



## Clinical trial results:

### A Phase 1b/2, Multicenter, Open-label, Dose-escalation Study of Elotuzumab (Humanized Anti-CS1 Monoclonal IgG1 Antibody) in Combination With Lenalidomide and Dexamethasone in Subjects With Relapsed Multiple Myeloma

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2007-006677-83  |
| Trial protocol           | DE GB           |
| Global end of trial date | 20 October 2016 |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 27 October 2017 |
| First version publication date | 27 October 2017 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | HuLuc631703 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00742560 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | AbbVie Deutschland GmbH & Co. KG  |
| Sponsor organisation address | AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB |
| Public contact               | Global Medical Services, AbbVie, 001 800-633-9110,  |
| Scientific contact           | Nilou Mobashery, MD, AbbVie, Nilou.mobashery@abbvie.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                       | 20 October 2016 |
| Is this the analysis of the primary completion data? | No              |

|                                  |                 |
|----------------------------------|-----------------|
| Global end of trial reached?     | Yes             |
| Global end of trial date         | 20 October 2016 |
| Was the trial ended prematurely? | No              |

Notes:

## General information about the trial

Main objective of the trial:

the purpose of this study is to evaluate the combination of elotuzumab, lenalidomide, and dexamethasone in subjects with relapsed relapsed multiple myeloma.

Protection of trial subjects:

Subject read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

|   |                |
|---|----------------|
| Actual start date of recruitment                          | 22 August 2008 |
| 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 | Canada: 10        |
| Country: Number of subjects enrolled | France: 24        |
| Country: Number of subjects enrolled | Germany: 8        |
| Country: Number of subjects enrolled | United States: 60 |
| Worldwide total number of subjects   | 102               |
| EEA total number of subjects         | 32                |

Notes:

### Subjects enrolled per age group

|   |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 64 |
| From 65 to 84 years                       | 38 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 101 participants were randomized (intent-to-treat [ITT] population); 1 subject did not receive study drug and is excluded from the analyses.

### Period 1

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

### Arms

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes   |
| <b>Arm title</b>             | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |

Arm description:

Elotuzumab 5 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.

|  |                                  |
|--|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | elotuzumab                       |
| Investigational medicinal product code |                                  |
| Other name                             | HuLuc63                          |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Humanized Anti-CS1 Monoclonal IgG1 Antibody (HuLuc63) administered as an intravenous infusion once a week during Cycles 1 and 2, and every other week beginning with Cycle 3.

|  |              |
|--|--------------|
| Investigational medicinal product name | lenalidomide |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Lenalidomide 25 mg administered orally once daily on Days 1 to 21 of each 28-day cycle

|  |                    |
|--|--------------------|
| Investigational medicinal product name | dexamethasone oral |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Oral solution      |
| Routes of administration               | Oral use           |

Dosage and administration details:

Dexamethasone 40 mg administered orally once weekly; during weeks when elotuzumab is also administered, dexamethasone was administered as a split dose (28 mg orally and 8 mg intravenously)

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

Dosage and administration details:

Dexamethasone 40 mg administered orally once weekly; during weeks when elotuzumab is also

administered, dexamethasone was administered as a split dose (28 mg orally and 8 mg intravenously)

|  |  |
|--|--|
| <b>Arm title</b>   | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
| Arm description:<br>Elotuzumab 10 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.   |  |
| Arm type   | Experimental   |
| Investigational medicinal product name   | elotuzumab   |
| Investigational medicinal product code   |  |
| Other name   | HuLuc63  |
| Pharmaceutical forms   | Powder for solution for infusion                               |
| Routes of administration   | Intravenous use  |
| Dosage and administration details:<br>Humanized Anti-CS1 Monoclonal IgG1 Antibody (HuLuc63) administered as an intravenous infusion once a week during Cycles 1 and 2, and every other week beginning with Cycle 3.                |  |
| Investigational medicinal product name   | lenalidomide   |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Capsule  |
| Routes of administration   | Oral use   |
| Dosage and administration details:<br>Lenalidomide 25 mg administered orally once daily on Days 1 to 21 of each 28-day cycle   |  |
| Investigational medicinal product name   | dexamethasone oral   |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Oral solution  |
| Routes of administration   | Oral use   |
| Dosage and administration details:<br>Dexamethasone 40 mg administered orally once weekly; during weeks when elotuzumab is also administered, dexamethasone was administered as a split dose (28 mg orally and 8 mg intravenously) |  |
| Investigational medicinal product name   | dexamethasone injection  |
| Investigational medicinal product code   |  |
| Other name   |  |
| Pharmaceutical forms   | Solution for injection   |
| Routes of administration   | Intravenous use  |
| Dosage and administration details:<br>Dexamethasone 40 mg administered orally once weekly; during weeks when elotuzumab is also administered, dexamethasone was administered as a split dose (28 mg orally and 8 mg intravenously) |  |
| <b>Arm title</b>   | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
| Arm description:<br>Elotuzumab 20 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.   |  |
| Arm type   | Experimental   |
| Investigational medicinal product name   | elotuzumab   |
| Investigational medicinal product code   |  |
| Other name   | HuLuc63  |
| Pharmaceutical forms   | Powder for solution for infusion                               |
| Routes of administration   | Intravenous use  |

Dosage and administration details:

Humanized Anti-CS1 Monoclonal IgG1 Antibody (HuLuc63) administered as an intravenous infusion once a week during Cycles 1 and 2, and every other week beginning with Cycle 3.

|  |              |
|--|--------------|
| Investigational medicinal product name | lenalidomide |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Lenalidomide 25 mg administered orally once daily on Days 1 to 21 of each 28-day cycle

|  |                    |
|--|--------------------|
| Investigational medicinal product name | dexamethasone oral |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Oral solution      |
| Routes of administration               | Oral use           |

Dosage and administration details:

Dexamethasone 40 mg administered orally once weekly; during weeks when elotuzumab is also administered, dexamethasone was administered as a split dose (28 mg orally and 8 mg intravenously)

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

Dosage and administration details:

Dexamethasone 40 mg administered orally once weekly; during weeks when elotuzumab is also administered, dexamethasone was administered as a split dose (28 mg orally and 8 mg intravenously)

|                  |  |
|------------------|--|
| <b>Arm title</b> | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
|------------------|--|

Arm description:

Elotuzumab 10 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.

|  |                                  |
|--|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | elotuzumab                       |
| Investigational medicinal product code |                                  |
| Other name                             | HuLuc63                          |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Humanized Anti-CS1 Monoclonal IgG1 Antibody (HuLuc63) administered as an intravenous infusion once a week during Cycles 1 and 2, and every other week beginning with Cycle 3.

|  |              |
|--|--------------|
| Investigational medicinal product name | lenalidomide |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Lenalidomide 25 mg administered orally once daily on Days 1 to 21 of each 28-day cycle

|  |                    |
|--|--------------------|
| Investigational medicinal product name | dexamethasone oral |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Oral solution      |
| Routes of administration               | Oral use           |

Dosage and administration details:

Dexamethasone 40 mg administered orally once weekly; during weeks when elotuzumab is also

administered, dexamethasone was administered as a split dose (28 mg orally and 8 mg intravenously)

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

Dosage and administration details:

Dexamethasone 40 mg administered orally once weekly; during weeks when elotuzumab is also administered, dexamethasone was administered as a split dose (28 mg orally and 8 mg intravenously)

|                  |  |
|------------------|--|
| <b>Arm title</b> | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
|------------------|--|

Arm description:

Elotuzumab 20 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.

|  |                                  |
|--|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | elotuzumab                       |
| Investigational medicinal product code |                                  |
| Other name                             | HuLuc63                          |
| Pharmaceutical forms                   | Powder for solution for infusion |
| Routes of administration               | Intravenous use                  |

Dosage and administration details:

Humanized Anti-CS1 Monoclonal IgG1 Antibody (HuLuc63) administered as an intravenous infusion once a week during Cycles 1 and 2, and every other week beginning with Cycle 3.

|  |              |
|--|--------------|
| Investigational medicinal product name | lenalidomide |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Lenalidomide 25 mg administered orally once daily on Days 1 to 21 of each 28-day cycle

|  |                    |
|--|--------------------|
| Investigational medicinal product name | dexamethasone oral |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Oral solution      |
| Routes of administration               | Oral use           |

Dosage and administration details:

Dexamethasone 40 mg administered orally once weekly; during weeks when elotuzumab is also administered, dexamethasone was administered as a split dose (28 mg orally and 8 mg intravenously)

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

Dosage and administration details:

Dexamethasone 40 mg administered orally once weekly; during weeks when elotuzumab is also administered, dexamethasone was administered as a split dose (28 mg orally and 8 mg intravenously)

| Number of subjects in period 1 <sup>[1]</sup> | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
|---|---|--|--|
|   |   |  |  |
| Started                                       | 3   | 3  | 22   |
| Completed                                     | 0   | 0  | 0  |
| Not completed                                 | 3   | 3  | 22   |
| Investigator's decision                       | -   | -  | 4  |
| Disease progression                           | 1   | -  | 5  |
| Death   | -   | 2  | -  |
| Not specified                                 | -   | 1  | 8  |
| Subject's decision                            | 1   | -  | 2  |
| New multiple myeloma therapy                  | 1   | -  | 2  |
| Adverse event                                 | -   | -  | 1  |
| Missing                                       | -   | -  | -  |

| Number of subjects in period 1 <sup>[1]</sup> | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
|---|--|--|
|   |  |  |
| Started                                       | 36   | 37   |
| Completed                                     | 0  | 0  |
| Not completed                                 | 36   | 37   |
| Investigator's decision                       | 1  | -  |
| Disease progression                           | 17   | 16   |
| Death   | 2  | 3  |
| Not specified                                 | 9  | 9  |
| Subject's decision                            | 3  | 3  |
| New multiple myeloma therapy                  | 3  | 4  |
| Adverse event                                 | 1  | 1  |
| Missing                                       | -  | 1  |

Notes:

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

Justification: A total of 101 participants were randomized (intent-to-treat [ITT] population); 1 subject did not receive study drug and is excluded from the analyses.

## Baseline characteristics

### Reporting groups

|  |  |
|--|--|
| Reporting group title  | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1)  |
| Reporting group description:<br>Elotuzumab 5 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.  |  |
| Reporting group title  | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
| Reporting group description:<br>Elotuzumab 10 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally. |  |
| Reporting group title  | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
| Reporting group description:<br>Elotuzumab 20 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally. |  |
| Reporting group title  | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
| Reporting group description:<br>Elotuzumab 10 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally. |  |
| Reporting group title  | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
| Reporting group description:<br>Elotuzumab 20 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally. |  |

| Reporting group values             | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
|------------------------------------|---|--|--|
| Number of subjects                 | 3   | 3  | 22   |
| Age categorical<br>Units: Subjects |   |  |  |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 68.3<br>± 7.23 | 64.7<br>± 6.94 | 59.3<br>± 10.87 |
| Gender categorical<br>Units: Subjects                                   |                |                |                 |
| Female  | 2              | 1              | 10              |
| Male  | 1              | 2              | 12              |

| Reporting group values | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) | Total |
|------------------------|--|--|-------|
| Number of subjects     | 36   | 37   | 101   |



|   |               |                |    |
|---|---------------|----------------|----|
| Age categorical<br>Units: Subjects                                      |               |                |    |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 60.6<br>± 9.7 | 63.3<br>± 9.76 | -  |
| Gender categorical<br>Units: Subjects                                   |               |                |    |
| Female  | 19            | 24             | 56 |
| Male  | 17            | 13             | 45 |

## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1)  |
| Reporting group description:<br>Elotuzumab 5 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.                              |  |
| Reporting group title  | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
| Reporting group description:<br>Elotuzumab 10 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.                             |  |
| Reporting group title  | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
| Reporting group description:<br>Elotuzumab 20 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.                             |  |
| Reporting group title  | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
| Reporting group description:<br>Elotuzumab 10 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.                             |  |
| Reporting group title  | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
| Reporting group description:<br>Elotuzumab 20 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.                             |  |
| Subject analysis set title   | Phase 1 Elotuzumab + Lenalidomide and Dexamethasone            |
| Subject analysis set type  | Intention-to-treat   |
| Subject analysis set description:<br>Elotuzumab 5, 10, or 20 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.              |  |
| Subject analysis set title   | Total (Phase 2)  |
| Subject analysis set type  | Intention-to-treat   |
| Subject analysis set description:<br>Elotuzumab (10 or 20 mg/kg) administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.                |  |
| Subject analysis set title   | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone           |
| Subject analysis set type  | Intention-to-treat   |
| Subject analysis set description:<br>Elotuzumab 10 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally in Phase 1 and Phase 2. |  |
| Subject analysis set title   | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone           |
| Subject analysis set type  | Intention-to-treat   |
| Subject analysis set description:<br>Elotuzumab 20 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally in Phase 1 and Phase 2. |  |
| Subject analysis set title   | Total (Phase 1)  |
| Subject analysis set type  | Intention-to-treat   |
| Subject analysis set description:<br>Elotuzumab (5, 10, or 20 mg/kg) administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.            |  |

## Primary: Maximum Tolerated Dose (MTD) of Elotuzumab in Combination With Lenalidomide and Dexamethasone (Phase 1)

|                 |  |
|-----------------|--|
| End point title | Maximum Tolerated Dose (MTD) of Elotuzumab in Combination With Lenalidomide and Dexamethasone (Phase 1) <sup>[1]</sup> |
|-----------------|--|

### End point description:

MTD was determined by testing increasing doses up to 20 mg/kg once daily dose escalation cohorts 1 to 3 with 3 patients each. MTD reflects highest dose of drug that did not cause an unacceptable side effect (dose limiting toxicity [DLT]) in more than 30% of patients; e.g., hematologic toxicities like Common Toxicity Criteria for Adverse Events (CTCAE) Grade 4 neutropenia in specific conditions, platelets < 10,000 cells/mm<sup>3</sup> that do not recover to 25,000 cells/mm<sup>3</sup>; and specific non-hematologic/biochemical toxicities CTCAE Grade 3 or 4 (except fatigue and Grade 3 infections); CTCAE version 3.0 were used.

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

### End point timeframe:

4 weeks

### Notes:

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

Justification: Descriptive data are summarized for this end point per protocol.

|                             |   |  |  |  |
|-----------------------------|---|--|--|--|
| <b>End point values</b>     | Phase 1<br>Elotuzumab +<br>Lenalidomide<br>and<br>Dexamethasone |  |  |  |
| Subject group type          | Subject analysis set  |  |  |  |
| Number of subjects analysed | 28 <sup>[2]</sup>   |  |  |  |
| Units: mg/kg                |   |  |  |  |
| number (not applicable)     | 20  |  |  |  |

### Notes:

[2] - All randomized participants who received at least 1 dose of study drug in phase 1 escalation cohorts

## Statistical analyses

No statistical analyses for this end point

## Primary: Objective Response Rate (ORR) According to the International Myeloma Working Group Uniform Response Criteria (Phase 2)

|                 |  |
|-----------------|--|
| End point title | Objective Response Rate (ORR) According to the International Myeloma Working Group Uniform Response Criteria (Phase 2) <sup>[3][4]</sup> |
|-----------------|--|

### End point description:

ORR: Percentage of participants with confirmed complete response (CR; negative immunofixation on the serum and urine, disappearance of any soft tissue plasmacytomas, and ≤5% plasma cells in bone marrow), partial response (PR; ≥50% reduction of serum M-protein and reduction in 24-hour urinary M-protein by ≥90% or to ≤200 mg per 24 hour; if serum and urine M-protein are unmeasurable, a ≥50% decrease in the difference between involved and uninvolved free light chain (FLC) levels is required in place of the M-protein criteria; if serum and urine M-protein are unmeasurable, and serum FLC is also unmeasurable, a ≥50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cell percentage was ≥30%; and, if present at baseline, a ≥50% reduction in the size of soft tissue plasmacytomas), very good PR (VGPR; normal FLC ratio and absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence), or stringent CR (sCR; CR plus VGPR).

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

### End point timeframe:

From date of randomization until 60 days following the last infusion (or before initiation of new therapy), up to 101 months

Notes:

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

Justification: Descriptive data are summarized for this end point per protocol.

[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: The primary end point included subjects enrolled in Phase 2 only.

| End point values                  | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) | Total (Phase 2)      |  |
|-----------------------------------|--|--|----------------------|--|
| Subject group type                | Reporting group  | Reporting group  | Subject analysis set |  |
| Number of subjects analysed       | 36 <sup>[5]</sup>  | 37 <sup>[6]</sup>  | 73 <sup>[7]</sup>    |  |
| Units: percentage of participants |  |  |                      |  |
| number (confidence interval 95%)  | 91.7 (77.5 to 98.2)  | 75.7 (58.8 to 88.2)  | 83.6 (73 to 91.2)    |  |

Notes:

[5] - Safety population: All randomized participants who received at least 1 dose of study drug

[6] - Safety population: All randomized participants who received at least 1 dose of study drug

[7] - Safety population: All randomized participants who received at least 1 dose of study drug

## Statistical analyses

No statistical analyses for this end point

## Secondary: Objective Response Rate (ORR) According to the International Myeloma Working Group Uniform Response Criteria (Phase 1)

|                 |   |
|-----------------|---|
| End point title | Objective Response Rate (ORR) According to the International Myeloma Working Group Uniform Response Criteria (Phase 1) <sup>[8]</sup> |
|-----------------|---|

End point description:

ORR: Percentage of participants with confirmed complete response (CR; negative immunofixation on the serum and urine, disappearance of any soft tissue plasmacytomas, and  $\leq 5\%$  plasma cells in bone marrow), partial response (PR;  $\geq 50\%$  reduction of serum M-protein and reduction in 24-hour urinary M-protein by  $\geq 90\%$  or to  $\leq 200$  mg per 24 hour; if serum and urine M-protein are unmeasurable, a  $\geq 50\%$  decrease in the difference between involved and uninvolved free light chain (FLC) levels is required in place of the M-protein criteria; if serum and urine M-protein are unmeasurable, and serum FLC is also unmeasurable, a  $\geq 50\%$  reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cell percentage was  $\geq 30\%$ ; and, if present at baseline, a  $\geq 50\%$  reduction in the size of soft tissue plasmacytomas), very good PR (VGPR; normal FLC ratio and absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence), or stringent CR (sCR; CR plus VGPR).

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

End point timeframe:

From first dose of elotuzumab until 60 days following the last infusion (or before initiation of new therapy), up to 100.5 months

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: The secondary end point included subjects enrolled in Phase 1 only.

| End point values                  | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Total (Phase 1)      |
|-----------------------------------|---|--|--|----------------------|
| Subject group type                | Reporting group   | Reporting group  | Reporting group  | Subject analysis set |
| Number of subjects analysed       | 3 <sup>[9]</sup>  | 3 <sup>[10]</sup>  | 22 <sup>[11]</sup>   | 28 <sup>[12]</sup>   |
| Units: percentage of participants |   |  |  |                      |
| number (confidence interval 95%)  | 100 (29.2 to 100)   | 100 (29.2 to 100)  | 77.3 (54.6 to 92.2)  | 82.1 (63.1 to 93.9)  |

Notes:

[9] - Safety population: All randomized participants who received at least 1 dose of study drug

[10] - Safety population: All randomized participants who received at least 1 dose of study drug

[11] - Safety population: All randomized participants who received at least 1 dose of study drug

[12] - Safety population: All randomized participants who received at least 1 dose of study drug

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Treatment-emergent Adverse Events (TEAEs)

|                 |   |
|-----------------|---|
| End point title | Number of Participants With Treatment-emergent Adverse Events (TEAEs) |
|-----------------|---|

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. The investigator assessed the relationship of each event to the use of study drug as either definitely related, probably related, possibly related or unrelated. A serious adverse event (SAE) is an event that results in death, is life-threatening, requires or prolongs hospitalization, results in a congenital anomaly, persistent or significant disability/incapacity or is an important medical event that, based on medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent any of the outcomes listed above. Treatment-emergent events (TEAEs/TESAEs) are defined as any event that began or worsened in severity after the first dose of study drug. For more details on adverse events please see the Adverse Event section.

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

End point timeframe:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) were collected from first dose of study drug until 60 days after the last dose of study drug (up to 95 months)

| End point values            | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
|-----------------------------|---|--|--|--|
| Subject group type          | Reporting group   | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed | 3 <sup>[13]</sup>   | 3 <sup>[14]</sup>  | 22 <sup>[15]</sup>   | 36 <sup>[16]</sup>   |
| Units: participants         |   |  |  |  |
| number (not applicable)     |   |  |  |  |
| Any TEAE                    | 3   | 3  | 22   | 36   |
| Any TESAE                   | 0   | 3  | 12   | 21   |
| TEAEs ≥ Grade 3             | 2   | 3  | 19   | 32   |
| TEAEs related to study drug | 3   | 3  | 16   | 29   |

|                              |   |   |   |   |
|------------------------------|---|---|---|---|
| TESAEs related to study drug | 0 | 0 | 2 | 2 |
|------------------------------|---|---|---|---|

Notes:

[13] - Safety population: All randomized participants who received at least 1 dose of study drug

[14] - Safety population: All randomized participants who received at least 1 dose of study drug

[15] - Safety population: All randomized participants who received at least 1 dose of study drug

[16] - Safety population: All randomized participants who received at least 1 dose of study drug

|                              |  |  |  |  |
|------------------------------|--|--|--|--|
| <b>End point values</b>      | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |  |  |  |
| Subject group type           | Reporting group  |  |  |  |
| Number of subjects analysed  | 37 <sup>[17]</sup>   |  |  |  |
| Units: participants          |  |  |  |  |
| number (not applicable)      |  |  |  |  |
| Any TEAE                     | 37   |  |  |  |
| Any TESAE                    | 21   |  |  |  |
| TEAEs ≥ Grade 3              | 25   |  |  |  |
| TEAEs related to study drug  | 26   |  |  |  |
| TESAEs related to study drug | 5  |  |  |  |

Notes:

[17] - Safety population: All randomized participants who received at least 1 dose of study drug

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Infusion Reactions

|                 |  |
|-----------------|--|
| End point title | Number of Participants With Infusion Reactions |
|-----------------|--|

End point description:

During Phase 1, a list of 118 pre-defined MedDRA preferred terms that had been adjudicated to be clinically relevant to infusion reactions by a safety committee was used to search for TEAEs that could potentially be associated with an infusion reaction following elotuzumab administration. Examples of these terms included angioedema, bronchospasm, chills, flushing, pyrexia, rash and urticaria. During Phase 2, the method for capturing TEAEs associated with an infusion reaction was modified to include investigators' designation of AEs judged as clinically relevant infusion reactions. The number of participants infusion reactions are provided overall and by highest toxicity grade (CTCAE v 3.0).

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

End point timeframe:

Cycles 1 and 2: Days 1, 8, 15, and 22 (day of infusion of elotuzumab) and Days 2, 9, 16, and 23 (day following infusion); and Cycles 3 and greater: Days 1 and 15 (day of infusion) and Days 2 and 16 (day after infusion) (up to 95 months)

|                             |   |  |  |  |
|-----------------------------|---|--|--|--|
| <b>End point values</b>     | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
| Subject group type          | Reporting group   | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed | 3 <sup>[18]</sup>   | 3 <sup>[19]</sup>  | 22 <sup>[20]</sup>   | 36 <sup>[21]</sup>   |

|                         |   |   |    |   |
|-------------------------|---|---|----|---|
| Units: participants     |   |   |    |   |
| number (not applicable) |   |   |    |   |
| Any reaction            | 2 | 3 | 20 | 5 |
| Grade 5                 | 0 | 0 | 0  | 0 |
| Grade 4                 | 0 | 0 | 1  | 0 |
| Grade 3                 | 0 | 0 | 2  | 1 |
| Grade 2                 | 0 | 1 | 5  | 1 |
| Grade 1                 | 2 | 2 | 12 | 3 |

Notes:

[18] - Safety population: All randomized participants who received at least 1 dose of study drug

[19] - Safety population: All randomized participants who received at least 1 dose of study drug

[20] - Safety population: All randomized participants who received at least 1 dose of study drug

[21] - Safety population: All randomized participants who received at least 1 dose of study drug

|                             |  |  |  |  |
|-----------------------------|--|--|--|--|
| <b>End point values</b>     | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |  |  |  |
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 37 <sup>[22]</sup>   |  |  |  |
| Units: participants         |  |  |  |  |
| number (not applicable)     |  |  |  |  |
| Any reaction                | 3  |  |  |  |
| Grade 5                     | 0  |  |  |  |
| Grade 4                     | 0  |  |  |  |
| Grade 3                     | 0  |  |  |  |
| Grade 2                     | 1  |  |  |  |
| Grade 1                     | 2  |  |  |  |

Notes:

[22] - Safety population: All randomized participants who received at least 1 dose of study drug

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Serum Concentrations of Elotuzumab During Cycle 1

|                 |  |
|-----------------|--|
| End point title | Mean Serum Concentrations of Elotuzumab During Cycle 1 <sup>[23]</sup> |
|-----------------|--|

End point description:

Blood samples were collected during Phase 1, Cycle 1, prior to elotuzumab infusion (time 0 hours) and 30 minutes (0.5 hours) and 4 hours post-infusion (Day 1), 30 minutes (0.5 hours) post-infusion (Day 8 and Day 15), or 30 minutes (0.5 hours), 2 hours, and 4 hours post-infusion (Day 15). Blood samples were collected during Phase 2, Cycle 1, prior to elotuzumab infusion (time 0 hours) and 30 minutes (0.5 hours), 2 hours, and 4 hours post-infusion (Day 1), 30 minutes (0.5 hours) and 2 hours post-infusion (Day 8 and Day 15), or 30 minutes (0.5 hours), 2 hours, and 4 hours post-infusion (Day 15). The samples were analyzed for the concentration of elotuzumab using validated analytical methods. Mean serum concentrations on Cycle 1, Days 1, 8, 15, and 22 (measured in µg/mL) are reported overall (across Phase 1 and Phase 2) by dose. 55555=The estimated standard deviation of one sample is undefined. 88888=Blood samples not collected at given timepoint.

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

End point timeframe:

Cycle 1: Days 1 (pre-infusion and 0.5, 2 and 4 hours post-infusion), 8 (pre-infusion and 0.5 and 2 hours post-infusion), 15 (pre-infusion and 0.5 hours and 2 hours post-infusion), and 22 (pre-infusion and 0.5, 2, and 4 hours post-infusion)

Notes:

[23] - 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: The end point is analyzed by dose (5, 10, and 20 mg/kg).

| End point values                     | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone |  |
|--------------------------------------|---|--|--|--|
| Subject group type                   | Reporting group   | Subject analysis set                                 | Subject analysis set                                 |  |
| Number of subjects analysed          | 3 <sup>[24]</sup>   | 39 <sup>[25]</sup>                                   | 58 <sup>[26]</sup>                                   |  |
| Units: µg/mL                         |   |  |  |  |
| arithmetic mean (standard deviation) |   |  |  |  |
| Day 1: 0.5 hours (N=3,39,58)         | 0 (± 0)   | 0 (± 0)  | 0 (± 0)  |  |
| Day 1: 0.5 hours (N=3,39,57)         | 78.48 (± 21.33)   | 217.9 (± 99.31)                                      | 434.2 (± 202.74)                                     |  |
| Day 1: 2 hours (N=0,36,43)           | 88888 (± 88888)   | 213.31 (± 91.3)                                      | 388.58 (± 112.94)                                    |  |
| Day 1: 4 hours (N=3,3,12)            | 85.56 (± 23.54)   | 251.34 (± 31.92)                                     | 525.98 (± 188.46)                                    |  |
| Day 8: 0 hours (N=3,37,55)           | 32.44 (± 8.91)  | 92.47 (± 61.16)                                      | 168.55 (± 56.43)                                     |  |
| Day 8: 0.5 hours(N=3,22,44)          | 133.37 (± 40.87)  | 281.53 (± 117.35)                                    | 593.8 (± 192.7)                                      |  |
| Day 8: 2 hours (N=0,12,9)            | 88888 (± 88888)   | 268.35 (± 107.44)                                    | 520.97 (± 207.28)                                    |  |
| Day 15: 0 hours (N=3,37,58)          | 49.84 (± 28.28)   | 111.11 (± 56.36)                                     | 298.82 (± 231.17)                                    |  |
| Day 15: 0.5 hours (N=3,36,55)        | 140.09 (± 32.28)  | 282.29 (± 100.29)                                    | 661.91 (± 251.08)                                    |  |
| Day 22: 0 hours (N=3,38,54)          | 61.93 (± 53.66)   | 135.92 (± 106.83)                                    | 308.02 (± 144.61)                                    |  |
| Day 22: 0.5 hours (N=3,38,54)        | 168.61 (± 59.31)  | 310.03 (± 165.14)                                    | 699.7 (± 230.41)                                     |  |
| Day 22: 2 hours (N=1,35,40)          | 268.53 (± 55555)  | 298.85 (± 114.35)                                    | 704.48 (± 234.98)                                    |  |
| Day 22: 4 hours (N=2,3,10)           | 128.94 (± 42.04)  | 538.88 (± 195.35)                                    | 981.16 (± 280.28)                                    |  |

Notes:

[24] - All participants in the safety population with evaluable data at given timepoint

[25] - All participants in the safety population with evaluable data at given timepoint

[26] - All participants in the safety population with evaluable data at given timepoint

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Serum Concentration (Cmax) of Elotuzumab

|                 |  |
|-----------------|--|
| End point title | Maximum Serum Concentration (Cmax) of Elotuzumab <sup>[27]</sup> |
|-----------------|--|

End point description:

The maximum plasma concentration (C<sub>max</sub>; measured in ng/mL) is the highest concentration that a drug achieves in the blood after administration in a dosing interval. The C<sub>max</sub> of elotuzumab was to be estimated using non-compartmental methods and data reported as the mean ± standard deviation. No noncompartmental pharmacokinetic parameters (e.g., AUC, CL, V, t<sub>1/2</sub>) were estimated due to sparse serum concentration collections.

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



End point timeframe:

Cycle 1: Days 1, 8, and 15; Cycle 2: Days 1 and 22; Cycle 3 and beyond: Day 1

Notes:

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

Justification: The end point was to be analyzed by dose (5, 10, and 20 mg/kg).

| End point values                     | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone |  |
|--------------------------------------|---|--|--|--|
| Subject group type                   | Reporting group   | Subject analysis set                                 | Subject analysis set                                 |  |
| Number of subjects analysed          | 0 <sup>[28]</sup>   | 0 <sup>[29]</sup>                                    | 0 <sup>[30]</sup>                                    |  |
| Units: ng/mL                         |   |  |  |  |
| arithmetic mean (standard deviation) | ()  | ()   | ()   |  |

Notes:

[28] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

[29] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

[30] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Concentration-time Curve From 0 to Infinity (AUC0-inf) of Elotuzumab

|                 |   |
|-----------------|---|
| End point title | Area Under the Concentration-time Curve From 0 to Infinity (AUC0-inf) of Elotuzumab <sup>[31]</sup> |
|-----------------|---|

End point description:

The area under the plasma concentration-time curve (AUC; measured in ng\*hr/mL) is a method of measurement to determine the total exposure of a drug in blood plasma. The AUC24 of elotuzumab was to be estimated using non-compartmental methods and data reported as the mean  $\pm$  standard deviation. No noncompartmental pharmacokinetic parameters (e.g., AUC, CL, V, t<sub>1/2</sub>) were estimated due to sparse serum concentration collections.

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

End point timeframe:

Cycle 1: Days 1, 8, and 15; Cycle 2: Days 1 and 22; Cycle 3 and beyond: Day 1

Notes:

[31] - 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: The end point was to be analyzed by dose (5, 10, and 20 mg/kg).

| End point values                     | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone |  |
|--------------------------------------|---|--|--|--|
| Subject group type                   | Reporting group   | Subject analysis set                                 | Subject analysis set                                 |  |
| Number of subjects analysed          | 0 <sup>[32]</sup>   | 0 <sup>[33]</sup>                                    | 0 <sup>[34]</sup>                                    |  |
| Units: ng*hr/mL                      |   |  |  |  |
| arithmetic mean (standard deviation) | ()  | ()   | ()   |  |

Notes:

[32] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

[33] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

[34] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

## Statistical analyses

No statistical analyses for this end point

### Secondary: Systemic Clearance (CL) of Elotuzumab

|                 |   |
|-----------------|---|
| End point title | Systemic Clearance (CL) of Elotuzumab <sup>[35]</sup> |
|-----------------|---|

End point description:

Systemic clearance (CL, measured in mL/kg/hr) is a measure of the efficiency with which a drug is irreversibly removed from the body. The CL of elotuzumab was to be estimated using non-compartmental methods and data reported as the mean  $\pm$  standard deviation. No noncompartmental pharmacokinetic parameters (e.g., AUC, CL, V, t 1/2) were estimated due to sparse serum concentration collections.

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

End point timeframe:

Cycle 1: Days 1, 8, and 15; Cycle 2: Days 1 and 22; Cycle 3 and beyond: Day 1

Notes:

[35] - 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: The end point was to be analyzed by dose (5, 10, and 20 mg/kg).

| End point values                     | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone |  |
|--------------------------------------|---|--|--|--|
| Subject group type                   | Reporting group   | Subject analysis set                                 | Subject analysis set                                 |  |
| Number of subjects analysed          | 0 <sup>[36]</sup>   | 0 <sup>[37]</sup>                                    | 0 <sup>[38]</sup>                                    |  |
| Units: mL/kg/hr                      |   |  |  |  |
| arithmetic mean (standard deviation) | ()  | ()   | ()   |  |

Notes:

[36] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

[37] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

[38] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

## Statistical analyses

No statistical analyses for this end point

### Secondary: Volume of Distribution (V) of Elotuzumab

|                 |  |
|-----------------|--|
| End point title | Volume of Distribution (V) of Elotuzumab <sup>[39]</sup> |
|-----------------|--|

End point description:

Volume of distribution (V, measured in L/kg) is the hypothetical volume of body fluid that would be required to dissolve the amount of drug needed to achieve the same concentration in the blood. The V of elotuzumab was to be estimated using non-compartmental methods and data reported as the mean  $\pm$  standard deviation. No noncompartmental pharmacokinetic parameters (e.g., AUC, CL, V, t 1/2) were estimated due to sparse serum concentration collections.

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

End point timeframe:

Cycle 1: Days 1, 8, and 15; Cycle 2: Days 1 and 22; Cycle 3 and beyond: Day 1

Notes:

[39] - 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: The end point was to be analyzed by dose (5, 10, and 20 mg/kg).

| End point values                     | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone |  |
|--------------------------------------|---|--|--|--|
| Subject group type                   | Reporting group   | Subject analysis set                                 | Subject analysis set                                 |  |
| Number of subjects analysed          | 0 <sup>[40]</sup>   | 0 <sup>[41]</sup>                                    | 0 <sup>[42]</sup>                                    |  |
| Units: L/kg                          |   |  |  |  |
| arithmetic mean (standard deviation) | ()  | ()   | ()   |  |

Notes:

[40] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

[41] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

[42] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

## Statistical analyses

No statistical analyses for this end point

## Secondary: Serum Half-life (t<sub>1/2</sub>) of Elotuzumab

|                 |   |
|-----------------|---|
| End point title | Serum Half-life (t <sub>1/2</sub> ) of Elotuzumab <sup>[43]</sup> |
|-----------------|---|

End point description:

The serum half-life of a drug (t<sub>1/2</sub>, measured in hours) is the time necessary to reduce the plasma concentration by half. The t<sub>1/2</sub> of elotuzumab was to be estimated using non-compartmental methods and data reported as the mean ± standard deviation. No noncompartmental pharmacokinetic parameters (e.g., AUC, CL, V, t<sub>1/2</sub>) were estimated due to sparse serum concentration collections.

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

End point timeframe:

Cycle 1: Days 1, 8, and 15; Cycle 2: Days 1 and 22; Cycle 3 and beyond: Day 1

Notes:

[43] - 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: The end point was to be analyzed by dose (5, 10, and 20 mg/kg).

| End point values                     | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone |  |
|--------------------------------------|---|--|--|--|
| Subject group type                   | Reporting group   | Subject analysis set                                 | Subject analysis set                                 |  |
| Number of subjects analysed          | 0 <sup>[44]</sup>   | 0 <sup>[45]</sup>                                    | 0 <sup>[46]</sup>                                    |  |
| Units: hours                         |   |  |  |  |
| arithmetic mean (standard deviation) | ()  | ()   | ()   |  |

Notes:

[44] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

[45] - No pharmacokinetic parameters were estimated due to sparse serum concentration collections

## Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Response

|                 |                      |
|-----------------|----------------------|
| End point title | Duration of Response |
|-----------------|----------------------|

End point description:

Duration of response is defined as the time from the initial objective response to disease progression or death, whichever occurs first. The distribution of duration of response was estimated for each treatment group using Kaplan-Meier methodology. Point estimates and 95% CIs for the median for the duration of response distribution are provided. 77777=Median was not reached (max value was 58.22). 11111=Lower limit not calculable due to insufficient progression events. 99999=upper limit not calculable due to insufficient progression events.

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

End point timeframe:

From first dose of elotuzumab (phase 1) or randomization (phase 2) until 60 days following the last infusion (or before initiation of new therapy), up to 101 months

| End point values                 | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
|----------------------------------|---|--|--|--|
| Subject group type               | Reporting group   | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed      | 3 <sup>[47]</sup>   | 3 <sup>[48]</sup>  | 22 <sup>[49]</sup>   | 36 <sup>[50]</sup>   |
| Units: months                    |   |  |  |  |
| median (confidence interval 95%) | 4.47 (1.45 to 4.47)   | 9.92 (0 to 99999)  | 77777 (11111 to 99999)   | 34.83 (14.6 to 99999)  |

Notes:

[47] - Safety population: All randomized participants who received at least 1 dose of study drug

[48] - Safety population: All randomized participants who received at least 1 dose of study drug

[49] - Safety population: All randomized participants who received at least 1 dose of study drug

[50] - Safety population: All randomized participants who received at least 1 dose of study drug

| End point values            | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) | Total (Phase 2)      | Total (Phase 1)      |  |
|-----------------------------|--|----------------------|----------------------|--|
| Subject group type          | Reporting group  | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed | 37 <sup>[51]</sup>   | 73 <sup>[52]</sup>   | 28 <sup>[53]</sup>   |  |
| Units: months               |  |                      |                      |  |

|                                  |                       |                       |                        |
|----------------------------------|-----------------------|-----------------------|------------------------|
| median (confidence interval 95%) | 29.01 (15.0 to 99999) | 29.24 (18.2 to 99999) | 77777 (11111 to 99999) |
|----------------------------------|-----------------------|-----------------------|------------------------|

Notes:

[51] - Safety population: All randomized participants who received at least 1 dose of study drug

[52] - Safety population: All randomized participants who received at least 1 dose of study drug

[53] - Safety population: All randomized participants who received at least 1 dose of study drug

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Progression (TTP)

|                 |                           |
|-----------------|---------------------------|
| End point title | Time to Progression (TTP) |
|-----------------|---------------------------|

End point description:

TTP is defined as the time from first dose (phase 1) or time from randomization (phase 2) to disease progression. The distribution of TTP was estimated for each treatment group using Kaplan-Meier methodology. Point estimates and 95% CIs for the median for the TTP distribution are provided. 11.111=Lower limit not calculable due to insufficient progression events. 99999=upper limit not calculable due to insufficient progression events

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

End point timeframe:

From first dose of elotuzumab (phase 1) or randomization (phase 2) until 60 days following the last infusion (or before initiation of new therapy), up to 101 months

| End point values                 | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
|----------------------------------|---|--|--|--|
| Subject group type               | Reporting group   | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed      | 3 <sup>[54]</sup>   | 3 <sup>[55]</sup>  | 22 <sup>[56]</sup>   | 36 <sup>[57]</sup>   |
| Units: months                    |   |  |  |  |
| median (confidence interval 95%) | 6.08 (6.05 to 6.08)   | 11.53 (11.111 to 99999)  | 52.93 (7.43 to 99999)  | 32.49 (14.9 to 99999)  |

Notes:

[54] - Safety population: All randomized participants who received at least 1 dose of study drug

[55] - Safety population: All randomized participants who received at least 1 dose of study drug

[56] - Safety population: All randomized participants who received at least 1 dose of study drug

[57] - Safety population: All randomized participants who received at least 1 dose of study drug

| End point values                 | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) | Total (Phase 2)      | Total (Phase 1)       |  |
|----------------------------------|--|----------------------|-----------------------|--|
| Subject group type               | Reporting group  | Subject analysis set | Subject analysis set  |  |
| Number of subjects analysed      | 37 <sup>[58]</sup>   | 73 <sup>[59]</sup>   | 28 <sup>[60]</sup>    |  |
| Units: months                    |  |                      |                       |  |
| median (confidence interval 95%) | 19.94 (12.9 to 35.7)   | 28.16 (15.4 to 35.8) | 52.93 (7.43 to 99999) |  |

Notes:

[58] - Safety population: All randomized participants who received at least 1 dose of study drug

[59] - Safety population: All randomized participants who received at least 1 dose of study drug

[60] - Safety population: All randomized participants who received at least 1 dose of study drug

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Treatment-emergent Anti-elotuzumab Antibody (ADA)

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants With Treatment-emergent Anti-elotuzumab Antibody (ADA) <sup>[61]</sup> |
|-----------------|---|

End point description:

Treatment-emergent (post-dose) positive elotuzumab-specific ADA is differentiated from pre-existing (positive at the predose time point) positive elotuzumab-specific ADA. The percentage of participants with confirmed treatment-emergent ADA overall by dose is provided.

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

End point timeframe:

From screening through 60-day follow up period (up to 101 months)

Notes:

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

Justification: The end point is analyzed by dose (5, 10, and 20 mg/kg).

| End point values            | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone |  |
|-----------------------------|---|--|--|--|
| Subject group type          | Reporting group   | Subject analysis set                                 | Subject analysis set                                 |  |
| Number of subjects analysed | 3 <sup>[62]</sup>   | 39 <sup>[63]</sup>                                   | 57 <sup>[64]</sup>                                   |  |
| Units: participants         |   |  |  |  |
| number (not applicable)     | 0   | 6  | 5  |  |

Notes:

[62] - All participants who received  $\geq 1$  dose of study drug and  $\geq 1$  evaluable post-dose sample

[63] - All participants who received  $\geq 1$  dose of study drug and  $\geq 1$  evaluable post-dose sample

[64] - All participants who received  $\geq 1$  dose of study drug and  $\geq 1$  evaluable post-dose sample

## Statistical analyses

No statistical analyses for this end point

### Secondary: Plasma Cell Myeloma Cytogenetic Subtype

|                 |   |
|-----------------|---|
| End point title | Plasma Cell Myeloma Cytogenetic Subtype |
|-----------------|---|

End point description:

Plasma cell myeloma cytogenetic subtype was assessed at the screening visit using standard karyotyping and/or fluorescence in situ hybridization. The number of participants in each cytogenetic risk category are provided: High Risk (International Staging System [ISS] stage II or III and t(4;14) or del(17p) abnormality); Standard Risk (not high or low risk); and Low Risk (ISS stage I or II and absence of t(4;14), del(17p) and 1q21 abnormalities AND age < 55).

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

End point timeframe:

Screening (up to 14 days prior to dosing)

| <b>End point values</b>     | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
|-----------------------------|---|--|--|--|
| Subject group type          | Reporting group   | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed | 3 <sup>[65]</sup>   | 3 <sup>[66]</sup>  | 22 <sup>[67]</sup>   | 36 <sup>[68]</sup>   |
| Units: participants         |   |  |  |  |
| number (not applicable)     |   |  |  |  |
| High Risk                   | 1   | 0  | 0  | 1  |
| Standard Risk               | 2   | 3  | 17   | 30   |
| Low Risk                    | 0   | 0  | 3  | 2  |
| Not Reported                | 0   | 0  | 2  | 3  |

Notes:

[65] - Safety population: All randomized participants who received at least 1 dose of study drug

[66] - Safety population: All randomized participants who received at least 1 dose of study drug

[67] - Safety population: All randomized participants who received at least 1 dose of study drug

[68] - Safety population: All randomized participants who received at least 1 dose of study drug

| <b>End point values</b>     | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |  |  |  |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 37 <sup>[69]</sup>   |  |  |  |
| Units: participants         |  |  |  |  |
| number (not applicable)     |  |  |  |  |
| High Risk                   | 3  |  |  |  |
| Standard Risk               | 24   |  |  |  |
| Low Risk                    | 3  |  |  |  |
| Not Reported                | 7  |  |  |  |

Notes:

[69] - Safety population: All randomized participants who received at least 1 dose of study drug

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-free Survival (PFS)

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

End point description:

PFS is defined as the time from first dose (phase 1) or time from randomization (phase 2) to disease progression or death. The distribution of PFS was estimated for each treatment group using Kaplan-Meier methodology. Point estimates and 95% CIs for the median for the PFS distribution are provided. 77777=Median was not reached (max value was 58.91). 11111=Lower limit not calculable due to insufficient progression events. 99999=upper limit not calculable due to insufficient progression events.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| From first dose of elotuzumab (phase 1) or randomization (phase 2) until 60 days following the last infusion (or before initiation of new therapy), up to 101 months |           |

| End point values                 | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
|----------------------------------|---|--|--|--|
| Subject group type               | Reporting group   | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed      | 3 <sup>[70]</sup>   | 3 <sup>[71]</sup>  | 22 <sup>[72]</sup>   | 36 <sup>[73]</sup>   |
| Units: months                    |   |  |  |  |
| median (confidence interval 95%) | 6.08 (6.05 to 6.08)   | 22.23 (11.5 to 32.9)   | 77777 (11111 to 99999)   | 32.49 (14.9 to 99999)  |

Notes:

[70] - Safety population: All randomized participants who received at least 1 dose of study drug

[71] - Safety population: All randomized participants who received at least 1 dose of study drug

[72] - Safety population: All randomized participants who received at least 1 dose of study drug

[73] - Safety population: All randomized participants who received at least 1 dose of study drug

| End point values                 | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) | Total (Phase 2)      | Total (Phase 1)       |  |
|----------------------------------|--|----------------------|-----------------------|--|
| Subject group type               | Reporting group  | Subject analysis set | Subject analysis set  |  |
| Number of subjects analysed      | 37 <sup>[74]</sup>   | 73 <sup>[75]</sup>   | 28 <sup>[76]</sup>    |  |
| Units: months                    |  |                      |                       |  |
| median (confidence interval 95%) | 25.00 (14.0 to 35.7)   | 28.62 (16.6 to 43.1) | 32.92 (7.43 to 99999) |  |

Notes:

[74] - Safety population: All randomized participants who received at least 1 dose of study drug

[75] - Safety population: All randomized participants who received at least 1 dose of study drug

[76] - Safety population: All randomized participants who received at least 1 dose of study drug

## Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) and serious adverse events (TESAEs) were collected from first dose of study drug until 60 days after the last dose of study drug (up to 95 months).

Adverse event reporting additional description:

TEAEs and TESAEs are defined as any adverse event or serious adverse event that begins or worsens in severity after initiation of study drug until 30 days after the last dose of study drug.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
|-----------------------|---|

Reporting group description:

Elotuzumab 5 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.

|                       |  |
|-----------------------|--|
| Reporting group title | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
|-----------------------|--|

Reporting group description:

Elotuzumab 10 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.

|                       |  |
|-----------------------|--|
| Reporting group title | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
|-----------------------|--|

Reporting group description:

Elotuzumab 20 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.

|                       |  |
|-----------------------|--|
| Reporting group title | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
|-----------------------|--|

Reporting group description:

Elotuzumab 10 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.

|                       |  |
|-----------------------|--|
| Reporting group title | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |
|-----------------------|--|

Reporting group description:

Elotuzumab 20 mg/kg administered as an IV infusion in combination with lenalidomide 25 mg and dexamethasone 40 mg administered orally.

| Serious adverse events  | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
|---|---|--|--|
| Total subjects affected by serious adverse events                   |   |  |  |
| subjects affected / exposed   | 0 / 3 (0.00%)   | 3 / 3 (100.00%)  | 12 / 22 (54.55%)   |
| number of deaths (all causes)                                       | 0   | 2  | 0  |
| number of deaths resulting from adverse events                      |   |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |  |  |

|   |               |               |                |
|---|---------------|---------------|----------------|
| BLADDER TRANSITIONAL CELL CARCINOMA             |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| LOBULAR BREAST CARCINOMA IN SITU                |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| MALIGNANT MELANOMA                              |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| MYELODYSPLASTIC SYNDROME                        |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| PROSTATE CANCER                                 |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| SQUAMOUS CELL CARCINOMA                         |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| SQUAMOUS CELL CARCINOMA OF SKIN                 |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Vascular disorders                              |               |               |                |
| ACCELERATED HYPERTENSION                        |               |               |                |

|  |               |               |                |
|--|---------------|---------------|----------------|
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0          |
| DEEP VEIN THROMBOSIS                                 |               |               |                |
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0          |
| PHLEBITIS  |               |               |                |
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0          |
| PHLEBITIS SUPERFICIAL                                |               |               |                |
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0          |
| General disorders and administration site conditions |               |               |                |
| CHEST PAIN   |               |               |                |
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0          |
| MULTIPLE ORGAN DYSFUNCTION SYNDROME                  |               |               |                |
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0          |
| PYREXIA  |               |               |                |
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0          |
| Immune system disorders                              |               |               |                |
| ANAPHYLACTIC REACTION                                |               |               |                |
| subjects affected / exposed                          | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0          |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Reproductive system and breast disorders        |               |               |                |
| BENIGN PROSTATIC HYPERPLASIA                    |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| PROSTATITIS                                     |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |               |               |                |
| ACUTE RESPIRATORY FAILURE                       |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| ASTHMA  |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| LUNG DISORDER                                   |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 22 (9.09%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 3          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| PNEUMONITIS                                     |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| PULMONARY EMBOLISM                              |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| STRIDOR   |               |               |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all                             | 0 / 0         | 0 / 0          | 2 / 2          |
| deaths causally related to treatment / all                                  | 0 / 0         | 0 / 0          | 0 / 0          |
| Psychiatric disorders<br>CONFUSIONAL STATE                                  |               |                |                |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                  | 0 / 0         | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications<br>GASTROENTERITIS RADIATION |               |                |                |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all                             | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                                  | 0 / 0         | 0 / 0          | 0 / 0          |
| Cardiac disorders<br>ANGINA PECTORIS  |               |                |                |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                  | 0 / 0         | 0 / 0          | 0 / 0          |
| ATRIAL FIBRILLATION   |               |                |                |
| subjects affected / exposed   | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all                             | 0 / 0         | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all                                  | 0 / 0         | 0 / 0          | 0 / 0          |
| BRADYCARDIA   |               |                |                |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                  | 0 / 0         | 0 / 0          | 0 / 0          |
| TACHYCARDIA   |               |                |                |
| subjects affected / exposed   | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all                             | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                                  | 0 / 0         | 0 / 0          | 0 / 0          |
| Nervous system disorders<br>CEREBROVASCULAR ACCIDENT                        |               |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| GENERALISED TONIC-CLONIC SEIZURE                |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| SYNCOPE   |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| TRANSIENT GLOBAL AMNESIA                        |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| TRANSIENT ISCHAEMIC ATTACK                      |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |               |                |                |
| FEBRILE NEUTROPENIA                             |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| LYMPHOPENIA                                     |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| NEUTROPENIA                                     |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| PANCYTOPENIA                                    |               |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| <b>Gastrointestinal disorders</b>               |               |                |                |
| <b>CONSTIPATION</b>                             |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| <b>DIARRHOEA</b>                                |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 22 (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          |
| <b>DIVERTICULAR PERFORATION</b>                 |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 22 (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          |
| <b>GASTROINTESTINAL HAEMORRHAGE</b>             |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 22 (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          |
| <b>GASTROINTESTINAL PERFORATION</b>             |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 1          | 0 / 0          |
| <b>HAEMATEMESIS</b>                             |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| <b>NAUSEA</b>                                   |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| <b>VARICES OESOPHAGEAL</b>                      |               |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| VOMITING  |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |               |                |                |
| CHOLECYSTITIS                                   |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |               |                |                |
| RASH  |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |               |                |                |
| ACUTE KIDNEY INJURY                             |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 22 (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          |
| RENAL COLIC                                     |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| RENAL FAILURE                                   |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |               |                |                |
| ARTHRALGIA                                      |               |                |                |



|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| BACK PAIN                                       |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| BONE PAIN                                       |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| MUSCULOSKELETAL PAIN                            |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| PAIN IN EXTREMITY                               |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Infections and infestations                     |               |               |                |
| ASPERGILLUS INFECTION                           |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| BRONCHITIS                                      |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| 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                                      |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| CLOSTRIDIUM DIFFICILE COLITIS                   |               |               |                |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| H1N1 INFLUENZA                                  |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| HERPES ZOSTER                                   |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| INFLUENZA                                       |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| LOCALISED INFECTION                             |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| LUNG INFECTION                                  |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| MENINGITIS                                      |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| PNEUMONIA                                       |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| PNEUMONIA KLEBSIELLA                            |               |               |                |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| PNEUMONIA VIRAL                                 |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| POSTOPERATIVE WOUND INFECTION                   |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| PYELONEPHRITIS                                  |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| SEPSIS  |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| URINARY TRACT INFECTION                         |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 22 (4.55%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| VISCERAL LEISHMANIASIS                          |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| 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              |               |               |                |
| ELECTROLYTE IMBALANCE                           |               |               |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| HYPERCALCAEMIA                                  |               |               |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| <b>HYPOKALAEMIA</b>                             |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| <b>METABOLIC ACIDOSIS</b>                       |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 22 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 1          | 0 / 0          |

| <b>Serious adverse events</b>  | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |  |
|--|--|--|--|
| Total subjects affected by serious adverse events                          |  |  |  |
| subjects affected / exposed  | 21 / 36 (58.33%)   | 21 / 37 (56.76%)   |  |
| number of deaths (all causes)  | 1  | 2  |  |
| number of deaths resulting from adverse events                             |  |  |  |
| <b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b> |  |  |  |
| <b>BLADDER TRANSITIONAL CELL CARCINOMA</b>                                 |  |  |  |
| subjects affected / exposed  | 0 / 36 (0.00%)   | 1 / 37 (2.70%)   |  |
| occurrences causally related to treatment / all                            | 0 / 0  | 0 / 1  |  |
| deaths causally related to treatment / all                                 | 0 / 0  | 0 / 0  |  |
| <b>LOBULAR BREAST CARCINOMA IN SITU</b>                                    |  |  |  |
| subjects affected / exposed  | 0 / 36 (0.00%)   | 1 / 37 (2.70%)   |  |
| occurrences causally related to treatment / all                            | 0 / 0  | 0 / 1  |  |
| deaths causally related to treatment / all                                 | 0 / 0  | 0 / 0  |  |
| <b>MALIGNANT MELANOMA</b>  |  |  |  |
| subjects affected / exposed  | 1 / 36 (2.78%)   | 0 / 37 (0.00%)   |  |
| occurrences causally related to treatment / all                            | 0 / 1  | 0 / 0  |  |
| deaths causally related to treatment / all                                 | 0 / 0  | 0 / 0  |  |
| <b>MYELODYSPLASTIC SYNDROME</b>  |  |  |  |

|  |                |                |  |
|--|----------------|----------------|--|
| subjects affected / exposed                          | 1 / 36 (2.78%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| PROSTATE CANCER                                      |                |                |  |
| subjects affected / exposed                          | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| SQUAMOUS CELL CARCINOMA                              |                |                |  |
| subjects affected / exposed                          | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| SQUAMOUS CELL CARCINOMA OF SKIN                      |                |                |  |
| subjects affected / exposed                          | 1 / 36 (2.78%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Vascular disorders                                   |                |                |  |
| ACCELERATED HYPERTENSION                             |                |                |  |
| subjects affected / exposed                          | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| DEEP VEIN THROMBOSIS                                 |                |                |  |
| subjects affected / exposed                          | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| PHLEBITIS  |                |                |  |
| subjects affected / exposed                          | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| PHLEBITIS SUPERFICIAL                                |                |                |  |
| subjects affected / exposed                          | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| General disorders and administration site conditions |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| CHEST PAIN                                      |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| MULTIPLE ORGAN DYSFUNCTION SYNDROME             |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| PYREXIA   |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 2 / 37 (5.41%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Immune system disorders                         |                |                |  |
| ANAPHYLACTIC REACTION                           |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 0 / 37 (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        |                |                |  |
| BENIGN PROSTATIC HYPERPLASIA                    |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| PROSTATITIS                                     |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders |                |                |  |
| ACUTE RESPIRATORY FAILURE                       |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| ASTHMA  |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                           | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          |  |
| <b>LUNG DISORDER</b>                                  |                |                |  |
| subjects affected / exposed                           | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          |  |
| <b>PNEUMONITIS</b>                                    |                |                |  |
| subjects affected / exposed                           | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          |  |
| <b>PULMONARY EMBOLISM</b>                             |                |                |  |
| subjects affected / exposed                           | 1 / 36 (2.78%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all       | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          |  |
| <b>STRIDOR</b>  |                |                |  |
| subjects affected / exposed                           | 0 / 36 (0.00%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          |  |
| <b>Psychiatric disorders</b>                          |                |                |  |
| <b>CONFUSIONAL STATE</b>                              |                |                |  |
| subjects affected / exposed                           | 0 / 36 (0.00%) | 2 / 37 (5.41%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          |  |
| <b>Injury, poisoning and procedural complications</b> |                |                |  |
| <b>GASTROENTERITIS RADIATION</b>                      |                |                |  |
| subjects affected / exposed                           | 0 / 36 (0.00%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          |  |
| <b>Cardiac disorders</b>                              |                |                |  |
| <b>ANGINA PECTORIS</b>                                |                |                |  |
| subjects affected / exposed                           | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          |  |

|   |                |                |  |
|---|----------------|----------------|--|
| ATRIAL FIBRILLATION                             |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| BRADYCARDIA                                     |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| TACHYCARDIA                                     |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Nervous system disorders                        |                |                |  |
| CEREBROVASCULAR ACCIDENT                        |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| GENERALISED TONIC-CLONIC SEIZURE                |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| SYNCOPE   |                |                |  |
| subjects affected / exposed                     | 2 / 36 (5.56%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| TRANSIENT GLOBAL AMNESIA                        |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| TRANSIENT ISCHAEMIC ATTACK                      |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |



|   |                |                |  |
|---|----------------|----------------|--|
| Blood and lymphatic system disorders            |                |                |  |
| FEBRILE NEUTROPENIA                             |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 2 / 37 (5.41%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| LYMPHOPENIA                                     |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| NEUTROPENIA                                     |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| PANCYTOPENIA                                    |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                      |                |                |  |
| CONSTIPATION                                    |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| DIARRHOEA                                       |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| DIVERTICULAR PERFORATION                        |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| GASTROINTESTINAL HAEMORRHAGE                    |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

|  |   |                |                |  |
|--|---|----------------|----------------|--|
| GASTROINTESTINAL PERFORATION           | subjects affected / exposed                     | 0 / 36 (0.00%) | 0 / 37 (0.00%) |  |
|  | occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
|  | deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| HAEMATEMESIS                           | subjects affected / exposed                     | 0 / 36 (0.00%) | 0 / 37 (0.00%) |  |
|  | occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
|  | deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| NAUSEA                                 | subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
|  | occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
|  | deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| VARICES OESOPHAGEAL                    | subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
|  | occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
|  | deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| VOMITING                               | subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
|  | occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
|  | deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatobiliary disorders                |   |                |                |  |
| CHOLECYSTITIS                          | subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
|  | occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
|  | deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Skin and subcutaneous tissue disorders |   |                |                |  |
| RASH                                   | subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
|  | occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
|  | deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Renal and urinary disorders            |   |                |                |  |
| ACUTE KIDNEY INJURY                    |   |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| RENAL COLIC                                     |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| RENAL FAILURE                                   |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 2 / 37 (5.41%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| ARTHRALGIA                                      |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| BACK PAIN                                       |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| BONE PAIN                                       |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| MUSCULOSKELETAL PAIN                            |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| PAIN IN EXTREMITY                               |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |

|   |                |                |  |
|---|----------------|----------------|--|
| ASPERGILLUS INFECTION                           |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| BRONCHITIS                                      |                |                |  |
| subjects affected / exposed                     | 2 / 36 (5.56%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| CELLULITIS                                      |                |                |  |
| subjects affected / exposed                     | 2 / 36 (5.56%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| CLOSTRIDIUM DIFFICILE COLITIS                   |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| H1N1 INFLUENZA                                  |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| HERPES ZOSTER                                   |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| INFLUENZA                                       |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| LOCALISED INFECTION                             |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| LUNG INFECTION                                  |                |                |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 36 (0.00%)  | 1 / 37 (2.70%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| MENINGITIS                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 36 (0.00%)  | 1 / 37 (2.70%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| PNEUMONIA                                       |                 |                 |  |
| subjects affected / exposed                     | 4 / 36 (11.11%) | 5 / 37 (13.51%) |  |
| occurrences causally related to treatment / all | 0 / 5           | 1 / 5           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           |  |
| PNEUMONIA KLEBSIELLA                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 36 (0.00%)  | 1 / 37 (2.70%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| PNEUMONIA VIRAL                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 36 (2.78%)  | 0 / 37 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| POSTOPERATIVE WOUND INFECTION                   |                 |                 |  |
| subjects affected / exposed                     | 1 / 36 (2.78%)  | 0 / 37 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| PYELONEPHRITIS                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 36 (0.00%)  | 1 / 37 (2.70%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| SEPSIS  |                 |                 |  |
| subjects affected / exposed                     | 3 / 36 (8.33%)  | 2 / 37 (5.41%)  |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 2           |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 1           |  |
| URINARY TRACT INFECTION                         |                 |                 |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 36 (0.00%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| VISCERAL LEISHMANIASIS                          |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Metabolism and nutrition disorders              |                |                |  |
| ELECTROLYTE IMBALANCE                           |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| HYPERCALCAEMIA                                  |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 1 / 37 (2.70%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| HYPOKALAEMIA                                    |                |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| METABOLIC ACIDOSIS                              |                |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%) | 0 / 37 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                                   | Elotuzumab 5 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 1) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 1) |
|---|---|--|--|
| Total subjects affected by non-serious adverse events               |   |  |  |
| subjects affected / exposed   | 3 / 3 (100.00%)   | 3 / 3 (100.00%)  | 22 / 22 (100.00%)  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |  |  |

|  |                     |                     |                       |
|--|---------------------|---------------------|-----------------------|
| BASAL CELL CARCINOMA<br>subjects affected / exposed<br>occurrences (all)         | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0   |
| Vascular disorders   |                     |                     |                       |
| DEEP VEIN THROMBOSIS<br>subjects affected / exposed<br>occurrences (all)         | 1 / 3 (33.33%)<br>1 | 0 / 3 (0.00%)<br>0  | 3 / 22 (13.64%)<br>4  |
| FLUSHING<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 1 / 22 (4.55%)<br>1   |
| HOT FLUSH<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 3 (0.00%)<br>0  | 1 / 3 (33.33%)<br>1 | 2 / 22 (9.09%)<br>2   |
| HYPERTENSION<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 2 / 22 (9.09%)<br>2   |
| HYPOTENSION<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 3 / 22 (13.64%)<br>4  |
| PHLEBITIS SUPERFICIAL<br>subjects affected / exposed<br>occurrences (all)        | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0   |
| THROMBOPHLEBITIS SUPERFICIAL<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0   |
| General disorders and administration<br>site conditions                          |                     |                     |                       |
| ASTHENIA<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 3 (0.00%)<br>0  | 1 / 3 (33.33%)<br>1 | 6 / 22 (27.27%)<br>12 |
| CHEST DISCOMFORT<br>subjects affected / exposed<br>occurrences (all)             | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 1 / 22 (4.55%)<br>1   |
| CHEST PAIN<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 3 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 1 / 22 (4.55%)<br>1   |
| CHILLS   |                     |                     |                       |

|                             |                |                |                  |
|-----------------------------|----------------|----------------|------------------|
| subjects affected / exposed | 2 / 3 (66.67%) | 2 / 3 (66.67%) | 1 / 22 (4.55%)   |
| occurrences (all)           | 2              | 3              | 1                |
| FATIGUE                     |                |                |                  |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 3 (66.67%) | 15 / 22 (68.18%) |
| occurrences (all)           | 1              | 2              | 21               |
| FEELING HOT                 |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |
| GAIT DISTURBANCE            |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)   |
| occurrences (all)           | 0              | 0              | 1                |
| INFLAMMATION                |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |
| INFLUENZA LIKE ILLNESS      |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 2 / 22 (9.09%)   |
| occurrences (all)           | 0              | 0              | 2                |
| IRRITABILITY                |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |
| NON-CARDIAC CHEST PAIN      |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)   |
| occurrences (all)           | 0              | 0              | 1                |
| OEDEMA                      |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |
| OEDEMA PERIPHERAL           |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 3 (33.33%) | 6 / 22 (27.27%)  |
| occurrences (all)           | 0              | 2              | 15               |
| PAIN                        |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 4 / 22 (18.18%)  |
| occurrences (all)           | 0              | 0              | 4                |
| PERIPHERAL SWELLING         |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 2 / 22 (9.09%)   |
| occurrences (all)           | 0              | 0              | 2                |
| PYREXIA                     |                |                |                  |



|  |                    |                     |                        |
|--|--------------------|---------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 10 / 22 (45.45%)<br>21 |
| Immune system disorders<br>DRUG HYPERSENSITIVITY<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 3 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0    |
| SEASONAL ALLERGY<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 1 / 3 (33.33%)<br>1 | 1 / 22 (4.55%)<br>2    |
| Reproductive system and breast disorders<br>BENIGN PROSTATIC HYPERPLASIA<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0    |
| VULVOVAGINAL PRURITUS<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0    |
| Respiratory, thoracic and mediastinal disorders<br>ASTHMA<br>subjects affected / exposed<br>occurrences (all)                | 0 / 3 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 22 (0.00%)<br>0    |
| COUGH<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 7 / 22 (31.82%)<br>11  |
| DYSPHONIA<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 1 / 22 (4.55%)<br>1    |
| DYSPNOEA<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 5 / 22 (22.73%)<br>7   |
| DYSPNOEA EXERTIONAL<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 2 / 22 (9.09%)<br>2    |
| EPISTAXIS<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 1 / 22 (4.55%)<br>1    |
| HICCUPS  |                    |                     |                        |

|                                   |               |                |                 |
|-----------------------------------|---------------|----------------|-----------------|
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0               |
| LUNG DISORDER                     |               |                |                 |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)                 | 0             | 0              | 3               |
| NASAL CONGESTION                  |               |                |                 |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)                 | 0             | 0              | 2               |
| OROPHARYNGEAL PAIN                |               |                |                 |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)                 | 0             | 0              | 2               |
| PARANASAL SINUS<br>HYPERSECRETION |               |                |                 |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)                 | 0             | 0              | 2               |
| PRODUCTIVE COUGH                  |               |                |                 |
| subjects affected / exposed       | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 22 (0.00%)  |
| occurrences (all)                 | 0             | 1              | 0               |
| PULMONARY EMBOLISM                |               |                |                 |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)                 | 0             | 0              | 1               |
| RALES                             |               |                |                 |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                 | 0             | 0              | 0               |
| RHINORRHOEA                       |               |                |                 |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 4 / 22 (18.18%) |
| occurrences (all)                 | 0             | 0              | 5               |
| SINUS CONGESTION                  |               |                |                 |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)                 | 0             | 0              | 1               |
| THROAT IRRITATION                 |               |                |                 |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)                 | 0             | 0              | 2               |
| UPPER-AIRWAY COUGH SYNDROME       |               |                |                 |
| subjects affected / exposed       | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)                 | 0             | 0              | 2               |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| Psychiatric disorders                                 |                |                |                 |
| AGGRESSION  |                |                |                 |
| subjects affected / exposed                           | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                                     | 0              | 0              | 0               |
| ANXIETY   |                |                |                 |
| subjects affected / exposed                           | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 4 / 22 (18.18%) |
| occurrences (all)                                     | 0              | 0              | 4               |
| CONFUSIONAL STATE                                     |                |                |                 |
| subjects affected / exposed                           | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                                     | 0              | 0              | 0               |
| DEPRESSED MOOD  |                |                |                 |
| subjects affected / exposed                           | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                                     | 0              | 0              | 0               |
| DEPRESSION  |                |                |                 |
| subjects affected / exposed                           | 1 / 3 (33.33%) | 0 / 3 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)                                     | 1              | 0              | 2               |
| INSOMNIA  |                |                |                 |
| subjects affected / exposed                           | 2 / 3 (66.67%) | 1 / 3 (33.33%) | 7 / 22 (31.82%) |
| occurrences (all)                                     | 2              | 1              | 9               |
| MOOD SWINGS   |                |                |                 |
| subjects affected / exposed                           | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)                                     | 0              | 0              | 2               |
| Investigations  |                |                |                 |
| ACTIVATED PARTIAL<br>THROMBOPLASTIN TIME<br>PROLONGED |                |                |                 |
| subjects affected / exposed                           | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                                     | 0              | 0              | 0               |
| ALANINE AMINOTRANSFERASE<br>INCREASED                 |                |                |                 |
| subjects affected / exposed                           | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)                                     | 0              | 0              | 1               |
| ASPARTATE AMINOTRANSFERASE<br>INCREASED               |                |                |                 |
| subjects affected / exposed                           | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                                     | 0              | 0              | 0               |
| BLOOD ALKALINE PHOSPHATASE<br>INCREASED               |                |                |                 |

|  |               |                |                |
|--|---------------|----------------|----------------|
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 2 / 22 (9.09%) |
| occurrences (all)                        | 0             | 0              | 2              |
| BLOOD BICARBONATE DECREASED              |               |                |                |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0              |
| BLOOD CREATININE INCREASED               |               |                |                |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 2 / 22 (9.09%) |
| occurrences (all)                        | 0             | 0              | 2              |
| BLOOD LACTATE DEHYDROGENASE INCREASED    |               |                |                |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0              |
| BLOOD MAGNESIUM DECREASED                |               |                |                |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%) |
| occurrences (all)                        | 0             | 0              | 1              |
| BLOOD PHOSPHORUS DECREASED               |               |                |                |
| subjects affected / exposed              | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 1 / 22 (4.55%) |
| occurrences (all)                        | 0             | 1              | 1              |
| BLOOD POTASSIUM DECREASED                |               |                |                |
| subjects affected / exposed              | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 1 / 22 (4.55%) |
| occurrences (all)                        | 0             | 1              | 1              |
| BLOOD UREA INCREASED                     |               |                |                |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0              |
| CARDIAC MURMUR                           |               |                |                |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0              |
| EJECTION FRACTION DECREASED              |               |                |                |
| subjects affected / exposed              | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                        | 0             | 0              | 0              |
| IMMUNOGLOBULINS DECREASED                |               |                |                |
| subjects affected / exposed              | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 22 (0.00%) |
| occurrences (all)                        | 0             | 1              | 0              |
| INTERNATIONAL NORMALISED RATIO INCREASED |               |                |                |

|  |               |               |                 |
|--|---------------|---------------|-----------------|
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0               |
| NEUTROPHIL COUNT INCREASED                     |               |               |                 |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0               |
| PROTEIN TOTAL INCREASED                        |               |               |                 |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0               |
| PROTHROMBIN TIME PROLONGED                     |               |               |                 |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0               |
| WEIGHT DECREASED                               |               |               |                 |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 3 / 22 (13.64%) |
| occurrences (all)                              | 0             | 0             | 3               |
| WEIGHT INCREASED                               |               |               |                 |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 22 (9.09%)  |
| occurrences (all)                              | 0             | 0             | 2               |
| WHITE BLOOD CELL COUNT DECREASED               |               |               |                 |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 22 (4.55%)  |
| occurrences (all)                              | 0             | 0             | 2               |
| Injury, poisoning and procedural complications |               |               |                 |
| ARTHROPOD BITE                                 |               |               |                 |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0               |
| CONTUSION                                      |               |               |                 |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 22 (4.55%)  |
| occurrences (all)                              | 0             | 0             | 1               |
| FALL   |               |               |                 |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 3 / 22 (13.64%) |
| occurrences (all)                              | 0             | 0             | 6               |
| JOINT DISLOCATION                              |               |               |                 |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 0 / 22 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0               |
| LIGAMENT SPRAIN                                |               |               |                 |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 3 (33.33%) | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| SKIN ABRASION               |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0              | 0              | 1               |
| STOMA SITE PAIN             |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 3 (33.33%) | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| SUNBURN                     |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Cardiac disorders           |                |                |                 |
| ATRIAL FIBRILLATION         |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 3 (33.33%) | 1 / 22 (4.55%)  |
| occurrences (all)           | 0              | 1              | 1               |
| PALPITATIONS                |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)           | 0              | 0              | 2               |
| Nervous system disorders    |                |                |                 |
| AMNESIA                     |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0              | 0              | 1               |
| BALANCE DISORDER            |                |                |                 |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| CARPAL TUNNEL SYNDROME      |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)           | 0              | 0              | 2               |
| DISTURBANCE IN ATTENTION    |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)           | 0              | 0              | 2               |
| DIZZINESS                   |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 4 / 22 (18.18%) |
| occurrences (all)           | 0              | 0              | 6               |
| DYSGEUSIA                   |                |                |                 |

|                               |                |               |                 |
|-------------------------------|----------------|---------------|-----------------|
| subjects affected / exposed   | 0 / 3 (0.00%)  | 0 / 3 (0.00%) | 2 / 22 (9.09%)  |
| occurrences (all)             | 0              | 0             | 2               |
| HEADACHE                      |                |               |                 |
| subjects affected / exposed   | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 5 / 22 (22.73%) |
| occurrences (all)             | 1              | 0             | 8               |
| HYPOAESTHESIA                 |                |               |                 |
| subjects affected / exposed   | 0 / 3 (0.00%)  | 0 / 3 (0.00%) | 1 / 22 (4.55%)  |
| occurrences (all)             | 0              | 0             | 1               |
| HYPOGEUSIA                    |                |               |                 |
| subjects affected / exposed   | 0 / 3 (0.00%)  | 0 / 3 (0.00%) | 0 / 22 (0.00%)  |
| occurrences (all)             | 0              | 0             | 0               |
| MEMORY IMPAIRMENT             |                |               |                 |
| subjects affected / exposed   | 0 / 3 (0.00%)  | 0 / 3 (0.00%) | 2 / 22 (9.09%)  |
| occurrences (all)             | 0              | 0             | 2               |
| NEURALGIA                     |                |               |                 |
| subjects affected / exposed   | 0 / 3 (0.00%)  | 0 / 3 (0.00%) | 0 / 22 (0.00%)  |
| occurrences (all)             | 0              | 0             | 0               |
| NEUROPATHY PERIPHERAL         |                |               |                 |
| subjects affected / exposed   | 0 / 3 (0.00%)  | 0 / 3 (0.00%) | 7 / 22 (31.82%) |
| occurrences (all)             | 0              | 0             | 10              |
| PARAESTHESIA                  |                |               |                 |
| subjects affected / exposed   | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 3 / 22 (13.64%) |
| occurrences (all)             | 1              | 0             | 3               |
| PERIPHERAL SENSORY NEUROPATHY |                |               |                 |
| subjects affected / exposed   | 0 / 3 (0.00%)  | 0 / 3 (0.00%) | 1 / 22 (4.55%)  |
| occurrences (all)             | 0              | 0             | 1               |
| PSYCHOMOTOR HYPERACTIVITY     |                |               |                 |
| subjects affected / exposed   | 0 / 3 (0.00%)  | 0 / 3 (0.00%) | 0 / 22 (0.00%)  |
| occurrences (all)             | 0              | 0             | 0               |
| SCIATICA                      |                |               |                 |
| subjects affected / exposed   | 0 / 3 (0.00%)  | 0 / 3 (0.00%) | 0 / 22 (0.00%)  |
| occurrences (all)             | 0              | 0             | 0               |
| SINUS HEADACHE                |                |               |                 |
| subjects affected / exposed   | 0 / 3 (0.00%)  | 0 / 3 (0.00%) | 1 / 22 (4.55%)  |
| occurrences (all)             | 0              | 0             | 1               |
| SOMNOLENCE                    |                |               |                 |

|                                      |                |                 |                  |
|--------------------------------------|----------------|-----------------|------------------|
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   | 0 / 22 (0.00%)   |
| occurrences (all)                    | 0              | 0               | 0                |
| SYNCOPE                              |                |                 |                  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   | 1 / 22 (4.55%)   |
| occurrences (all)                    | 0              | 0               | 1                |
| TREMOR                               |                |                 |                  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   | 0 / 22 (0.00%)   |
| occurrences (all)                    | 0              | 0               | 0                |
| Blood and lymphatic system disorders |                |                 |                  |
| ANAEMIA                              |                |                 |                  |
| subjects affected / exposed          | 2 / 3 (66.67%) | 2 / 3 (66.67%)  | 10 / 22 (45.45%) |
| occurrences (all)                    | 2              | 3               | 17               |
| FEBRILE NEUTROPENIA                  |                |                 |                  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 3 (33.33%)  | 1 / 22 (4.55%)   |
| occurrences (all)                    | 0              | 1               | 2                |
| HAEMOGLOBINAEMIA                     |                |                 |                  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 3 (33.33%)  | 0 / 22 (0.00%)   |
| occurrences (all)                    | 0              | 1               | 0                |
| INCREASED TENDENCY TO BRUISE         |                |                 |                  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   | 0 / 22 (0.00%)   |
| occurrences (all)                    | 0              | 0               | 0                |
| IRON DEFICIENCY ANAEMIA              |                |                 |                  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   | 0 / 22 (0.00%)   |
| occurrences (all)                    | 0              | 0               | 0                |
| LEUKOPENIA                           |                |                 |                  |
| subjects affected / exposed          | 1 / 3 (33.33%) | 1 / 3 (33.33%)  | 2 / 22 (9.09%)   |
| occurrences (all)                    | 1              | 3               | 2                |
| LYMPHADENOPATHY                      |                |                 |                  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 0 / 3 (0.00%)   | 0 / 22 (0.00%)   |
| occurrences (all)                    | 0              | 0               | 0                |
| LYMPHOPENIA                          |                |                 |                  |
| subjects affected / exposed          | 0 / 3 (0.00%)  | 1 / 3 (33.33%)  | 1 / 22 (4.55%)   |
| occurrences (all)                    | 0              | 2               | 1                |
| NEUTROPENIA                          |                |                 |                  |
| subjects affected / exposed          | 2 / 3 (66.67%) | 3 / 3 (100.00%) | 7 / 22 (31.82%)  |
| occurrences (all)                    | 3              | 8               | 11               |



|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| PANCYTOPENIA                |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| THROMBOCYTOPENIA            |                |                |                 |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 3 (66.67%) | 5 / 22 (22.73%) |
| occurrences (all)           | 3              | 3              | 5               |
| Ear and labyrinth disorders |                |                |                 |
| HYPOACUSIS                  |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0              | 0              | 1               |
| TINNITUS                    |                |                |                 |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 1              | 0              | 1               |
| VERTIGO                     |                |                |                 |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 2              | 0              | 0               |
| Eye disorders               |                |                |                 |
| CATARACT                    |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)           | 0              | 0              | 2               |
| DRY EYE                     |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0              | 0              | 1               |
| EYE IRRITATION              |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0              | 0              | 1               |
| OCULAR HYPERAEMIA           |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| VISION BLURRED              |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 4 / 22 (18.18%) |
| occurrences (all)           | 0              | 0              | 4               |
| VISUAL ACUITY REDUCED       |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| VITREOUS FLOATERS           |                |                |                 |

|  |                    |                    |                     |
|--|--------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 1 / 22 (4.55%)<br>1 |
| Gastrointestinal disorders                       |                    |                    |                     |
| ABDOMINAL DISTENSION                             |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 1 / 22 (4.55%)      |
| occurrences (all)                                | 0                  | 0                  | 1                   |
| ABDOMINAL PAIN                                   |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 1 / 22 (4.55%)      |
| occurrences (all)                                | 0                  | 0                  | 1                   |
| ABDOMINAL PAIN UPPER                             |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 0 / 22 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                   |
| CONSTIPATION                                     |                    |                    |                     |
| subjects affected / exposed                      | 1 / 3 (33.33%)     | 2 / 3 (66.67%)     | 11 / 22 (50.00%)    |
| occurrences (all)                                | 2                  | 2                  | 13                  |
| DIARRHOEA  |                    |                    |                     |
| subjects affected / exposed                      | 1 / 3 (33.33%)     | 2 / 3 (66.67%)     | 14 / 22 (63.64%)    |
| occurrences (all)                                | 1                  | 3                  | 29                  |
| DIVERTICULAR PERFORATION                         |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 1 / 3 (33.33%)     | 0 / 22 (0.00%)      |
| occurrences (all)                                | 0                  | 1                  | 0                   |
| DRY MOUTH  |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 0 / 22 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                   |
| DYSPEPSIA  |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 1 / 22 (4.55%)      |
| occurrences (all)                                | 0                  | 0                  | 1                   |
| FLATULENCE                                       |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 2 / 22 (9.09%)      |
| occurrences (all)                                | 0                  | 0                  | 2                   |
| GASTROINTESTINAL HAEMORRHAGE                     |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 1 / 3 (33.33%)     | 0 / 22 (0.00%)      |
| occurrences (all)                                | 0                  | 1                  | 0                   |
| GASTROINTESTINAL MOTILITY<br>DISORDER            |                    |                    |                     |

|                                  |               |                 |                  |
|----------------------------------|---------------|-----------------|------------------|
| subjects affected / exposed      | 0 / 3 (0.00%) | 0 / 3 (0.00%)   | 2 / 22 (9.09%)   |
| occurrences (all)                | 0             | 0               | 3                |
| GASTROINTESTINAL PERFORATION     |               |                 |                  |
| subjects affected / exposed      | 0 / 3 (0.00%) | 1 / 3 (33.33%)  | 0 / 22 (0.00%)   |
| occurrences (all)                | 0             | 1               | 0                |
| GASTROOESOPHAGEAL REFLUX DISEASE |               |                 |                  |
| subjects affected / exposed      | 0 / 3 (0.00%) | 0 / 3 (0.00%)   | 1 / 22 (4.55%)   |
| occurrences (all)                | 0             | 0               | 1                |
| HAEMATOCHESIA                    |               |                 |                  |
| subjects affected / exposed      | 0 / 3 (0.00%) | 0 / 3 (0.00%)   | 0 / 22 (0.00%)   |
| occurrences (all)                | 0             | 0               | 0                |
| HAEMORRHOIDS                     |               |                 |                  |
| subjects affected / exposed      | 0 / 3 (0.00%) | 1 / 3 (33.33%)  | 2 / 22 (9.09%)   |
| occurrences (all)                | 0             | 1               | 2                |
| NAUSEA                           |               |                 |                  |
| subjects affected / exposed      | 0 / 3 (0.00%) | 3 / 3 (100.00%) | 11 / 22 (50.00%) |
| occurrences (all)                | 0             | 4               | 13               |
| PARAESTHESIA ORAL                |               |                 |                  |
| subjects affected / exposed      | 0 / 3 (0.00%) | 0 / 3 (0.00%)   | 0 / 22 (0.00%)   |
| occurrences (all)                | 0             | 0               | 0                |
| STOMATITIS                       |               |                 |                  |
| subjects affected / exposed      | 0 / 3 (0.00%) | 1 / 3 (33.33%)  | 1 / 22 (4.55%)   |
| occurrences (all)                | 0             | 1               | 1                |
| TOOTH DISORDER                   |               |                 |                  |
| subjects affected / exposed      | 0 / 3 (0.00%) | 0 / 3 (0.00%)   | 0 / 22 (0.00%)   |
| occurrences (all)                | 0             | 0               | 0                |
| TOOTHACHE                        |               |                 |                  |
| subjects affected / exposed      | 0 / 3 (0.00%) | 0 / 3 (0.00%)   | 2 / 22 (9.09%)   |
| occurrences (all)                | 0             | 0               | 2                |
| VOMITING                         |               |                 |                  |
| subjects affected / exposed      | 0 / 3 (0.00%) | 0 / 3 (0.00%)   | 6 / 22 (27.27%)  |
| occurrences (all)                | 0             | 0               | 6                |
| Hepatobiliary disorders          |               |                 |                  |
| HYPERBILIRUBINAEMIA              |               |                 |                  |

|  |                    |                    |                     |
|--|--------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0 | 1 / 22 (4.55%)<br>1 |
| Skin and subcutaneous tissue disorders           |                    |                    |                     |
| ALOPECIA   |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 0 / 22 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                   |
| BLISTER  |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 0 / 22 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                   |
| DRY SKIN   |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 2 / 22 (9.09%)      |
| occurrences (all)                                | 0                  | 0                  | 2                   |
| ECCHYMOSIS                                       |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 1 / 22 (4.55%)      |
| occurrences (all)                                | 0                  | 0                  | 1                   |
| ERYTHEMA   |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 2 / 22 (9.09%)      |
| occurrences (all)                                | 0                  | 0                  | 2                   |
| HYPERHIDROSIS                                    |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 3 / 22 (13.64%)     |
| occurrences (all)                                | 0                  | 0                  | 5                   |
| INGROWING NAIL                                   |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 2 / 22 (9.09%)      |
| occurrences (all)                                | 0                  | 0                  | 3                   |
| NIGHT SWEATS                                     |                    |                    |                     |
| subjects affected / exposed                      | 0 / 3 (0.00%)      | 0 / 3 (0.00%)      | 1 / 22 (4.55%)      |
| occurrences (all)                                | 0                  | 0                  | 1                   |
| PRURITUS   |                    |                    |                     |
| subjects affected / exposed                      | 1 / 3 (33.33%)     | 0 / 3 (0.00%)      | 2 / 22 (9.09%)      |
| occurrences (all)                                | 1                  | 0                  | 2                   |
| RASH   |                    |                    |                     |
| subjects affected / exposed                      | 1 / 3 (33.33%)     | 1 / 3 (33.33%)     | 3 / 22 (13.64%)     |
| occurrences (all)                                | 1                  | 1                  | 7                   |
| RASH GENERALISED                                 |                    |                    |                     |
| subjects affected / exposed                      | 1 / 3 (33.33%)     | 0 / 3 (0.00%)      | 1 / 22 (4.55%)      |
| occurrences (all)                                | 1                  | 0                  | 1                   |

|   |               |                |                |
|---|---------------|----------------|----------------|
| RASH MACULAR                                    |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 22 (0.00%) |
| occurrences (all)                               | 0             | 1              | 0              |
| RASH MACULO-PAPULAR                             |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%) |
| occurrences (all)                               | 0             | 0              | 1              |
| SCAB  |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| SKIN DISCOLOURATION                             |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| SKIN LESION                                     |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 2 / 22 (9.09%) |
| occurrences (all)                               | 0             | 0              | 2              |
| URTICARIA                                       |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 2 / 22 (9.09%) |
| occurrences (all)                               | 0             | 0              | 3              |
| Renal and urinary disorders                     |               |                |                |
| ACUTE KIDNEY INJURY                             |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 22 (0.00%) |
| occurrences (all)                               | 0             | 1              | 0              |
| DYSURIA   |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%) |
| occurrences (all)                               | 0             | 0              | 1              |
| HAEMATURIA                                      |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| POLLAKIURIA                                     |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| RENAL FAILURE                                   |               |                |                |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| Musculoskeletal and connective tissue disorders |               |                |                |

|                             |                |                |                  |
|-----------------------------|----------------|----------------|------------------|
| ARTHRALGIA                  |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 2 / 3 (66.67%) | 7 / 22 (31.82%)  |
| occurrences (all)           | 0              | 2              | 12               |
| BACK PAIN                   |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 3 (33.33%) | 7 / 22 (31.82%)  |
| occurrences (all)           | 0              | 1              | 11               |
| BONE PAIN                   |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 2 / 22 (9.09%)   |
| occurrences (all)           | 0              | 0              | 3                |
| MUSCLE SPASMS               |                |                |                  |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 10 / 22 (45.45%) |
| occurrences (all)           | 2              | 1              | 12               |
| MUSCULAR WEAKNESS           |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)   |
| occurrences (all)           | 0              | 0              | 1                |
| MUSCULOSKELETAL CHEST PAIN  |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 5 / 22 (22.73%)  |
| occurrences (all)           | 0              | 0              | 8                |
| MUSCULOSKELETAL DISCOMFORT  |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |
| MUSCULOSKELETAL PAIN        |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 3 / 22 (13.64%)  |
| occurrences (all)           | 0              | 0              | 3                |
| MUSCULOSKELETAL STIFFNESS   |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |
| MYALGIA                     |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 3 / 22 (13.64%)  |
| occurrences (all)           | 0              | 0              | 3                |
| NECK PAIN                   |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)   |
| occurrences (all)           | 0              | 0              | 1                |
| OSTEONECROSIS OF JAW        |                |                |                  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)   |
| occurrences (all)           | 0              | 0              | 0                |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| PAIN IN EXTREMITY           |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 3 (33.33%) | 5 / 22 (22.73%) |
| occurrences (all)           | 0              | 1              | 6               |
| PAIN IN JAW                 |                |                |                 |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 1              | 0              | 2               |
| Infections and infestations |                |                |                 |
| BRONCHITIS                  |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 5 / 22 (22.73%) |
| occurrences (all)           | 0              | 0              | 14              |
| CELLULITIS                  |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| CONJUNCTIVITIS              |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 4 / 22 (18.18%) |
| occurrences (all)           | 0              | 0              | 4               |
| EAR INFECTION               |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| FUNGAL INFECTION            |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 3 (33.33%) | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| GASTROENTERITIS             |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| GASTROENTERITIS VIRAL       |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0              | 0              | 1               |
| GINGIVITIS                  |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 2 / 22 (9.09%)  |
| occurrences (all)           | 0              | 0              | 2               |
| HERPES ZOSTER               |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| INFLUENZA                   |                |                |                 |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0              | 0              | 1               |
| LOCALISED INFECTION         |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0              | 0              | 1               |
| LUNG INFECTION              |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| NASOPHARYNGITIS             |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 3 / 22 (13.64%) |
| occurrences (all)           | 0              | 0              | 4               |
| ORAL CANDIDIASIS            |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 1 / 3 (33.33%) | 1 / 22 (4.55%)  |
| occurrences (all)           | 0              | 1              | 2               |
| ORAL HERPES                 |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| PHARYNGITIS                 |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| PNEUMONIA                   |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 4 / 22 (18.18%) |
| occurrences (all)           | 0              | 0              | 5               |
| PNEUMONIA VIRAL             |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| RHINITIS                    |                |                |                 |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 1              | 0              | 1               |
| SEPSIS                      |                |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0              | 0              | 1               |
| SINUSITIS                   |                |                |                 |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%)  | 3 / 22 (13.64%) |
| occurrences (all)           | 1              | 0              | 8               |
| UPPER RESPIRATORY TRACT     |                |                |                 |



|   |               |                |                 |
|---|---------------|----------------|-----------------|
| INFECTION                                   |               |                |                 |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 7 / 22 (31.82%) |
| occurrences (all)                           | 0             | 2              | 44              |
| UPPER RESPIRATORY TRACT INFECTION BACTERIAL |               |                |                 |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 22 (0.00%)  |
| occurrences (all)                           | 0             | 1              | 0               |
| URINARY TRACT INFECTION                     |               |                |                 |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 4 / 22 (18.18%) |
| occurrences (all)                           | 0             | 0              | 19              |
| VIRAL INFECTION                             |               |                |                 |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 1 / 22 (4.55%)  |
| occurrences (all)                           | 0             | 1              | 1               |
| VIRAL UPPER RESPIRATORY TRACT INFECTION     |               |                |                 |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)                           | 0             | 0              | 1               |
| Metabolism and nutrition disorders          |               |                |                 |
| DECREASED APPETITE                          |               |                |                 |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 3 / 22 (13.64%) |
| occurrences (all)                           | 0             | 0              | 3               |
| DEHYDRATION                                 |               |                |                 |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)                           | 0             | 0              | 1               |
| DIABETES MELLITUS                           |               |                |                 |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                           | 0             | 0              | 0               |
| GOUT  |               |                |                 |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)                           | 0             | 0              | 1               |
| HYPERCALCAEMIA                              |               |                |                 |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)                           | 0             | 0              | 0               |
| HYPERGLYCAEMIA                              |               |                |                 |
| subjects affected / exposed                 | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 3 / 22 (13.64%) |
| occurrences (all)                           | 0             | 0              | 4               |
| HYPERKALAEMIA                               |               |                |                 |

|                             |               |                |                 |
|-----------------------------|---------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0             | 0              | 1               |
| HYPERNATRAEMIA              |               |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| HYPOALBUMINAEMIA            |               |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| HYPOCALCAEMIA               |               |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| HYPOKALAEMIA                |               |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 6 / 22 (27.27%) |
| occurrences (all)           | 0             | 2              | 13              |
| HYPOMAGNESAEMIA             |               |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| HYPONATRAEMIA               |               |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0             | 0              | 1               |
| HYPOPHOSPHATAEMIA           |               |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 0 / 22 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0               |
| METABOLIC ACIDOSIS          |               |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 22 (0.00%)  |
| occurrences (all)           | 0             | 2              | 0               |
| VITAMIN D DEFICIENCY        |               |                |                 |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%)  | 1 / 22 (4.55%)  |
| occurrences (all)           | 0             | 0              | 1               |

| <b>Non-serious adverse events</b>                                   | Elotuzumab 10 mg/kg + Lenalidomide and Dexamethasone (Phase 2) | Elotuzumab 20 mg/kg + Lenalidomide and Dexamethasone (Phase 2) |  |
|---|--|--|--|
| Total subjects affected by non-serious adverse events               |  |  |  |
| subjects affected / exposed   | 36 / 36 (100.00%)  | 37 / 37 (100.00%)  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |

|  |                       |                        |  |
|--|-----------------------|------------------------|--|
| BASAL CELL CARCINOMA<br>subjects affected / exposed<br>occurrences (all)         | 1 / 36 (2.78%)<br>1   | 2 / 37 (5.41%)<br>2    |  |
| Vascular disorders   |                       |                        |  |
| DEEP VEIN THROMBOSIS<br>subjects affected / exposed<br>occurrences (all)         | 2 / 36 (5.56%)<br>2   | 2 / 37 (5.41%)<br>2    |  |
| FLUSHING<br>subjects affected / exposed<br>occurrences (all)                     | 4 / 36 (11.11%)<br>5  | 2 / 37 (5.41%)<br>3    |  |
| HOT FLUSH<br>subjects affected / exposed<br>occurrences (all)                    | 2 / 36 (5.56%)<br>3   | 2 / 37 (5.41%)<br>3    |  |
| HYPERTENSION<br>subjects affected / exposed<br>occurrences (all)                 | 2 / 36 (5.56%)<br>2   | 2 / 37 (5.41%)<br>5    |  |
| HYPOTENSION<br>subjects affected / exposed<br>occurrences (all)                  | 4 / 36 (11.11%)<br>5  | 4 / 37 (10.81%)<br>8   |  |
| PHLEBITIS SUPERFICIAL<br>subjects affected / exposed<br>occurrences (all)        | 2 / 36 (5.56%)<br>2   | 0 / 37 (0.00%)<br>0    |  |
| THROMBOPHLEBITIS SUPERFICIAL<br>subjects affected / exposed<br>occurrences (all) | 2 / 36 (5.56%)<br>2   | 0 / 37 (0.00%)<br>0    |  |
| General disorders and administration<br>site conditions                          |                       |                        |  |
| ASTHENIA<br>subjects affected / exposed<br>occurrences (all)                     | 7 / 36 (19.44%)<br>10 | 12 / 37 (32.43%)<br>22 |  |
| CHEST DISCOMFORT<br>subjects affected / exposed<br>occurrences (all)             | 1 / 36 (2.78%)<br>2   | 2 / 37 (5.41%)<br>2    |  |
| CHEST PAIN<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 36 (0.00%)<br>0   | 3 / 37 (8.11%)<br>3    |  |
| CHILLS   |                       |                        |  |

|                             |                  |                  |
|-----------------------------|------------------|------------------|
| subjects affected / exposed | 6 / 36 (16.67%)  | 2 / 37 (5.41%)   |
| occurrences (all)           | 8                | 4                |
| FATIGUE                     |                  |                  |
| subjects affected / exposed | 24 / 36 (66.67%) | 18 / 37 (48.65%) |
| occurrences (all)           | 36               | 24               |
| FEELING HOT                 |                  |                  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 0 / 37 (0.00%)   |
| occurrences (all)           | 2                | 0                |
| GAIT DISTURBANCE            |                  |                  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 2 / 37 (5.41%)   |
| occurrences (all)           | 2                | 2                |
| INFLAMMATION                |                  |                  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 0 / 37 (0.00%)   |
| occurrences (all)           | 2                | 0                |
| INFLUENZA LIKE ILLNESS      |                  |                  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 0 / 37 (0.00%)   |
| occurrences (all)           | 2                | 0                |
| IRRITABILITY                |                  |                  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 1 / 37 (2.70%)   |
| occurrences (all)           | 3                | 1                |
| NON-CARDIAC CHEST PAIN      |                  |                  |
| subjects affected / exposed | 5 / 36 (13.89%)  | 2 / 37 (5.41%)   |
| occurrences (all)           | 5                | 2                |
| OEDEMA                      |                  |                  |
| subjects affected / exposed | 5 / 36 (13.89%)  | 1 / 37 (2.70%)   |
| occurrences (all)           | 8                | 1                |
| OEDEMA PERIPHERAL           |                  |                  |
| subjects affected / exposed | 14 / 36 (38.89%) | 9 / 37 (24.32%)  |
| occurrences (all)           | 23               | 14               |
| PAIN                        |                  |                  |
| subjects affected / exposed | 1 / 36 (2.78%)   | 5 / 37 (13.51%)  |
| occurrences (all)           | 1                | 5                |
| PERIPHERAL SWELLING         |                  |                  |
| subjects affected / exposed | 5 / 36 (13.89%)  | 7 / 37 (18.92%)  |
| occurrences (all)           | 14               | 9                |
| PYREXIA                     |                  |                  |

|  |                        |                        |  |
|--|------------------------|------------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 14 / 36 (38.89%)<br>22 | 17 / 37 (45.95%)<br>23 |  |
| Immune system disorders<br>DRUG HYPERSENSITIVITY<br>subjects affected / exposed<br>occurrences (all)                         | 2 / 36 (5.56%)<br>2    | 1 / 37 (2.70%)<br>1    |  |
| SEASONAL ALLERGY<br>subjects affected / exposed<br>occurrences (all)   | 3 / 36 (8.33%)<br>3    | 0 / 37 (0.00%)<br>0    |  |
| Reproductive system and breast disorders<br>BENIGN PROSTATIC HYPERPLASIA<br>subjects affected / exposed<br>occurrences (all) | 0 / 36 (0.00%)<br>0    | 3 / 37 (8.11%)<br>3    |  |
| VULVOVAGINAL PRURITUS<br>subjects affected / exposed<br>occurrences (all)  | 2 / 36 (5.56%)<br>2    | 0 / 37 (0.00%)<br>0    |  |
| Respiratory, thoracic and mediastinal disorders<br>ASTHMA<br>subjects affected / exposed<br>occurrences (all)                | 2 / 36 (5.56%)<br>2    | 0 / 37 (0.00%)<br>0    |  |
| COUGH<br>subjects affected / exposed<br>occurrences (all)  | 12 / 36 (33.33%)<br>20 | 13 / 37 (35.14%)<br>20 |  |
| DYSPHONIA<br>subjects affected / exposed<br>occurrences (all)  | 6 / 36 (16.67%)<br>7   | 3 / 37 (8.11%)<br>4    |  |
| DYSPNOEA<br>subjects affected / exposed<br>occurrences (all)   | 11 / 36 (30.56%)<br>15 | 10 / 37 (27.03%)<br>15 |  |
| DYSPNOEA EXERTIONAL<br>subjects affected / exposed<br>occurrences (all)  | 9 / 36 (25.00%)<br>11  | 5 / 37 (13.51%)<br>6   |  |
| EPISTAXIS<br>subjects affected / exposed<br>occurrences (all)  | 6 / 36 (16.67%)<br>6   | 6 / 37 (16.22%)<br>8   |  |
| HICCUPS  |                        |                        |  |

|                                   |                 |                 |
|-----------------------------------|-----------------|-----------------|
| subjects affected / exposed       | 1 / 36 (2.78%)  | 3 / 37 (8.11%)  |
| occurrences (all)                 | 1               | 3               |
| LUNG DISORDER                     |                 |                 |
| subjects affected / exposed       | 1 / 36 (2.78%)  | 2 / 37 (5.41%)  |
| occurrences (all)                 | 1               | 2               |
| NASAL CONGESTION                  |                 |                 |
| subjects affected / exposed       | 2 / 36 (5.56%)  | 5 / 37 (13.51%) |
| occurrences (all)                 | 2               | 6               |
| OROPHARYNGEAL PAIN                |                 |                 |
| subjects affected / exposed       | 5 / 36 (13.89%) | 4 / 37 (10.81%) |
| occurrences (all)                 | 8               | 5               |
| PARANASAL SINUS<br>HYPERSECRETION |                 |                 |
| subjects affected / exposed       | 2 / 36 (5.56%)  | 1 / 37 (2.70%)  |
| occurrences (all)                 | 2               | 1               |
| PRODUCTIVE COUGH                  |                 |                 |
| subjects affected / exposed       | 5 / 36 (13.89%) | 2 / 37 (5.41%)  |
| occurrences (all)                 | 5               | 3               |
| PULMONARY EMBOLISM                |                 |                 |
| subjects affected / exposed       | 2 / 36 (5.56%)  | 2 / 37 (5.41%)  |
| occurrences (all)                 | 2               | 2               |
| RALES                             |                 |                 |
| subjects affected / exposed       | 2 / 36 (5.56%)  | 0 / 37 (0.00%)  |
| occurrences (all)                 | 2               | 0               |
| RHINORRHOEA                       |                 |                 |
| subjects affected / exposed       | 4 / 36 (11.11%) | 5 / 37 (13.51%) |
| occurrences (all)                 | 4               | 7               |
| SINUS CONGESTION                  |                 |                 |
| subjects affected / exposed       | 4 / 36 (11.11%) | 2 / 37 (5.41%)  |
| occurrences (all)                 | 4               | 2               |
| THROAT IRRITATION                 |                 |                 |
| subjects affected / exposed       | 0 / 36 (0.00%)  | 1 / 37 (2.70%)  |
| occurrences (all)                 | 0               | 1               |
| UPPER-AIRWAY COUGH SYNDROME       |                 |                 |
| subjects affected / exposed       | 2 / 36 (5.56%)  | 1 / 37 (2.70%)  |
| occurrences (all)                 | 2               | 1               |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Psychiatric disorders                                 |                  |                  |  |
| AGGRESSION  |                  |                  |  |
| subjects affected / exposed                           | 2 / 36 (5.56%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                                     | 2                | 0                |  |
| ANXIETY   |                  |                  |  |
| subjects affected / exposed                           | 5 / 36 (13.89%)  | 1 / 37 (2.70%)   |  |
| occurrences (all)                                     | 5                | 1                |  |
| CONFUSIONAL STATE                                     |                  |                  |  |
| subjects affected / exposed                           | 1 / 36 (2.78%)   | 3 / 37 (8.11%)   |  |
| occurrences (all)                                     | 1                | 3                |  |
| DEPRESSED MOOD  |                  |                  |  |
| subjects affected / exposed                           | 2 / 36 (5.56%)   | 1 / 37 (2.70%)   |  |
| occurrences (all)                                     | 2                | 1                |  |
| DEPRESSION  |                  |                  |  |
| subjects affected / exposed                           | 4 / 36 (11.11%)  | 3 / 37 (8.11%)   |  |
| occurrences (all)                                     | 4                | 4                |  |
| INSOMNIA  |                  |                  |  |
| subjects affected / exposed                           | 10 / 36 (27.78%) | 15 / 37 (40.54%) |  |
| occurrences (all)                                     | 12               | 16               |  |
| MOOD SWINGS   |                  |                  |  |
| subjects affected / exposed                           | 1 / 36 (2.78%)   | 2 / 37 (5.41%)   |  |
| occurrences (all)                                     | 1                | 2                |  |
| Investigations  |                  |                  |  |
| ACTIVATED PARTIAL<br>THROMBOPLASTIN TIME<br>PROLONGED |                  |                  |  |
| subjects affected / exposed                           | 2 / 36 (5.56%)   | 1 / 37 (2.70%)   |  |
| occurrences (all)                                     | 2                | 1                |  |
| ALANINE AMINOTRANSFERASE<br>INCREASED                 |                  |                  |  |
| subjects affected / exposed                           | 5 / 36 (13.89%)  | 4 / 37 (10.81%)  |  |
| occurrences (all)                                     | 8                | 8                |  |
| ASPARTATE AMINOTRANSFERASE<br>INCREASED               |                  |                  |  |
| subjects affected / exposed                           | 3 / 36 (8.33%)   | 4 / 37 (10.81%)  |  |
| occurrences (all)                                     | 4                | 6                |  |
| BLOOD ALKALINE PHOSPHATASE<br>INCREASED               |                  |                  |  |

|  |                 |                 |
|--|-----------------|-----------------|
| subjects affected / exposed              | 3 / 36 (8.33%)  | 1 / 37 (2.70%)  |
| occurrences (all)                        | 3               | 2               |
| BLOOD BICARBONATE DECREASED              |                 |                 |
| subjects affected / exposed              | 7 / 36 (19.44%) | 4 / 37 (10.81%) |
| occurrences (all)                        | 13              | 9               |
| BLOOD CREATININE INCREASED               |                 |                 |
| subjects affected / exposed              | 5 / 36 (13.89%) | 4 / 37 (10.81%) |
| occurrences (all)                        | 8               | 10              |
| BLOOD LACTATE DEHYDROGENASE INCREASED    |                 |                 |
| subjects affected / exposed              | 4 / 36 (11.11%) | 1 / 37 (2.70%)  |
| occurrences (all)                        | 7               | 4               |
| BLOOD MAGNESIUM DECREASED                |                 |                 |
| subjects affected / exposed              | 2 / 36 (5.56%)  | 0 / 37 (0.00%)  |
| occurrences (all)                        | 2               | 0               |
| BLOOD PHOSPHORUS DECREASED               |                 |                 |
| subjects affected / exposed              | 0 / 36 (0.00%)  | 0 / 37 (0.00%)  |
| occurrences (all)                        | 0               | 0               |
| BLOOD POTASSIUM DECREASED                |                 |                 |
| subjects affected / exposed              | 0 / 36 (0.00%)  | 0 / 37 (0.00%)  |
| occurrences (all)                        | 0               | 0               |
| BLOOD UREA INCREASED                     |                 |                 |
| subjects affected / exposed              | 2 / 36 (5.56%)  | 2 / 37 (5.41%)  |
| occurrences (all)                        | 2               | 3               |
| CARDIAC MURMUR                           |                 |                 |
| subjects affected / exposed              | 3 / 36 (8.33%)  | 1 / 37 (2.70%)  |
| occurrences (all)                        | 3               | 1               |
| EJECTION FRACTION DECREASED              |                 |                 |
| subjects affected / exposed              | 2 / 36 (5.56%)  | 0 / 37 (0.00%)  |
| occurrences (all)                        | 2               | 0               |
| IMMUNOGLOBULINS DECREASED                |                 |                 |
| subjects affected / exposed              | 0 / 36 (0.00%)  | 0 / 37 (0.00%)  |
| occurrences (all)                        | 0               | 0               |
| INTERNATIONAL NORMALISED RATIO INCREASED |                 |                 |



|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                    | 3 / 36 (8.33%)  | 1 / 37 (2.70%)  |  |
| occurrences (all)                              | 7               | 1               |  |
| NEUTROPHIL COUNT INCREASED                     |                 |                 |  |
| subjects affected / exposed                    | 3 / 36 (8.33%)  | 1 / 37 (2.70%)  |  |
| occurrences (all)                              | 3               | 2               |  |
| PROTEIN TOTAL INCREASED                        |                 |                 |  |
| subjects affected / exposed                    | 2 / 36 (5.56%)  | 0 / 37 (0.00%)  |  |
| occurrences (all)                              | 2               | 0               |  |
| PROTHROMBIN TIME PROLONGED                     |                 |                 |  |
| subjects affected / exposed                    | 2 / 36 (5.56%)  | 1 / 37 (2.70%)  |  |
| occurrences (all)                              | 3               | 3               |  |
| WEIGHT DECREASED                               |                 |                 |  |
| subjects affected / exposed                    | 7 / 36 (19.44%) | 4 / 37 (10.81%) |  |
| occurrences (all)                              | 9               | 4               |  |
| WEIGHT INCREASED                               |                 |                 |  |
| subjects affected / exposed                    | 1 / 36 (2.78%)  | 3 / 37 (8.11%)  |  |
| occurrences (all)                              | 1               | 3               |  |
| WHITE BLOOD CELL COUNT DECREASED               |                 |                 |  |
| subjects affected / exposed                    | 2 / 36 (5.56%)  | 2 / 37 (5.41%)  |  |
| occurrences (all)                              | 2               | 3               |  |
| Injury, poisoning and procedural complications |                 |                 |  |
| ARTHROPOD BITE                                 |                 |                 |  |
| subjects affected / exposed                    | 0 / 36 (0.00%)  | 2 / 37 (5.41%)  |  |
| occurrences (all)                              | 0               | 2               |  |
| CONTUSION                                      |                 |                 |  |
| subjects affected / exposed                    | 4 / 36 (11.11%) | 4 / 37 (10.81%) |  |
| occurrences (all)                              | 4               | 5               |  |
| FALL   |                 |                 |  |
| subjects affected / exposed                    | 5 / 36 (13.89%) | 4 / 37 (10.81%) |  |
| occurrences (all)                              | 5               | 4               |  |
| JOINT DISLOCATION                              |                 |                 |  |
| subjects affected / exposed                    | 2 / 36 (5.56%)  | 0 / 37 (0.00%)  |  |
| occurrences (all)                              | 2               | 0               |  |
| LIGAMENT SPRAIN                                |                 |                 |  |

|                             |                  |                 |  |
|-----------------------------|------------------|-----------------|--|
| subjects affected / exposed | 1 / 36 (2.78%)   | 0 / 37 (0.00%)  |  |
| occurrences (all)           | 1                | 0               |  |
| SKIN ABRASION               |                  |                 |  |
| subjects affected / exposed | 0 / 36 (0.00%)   | 2 / 37 (5.41%)  |  |
| occurrences (all)           | 0                | 2               |  |
| STOMA SITE PAIN             |                  |                 |  |
| subjects affected / exposed | 0 / 36 (0.00%)   | 0 / 37 (0.00%)  |  |
| occurrences (all)           | 0                | 0               |  |
| SUNBURN                     |                  |                 |  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 0 / 37 (0.00%)  |  |
| occurrences (all)           | 2                | 0               |  |
| Cardiac disorders           |                  |                 |  |
| ATRIAL FIBRILLATION         |                  |                 |  |
| subjects affected / exposed | 1 / 36 (2.78%)   | 3 / 37 (8.11%)  |  |
| occurrences (all)           | 1                | 3               |  |
| PALPITATIONS                |                  |                 |  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 2 / 37 (5.41%)  |  |
| occurrences (all)           | 3                | 2               |  |
| Nervous system disorders    |                  |                 |  |
| AMNESIA                     |                  |                 |  |
| subjects affected / exposed | 0 / 36 (0.00%)   | 2 / 37 (5.41%)  |  |
| occurrences (all)           | 0                | 2               |  |
| BALANCE DISORDER            |                  |                 |  |
| subjects affected / exposed | 1 / 36 (2.78%)   | 1 / 37 (2.70%)  |  |
| occurrences (all)           | 2                | 1               |  |
| CARPAL TUNNEL SYNDROME      |                  |                 |  |
| subjects affected / exposed | 0 / 36 (0.00%)   | 0 / 37 (0.00%)  |  |
| occurrences (all)           | 0                | 0               |  |
| DISTURBANCE IN ATTENTION    |                  |                 |  |
| subjects affected / exposed | 0 / 36 (0.00%)   | 0 / 37 (0.00%)  |  |
| occurrences (all)           | 0                | 0               |  |
| DIZZINESS                   |                  |                 |  |
| subjects affected / exposed | 12 / 36 (33.33%) | 7 / 37 (18.92%) |  |
| occurrences (all)           | 16               | 12              |  |
| DYSGEUSIA                   |                  |                 |  |

|                               |                  |                 |
|-------------------------------|------------------|-----------------|
| subjects affected / exposed   | 9 / 36 (25.00%)  | 6 / 37 (16.22%) |
| occurrences (all)             | 10               | 7               |
| HEADACHE                      |                  |                 |
| subjects affected / exposed   | 14 / 36 (38.89%) | 7 / 37 (18.92%) |
| occurrences (all)             | 20               | 8               |
| HYPOAESTHESIA                 |                  |                 |
| subjects affected / exposed   | 5 / 36 (13.89%)  | 3 / 37 (8.11%)  |
| occurrences (all)             | 5                | 3               |
| HYPOGEUSIA                    |                  |                 |
| subjects affected / exposed   | 2 / 36 (5.56%)   | 0 / 37 (0.00%)  |
| occurrences (all)             | 2                | 0               |
| MEMORY IMPAIRMENT             |                  |                 |
| subjects affected / exposed   | 2 / 36 (5.56%)   | 2 / 37 (5.41%)  |
| occurrences (all)             | 2                | 2               |
| NEURALGIA                     |                  |                 |
| subjects affected / exposed   | 2 / 36 (5.56%)   | 1 / 37 (2.70%)  |
| occurrences (all)             | 2                | 1               |
| NEUROPATHY PERIPHERAL         |                  |                 |
| subjects affected / exposed   | 8 / 36 (22.22%)  | 7 / 37 (18.92%) |
| occurrences (all)             | 11               | 8               |
| PARAESTHESIA                  |                  |                 |
| subjects affected / exposed   | 6 / 36 (16.67%)  | 3 / 37 (8.11%)  |
| occurrences (all)             | 7                | 3               |
| PERIPHERAL SENSORY NEUROPATHY |                  |                 |
| subjects affected / exposed   | 3 / 36 (8.33%)   | 5 / 37 (13.51%) |
| occurrences (all)             | 3                | 5               |
| PSYCHOMOTOR HYPERACTIVITY     |                  |                 |
| subjects affected / exposed   | 3 / 36 (8.33%)   | 0 / 37 (0.00%)  |
| occurrences (all)             | 3                | 0               |
| SCIATICA                      |                  |                 |
| subjects affected / exposed   | 2 / 36 (5.56%)   | 0 / 37 (0.00%)  |
| occurrences (all)             | 2                | 0               |
| SINUS HEADACHE                |                  |                 |
| subjects affected / exposed   | 3 / 36 (8.33%)   | 1 / 37 (2.70%)  |
| occurrences (all)             | 3                | 1               |
| SOMNOLENCE                    |                  |                 |

|                                      |                  |                  |  |
|--------------------------------------|------------------|------------------|--|
| subjects affected / exposed          | 2 / 36 (5.56%)   | 1 / 37 (2.70%)   |  |
| occurrences (all)                    | 2                | 1                |  |
| SYNCOPE                              |                  |                  |  |
| subjects affected / exposed          | 6 / 36 (16.67%)  | 1 / 37 (2.70%)   |  |
| occurrences (all)                    | 7                | 1                |  |
| TREMOR                               |                  |                  |  |
| subjects affected / exposed          | 3 / 36 (8.33%)   | 5 / 37 (13.51%)  |  |
| occurrences (all)                    | 3                | 6                |  |
| Blood and lymphatic system disorders |                  |                  |  |
| ANAEMIA                              |                  |                  |  |
| subjects affected / exposed          | 17 / 36 (47.22%) | 13 / 37 (35.14%) |  |
| occurrences (all)                    | 29               | 24               |  |
| FEBRILE NEUTROPENIA                  |                  |                  |  |
| subjects affected / exposed          | 2 / 36 (5.56%)   | 3 / 37 (8.11%)   |  |
| occurrences (all)                    | 2                | 3                |  |
| HAEMOGLOBINAEMIA                     |                  |                  |  |
| subjects affected / exposed          | 0 / 36 (0.00%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                    | 0                | 0                |  |
| INCREASED TENDENCY TO BRUISE         |                  |                  |  |
| subjects affected / exposed          | 2 / 36 (5.56%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                    | 2                | 0                |  |
| IRON DEFICIENCY ANAEMIA              |                  |                  |  |
| subjects affected / exposed          | 2 / 36 (5.56%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                    | 2                | 0                |  |
| LEUKOPENIA                           |                  |                  |  |
| subjects affected / exposed          | 8 / 36 (22.22%)  | 6 / 37 (16.22%)  |  |
| occurrences (all)                    | 13               | 8                |  |
| LYMPHADENOPATHY                      |                  |                  |  |
| subjects affected / exposed          | 2 / 36 (5.56%)   | 2 / 37 (5.41%)   |  |
| occurrences (all)                    | 3                | 3                |  |
| LYMPHOPENIA                          |                  |                  |  |
| subjects affected / exposed          | 12 / 36 (33.33%) | 8 / 37 (21.62%)  |  |
| occurrences (all)                    | 23               | 11               |  |
| NEUTROPENIA                          |                  |                  |  |
| subjects affected / exposed          | 12 / 36 (33.33%) | 9 / 37 (24.32%)  |  |
| occurrences (all)                    | 25               | 17               |  |

|                             |                  |                  |  |
|-----------------------------|------------------|------------------|--|
| PANCYTOPENIA                |                  |                  |  |
| subjects affected / exposed | 0 / 36 (0.00%)   | 3 / 37 (8.11%)   |  |
| occurrences (all)           | 0                | 3                |  |
| THROMBOCYTOPENIA            |                  |                  |  |
| subjects affected / exposed | 12 / 36 (33.33%) | 10 / 37 (27.03%) |  |
| occurrences (all)           | 21               | 18               |  |
| Ear and labyrinth disorders |                  |                  |  |
| HYPOACUSIS                  |                  |                  |  |
| subjects affected / exposed | 1 / 36 (2.78%)   | 3 / 37 (8.11%)   |  |
| occurrences (all)           | 1                | 3                |  |
| TINNITUS                    |                  |                  |  |
| subjects affected / exposed | 0 / 36 (0.00%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)           | 0                | 0                |  |
| VERTIGO                     |                  |                  |  |
| subjects affected / exposed | 3 / 36 (8.33%)   | 3 / 37 (8.11%)   |  |
| occurrences (all)           | 3                | 4                |  |
| Eye disorders               |                  |                  |  |
| CATARACT                    |                  |                  |  |
| subjects affected / exposed | 4 / 36 (11.11%)  | 6 / 37 (16.22%)  |  |
| occurrences (all)           | 4                | 7                |  |
| DRY EYE                     |                  |                  |  |
| subjects affected / exposed | 0 / 36 (0.00%)   | 2 / 37 (5.41%)   |  |
| occurrences (all)           | 0                | 2                |  |
| EYE IRRITATION              |                  |                  |  |
| subjects affected / exposed | 3 / 36 (8.33%)   | 3 / 37 (8.11%)   |  |
| occurrences (all)           | 3                | 3                |  |
| OCULAR HYPERAEMIA           |                  |                  |  |
| subjects affected / exposed | 1 / 36 (2.78%)   | 3 / 37 (8.11%)   |  |
| occurrences (all)           | 1                | 4                |  |
| VISION BLURRED              |                  |                  |  |
| subjects affected / exposed | 9 / 36 (25.00%)  | 5 / 37 (13.51%)  |  |
| occurrences (all)           | 14               | 5                |  |
| VISUAL ACUITY REDUCED       |                  |                  |  |
| subjects affected / exposed | 3 / 36 (8.33%)   | 1 / 37 (2.70%)   |  |
| occurrences (all)           | 3                | 1                |  |
| VITREOUS FLOATERS           |                  |                  |  |

|                                    |                  |                  |  |
|------------------------------------|------------------|------------------|--|
| subjects affected / exposed        | 0 / 36 (0.00%)   | 2 / 37 (5.41%)   |  |
| occurrences (all)                  | 0                | 2                |  |
| Gastrointestinal disorders         |                  |                  |  |
| ABDOMINAL DISTENSION               |                  |                  |  |
| subjects affected / exposed        | 4 / 36 (11.11%)  | 2 / 37 (5.41%)   |  |
| occurrences (all)                  | 7                | 2                |  |
| ABDOMINAL PAIN                     |                  |                  |  |
| subjects affected / exposed        | 7 / 36 (19.44%)  | 7 / 37 (18.92%)  |  |
| occurrences (all)                  | 9                | 8                |  |
| ABDOMINAL PAIN UPPER               |                  |                  |  |
| subjects affected / exposed        | 5 / 36 (13.89%)  | 4 / 37 (10.81%)  |  |
| occurrences (all)                  | 6                | 6                |  |
| CONSTIPATION                       |                  |                  |  |
| subjects affected / exposed        | 18 / 36 (50.00%) | 19 / 37 (51.35%) |  |
| occurrences (all)                  | 25               | 22               |  |
| DIARRHOEA                          |                  |                  |  |
| subjects affected / exposed        | 24 / 36 (66.67%) | 25 / 37 (67.57%) |  |
| occurrences (all)                  | 71               | 56               |  |
| DIVERTICULAR PERFORATION           |                  |                  |  |
| subjects affected / exposed        | 0 / 36 (0.00%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                  | 0                | 0                |  |
| DRY MOUTH                          |                  |                  |  |
| subjects affected / exposed        | 3 / 36 (8.33%)   | 2 / 37 (5.41%)   |  |
| occurrences (all)                  | 3                | 2                |  |
| DYSPEPSIA                          |                  |                  |  |
| subjects affected / exposed        | 8 / 36 (22.22%)  | 2 / 37 (5.41%)   |  |
| occurrences (all)                  | 10               | 2                |  |
| FLATULENCE                         |                  |                  |  |
| subjects affected / exposed        | 2 / 36 (5.56%)   | 1 / 37 (2.70%)   |  |
| occurrences (all)                  | 2                | 1                |  |
| GASTROINTESTINAL HAEMORRHAGE       |                  |                  |  |
| subjects affected / exposed        | 0 / 36 (0.00%)   | 1 / 37 (2.70%)   |  |
| occurrences (all)                  | 0                | 1                |  |
| GASTROINTESTINAL MOTILITY DISORDER |                  |                  |  |

|                                  |                  |                  |  |
|----------------------------------|------------------|------------------|--|
| subjects affected / exposed      | 0 / 36 (0.00%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                | 0                | 0                |  |
| GASTROINTESTINAL PERFORATION     |                  |                  |  |
| subjects affected / exposed      | 0 / 36 (0.00%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                | 0                | 0                |  |
| GASTROOESOPHAGEAL REFLUX DISEASE |                  |                  |  |
| subjects affected / exposed      | 3 / 36 (8.33%)   | 4 / 37 (10.81%)  |  |
| occurrences (all)                | 3                | 5                |  |
| HAEMATOCHEZIA                    |                  |                  |  |
| subjects affected / exposed      | 3 / 36 (8.33%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                | 5                | 0                |  |
| HAEMORRHOIDS                     |                  |                  |  |
| subjects affected / exposed      | 2 / 36 (5.56%)   | 1 / 37 (2.70%)   |  |
| occurrences (all)                | 2                | 1                |  |
| NAUSEA                           |                  |                  |  |
| subjects affected / exposed      | 18 / 36 (50.00%) | 17 / 37 (45.95%) |  |
| occurrences (all)                | 35               | 27               |  |
| PARAESTHESIA ORAL                |                  |                  |  |
| subjects affected / exposed      | 3 / 36 (8.33%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                | 3                | 0                |  |
| STOMATITIS                       |                  |                  |  |
| subjects affected / exposed      | 3 / 36 (8.33%)   | 1 / 37 (2.70%)   |  |
| occurrences (all)                | 5                | 1                |  |
| TOOTH DISORDER                   |                  |                  |  |
| subjects affected / exposed      | 2 / 36 (5.56%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                | 2                | 0                |  |
| TOOTHACHE                        |                  |                  |  |
| subjects affected / exposed      | 3 / 36 (8.33%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                | 3                | 0                |  |
| VOMITING                         |                  |                  |  |
| subjects affected / exposed      | 11 / 36 (30.56%) | 6 / 37 (16.22%)  |  |
| occurrences (all)                | 18               | 8                |  |
| Hepatobiliary disorders          |                  |                  |  |
| HYPERBILIRUBINAEMIA              |                  |                  |  |

|  |                     |                     |  |
|--|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all) | 2 / 36 (5.56%)<br>3 | 0 / 37 (0.00%)<br>0 |  |
| Skin and subcutaneous tissue disorders           |                     |                     |  |
| ALOPECIA   |                     |                     |  |
| subjects affected / exposed                      | 3 / 36 (8.33%)      | 0 / 37 (0.00%)      |  |
| occurrences (all)                                | 3                   | 0                   |  |
| BLISTER  |                     |                     |  |
| subjects affected / exposed                      | 0 / 36 (0.00%)      | 2 / 37 (5.41%)      |  |
| occurrences (all)                                | 0                   | 2                   |  |
| DRY SKIN   |                     |                     |  |
| subjects affected / exposed                      | 1 / 36 (2.78%)      | 1 / 37 (2.70%)      |  |
| occurrences (all)                                | 1                   | 3                   |  |
| ECCHYMOSIS                                       |                     |                     |  |
| subjects affected / exposed                      | 3 / 36 (8.33%)      | 3 / 37 (8.11%)      |  |
| occurrences (all)                                | 3                   | 3                   |  |
| ERYTHEMA   |                     |                     |  |
| subjects affected / exposed                      | 3 / 36 (8.33%)      | 4 / 37 (10.81%)     |  |
| occurrences (all)                                | 3                   | 5                   |  |
| HYPERHIDROSIS                                    |                     |                     |  |
| subjects affected / exposed                      | 4 / 36 (11.11%)     | 5 / 37 (13.51%)     |  |
| occurrences (all)                                | 5                   | 5                   |  |
| INGROWING NAIL                                   |                     |                     |  |
| subjects affected / exposed                      | 0 / 36 (0.00%)      | 0 / 37 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                   |  |
| NIGHT SWEATS                                     |                     |                     |  |
| subjects affected / exposed                      | 8 / 36 (22.22%)     | 10 / 37 (27.03%)    |  |
| occurrences (all)                                | 12                  | 12                  |  |
| PRURITUS   |                     |                     |  |
| subjects affected / exposed                      | 2 / 36 (5.56%)      | 2 / 37 (5.41%)      |  |
| occurrences (all)                                | 2                   | 2                   |  |
| RASH   |                     |                     |  |
| subjects affected / exposed                      | 9 / 36 (25.00%)     | 9 / 37 (24.32%)     |  |
| occurrences (all)                                | 16                  | 15                  |  |
| RASH GENERALISED                                 |                     |                     |  |
| subjects affected / exposed                      | 2 / 36 (5.56%)      | 2 / 37 (5.41%)      |  |
| occurrences (all)                                | 2                   | 3                   |  |



|   |                 |                |  |
|---|-----------------|----------------|--|
| RASH MACULAR                                    |                 |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%)  | 0 / 37 (0.00%) |  |
| occurrences (all)                               | 0               | 0              |  |
| RASH MACULO-PAPULAR                             |                 |                |  |
| subjects affected / exposed                     | 2 / 36 (5.56%)  | 1 / 37 (2.70%) |  |
| occurrences (all)                               | 3               | 1              |  |
| SCAB  |                 |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%)  | 2 / 37 (5.41%) |  |
| occurrences (all)                               | 0               | 2              |  |
| SKIN DISCOLOURATION                             |                 |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%)  | 2 / 37 (5.41%) |  |
| occurrences (all)                               | 0               | 2              |  |
| SKIN LESION                                     |                 |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%)  | 1 / 37 (2.70%) |  |
| occurrences (all)                               | 0               | 2              |  |
| URTICARIA                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%)  | 0 / 37 (0.00%) |  |
| occurrences (all)                               | 1               | 0              |  |
| Renal and urinary disorders                     |                 |                |  |
| ACUTE KIDNEY INJURY                             |                 |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%)  | 0 / 37 (0.00%) |  |
| occurrences (all)                               | 1               | 0              |  |
| DYSURIA   |                 |                |  |
| subjects affected / exposed                     | 4 / 36 (11.11%) | 2 / 37 (5.41%) |  |
| occurrences (all)                               | 4               | 2              |  |
| HAEMATURIA                                      |                 |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%)  | 2 / 37 (5.41%) |  |
| occurrences (all)                               | 1               | 2              |  |
| POLLAKIURIA                                     |                 |                |  |
| subjects affected / exposed                     | 0 / 36 (0.00%)  | 2 / 37 (5.41%) |  |
| occurrences (all)                               | 0               | 2              |  |
| RENAL FAILURE                                   |                 |                |  |
| subjects affected / exposed                     | 1 / 36 (2.78%)  | 2 / 37 (5.41%) |  |
| occurrences (all)                               | 1               | 3              |  |
| Musculoskeletal and connective tissue disorders |                 |                |  |

|                             |                  |                  |
|-----------------------------|------------------|------------------|
| ARTHRALGIA                  |                  |                  |
| subjects affected / exposed | 12 / 36 (33.33%) | 8 / 37 (21.62%)  |
| occurrences (all)           | 13               | 9                |
| BACK PAIN                   |                  |                  |
| subjects affected / exposed | 17 / 36 (47.22%) | 14 / 37 (37.84%) |
| occurrences (all)           | 27               | 15               |
| BONE PAIN                   |                  |                  |
| subjects affected / exposed | 4 / 36 (11.11%)  | 8 / 37 (21.62%)  |
| occurrences (all)           | 5                | 12               |
| MUSCLE SPASMS               |                  |                  |
| subjects affected / exposed | 22 / 36 (61.11%) | 23 / 37 (62.16%) |
| occurrences (all)           | 28               | 32               |
| MUSCULAR WEAKNESS           |                  |                  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 1 / 37 (2.70%)   |
| occurrences (all)           | 2                | 1                |
| MUSCULOSKELETAL CHEST PAIN  |                  |                  |
| subjects affected / exposed | 4 / 36 (11.11%)  | 3 / 37 (8.11%)   |
| occurrences (all)           | 7                | 3                |
| MUSCULOSKELETAL DISCOMFORT  |                  |                  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 1 / 37 (2.70%)   |
| occurrences (all)           | 2                | 1                |
| MUSCULOSKELETAL PAIN        |                  |                  |
| subjects affected / exposed | 6 / 36 (16.67%)  | 4 / 37 (10.81%)  |
| occurrences (all)           | 8                | 4                |
| MUSCULOSKELETAL STIFFNESS   |                  |                  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 1 / 37 (2.70%)   |
| occurrences (all)           | 3                | 1                |
| MYALGIA                     |                  |                  |
| subjects affected / exposed | 6 / 36 (16.67%)  | 1 / 37 (2.70%)   |
| occurrences (all)           | 8                | 1                |
| NECK PAIN                   |                  |                  |
| subjects affected / exposed | 4 / 36 (11.11%)  | 3 / 37 (8.11%)   |
| occurrences (all)           | 4                | 4                |
| OSTEONECROSIS OF JAW        |                  |                  |
| subjects affected / exposed | 0 / 36 (0.00%)   | 2 / 37 (5.41%)   |
| occurrences (all)           | 0                | 2                |

|                             |                  |                  |  |
|-----------------------------|------------------|------------------|--|
| PAIN IN EXTREMITY           |                  |                  |  |
| subjects affected / exposed | 10 / 36 (27.78%) | 13 / 37 (35.14%) |  |
| occurrences (all)           | 10               | 16               |  |
| PAIN IN JAW                 |                  |                  |  |
| subjects affected / exposed | 0 / 36 (0.00%)   | 1 / 37 (2.70%)   |  |
| occurrences (all)           | 0                | 1                |  |
| Infections and infestations |                  |                  |  |
| BRONCHITIS                  |                  |                  |  |
| subjects affected / exposed | 8 / 36 (22.22%)  | 10 / 37 (27.03%) |  |
| occurrences (all)           | 10               | 15               |  |
| CELLULITIS                  |                  |                  |  |
| subjects affected / exposed | 4 / 36 (11.11%)  | 4 / 37 (10.81%)  |  |
| occurrences (all)           | 8                | 5                |  |
| CONJUNCTIVITIS              |                  |                  |  |
| subjects affected / exposed | 1 / 36 (2.78%)   | 2 / 37 (5.41%)   |  |
| occurrences (all)           | 2                | 2                |  |
| EAR INFECTION               |                  |                  |  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)           | 4                | 0                |  |
| FUNGAL INFECTION            |                  |                  |  |
| subjects affected / exposed | 1 / 36 (2.78%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)           | 1                | 0                |  |
| GASTROENTERITIS             |                  |                  |  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 3 / 37 (8.11%)   |  |
| occurrences (all)           | 4                | 4                |  |
| GASTROENTERITIS VIRAL       |                  |                  |  |
| subjects affected / exposed | 2 / 36 (5.56%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)           | 4                | 0                |  |
| GINGIVITIS                  |                  |                  |  |
| subjects affected / exposed | 1 / 36 (2.78%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)           | 2                | 0                |  |
| HERPES ZOSTER               |                  |                  |  |
| subjects affected / exposed | 4 / 36 (11.11%)  | 0 / 37 (0.00%)   |  |
| occurrences (all)           | 4                | 0                |  |
| INFLUENZA                   |                  |                  |  |

|                             |                  |                 |
|-----------------------------|------------------|-----------------|
| subjects affected / exposed | 8 / 36 (22.22%)  | 3 / 37 (8.11%)  |
| occurrences (all)           | 9                | 4               |
| LOCALISED INFECTION         |                  |                 |
| subjects affected / exposed | 2 / 36 (5.56%)   | 2 / 37 (5.41%)  |
| occurrences (all)           | 2                | 2               |
| LUNG INFECTION              |                  |                 |
| subjects affected / exposed | 0 / 36 (0.00%)   | 3 / 37 (8.11%)  |
| occurrences (all)           | 0                | 3               |
| NASOPHARYNGITIS             |                  |                 |
| subjects affected / exposed | 10 / 36 (27.78%) | 9 / 37 (24.32%) |
| occurrences (all)           | 21               | 15              |
| ORAL CANDIDIASIS            |                  |                 |
| subjects affected / exposed | 1 / 36 (2.78%)   | 5 / 37 (13.51%) |
| occurrences (all)           | 1                | 6               |
| ORAL HERPES                 |                  |                 |
| subjects affected / exposed | 2 / 36 (5.56%)   | 1 / 37 (2.70%)  |
| occurrences (all)           | 2                | 1               |
| PHARYNGITIS                 |                  |                 |
| subjects affected / exposed | 1 / 36 (2.78%)   | 2 / 37 (5.41%)  |
| occurrences (all)           | 1                | 2               |
| PNEUMONIA                   |                  |                 |
| subjects affected / exposed | 7 / 36 (19.44%)  | 9 / 37 (24.32%) |
| occurrences (all)           | 10               | 11              |
| PNEUMONIA VIRAL             |                  |                 |
| subjects affected / exposed | 2 / 36 (5.56%)   | 0 / 37 (0.00%)  |
| occurrences (all)           | 2                | 0               |
| RHINITIS                    |                  |                 |
| subjects affected / exposed | 5 / 36 (13.89%)  | 8 / 37 (21.62%) |
| occurrences (all)           | 8                | 10              |
| SEPSIS                      |                  |                 |
| subjects affected / exposed | 3 / 36 (8.33%)   | 2 / 37 (5.41%)  |
| occurrences (all)           | 3                | 2               |
| SINUSITIS                   |                  |                 |
| subjects affected / exposed | 5 / 36 (13.89%)  | 3 / 37 (8.11%)  |
| occurrences (all)           | 6                | 11              |
| UPPER RESPIRATORY TRACT     |                  |                 |

|   |                  |                  |  |
|---|------------------|------------------|--|
| INFECTION                                   |                  |                  |  |
| subjects affected / exposed                 | 19 / 36 (52.78%) | 15 / 37 (40.54%) |  |
| occurrences (all)                           | 46               | 54               |  |
| UPPER RESPIRATORY TRACT INFECTION BACTERIAL |                  |                  |  |
| subjects affected / exposed                 | 0 / 36 (0.00%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                           | 0                | 0                |  |
| URINARY TRACT INFECTION                     |                  |                  |  |
| subjects affected / exposed                 | 6 / 36 (16.67%)  | 5 / 37 (13.51%)  |  |
| occurrences (all)                           | 13               | 5                |  |
| VIRAL INFECTION                             |                  |                  |  |
| subjects affected / exposed                 | 0 / 36 (0.00%)   | 0 / 37 (0.00%)   |  |
| occurrences (all)                           | 0                | 0                |  |
| VIRAL UPPER RESPIRATORY TRACT INFECTION     |                  |                  |  |
| subjects affected / exposed                 | 0 / 36 (0.00%)   | 2 / 37 (5.41%)   |  |
| occurrences (all)                           | 0                | 2                |  |
| Metabolism and nutrition disorders          |                  |                  |  |
| DECREASED APPETITE                          |                  |                  |  |
| subjects affected / exposed                 | 10 / 36 (27.78%) | 8 / 37 (21.62%)  |  |
| occurrences (all)                           | 12               | 11               |  |
| DEHYDRATION                                 |                  |                  |  |
| subjects affected / exposed                 | 3 / 36 (8.33%)   | 2 / 37 (5.41%)   |  |
| occurrences (all)                           | 4                | 2                |  |
| DIABETES MELLITUS                           |                  |                  |  |
| subjects affected / exposed                 | 1 / 36 (2.78%)   | 2 / 37 (5.41%)   |  |
| occurrences (all)                           | 1                | 2                |  |
| GOUT  |                  |                  |  |
| subjects affected / exposed                 | 0 / 36 (0.00%)   | 2 / 37 (5.41%)   |  |
| occurrences (all)                           | 0                | 2                |  |
| HYPERCALCAEMIA                              |                  |                  |  |
| subjects affected / exposed                 | 1 / 36 (2.78%)   | 3 / 37 (8.11%)   |  |
| occurrences (all)                           | 1                | 3                |  |
| HYPERGLYCAEMIA                              |                  |                  |  |
| subjects affected / exposed                 | 9 / 36 (25.00%)  | 12 / 37 (32.43%) |  |
| occurrences (all)                           | 24               | 24               |  |
| HYPERKALAEMIA                               |                  |                  |  |

|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 36 (8.33%)  | 1 / 37 (2.70%)  |
| occurrences (all)           | 3               | 1               |
| HYPERNATRAEMIA              |                 |                 |
| subjects affected / exposed | 3 / 36 (8.33%)  | 0 / 37 (0.00%)  |
| occurrences (all)           | 3               | 0               |
| HYPOALBUMINAEMIA            |                 |                 |
| subjects affected / exposed | 5 / 36 (13.89%) | 3 / 37 (8.11%)  |
| occurrences (all)           | 6               | 8               |
| HYPOCALCAEMIA               |                 |                 |
| subjects affected / exposed | 3 / 36 (8.33%)  | 3 / 37 (8.11%)  |
| occurrences (all)           | 3               | 3               |
| HYPOKALAEMIA                |                 |                 |
| subjects affected / exposed | 7 / 36 (19.44%) | 7 / 37 (18.92%) |
| occurrences (all)           | 21              | 12              |
| HYPOMAGNESAEMIA             |                 |                 |
| subjects affected / exposed | 2 / 36 (5.56%)  | 2 / 37 (5.41%)  |
| occurrences (all)           | 4               | 4               |
| HYPONATRAEMIA               |                 |                 |
| subjects affected / exposed | 3 / 36 (8.33%)  | 2 / 37 (5.41%)  |
| occurrences (all)           | 3               | 2               |
| HYPOPHOSPHATAEMIA           |                 |                 |
| subjects affected / exposed | 2 / 36 (5.56%)  | 5 / 37 (13.51%) |
| occurrences (all)           | 2               | 6               |
| METABOLIC ACIDOSIS          |                 |                 |
| subjects affected / exposed | 0 / 36 (0.00%)  | 0 / 37 (0.00%)  |
| occurrences (all)           | 0               | 0               |
| VITAMIN D DEFICIENCY        |                 |                 |
| subjects affected / exposed | 0 / 36 (0.00%)  | 3 / 37 (8.11%)  |
| occurrences (all)           | 0               | 3               |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 29 August 2008    | The primary purpose of this amendment was to add pretreatment with an antihistamine and acetaminophen before or during study drug infusion and to slow the infusion rate of the elotuzumab dose.   |
| 23 April 2009     | The primary purpose of this amendment was to reduce the maximum number of subjects in phase 1 treated at the maximum tolerated dose (MTD) from 36 to 33 subjects because no dose-limiting toxicities (DLTs) were observed; extend the duration of the treatment period beyond 6 cycles to allow treatment to continue until the subject experienced disease progression or unacceptable toxicity; and increase the flow rate of elotuzumab infusion as the subject was able to tolerate (the rate remained capped at 2 mL/min).  |
| 30 September 2009 | The primary purpose of this amendment was to expand the study design from phase 1b to phase 1b/2 and to enroll an additional 60 subjects; include pretreatment with IV methylprednisolone, diphenhydramine and acetaminophen before every elotuzumab infusion; and specify that the weekly dose of dexamethasone was to be administered 12 hours before all elotuzumab infusions.  |
| 19 March 2010     | The primary purpose of this amendment was to revise predosing instructions (change the first weekly 40 mg oral dexamethasone administration from 2 to 4 hours to 1 to 3 hours prior to elotuzumab, and to allow split dosing of dexamethasone prior to the second dose and all subsequent doses of elotuzumab)   |
| 29 July 2010      | The primary purpose of this amendment was to enroll an additional 10 subjects; update the predose of dexamethasone to a split dose of 28 mg orally (between 3 – 24 hours prior to elotuzumab infusion) and 8 mg IV (at least 45 minutes prior to infusion), and dexamethasone 28 mg orally was given on elotuzumab dosing days to reducing total dexamethasone dosing to a total biologic equivalent dose of 40 mg oral dexamethasone, the standard of care with a maximum 40 mg; and increase the maximum allowable elotuzumab infusion rate to 5 mL/min for subjects who had completed at least 4 cycles without an infusion reaction. |
| 28 January 2011   | The primary purpose of this amendment was to allow reduction to 20 mg weekly dexamethasone dose for subjects who developed intolerance to dexamethasone.   |
| 23 May 2012       | The primary purpose of this amendment was to decrease the frequency of vital sign measurements and blood tests; and to discontinue DMC oversight (safety to be monitored by Bristol-Myers Squibb and Abbott).  |
| 20 November 2012  | The primary purpose of this amendment was to remove serum soluble SLAMF7 and cytokines at the last cycle Day 28/early termination visit and the 30- and 60-day follow-up visits; and to incorporate changes related to Sponsor changing from Abbott to AbbVie (Abbott separated into 2 publicly traded companies, Abbott and AbbVie).  |
| 21 November 2013  | The primary purpose of this amendment was to reduce the burden of assessments during treatment and the burden of long-term follow-up.  |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported