemia       |                |                |                 |
| subjects affected / exposed      | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                | 1              | 0              | 0               |
| Stenotrophomonas Infection       |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                | 0              | 0              | 1               |
| Tonsillitis                      |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                | 0              | 0              | 0               |
| Tonsillitis Bacterial            |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                | 0              | 0              | 1               |
| Tooth Abscess                    |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                | 0              | 0              | 1               |
| Tooth Infection                  |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                | 0              | 0              | 0               |
| Varicella Zoster Virus Infection |                |                |                 |
| subjects affected / exposed      | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                | 1              | 0              | 0               |
| Hallucination                    |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences (all)                | 0              | 0              | 3               |
| Personality Change               |                |                |                 |
| subjects affected / exposed      | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)                | 1              | 0              | 2               |
| Facial Bones Fracture            |                |                |                 |
| subjects affected / exposed      | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                | 0              | 0              | 0               |

|                                    |                  |                 |                   |
|------------------------------------|------------------|-----------------|-------------------|
| Metabolism and nutrition disorders |                  |                 |                   |
| Hyponatraemia                      |                  |                 |                   |
| subjects affected / exposed        | 26 / 71 (36.62%) | 6 / 27 (22.22%) | 25 / 115 (21.74%) |
| occurrences (all)                  | 26               | 6               | 25                |
| Hypokalaemia                       |                  |                 |                   |
| subjects affected / exposed        | 10 / 71 (14.08%) | 1 / 27 (3.70%)  | 9 / 115 (7.83%)   |
| occurrences (all)                  | 10               | 1               | 9                 |
| Hypocalcaemia                      |                  |                 |                   |
| subjects affected / exposed        | 5 / 71 (7.04%)   | 2 / 27 (7.41%)  | 11 / 115 (9.57%)  |
| occurrences (all)                  | 5                | 2               | 11                |
| Hypercreatininaemia                |                  |                 |                   |
| subjects affected / exposed        | 5 / 71 (7.04%)   | 0 / 27 (0.00%)  | 13 / 115 (11.30%) |
| occurrences (all)                  | 5                | 0               | 13                |
| Hypomagnesaemia                    |                  |                 |                   |
| subjects affected / exposed        | 7 / 71 (9.86%)   | 0 / 27 (0.00%)  | 9 / 115 (7.83%)   |
| occurrences (all)                  | 7                | 0               | 9                 |
| Hyperglycaemia                     |                  |                 |                   |
| subjects affected / exposed        | 6 / 71 (8.45%)   | 3 / 27 (11.11%) | 7 / 115 (6.09%)   |
| occurrences (all)                  | 6                | 3               | 7                 |
| Hyperkalaemia                      |                  |                 |                   |
| subjects affected / exposed        | 8 / 71 (11.27%)  | 2 / 27 (7.41%)  | 9 / 115 (7.83%)   |
| occurrences (all)                  | 8                | 2               | 9                 |
| Dehydration                        |                  |                 |                   |
| subjects affected / exposed        | 8 / 71 (11.27%)  | 0 / 27 (0.00%)  | 6 / 115 (5.22%)   |
| occurrences (all)                  | 8                | 0               | 6                 |
| Hypophosphataemia                  |                  |                 |                   |
| subjects affected / exposed        | 9 / 71 (12.68%)  | 1 / 27 (3.70%)  | 5 / 115 (4.35%)   |
| occurrences (all)                  | 9                | 1               | 5                 |
| Hyperuricaemia                     |                  |                 |                   |
| subjects affected / exposed        | 5 / 71 (7.04%)   | 1 / 27 (3.70%)  | 2 / 115 (1.74%)   |
| occurrences (all)                  | 5                | 1               | 2                 |
| Hypoalbuminaemia                   |                  |                 |                   |
| subjects affected / exposed        | 4 / 71 (5.63%)   | 1 / 27 (3.70%)  | 1 / 115 (0.87%)   |
| occurrences (all)                  | 4                | 1               | 1                 |
| Hypercalcaemia                     |                  |                 |                   |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 4 / 115 (3.48%) |
| occurrences (all)           | 0              | 0              | 4               |
| Hypermagnesaemia            |                |                |                 |
| subjects affected / exposed | 3 / 71 (4.23%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 3              | 0              | 1               |
| Cachexia                    |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 3 / 115 (2.61%) |
| occurrences (all)           | 0              | 1              | 3               |
| Hyperlipasaemia             |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences (all)           | 1              | 0              | 3               |
| Hyperphosphataemia          |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 3 / 115 (2.61%) |
| occurrences (all)           | 0              | 0              | 3               |
| Hypoglycaemia               |                |                |                 |
| subjects affected / exposed | 3 / 71 (4.23%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 3              | 0              | 1               |
| Fluid Retention             |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Hyperamylasaemia            |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 2 / 115 (1.74%) |
| occurrences (all)           | 1              | 0              | 2               |
| Fluid Overload              |                |                |                 |
| subjects affected / exposed | 2 / 71 (2.82%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 2              | 0              | 0               |
| Tumour Lysis Syndrome       |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Type 2 Diabetes Mellitus    |                |                |                 |
| subjects affected / exposed | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)           | 1              | 0              | 0               |
| Diabetes Mellitus           |                |                |                 |
| subjects affected / exposed | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)           | 0              | 0              | 1               |
| Failure To Thrive           |                |                |                 |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed                        | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                                  | 1              | 0              | 0               |
| Gout   |                |                |                 |
| subjects affected / exposed                        | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                                  | 1              | 0              | 0               |
| Hyperglycaemic Hyperosmolar<br>Nonketotic Syndrome |                |                |                 |
| subjects affected / exposed                        | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                                  | 1              | 0              | 0               |
| Hyperhomocysteinaemia                              |                |                |                 |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                                  | 0              | 0              | 1               |
| Hypernatraemia                                     |                |                |                 |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                                  | 0              | 0              | 1               |
| Hypouricaemia                                      |                |                |                 |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 1 / 27 (3.70%) | 0 / 115 (0.00%) |
| occurrences (all)                                  | 0              | 1              | 0               |
| Metabolic Acidosis                                 |                |                |                 |
| subjects affected / exposed                        | 1 / 71 (1.41%) | 0 / 27 (0.00%) | 0 / 115 (0.00%) |
| occurrences (all)                                  | 1              | 0              | 0               |
| Polydipsia   |                |                |                 |
| subjects affected / exposed                        | 0 / 71 (0.00%) | 0 / 27 (0.00%) | 1 / 115 (0.87%) |
| occurrences (all)                                  | 0              | 0              | 1               |

| <b>Non-serious adverse events</b>                                      | Physician's Choice 1<br>(PV <5) | Physician's Choice 2<br>(PV ≥5) |  |
|--|---------------------------------|---------------------------------|--|
| Total subjects affected by non-serious<br>adverse events               |                                 |                                 |  |
| subjects affected / exposed  | 37 / 39 (94.87%)                | 40 / 45 (88.89%)                |  |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps) |                                 |                                 |  |
| Acute Myeloid Leukaemia  |                                 |                                 |  |
| subjects affected / exposed  | 1 / 39 (2.56%)                  | 0 / 45 (0.00%)                  |  |
| occurrences (all)  | 1                               | 0                               |  |
| Basal Cell Carcinoma   |                                 |                                 |  |
| subjects affected / exposed  | 0 / 39 (0.00%)                  | 1 / 45 (2.22%)                  |  |
| occurrences (all)  | 0                               | 1                               |  |
| Chloroma   |                                 |                                 |  |



|                             |                 |                |  |
|-----------------------------|-----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%)  | 1 / 45 (2.22%) |  |
| occurrences (all)           | 0               | 1              |  |
| Leukaemic Infiltration      |                 |                |  |
| subjects affected / exposed | 1 / 39 (2.56%)  | 0 / 45 (0.00%) |  |
| occurrences (all)           | 1               | 0              |  |
| Uterine Leiomyoma           |                 |                |  |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |
| Vascular disorders          |                 |                |  |
| Hypotension                 |                 |                |  |
| subjects affected / exposed | 4 / 39 (10.26%) | 1 / 45 (2.22%) |  |
| occurrences (all)           | 4               | 1              |  |
| Haematoma                   |                 |                |  |
| subjects affected / exposed | 7 / 39 (17.95%) | 1 / 45 (2.22%) |  |
| occurrences (all)           | 7               | 1              |  |
| Hypertension                |                 |                |  |
| subjects affected / exposed | 1 / 39 (2.56%)  | 1 / 45 (2.22%) |  |
| occurrences (all)           | 1               | 1              |  |
| Pallor                      |                 |                |  |
| subjects affected / exposed | 2 / 39 (5.13%)  | 1 / 45 (2.22%) |  |
| occurrences (all)           | 2               | 1              |  |
| Haemorrhage                 |                 |                |  |
| subjects affected / exposed | 0 / 39 (0.00%)  | 1 / 45 (2.22%) |  |
| occurrences (all)           | 0               | 1              |  |
| Phlebitis                   |                 |                |  |
| subjects affected / exposed | 3 / 39 (7.69%)  | 0 / 45 (0.00%) |  |
| occurrences (all)           | 3               | 0              |  |
| Thrombophlebitis            |                 |                |  |
| subjects affected / exposed | 1 / 39 (2.56%)  | 1 / 45 (2.22%) |  |
| occurrences (all)           | 1               | 1              |  |
| Orthostatic Hypotension     |                 |                |  |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |
| Deep Vein Thrombosis        |                 |                |  |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |

|  |                  |                  |  |
|--|------------------|------------------|--|
| Flushing   |                  |                  |  |
| subjects affected / exposed                          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                                    | 0                | 0                |  |
| Circulatory Collapse                                 |                  |                  |  |
| subjects affected / exposed                          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                                    | 0                | 0                |  |
| Embolism   |                  |                  |  |
| subjects affected / exposed                          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                                    | 0                | 0                |  |
| Hot Flush  |                  |                  |  |
| subjects affected / exposed                          | 1 / 39 (2.56%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                                    | 1                | 0                |  |
| Intermittent Claudication                            |                  |                  |  |
| subjects affected / exposed                          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                                    | 0                | 0                |  |
| Lymphoedema  |                  |                  |  |
| subjects affected / exposed                          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                                    | 0                | 0                |  |
| Poor Peripheral Circulation                          |                  |                  |  |
| subjects affected / exposed                          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                                    | 0                | 0                |  |
| Thrombophlebitis Superficial                         |                  |                  |  |
| subjects affected / exposed                          | 0 / 39 (0.00%)   | 1 / 45 (2.22%)   |  |
| occurrences (all)                                    | 0                | 1                |  |
| Venous Thrombosis                                    |                  |                  |  |
| subjects affected / exposed                          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                                    | 0                | 0                |  |
| General disorders and administration site conditions |                  |                  |  |
| Fatigue  |                  |                  |  |
| subjects affected / exposed                          | 15 / 39 (38.46%) | 13 / 45 (28.89%) |  |
| occurrences (all)                                    | 15               | 13               |  |
| Pyrexia  |                  |                  |  |
| alternative assessment type: Systematic              |                  |                  |  |
| subjects affected / exposed                          | 13 / 39 (33.33%) | 13 / 45 (28.89%) |  |
| occurrences (all)                                    | 13               | 13               |  |
| Oedema peripheral                                    |                  |                  |  |

|  |                  |                 |  |
|--|------------------|-----------------|--|
| alternative assessment type:<br>Systematic |                  |                 |  |
| subjects affected / exposed                | 10 / 39 (25.64%) | 5 / 45 (11.11%) |  |
| occurrences (all)                          | 10               | 5               |  |
| Asthenia                                   |                  |                 |  |
| alternative assessment type:<br>Systematic |                  |                 |  |
| subjects affected / exposed                | 5 / 39 (12.82%)  | 5 / 45 (11.11%) |  |
| occurrences (all)                          | 5                | 5               |  |
| Malaise                                    |                  |                 |  |
| subjects affected / exposed                | 3 / 39 (7.69%)   | 1 / 45 (2.22%)  |  |
| occurrences (all)                          | 3                | 1               |  |
| Oedema                                     |                  |                 |  |
| subjects affected / exposed                | 4 / 39 (10.26%)  | 2 / 45 (4.44%)  |  |
| occurrences (all)                          | 4                | 2               |  |
| Chills                                     |                  |                 |  |
| subjects affected / exposed                | 3 / 39 (7.69%)   | 1 / 45 (2.22%)  |  |
| occurrences (all)                          | 3                | 1               |  |
| Mucosal Inflammation                       |                  |                 |  |
| subjects affected / exposed                | 4 / 39 (10.26%)  | 3 / 45 (6.67%)  |  |
| occurrences (all)                          | 4                | 3               |  |
| Pain                                       |                  |                 |  |
| subjects affected / exposed                | 1 / 39 (2.56%)   | 1 / 45 (2.22%)  |  |
| occurrences (all)                          | 1                | 1               |  |
| Gait Disturbance                           |                  |                 |  |
| subjects affected / exposed                | 0 / 39 (0.00%)   | 0 / 45 (0.00%)  |  |
| occurrences (all)                          | 0                | 0               |  |
| General Physical Health Deterioration      |                  |                 |  |
| subjects affected / exposed                | 0 / 39 (0.00%)   | 0 / 45 (0.00%)  |  |
| occurrences (all)                          | 0                | 0               |  |
| Injection Site Bruising                    |                  |                 |  |
| subjects affected / exposed                | 1 / 39 (2.56%)   | 1 / 45 (2.22%)  |  |
| occurrences (all)                          | 1                | 1               |  |
| Non-Cardiac Chest Pain                     |                  |                 |  |
| subjects affected / exposed                | 0 / 39 (0.00%)   | 0 / 45 (0.00%)  |  |
| occurrences (all)                          | 0                | 0               |  |
| Ulcer                                      |                  |                 |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Catheter Site Haemorrhage   |                |                |  |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Face Oedema                 |                |                |  |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Generalised Oedema          |                |                |  |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Secretion Discharge         |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Catheter Site Haematoma     |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Chest Pain                  |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Drug Intolerance            |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Extravasation               |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Feeling Cold                |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Granuloma                   |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences (all)           | 0              | 1              |  |
| Hernia                      |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Impaired Healing            |                |                |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed              | 0 / 39 (0.00%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                        | 0               | 0               |  |
| Infusion Site Haemorrhage                |                 |                 |  |
| subjects affected / exposed              | 0 / 39 (0.00%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                        | 0               | 0               |  |
| Injection Site Discolouration            |                 |                 |  |
| subjects affected / exposed              | 1 / 39 (2.56%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                        | 1               | 0               |  |
| Injection Site Pain                      |                 |                 |  |
| subjects affected / exposed              | 0 / 39 (0.00%)  | 1 / 45 (2.22%)  |  |
| occurrences (all)                        | 0               | 1               |  |
| Mucosal Dryness                          |                 |                 |  |
| subjects affected / exposed              | 0 / 39 (0.00%)  | 1 / 45 (2.22%)  |  |
| occurrences (all)                        | 0               | 1               |  |
| Nodule                                   |                 |                 |  |
| subjects affected / exposed              | 1 / 39 (2.56%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                        | 1               | 0               |  |
| Peripheral Swelling                      |                 |                 |  |
| subjects affected / exposed              | 0 / 39 (0.00%)  | 1 / 45 (2.22%)  |  |
| occurrences (all)                        | 0               | 1               |  |
| Swelling                                 |                 |                 |  |
| subjects affected / exposed              | 0 / 39 (0.00%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                        | 0               | 0               |  |
| Decreased appetite                       |                 |                 |  |
| subjects affected / exposed              | 9 / 39 (23.08%) | 7 / 45 (15.56%) |  |
| occurrences (all)                        | 9               | 7               |  |
| Immune system disorders                  |                 |                 |  |
| Hypersensitivity                         |                 |                 |  |
| subjects affected / exposed              | 0 / 39 (0.00%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                        | 0               | 0               |  |
| Reproductive system and breast disorders |                 |                 |  |
| Breast Pain                              |                 |                 |  |
| subjects affected / exposed              | 0 / 39 (0.00%)  | 1 / 45 (2.22%)  |  |
| occurrences (all)                        | 0               | 1               |  |
| Breast Swelling                          |                 |                 |  |

|   |                 |                  |  |
|---|-----------------|------------------|--|
| subjects affected / exposed                     | 0 / 39 (0.00%)  | 0 / 45 (0.00%)   |  |
| occurrences (all)                               | 0               | 0                |  |
| Gynaecomastia                                   |                 |                  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%)  | 1 / 45 (2.22%)   |  |
| occurrences (all)                               | 0               | 1                |  |
| Nipple Pain                                     |                 |                  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%)  | 0 / 45 (0.00%)   |  |
| occurrences (all)                               | 0               | 0                |  |
| Oedema Genital                                  |                 |                  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%)  | 0 / 45 (0.00%)   |  |
| occurrences (all)                               | 0               | 0                |  |
| Ovarian Cyst                                    |                 |                  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%)  | 0 / 45 (0.00%)   |  |
| occurrences (all)                               | 0               | 0                |  |
| Testicular Oedema                               |                 |                  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%)  | 1 / 45 (2.22%)   |  |
| occurrences (all)                               | 0               | 1                |  |
| Vaginal Haemorrhage                             |                 |                  |  |
| subjects affected / exposed                     | 0 / 39 (0.00%)  | 0 / 45 (0.00%)   |  |
| occurrences (all)                               | 0               | 0                |  |
| Respiratory, thoracic and mediastinal disorders |                 |                  |  |
| Dyspnoea  |                 |                  |  |
| subjects affected / exposed                     | 8 / 39 (20.51%) | 10 / 45 (22.22%) |  |
| occurrences (all)                               | 8               | 10               |  |
| Epistaxis                                       |                 |                  |  |
| subjects affected / exposed                     | 7 / 39 (17.95%) | 7 / 45 (15.56%)  |  |
| occurrences (all)                               | 7               | 7                |  |
| Cough   |                 |                  |  |
| subjects affected / exposed                     | 5 / 39 (12.82%) | 8 / 45 (17.78%)  |  |
| occurrences (all)                               | 5               | 8                |  |
| Oropharyngeal Pain                              |                 |                  |  |
| subjects affected / exposed                     | 2 / 39 (5.13%)  | 3 / 45 (6.67%)   |  |
| occurrences (all)                               | 2               | 3                |  |
| Productive Cough                                |                 |                  |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 3 / 39 (7.69%) | 1 / 45 (2.22%) |
| occurrences (all)           | 3              | 1              |
| Haemoptysis                 |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 3 / 45 (6.67%) |
| occurrences (all)           | 1              | 3              |
| Dyspnoea Exertional         |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)           | 1              | 1              |
| Nasal Congestion            |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Pleural Effusion            |                |                |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 45 (0.00%) |
| occurrences (all)           | 2              | 0              |
| Hypoxia                     |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 45 (4.44%) |
| occurrences (all)           | 1              | 2              |
| Rhinorrhoea                 |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 45 (4.44%) |
| occurrences (all)           | 0              | 2              |
| Wheezing                    |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 45 (4.44%) |
| occurrences (all)           | 1              | 2              |
| Atelectasis                 |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Hiccups                     |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Pleuritic Pain              |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)           | 1              | 1              |
| Respiratory Failure         |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Pulmonary Oedema            |                |                |

|                                       |                |                |
|---------------------------------------|----------------|----------------|
| subjects affected / exposed           | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 1              | 0              |
| Sinus Congestion                      |                |                |
| subjects affected / exposed           | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Sinus Pain                            |                |                |
| subjects affected / exposed           | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Upper-Airway Cough Syndrome           |                |                |
| subjects affected / exposed           | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)                     | 1              | 1              |
| Chronic Obstructive Pulmonary Disease |                |                |
| subjects affected / exposed           | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                     | 0              | 1              |
| Dysphonia                             |                |                |
| subjects affected / exposed           | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Laryngeal Pain                        |                |                |
| subjects affected / exposed           | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 1              | 0              |
| Lung Consolidation                    |                |                |
| subjects affected / exposed           | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                     | 0              | 1              |
| Lung Infiltration                     |                |                |
| subjects affected / exposed           | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Nasal Dryness                         |                |                |
| subjects affected / exposed           | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Nasal Inflammation                    |                |                |
| subjects affected / exposed           | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Paranasal Sinus Discomfort            |                |                |
| subjects affected / exposed           | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                     | 0              | 0              |



|                              |                |                |  |
|------------------------------|----------------|----------------|--|
| Pharyngeal Inflammation      |                |                |  |
| subjects affected / exposed  | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Pneumonitis                  |                |                |  |
| subjects affected / exposed  | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Pulmonary Mass               |                |                |  |
| subjects affected / exposed  | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences (all)            | 0              | 1              |  |
| Rales                        |                |                |  |
| subjects affected / exposed  | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences (all)            | 0              | 1              |  |
| Respiratory Tract Congestion |                |                |  |
| subjects affected / exposed  | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences (all)            | 1              | 0              |  |
| Rhinitis Allergic            |                |                |  |
| subjects affected / exposed  | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Rhonchi                      |                |                |  |
| subjects affected / exposed  | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Sinus Disorder               |                |                |  |
| subjects affected / exposed  | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences (all)            | 1              | 0              |  |
| Tachypnoea                   |                |                |  |
| subjects affected / exposed  | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Tonsillar Erythema           |                |                |  |
| subjects affected / exposed  | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences (all)            | 1              | 0              |  |
| Tonsillar Hypertrophy        |                |                |  |
| subjects affected / exposed  | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences (all)            | 1              | 0              |  |
| Psychiatric disorders        |                |                |  |
| Insomnia                     |                |                |  |

|                             |                 |                |
|-----------------------------|-----------------|----------------|
| subjects affected / exposed | 4 / 39 (10.26%) | 3 / 45 (6.67%) |
| occurrences (all)           | 4               | 3              |
| Confusional State           |                 |                |
| subjects affected / exposed | 2 / 39 (5.13%)  | 3 / 45 (6.67%) |
| occurrences (all)           | 2               | 3              |
| Anxiety                     |                 |                |
| subjects affected / exposed | 2 / 39 (5.13%)  | 1 / 45 (2.22%) |
| occurrences (all)           | 2               | 1              |
| Depression                  |                 |                |
| subjects affected / exposed | 3 / 39 (7.69%)  | 1 / 45 (2.22%) |
| occurrences (all)           | 3               | 1              |
| Agitation                   |                 |                |
| subjects affected / exposed | 1 / 39 (2.56%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 1               | 0              |
| Restlessness                |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 1 / 45 (2.22%) |
| occurrences (all)           | 0               | 1              |
| Abnormal Dreams             |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Bulimia Nervosa             |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Delirium                    |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Disorientation              |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Flat Affect                 |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Hallucination, Visual       |                 |                |
| subjects affected / exposed | 1 / 39 (2.56%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 1               | 0              |
| Irritability                |                 |                |

|  |                      |                     |  |
|--|----------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 39 (0.00%)<br>0  | 0 / 45 (0.00%)<br>0 |  |
| Listless<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 39 (0.00%)<br>0  | 0 / 45 (0.00%)<br>0 |  |
| Mental Disorder<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 39 (0.00%)<br>0  | 0 / 45 (0.00%)<br>0 |  |
| Mental Status Changes<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 39 (0.00%)<br>0  | 0 / 45 (0.00%)<br>0 |  |
| Nervousness<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 39 (0.00%)<br>0  | 0 / 45 (0.00%)<br>0 |  |
| Psychomotor Retardation<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 39 (0.00%)<br>0  | 0 / 45 (0.00%)<br>0 |  |
| Investigations<br>Weight Decreased<br>subjects affected / exposed<br>occurrences (all)       | 3 / 39 (7.69%)<br>3  | 3 / 45 (6.67%)<br>3 |  |
| Alanine Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all)       | 2 / 39 (5.13%)<br>2  | 1 / 45 (2.22%)<br>1 |  |
| Aspartate Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all)     | 2 / 39 (5.13%)<br>2  | 1 / 45 (2.22%)<br>1 |  |
| International Normalised Ratio Increased<br>subjects affected / exposed<br>occurrences (all) | 3 / 39 (7.69%)<br>3  | 0 / 45 (0.00%)<br>0 |  |
| Weight Increased<br>subjects affected / exposed<br>occurrences (all)                         | 6 / 39 (15.38%)<br>6 | 1 / 45 (2.22%)<br>1 |  |
| Blood Lactate Dehydrogenase Increased  |                      |                     |  |

|   |                |                |
|---|----------------|----------------|
| subjects affected / exposed                     | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                               | 1              | 0              |
| Blood Alkaline Phosphatase Increased            |                |                |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)                               | 1              | 1              |
| C-Reactive Protein Increased                    |                |                |
| subjects affected / exposed                     | 2 / 39 (5.13%) | 0 / 45 (0.00%) |
| occurrences (all)                               | 2              | 0              |
| Blood Uric Acid Increased                       |                |                |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                               | 1              | 0              |
| Electrocardiogram Qt Prolonged                  |                |                |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)                               | 1              | 1              |
| Activated Partial Thromboplastin Time Prolonged |                |                |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                               | 0              | 0              |
| Blood Creatine Phosphokinase Increased          |                |                |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                               | 1              | 0              |
| Blood Thyroid Stimulating Hormone Increased     |                |                |
| subjects affected / exposed                     | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                               | 1              | 0              |
| General Physical Condition Abnormal             |                |                |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 2 / 45 (4.44%) |
| occurrences (all)                               | 0              | 2              |
| Blood Creatine Phosphokinase Decreased          |                |                |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                               | 0              | 0              |
| Blood Pressure Decreased                        |                |                |
| subjects affected / exposed                     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                               | 0              | 1              |
| Blood Urea Increased                            |                |                |

|                                |                |                |
|--------------------------------|----------------|----------------|
| subjects affected / exposed    | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)              | 1              | 0              |
| Cardiac Murmur                 |                |                |
| subjects affected / exposed    | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Ejection Fraction Decreased    |                |                |
| subjects affected / exposed    | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Electrocardiogram Change       |                |                |
| subjects affected / exposed    | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Hypophonesis                   |                |                |
| subjects affected / exposed    | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Oxygen Saturation Decreased    |                |                |
| subjects affected / exposed    | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Transaminases Increased        |                |                |
| subjects affected / exposed    | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)              | 0              | 1              |
| Alpha 1 Foetoprotein Increased |                |                |
| subjects affected / exposed    | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)              | 1              | 0              |
| Astrovirus Test Positive       |                |                |
| subjects affected / exposed    | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Bilirubin Urine                |                |                |
| subjects affected / exposed    | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Blast Cell Count Increased     |                |                |
| subjects affected / exposed    | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)              | 1              | 0              |
| Bleeding Time Prolonged        |                |                |
| subjects affected / exposed    | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Blood Alkaline Phosphatase     |                |                |

|  |                     |                     |  |
|--|---------------------|---------------------|--|
| Decreased<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 39 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |  |
| Blood Lactic Acid Increased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 39 (0.00%)<br>0 | 1 / 45 (2.22%)<br>1 |  |
| Blood Test Abnormal<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 39 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |  |
| Body Temperature Increased<br>subjects affected / exposed<br>occurrences (all)           | 1 / 39 (2.56%)<br>1 | 0 / 45 (0.00%)<br>0 |  |
| Gamma-Glutamyltransferase Increased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 39 (2.56%)<br>1 | 0 / 45 (0.00%)<br>0 |  |
| Glomerular Filtration Rate Decreased<br>subjects affected / exposed<br>occurrences (all) | 0 / 39 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |  |
| Liver Function Test Increased<br>subjects affected / exposed<br>occurrences (all)        | 0 / 39 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |  |
| Prothrombin Time Prolonged<br>subjects affected / exposed<br>occurrences (all)           | 0 / 39 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |  |
| White Blood Cell Count<br>subjects affected / exposed<br>occurrences (all)               | 0 / 39 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |  |
| White Blood Cell Count Increased<br>subjects affected / exposed<br>occurrences (all)     | 0 / 39 (0.00%)<br>0 | 1 / 45 (2.22%)<br>1 |  |
| Injury, poisoning and procedural complications   |                     |                     |  |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                            | 3 / 39 (7.69%)<br>3 | 1 / 45 (2.22%)<br>1 |  |
| Fall   |                     |                     |  |

|                               |                |                |
|-------------------------------|----------------|----------------|
| subjects affected / exposed   | 2 / 39 (5.13%) | 2 / 45 (4.44%) |
| occurrences (all)             | 2              | 2              |
| Infusion Related Reaction     |                |                |
| subjects affected / exposed   | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)             | 1              | 1              |
| Laceration                    |                |                |
| subjects affected / exposed   | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)             | 1              | 0              |
| Procedural Pain               |                |                |
| subjects affected / exposed   | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)             | 0              | 1              |
| Skin Abrasion                 |                |                |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)             | 0              | 0              |
| Transfusion Reaction          |                |                |
| subjects affected / exposed   | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)             | 1              | 0              |
| Allergic Transfusion Reaction |                |                |
| subjects affected / exposed   | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)             | 1              | 0              |
| Animal Bite                   |                |                |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)             | 0              | 0              |
| Head Injury                   |                |                |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)             | 0              | 0              |
| Joint Injury                  |                |                |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)             | 0              | 0              |
| Overdose                      |                |                |
| subjects affected / exposed   | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)             | 0              | 0              |
| Periorbital Haematoma         |                |                |
| subjects affected / exposed   | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)             | 0              | 1              |
| Post Procedural Contusion     |                |                |

|                                |                |                |  |
|--------------------------------|----------------|----------------|--|
| subjects affected / exposed    | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Post Procedural Haemorrhage    |                |                |  |
| subjects affected / exposed    | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences (all)              | 0              | 1              |  |
| Sunburn                        |                |                |  |
| subjects affected / exposed    | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences (all)              | 1              | 0              |  |
| Tooth Fracture                 |                |                |  |
| subjects affected / exposed    | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Wound                          |                |                |  |
| subjects affected / exposed    | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Cardiac disorders              |                |                |  |
| Tachycardia                    |                |                |  |
| subjects affected / exposed    | 0 / 39 (0.00%) | 2 / 45 (4.44%) |  |
| occurrences (all)              | 0              | 2              |  |
| Sinus Tachycardia              |                |                |  |
| subjects affected / exposed    | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences (all)              | 1              | 0              |  |
| Atrial Fibrillation            |                |                |  |
| subjects affected / exposed    | 2 / 39 (5.13%) | 1 / 45 (2.22%) |  |
| occurrences (all)              | 2              | 1              |  |
| Bradycardia                    |                |                |  |
| subjects affected / exposed    | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences (all)              | 0              | 1              |  |
| Acute Left Ventricular Failure |                |                |  |
| subjects affected / exposed    | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences (all)              | 0              | 1              |  |
| Angina Pectoris                |                |                |  |
| subjects affected / exposed    | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Arrhythmia                     |                |                |  |
| subjects affected / exposed    | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences (all)              | 1              | 0              |  |



|                              |                 |                 |  |
|------------------------------|-----------------|-----------------|--|
| Bundle Branch Block Right    |                 |                 |  |
| subjects affected / exposed  | 1 / 39 (2.56%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)            | 1               | 0               |  |
| Cardiac Failure              |                 |                 |  |
| subjects affected / exposed  | 0 / 39 (0.00%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)            | 0               | 0               |  |
| Cardiac Flutter              |                 |                 |  |
| subjects affected / exposed  | 1 / 39 (2.56%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)            | 1               | 0               |  |
| Extrasystoles                |                 |                 |  |
| subjects affected / exposed  | 1 / 39 (2.56%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)            | 1               | 0               |  |
| Palpitations                 |                 |                 |  |
| subjects affected / exposed  | 0 / 39 (0.00%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)            | 0               | 0               |  |
| Sinus Bradycardia            |                 |                 |  |
| subjects affected / exposed  | 0 / 39 (0.00%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)            | 0               | 0               |  |
| Supraventricular Tachycardia |                 |                 |  |
| subjects affected / exposed  | 0 / 39 (0.00%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)            | 0               | 0               |  |
| Tachycardia Paroxysmal       |                 |                 |  |
| subjects affected / exposed  | 1 / 39 (2.56%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)            | 1               | 0               |  |
| Nervous system disorders     |                 |                 |  |
| Dysgeusia                    |                 |                 |  |
| subjects affected / exposed  | 3 / 39 (7.69%)  | 2 / 45 (4.44%)  |  |
| occurrences (all)            | 3               | 2               |  |
| Headache                     |                 |                 |  |
| subjects affected / exposed  | 7 / 39 (17.95%) | 6 / 45 (13.33%) |  |
| occurrences (all)            | 7               | 6               |  |
| Syncope                      |                 |                 |  |
| subjects affected / exposed  | 2 / 39 (5.13%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)            | 2               | 0               |  |
| Dizziness                    |                 |                 |  |

|                             |                 |                |
|-----------------------------|-----------------|----------------|
| subjects affected / exposed | 8 / 39 (20.51%) | 2 / 45 (4.44%) |
| occurrences (all)           | 8               | 2              |
| Presyncope                  |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 2 / 45 (4.44%) |
| occurrences (all)           | 0               | 2              |
| Somnolence                  |                 |                |
| subjects affected / exposed | 1 / 39 (2.56%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 1               | 0              |
| Ageusia                     |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Balance Disorder            |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Memory Impairment           |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Ataxia                      |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Lethargy                    |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 1 / 45 (2.22%) |
| occurrences (all)           | 0               | 1              |
| Polyneuropathy              |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 1 / 45 (2.22%) |
| occurrences (all)           | 0               | 1              |
| Tremor                      |                 |                |
| subjects affected / exposed | 1 / 39 (2.56%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 1               | 0              |
| Aphasia                     |                 |                |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Cognitive Disorder          |                 |                |
| subjects affected / exposed | 1 / 39 (2.56%)  | 0 / 45 (0.00%) |
| occurrences (all)           | 1               | 0              |
| Dysarthria                  |                 |                |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Neuropathy Peripheral       |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Paraesthesia                |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Speech Disorder             |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Aphonia                     |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Cogwheel Rigidity           |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Coordination Abnormal       |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Drooling                    |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Dysaesthesia                |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Encephalopathy              |                |                |  |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Haemorrhage Intracranial    |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Hemianopia                  |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Hemianopia Homonymous       |                |                |  |

|                                      |                  |                  |  |
|--------------------------------------|------------------|------------------|--|
| subjects affected / exposed          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                    | 0                | 0                |  |
| Hypersomnia                          |                  |                  |  |
| subjects affected / exposed          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                    | 0                | 0                |  |
| Hypoaesthesia                        |                  |                  |  |
| subjects affected / exposed          | 0 / 39 (0.00%)   | 1 / 45 (2.22%)   |  |
| occurrences (all)                    | 0                | 1                |  |
| Hyposmia                             |                  |                  |  |
| subjects affected / exposed          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                    | 0                | 0                |  |
| Migraine                             |                  |                  |  |
| subjects affected / exposed          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                    | 0                | 0                |  |
| Parosmia                             |                  |                  |  |
| subjects affected / exposed          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                    | 0                | 0                |  |
| Peripheral Sensory Neuropathy        |                  |                  |  |
| subjects affected / exposed          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                    | 0                | 0                |  |
| Sensory Loss                         |                  |                  |  |
| subjects affected / exposed          | 1 / 39 (2.56%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                    | 1                | 0                |  |
| Synaesthesia                         |                  |                  |  |
| subjects affected / exposed          | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                    | 0                | 0                |  |
| Blood and lymphatic system disorders |                  |                  |  |
| Thrombocytopenia                     |                  |                  |  |
| subjects affected / exposed          | 18 / 39 (46.15%) | 11 / 45 (24.44%) |  |
| occurrences (all)                    | 18               | 11               |  |
| Anaemia                              |                  |                  |  |
| subjects affected / exposed          | 17 / 39 (43.59%) | 10 / 45 (22.22%) |  |
| occurrences (all)                    | 17               | 10               |  |
| Neutropenia                          |                  |                  |  |
| subjects affected / exposed          | 10 / 39 (25.64%) | 9 / 45 (20.00%)  |  |
| occurrences (all)                    | 10               | 9                |  |

|                              |                 |                |  |
|------------------------------|-----------------|----------------|--|
| Leukopenia                   |                 |                |  |
| subjects affected / exposed  | 5 / 39 (12.82%) | 4 / 45 (8.89%) |  |
| occurrences (all)            | 5               | 4              |  |
| Febrile neutropenia          |                 |                |  |
| subjects affected / exposed  | 3 / 39 (7.69%)  | 2 / 45 (4.44%) |  |
| occurrences (all)            | 3               | 2              |  |
| Leukocytosis                 |                 |                |  |
| subjects affected / exposed  | 4 / 39 (10.26%) | 0 / 45 (0.00%) |  |
| occurrences (all)            | 4               | 0              |  |
| Lymphopenia                  |                 |                |  |
| subjects affected / exposed  | 2 / 39 (5.13%)  | 1 / 45 (2.22%) |  |
| occurrences (all)            | 2               | 1              |  |
| Pancytopenia                 |                 |                |  |
| subjects affected / exposed  | 2 / 39 (5.13%)  | 0 / 45 (0.00%) |  |
| occurrences (all)            | 2               | 0              |  |
| Coagulopathy                 |                 |                |  |
| subjects affected / exposed  | 1 / 39 (2.56%)  | 0 / 45 (0.00%) |  |
| occurrences (all)            | 1               | 0              |  |
| Lymphadenopathy              |                 |                |  |
| subjects affected / exposed  | 1 / 39 (2.56%)  | 1 / 45 (2.22%) |  |
| occurrences (all)            | 1               | 1              |  |
| Increased Tendency To Bruise |                 |                |  |
| subjects affected / exposed  | 0 / 39 (0.00%)  | 1 / 45 (2.22%) |  |
| occurrences (all)            | 0               | 0              |  |
| Polycythaemia                |                 |                |  |
| subjects affected / exposed  | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |  |
| occurrences (all)            | 0               | 0              |  |
| Splenomegaly                 |                 |                |  |
| subjects affected / exposed  | 0 / 39 (0.00%)  | 1 / 45 (2.22%) |  |
| occurrences (all)            | 0               | 1              |  |
| Thrombocytosis               |                 |                |  |
| subjects affected / exposed  | 1 / 39 (2.56%)  | 0 / 45 (0.00%) |  |
| occurrences (all)            | 1               | 0              |  |
| Ear and labyrinth disorders  |                 |                |  |
| Deafness                     |                 |                |  |

|  |                |                |  |
|--|----------------|----------------|--|
| subjects affected / exposed                | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences (all)                          | 0              | 1              |  |
| Ear Discomfort                             |                |                |  |
| subjects affected / exposed                | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences (all)                          | 0              | 1              |  |
| Vertigo                                    |                |                |  |
| subjects affected / exposed                | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences (all)                          | 0              | 1              |  |
| Ear Pain                                   |                |                |  |
| subjects affected / exposed                | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)                          | 0              | 0              |  |
| Tinnitus                                   |                |                |  |
| subjects affected / exposed                | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)                          | 0              | 0              |  |
| Ear Congestion                             |                |                |  |
| subjects affected / exposed                | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)                          | 0              | 0              |  |
| Eustachian Tube Dysfunction                |                |                |  |
| subjects affected / exposed                | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)                          | 0              | 0              |  |
| Excessive Cerumen Production               |                |                |  |
| subjects affected / exposed                | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)                          | 0              | 0              |  |
| Hypoacusis                                 |                |                |  |
| subjects affected / exposed                | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)                          | 0              | 0              |  |
| Eye disorders                              |                |                |  |
| Vision blurred                             |                |                |  |
| alternative assessment type:<br>Systematic |                |                |  |
| subjects affected / exposed                | 1 / 39 (2.56%) | 0 / 45 (0.00%) |  |
| occurrences (all)                          | 1              | 0              |  |
| Visual Impairment                          |                |                |  |
| subjects affected / exposed                | 0 / 39 (0.00%) | 1 / 45 (2.22%) |  |
| occurrences (all)                          | 0              | 1              |  |
| Cataract                                   |                |                |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Dry Eye                     |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Visual Acuity Reduced       |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Conjunctival Haemorrhage    |                |                |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 45 (0.00%) |
| occurrences (all)           | 2              | 0              |
| Eye Pain                    |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Lacrimation Increased       |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Eye Haemorrhage             |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Eyelid Oedema               |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Ocular Hyperaemia           |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Periorbital Oedema          |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Photopsia                   |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Retinal Haemorrhage         |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Diplopia                    |                |                |

|  |                  |                  |  |
|--|------------------|------------------|--|
| subjects affected / exposed                | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                          | 0                | 0                |  |
| Eye Inflammation                           |                  |                  |  |
| subjects affected / exposed                | 0 / 39 (0.00%)   | 1 / 45 (2.22%)   |  |
| occurrences (all)                          | 0                | 1                |  |
| Eye Swelling                               |                  |                  |  |
| subjects affected / exposed                | 1 / 39 (2.56%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                          | 1                | 0                |  |
| Eyelid Ptosis                              |                  |                  |  |
| subjects affected / exposed                | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                          | 0                | 0                |  |
| Vitreous Floaters                          |                  |                  |  |
| subjects affected / exposed                | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                          | 0                | 0                |  |
| Vitreous Haemorrhage                       |                  |                  |  |
| subjects affected / exposed                | 0 / 39 (0.00%)   | 0 / 45 (0.00%)   |  |
| occurrences (all)                          | 0                | 0                |  |
| Gastrointestinal disorders                 |                  |                  |  |
| Nausea                                     |                  |                  |  |
| alternative assessment type:<br>Systematic |                  |                  |  |
| subjects affected / exposed                | 13 / 39 (33.33%) | 8 / 45 (17.78%)  |  |
| occurrences (all)                          | 13               | 8                |  |
| Diarrhoea                                  |                  |                  |  |
| alternative assessment type:<br>Systematic |                  |                  |  |
| subjects affected / exposed                | 8 / 39 (20.51%)  | 6 / 45 (13.33%)  |  |
| occurrences (all)                          | 8                | 6                |  |
| Constipation                               |                  |                  |  |
| alternative assessment type:<br>Systematic |                  |                  |  |
| subjects affected / exposed                | 16 / 39 (41.03%) | 15 / 45 (33.33%) |  |
| occurrences (all)                          | 16               | 15               |  |
| Vomiting                                   |                  |                  |  |
| alternative assessment type:<br>Systematic |                  |                  |  |
| subjects affected / exposed                | 7 / 39 (17.95%)  | 6 / 45 (13.33%)  |  |
| occurrences (all)                          | 7                | 6                |  |
| Stomatitis                                 |                  |                  |  |



|  |                |                 |
|--|----------------|-----------------|
| alternative assessment type:<br>Systematic |                |                 |
| subjects affected / exposed                | 3 / 39 (7.69%) | 3 / 45 (6.67%)  |
| occurrences (all)                          | 3              | 3               |
| Abdominal pain                             |                |                 |
| alternative assessment type:<br>Systematic |                |                 |
| subjects affected / exposed                | 2 / 39 (5.13%) | 6 / 45 (13.33%) |
| occurrences (all)                          | 2              | 6               |
| Abdominal Pain Upper                       |                |                 |
| subjects affected / exposed                | 1 / 39 (2.56%) | 1 / 45 (2.22%)  |
| occurrences (all)                          | 1              | 1               |
| Dyspepsia                                  |                |                 |
| subjects affected / exposed                | 1 / 39 (2.56%) | 1 / 45 (2.22%)  |
| occurrences (all)                          | 1              | 1               |
| Gingival Bleeding                          |                |                 |
| subjects affected / exposed                | 1 / 39 (2.56%) | 2 / 45 (4.44%)  |
| occurrences (all)                          | 1              | 2               |
| Haemorrhoids                               |                |                 |
| subjects affected / exposed                | 2 / 39 (5.13%) | 3 / 45 (6.67%)  |
| occurrences (all)                          | 2              | 3               |
| Aphthous Ulcer                             |                |                 |
| subjects affected / exposed                | 2 / 39 (5.13%) | 2 / 45 (4.44%)  |
| occurrences (all)                          | 2              | 2               |
| Mouth Haemorrhage                          |                |                 |
| subjects affected / exposed                | 1 / 39 (2.56%) | 0 / 45 (0.00%)  |
| occurrences (all)                          | 1              | 0               |
| Abdominal Discomfort                       |                |                 |
| subjects affected / exposed                | 2 / 39 (5.13%) | 2 / 45 (4.44%)  |
| occurrences (all)                          | 2              | 2               |
| Gingival Pain                              |                |                 |
| subjects affected / exposed                | 2 / 39 (5.13%) | 0 / 45 (0.00%)  |
| occurrences (all)                          | 2              | 0               |
| Odynophagia                                |                |                 |
| subjects affected / exposed                | 2 / 39 (5.13%) | 2 / 45 (4.44%)  |
| occurrences (all)                          | 2              | 2               |
| Toothache                                  |                |                 |

|                                  |                |                |
|----------------------------------|----------------|----------------|
| subjects affected / exposed      | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                | 0              | 1              |
| Dry Mouth                        |                |                |
| subjects affected / exposed      | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                | 1              | 0              |
| Gastrooesophageal Reflux Disease |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Dysphagia                        |                |                |
| subjects affected / exposed      | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                | 1              | 0              |
| Flatulence                       |                |                |
| subjects affected / exposed      | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                | 1              | 0              |
| Melaena                          |                |                |
| subjects affected / exposed      | 1 / 39 (2.56%) | 2 / 45 (4.44%) |
| occurrences (all)                | 1              | 2              |
| Abdominal Pain Lower             |                |                |
| subjects affected / exposed      | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                | 1              | 0              |
| Anal Fissure                     |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                | 0              | 1              |
| Angina Bullosa Haemorrhagica     |                |                |
| subjects affected / exposed      | 2 / 39 (5.13%) | 0 / 45 (0.00%) |
| occurrences (all)                | 2              | 0              |
| Enterocolitis                    |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Eructation                       |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Gastritis                        |                |                |
| subjects affected / exposed      | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                | 1              | 0              |
| Gastrointestinal Haemorrhage     |                |                |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Mouth Ulceration            |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Oral Disorder               |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Oral Mucosa Haematoma       |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Oral Mucosal Blistering     |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Abdominal Tenderness        |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Anal Incontinence           |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Breath Odour                |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Diverticulum                |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Faeces Soft                 |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Gastrointestinal Pain       |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Gingival Hypertrophy        |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Glossitis                   |                |                |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Ileus                       |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Inguinal Hernia             |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Lip Blister                 |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Lip Dry                     |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Lip Oedema                  |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Lip Pain                    |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Lip Swelling                |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Lip Ulceration              |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Mouth Swelling              |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Oesophagitis                |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Oral Dysaesthesia           |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Palatal Disorder            |                |                |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Perianal Erythema           |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Proctalgia                  |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Rectal Fissure              |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Rectal Haemorrhage          |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Retching                    |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Salivary Hypersecretion     |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Tongue Haematoma            |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Tongue Ulceration           |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Tooth Loss                  |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Trichoglossia               |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Oral Contusion              |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Oral Pain                   |                |                |

|  |                     |                     |  |
|--|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all) | 2 / 39 (5.13%)<br>2 | 0 / 45 (0.00%)<br>0 |  |
| Hepatobiliary disorders                          |                     |                     |  |
| Hyperbilirubinaemia                              |                     |                     |  |
| subjects affected / exposed                      | 1 / 39 (2.56%)      | 1 / 45 (2.22%)      |  |
| occurrences (all)                                | 1                   | 1                   |  |
| Cholelithiasis                                   |                     |                     |  |
| subjects affected / exposed                      | 0 / 39 (0.00%)      | 0 / 45 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                   |  |
| Hepatomegaly                                     |                     |                     |  |
| subjects affected / exposed                      | 0 / 39 (0.00%)      | 1 / 45 (2.22%)      |  |
| occurrences (all)                                | 0                   | 1                   |  |
| Jaundice   |                     |                     |  |
| subjects affected / exposed                      | 0 / 39 (0.00%)      | 0 / 45 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                   |  |
| Ocular Icterus                                   |                     |                     |  |
| subjects affected / exposed                      | 0 / 39 (0.00%)      | 0 / 45 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                   |  |
| Skin and subcutaneous tissue disorders           |                     |                     |  |
| Night sweats                                     |                     |                     |  |
| subjects affected / exposed                      | 1 / 39 (2.56%)      | 4 / 45 (8.89%)      |  |
| occurrences (all)                                | 1                   | 4                   |  |
| Petechiae  |                     |                     |  |
| subjects affected / exposed                      | 7 / 39 (17.95%)     | 6 / 45 (13.33%)     |  |
| occurrences (all)                                | 7                   | 6                   |  |
| Hyperhidrosis                                    |                     |                     |  |
| subjects affected / exposed                      | 1 / 39 (2.56%)      | 1 / 45 (2.22%)      |  |
| occurrences (all)                                | 1                   | 1                   |  |
| Rash   |                     |                     |  |
| subjects affected / exposed                      | 4 / 39 (10.26%)     | 2 / 45 (4.44%)      |  |
| occurrences (all)                                | 4                   | 2                   |  |
| Rash Maculo-Papular                              |                     |                     |  |
| subjects affected / exposed                      | 2 / 39 (5.13%)      | 2 / 45 (4.44%)      |  |
| occurrences (all)                                | 2                   | 2                   |  |
| Ecchymosis                                       |                     |                     |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 45 (4.44%) |
| occurrences (all)           | 1              | 2              |
| Pruritus                    |                |                |
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 45 (2.22%) |
| occurrences (all)           | 2              | 1              |
| Skin Lesion                 |                |                |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 45 (0.00%) |
| occurrences (all)           | 2              | 0              |
| Skin Ulcer                  |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Alopecia                    |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Decubitus Ulcer             |                |                |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 45 (0.00%) |
| occurrences (all)           | 2              | 0              |
| Erythema                    |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 2 / 45 (4.44%) |
| occurrences (all)           | 0              | 2              |
| Cold Sweat                  |                |                |
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 45 (0.00%) |
| occurrences (all)           | 2              | 0              |
| Dermatitis                  |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Purpura                     |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Skin Mass                   |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Swelling Face               |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Dermal Cyst                 |                |                |

|                                  |                |                |
|----------------------------------|----------------|----------------|
| subjects affected / exposed      | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                | 1              | 0              |
| <b>Dermatitis Acneiform</b>      |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                | 0              | 0              |
| <b>Dermatitis Bullous</b>        |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                | 0              | 0              |
| <b>Dry Skin</b>                  |                |                |
| subjects affected / exposed      | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                | 1              | 0              |
| <b>Facial Wasting</b>            |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                | 0              | 0              |
| <b>Macule</b>                    |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                | 0              | 0              |
| <b>Miliaria</b>                  |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                | 0              | 0              |
| <b>Nail Disorder</b>             |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                | 0              | 0              |
| <b>Photosensitivity Reaction</b> |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                | 0              | 0              |
| <b>Rash Erythematous</b>         |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                | 0              | 1              |
| <b>Rash Pruritic</b>             |                |                |
| subjects affected / exposed      | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                | 1              | 0              |
| <b>Skin Discolouration</b>       |                |                |
| subjects affected / exposed      | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                | 0              | 0              |
| <b>Skin Hyperpigmentation</b>    |                |                |



|  |                     |                     |  |
|--|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 39 (0.00%)<br>0 | 0 / 45 (0.00%)<br>0 |  |
| Skin Induration<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 39 (0.00%)<br>0 | 1 / 45 (2.22%)<br>1 |  |
| Skin Maceration<br>subjects affected / exposed<br>occurrences (all)                                    | 1 / 39 (2.56%)<br>1 | 0 / 45 (0.00%)<br>0 |  |
| Urticaria<br>subjects affected / exposed<br>occurrences (all)  | 1 / 39 (2.56%)<br>1 | 0 / 45 (0.00%)<br>0 |  |
| Renal and urinary disorders<br>Acute Kidney Injury<br>subjects affected / exposed<br>occurrences (all) | 2 / 39 (5.13%)<br>2 | 3 / 45 (6.67%)<br>3 |  |
| Haematuria<br>subjects affected / exposed<br>occurrences (all)   | 2 / 39 (5.13%)<br>2 | 3 / 45 (6.67%)<br>3 |  |
| Pollakiuria<br>subjects affected / exposed<br>occurrences (all)  | 1 / 39 (2.56%)<br>1 | 2 / 45 (4.44%)<br>2 |  |
| Proteinuria<br>subjects affected / exposed<br>occurrences (all)  | 2 / 39 (5.13%)<br>2 | 1 / 45 (2.22%)<br>1 |  |
| Dysuria<br>subjects affected / exposed<br>occurrences (all)  | 0 / 39 (0.00%)<br>0 | 2 / 45 (4.44%)<br>2 |  |
| Renal Failure<br>subjects affected / exposed<br>occurrences (all)                                      | 1 / 39 (2.56%)<br>1 | 1 / 45 (2.22%)<br>1 |  |
| Urinary Incontinence<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 39 (2.56%)<br>1 | 0 / 45 (0.00%)<br>0 |  |
| Urinary Retention<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 39 (2.56%)<br>1 | 0 / 45 (0.00%)<br>0 |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Bladder Dilatation          |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Chronic Kidney Disease      |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Micturition Urgency         |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Bladder Pain                |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Chromaturia                 |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Incontinence                |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Nocturia                    |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Polyuria                    |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Urethral Caruncle           |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Urethral Haemorrhage        |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Urge Incontinence           |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Urinary Tract Obstruction   |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |

|  |                      |                      |  |
|--|----------------------|----------------------|--|
| Urinary Tract Pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 39 (0.00%)<br>0  | 0 / 45 (0.00%)<br>0  |  |
| Endocrine disorders  |                      |                      |  |
| Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)       | 1 / 39 (2.56%)<br>1  | 0 / 45 (0.00%)<br>0  |  |
| Cushingoid<br>subjects affected / exposed<br>occurrences (all)           | 0 / 39 (0.00%)<br>0  | 0 / 45 (0.00%)<br>0  |  |
| Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)      | 0 / 39 (0.00%)<br>0  | 0 / 45 (0.00%)<br>0  |  |
| Musculoskeletal and connective tissue disorders                          |                      |                      |  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)           | 5 / 39 (12.82%)<br>5 | 1 / 45 (2.22%)<br>1  |  |
| Back Pain<br>subjects affected / exposed<br>occurrences (all)            | 5 / 39 (12.82%)<br>5 | 5 / 45 (11.11%)<br>5 |  |
| Muscular Weakness<br>subjects affected / exposed<br>occurrences (all)    | 3 / 39 (7.69%)<br>3  | 0 / 45 (0.00%)<br>0  |  |
| Pain In Extremity<br>subjects affected / exposed<br>occurrences (all)    | 1 / 39 (2.56%)<br>1  | 2 / 45 (4.44%)<br>2  |  |
| Muscle Spasms<br>subjects affected / exposed<br>occurrences (all)        | 1 / 39 (2.56%)<br>1  | 3 / 45 (6.67%)<br>3  |  |
| Bone Pain<br>subjects affected / exposed<br>occurrences (all)            | 1 / 39 (2.56%)<br>1  | 0 / 45 (0.00%)<br>0  |  |
| Musculoskeletal Pain<br>subjects affected / exposed<br>occurrences (all) | 2 / 39 (5.13%)<br>2  | 0 / 45 (0.00%)<br>0  |  |
| Myalgia  |                      |                      |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 2 / 39 (5.13%) | 0 / 45 (0.00%) |
| occurrences (all)           | 2              | 0              |
| Neck Pain                   |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 2 / 45 (4.44%) |
| occurrences (all)           | 1              | 2              |
| Arthritis                   |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Flank Pain                  |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)           | 1              | 1              |
| Hypercreatinaemia           |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Joint Swelling              |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Musculoskeletal Chest Pain  |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)           | 1              | 1              |
| Pain In Jaw                 |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Bursitis                    |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Groin Pain                  |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Ligament Pain               |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Limb Discomfort             |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Limb Mass                   |                |                |

|                             |                 |                |  |
|-----------------------------|-----------------|----------------|--|
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |
| Muscle Mass                 |                 |                |  |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |
| Muscle Tightness            |                 |                |  |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |
| Muscle Twitching            |                 |                |  |
| subjects affected / exposed | 0 / 39 (0.00%)  | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |
| Osteitis                    |                 |                |  |
| subjects affected / exposed | 1 / 39 (2.56%)  | 0 / 45 (0.00%) |  |
| occurrences (all)           | 1               | 0              |  |
| Osteoarthritis              |                 |                |  |
| subjects affected / exposed | 1 / 39 (2.56%)  | 0 / 45 (0.00%) |  |
| occurrences (all)           | 1               | 0              |  |
| Spinal Osteoarthritis       |                 |                |  |
| subjects affected / exposed | 0 / 39 (0.00%)  | 1 / 45 (2.22%) |  |
| occurrences (all)           | 0               | 1              |  |
| Torticollis                 |                 |                |  |
| subjects affected / exposed | 0 / 39 (0.00%)  | 1 / 45 (2.22%) |  |
| occurrences (all)           | 0               | 1              |  |
| Infections and infestations |                 |                |  |
| Urinary Tract Infection     |                 |                |  |
| subjects affected / exposed | 5 / 39 (12.82%) | 2 / 45 (4.44%) |  |
| occurrences (all)           | 5               | 2              |  |
| Oral Herpes                 |                 |                |  |
| subjects affected / exposed | 4 / 39 (10.26%) | 4 / 45 (8.89%) |  |
| occurrences (all)           | 4               | 4              |  |
| Nasopharyngitis             |                 |                |  |
| subjects affected / exposed | 1 / 39 (2.56%)  | 3 / 45 (6.67%) |  |
| occurrences (all)           | 1               | 3              |  |
| Oral Candidiasis            |                 |                |  |
| subjects affected / exposed | 1 / 39 (2.56%)  | 1 / 45 (2.22%) |  |
| occurrences (all)           | 1               | 1              |  |

|                                   |                |                |
|-----------------------------------|----------------|----------------|
| Pneumonia                         |                |                |
| subjects affected / exposed       | 3 / 39 (7.69%) | 1 / 45 (2.22%) |
| occurrences (all)                 | 3              | 1              |
| Cellulitis                        |                |                |
| subjects affected / exposed       | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)                 | 1              | 1              |
| Lung Infection                    |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                 | 0              | 1              |
| Sinusitis                         |                |                |
| subjects affected / exposed       | 2 / 39 (5.13%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 2              | 0              |
| Upper Respiratory Tract Infection |                |                |
| subjects affected / exposed       | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)                 | 1              | 1              |
| Device Related Infection          |                |                |
| subjects affected / exposed       | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 1              | 0              |
| Periodontitis                     |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 2 / 45 (4.44%) |
| occurrences (all)                 | 0              | 2              |
| Pneumonia Fungal                  |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 3 / 45 (6.67%) |
| occurrences (all)                 | 0              | 3              |
| Sepsis                            |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                 | 0              | 1              |
| Candida Infection                 |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Folliculitis                      |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Oesophageal Candidiasis           |                |                |
| subjects affected / exposed       | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 1              | 0              |

|                                 |                |                |
|---------------------------------|----------------|----------------|
| Skin Infection                  |                |                |
| subjects affected / exposed     | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)               | 1              | 0              |
| Staphylococcal Infection        |                |                |
| subjects affected / exposed     | 0 / 39 (0.00%) | 2 / 45 (4.44%) |
| occurrences (all)               | 0              | 2              |
| Clostridium Difficile Colitis   |                |                |
| subjects affected / exposed     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Clostridium Difficile Infection |                |                |
| subjects affected / exposed     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)               | 0              | 1              |
| Conjunctivitis                  |                |                |
| subjects affected / exposed     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Ear Infection                   |                |                |
| subjects affected / exposed     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Fungal Infection                |                |                |
| subjects affected / exposed     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Herpes Dermatitis               |                |                |
| subjects affected / exposed     | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)               | 0              | 1              |
| Infection                       |                |                |
| subjects affected / exposed     | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)               | 1              | 1              |
| Lip Infection                   |                |                |
| subjects affected / exposed     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Nasal Herpes                    |                |                |
| subjects affected / exposed     | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Pharyngitis                     |                |                |
| subjects affected / exposed     | 2 / 39 (5.13%) | 0 / 45 (0.00%) |
| occurrences (all)               | 2              | 0              |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Pseudomonas Infection       |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Rash Pustular               |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Rhinovirus Infection        |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Soft Tissue Infection       |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Abscess Limb                |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Acute Sinusitis             |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Anal Abscess                |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Aspergillus Infection       |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Asymptomatic Bacteriuria    |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Bacterial Infection         |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Bacteriuria                 |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Bronchitis                  |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |



|                             |                |                |
|-----------------------------|----------------|----------------|
| Catheter Site Cellulitis    |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Clostridium Colitis         |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Dermo-Hypodermatitis        |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Diverticulitis              |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Empyema                     |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Encephalitis                |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Enterobiasis                |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Enterococcal Infection      |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Furuncle                    |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Genital Herpes              |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Gingivitis                  |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Groin Infection             |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                                   |                |                |
|-----------------------------------|----------------|----------------|
| Herpes Simplex                    |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                 | 0              | 1              |
| Herpes Zoster                     |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                 | 0              | 1              |
| Infected Dermal Cyst              |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Influenza                         |                |                |
| subjects affected / exposed       | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 1              | 0              |
| Lower Respiratory Tract Infection |                |                |
| subjects affected / exposed       | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 1              | 0              |
| Lymph Gland Infection             |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Meningitis                        |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Metapneumovirus Infection         |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Mucosal Infection                 |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Oesophageal Infection             |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Ophthalmic Herpes Simplex         |                |                |
| subjects affected / exposed       | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                 | 0              | 1              |
| Oral Fungal Infection             |                |                |
| subjects affected / exposed       | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                 | 1              | 0              |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Oral Infection              |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Osteomyelitis               |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Parotitis                   |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Pneumonia Klebsiella        |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Proteus Infection           |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Pseudomembranous Colitis    |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Respiratory Tract Infection |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Rhinitis                    |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Septic Shock                |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Sialoadenitis               |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Staphylococcal Bacteraemia  |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Stenotrophomonas Infection  |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                                    |                 |                 |  |
|------------------------------------|-----------------|-----------------|--|
| Tonsillitis                        |                 |                 |  |
| subjects affected / exposed        | 1 / 39 (2.56%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                  | 1               | 0               |  |
| Tonsillitis Bacterial              |                 |                 |  |
| subjects affected / exposed        | 0 / 39 (0.00%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                  | 0               | 0               |  |
| Tooth Abscess                      |                 |                 |  |
| subjects affected / exposed        | 0 / 39 (0.00%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                  | 0               | 0               |  |
| Tooth Infection                    |                 |                 |  |
| subjects affected / exposed        | 1 / 39 (2.56%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                  | 1               | 0               |  |
| Varicella Zoster Virus Infection   |                 |                 |  |
| subjects affected / exposed        | 0 / 39 (0.00%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                  | 0               | 0               |  |
| Hallucination                      |                 |                 |  |
| subjects affected / exposed        | 0 / 39 (0.00%)  | 1 / 45 (2.22%)  |  |
| occurrences (all)                  | 0               | 1               |  |
| Personality Change                 |                 |                 |  |
| subjects affected / exposed        | 0 / 39 (0.00%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                  | 0               | 0               |  |
| Facial Bones Fracture              |                 |                 |  |
| subjects affected / exposed        | 1 / 39 (2.56%)  | 0 / 45 (0.00%)  |  |
| occurrences (all)                  | 1               | 0               |  |
| Metabolism and nutrition disorders |                 |                 |  |
| Hyponatraemia                      |                 |                 |  |
| subjects affected / exposed        | 3 / 39 (7.69%)  | 1 / 45 (2.22%)  |  |
| occurrences (all)                  | 3               | 1               |  |
| Hypokalaemia                       |                 |                 |  |
| subjects affected / exposed        | 5 / 39 (12.82%) | 6 / 45 (13.33%) |  |
| occurrences (all)                  | 5               | 6               |  |
| Hypocalcaemia                      |                 |                 |  |
| subjects affected / exposed        | 2 / 39 (5.13%)  | 4 / 45 (8.89%)  |  |
| occurrences (all)                  | 2               | 4               |  |
| Hypercreatininaemia                |                 |                 |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 2 / 39 (5.13%) | 1 / 45 (2.22%) |
| occurrences (all)           | 2              | 1              |
| Hypomagnesaemia             |                |                |
| subjects affected / exposed | 2 / 39 (5.13%) | 3 / 45 (6.67%) |
| occurrences (all)           | 2              | 3              |
| Hyperglycaemia              |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 3 / 45 (6.67%) |
| occurrences (all)           | 1              | 3              |
| Hyperkalaemia               |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Dehydration                 |                |                |
| subjects affected / exposed | 3 / 39 (7.69%) | 2 / 45 (4.44%) |
| occurrences (all)           | 3              | 2              |
| Hypophosphataemia           |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Hyperuricaemia              |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)           | 1              | 1              |
| Hypoalbuminaemia            |                |                |
| subjects affected / exposed | 2 / 39 (5.13%) | 2 / 45 (4.44%) |
| occurrences (all)           | 2              | 2              |
| Hypercalcaemia              |                |                |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Hypermagnesaemia            |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)           | 0              | 1              |
| Cachexia                    |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hyperlipasaemia             |                |                |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hyperphosphataemia          |                |                |

|  |                |                |
|--|----------------|----------------|
| subjects affected / exposed                        | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                                  | 0              | 1              |
| Hypoglycaemia                                      |                |                |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                  | 0              | 0              |
| Fluid Retention                                    |                |                |
| subjects affected / exposed                        | 1 / 39 (2.56%) | 1 / 45 (2.22%) |
| occurrences (all)                                  | 1              | 1              |
| Hyperamylasaemia                                   |                |                |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                  | 0              | 0              |
| Fluid Overload                                     |                |                |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                  | 0              | 0              |
| Tumour Lysis Syndrome                              |                |                |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all)                                  | 0              | 1              |
| Type 2 Diabetes Mellitus                           |                |                |
| subjects affected / exposed                        | 1 / 39 (2.56%) | 0 / 45 (0.00%) |
| occurrences (all)                                  | 1              | 0              |
| Diabetes Mellitus                                  |                |                |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                  | 0              | 0              |
| Failure To Thrive                                  |                |                |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                  | 0              | 0              |
| Gout   |                |                |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                  | 0              | 0              |
| Hyperglycaemic Hyperosmolar<br>Nonketotic Syndrome |                |                |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                  | 0              | 0              |
| Hyperhomocysteinaemia                              |                |                |
| subjects affected / exposed                        | 0 / 39 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all)                                  | 0              | 0              |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| Hypernatraemia              |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Hypouricaemia               |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Metabolic Acidosis          |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Polydipsia                  |                |                |  |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 45 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 03 July 2014     | Revise the treatment goal for hypertension to be lower than Blood pressure = 150/100 mmHg, the original protocol limit, to reduce the risk of CNS bleeding given that thrombocytopenia was expected in subjects with this protocol regimen. The recommendation for treatment of hypertension was removed thereby allowing study sites to use their standard protocols.   |
| 25 November 2014 | <ul style="list-style-type: none"><li>• Address feedback from study Investigators regarding use of hydroxyurea and timing of dosing days and screening bone marrow aspirate.</li><li>• Remove the restriction on acetaminophen except on days of selinexor dosing (<math>\leq 1</math> g total daily dose of acetaminophen) and to add restrictions for products that may alter selinexor metabolism.</li><li>• Update the supportive care guidance and selinexor dose adjustment information, as well as study procedures including ophthalmological exam.</li><li>• Standardize reporting requirements for cerebellar toxicities (expanded reporting beyond FDA and the MHRA as in Version 2.1).</li></ul>   |
| 24 April 2015    | <ul style="list-style-type: none"><li>• Increase the assumed dropout rate to <math>\sim 20\%</math> to align with the actual rate at study sites and increase the sample size to 170 subject to maintain power with the increased dropout rate.</li><li>• Expand exclusion criteria to exclude subject with concurrent active malignancies that were not being treated.</li><li>• Add EQ-5D-5L QoL questionnaire.</li><li>• Add 20 mg tablets in blister packs as an option for selinexor drug product.</li><li>• Remove specific recommendation for the use of dexamethasone as a supportive care agent.</li></ul>  |
| 04 August 2015   | <ul style="list-style-type: none"><li>• Address the unexpected increase in the number of infection-related AEs in subjects randomised to selinexor as compared to subjects randomised to the PC arm.</li><li>• Reduce the selinexor dose from <math>\sim 55</math> mg/square-metre (<math>\sim 80</math> to <math>100</math> mg) to a fixed dose of <math>60</math> mg (<math>\sim 35</math> mg/square-metre) to reduce selinexor-related adverse events, especially suspected sepsis cases as well as and pneumonia/lung infections in this highly compromised subjects population.</li><li>• Revise the inclusion criteria to require at least 2 prior lines of AML therapy, including (1) at least 1 regimen including Ara-C and (2) at least 1 regimen including an adequate trial of an HMA in order to insure that subjects entering the study had been offered an adequate trial of agents currently used to treat AML in subjects ineligible for intensive chemotherapy with transplantation.</li><li>• Add the exclusion criterion for subjects whose AML was classified as favorable according to the ELN disease risk assessment.</li><li>• Revise the stratification to add a stratum for peripheral leukemic blast counts <math>\geq 10,000/\text{mCL}</math> versus <math>&lt; 10,000/\text{mCL}</math> and to reduce the duration of the first CR on prior therapy from 1 year to 6 months.</li></ul> |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported