



## Clinical trial results:

### A Phase 1/2 Dose Escalation Safety, Pharmacokinetic and Efficacy Study of Multiple Intravenous Administrations of a Humanized Monoclonal Antibody (SAR650984) Against CD38 in Patients With Selected CD38+ Hematological Malignancies

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2013-001418-13    |
| Trial protocol           | IT GR GB FI BE AT |
| Global end of trial date | 13 July 2023      |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1           |
| This version publication date  | 14 July 2024 |
| First version publication date | 14 July 2024 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | TED10893 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |                 |
|------------------------------------|-----------------|
| ISRCTN number                      | -               |
| ClinicalTrials.gov id (NCT number) | NCT01084252     |
| WHO universal trial number (UTN)   | U1111-1116-5472 |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Sanofi aventis recherche & développement   |
| Sponsor organisation address | 1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380                               |
| Public contact               | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com |
| Scientific contact           | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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                       | 02 August 2023 |
| Is this the analysis of the primary completion data? | No             |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 13 July 2023   |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

Phase 1: To determine the maximum tolerated/administered dose (MTD/MAD) of isatuximab according to the investigational product (IP)-related dose limiting toxicities (DLTs) observed in participants with cluster of differentiation (CD)38+-selected hematological malignancies.

Phase 2 Stage 1: To evaluate the activity of single agent isatuximab at different doses/schedules and to select dose and regimen for Phase 2 Stage 2.

Phase 2 Stage 2: To further evaluate the activity in terms of overall response rate (ORR) of isatuximab (SAR650984) at the selected dose/schedule from Stage 1, as single agent (isatuximab arm) and in combination with dexamethasone in participants with relapsed or relapsed/refractory multiple myeloma (RRMM)

Protection of trial subjects:

Participants were fully informed of all pertinent aspects of clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the participant and considering the local culture. During the course of the trial, participants were provided with individual participant cards indicating the nature of the trial the participant is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 11 May 2010 |
| 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 | Argentina: 5 |
| Country: Number of subjects enrolled | Belgium: 4   |
| Country: Number of subjects enrolled | Brazil: 17   |
| Country: Number of subjects enrolled | Chile: 6     |
| Country: Number of subjects enrolled | Finland: 10  |
| Country: Number of subjects enrolled | France: 12   |
| Country: Number of subjects enrolled | Greece: 21   |
| Country: Number of subjects enrolled | Israel: 3    |
| Country: Number of subjects enrolled | Italy: 15    |
| Country: Number of subjects enrolled | Mexico: 5    |
| Country: Number of subjects enrolled | Peru: 7      |

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Russian Federation: 13 |
| Country: Number of subjects enrolled | Spain: 16              |
| Country: Number of subjects enrolled | Türkiye: 9             |
| Country: Number of subjects enrolled | Ukraine: 7             |
| Country: Number of subjects enrolled | United Kingdom: 9      |
| Country: Number of subjects enrolled | United States: 191     |
| Worldwide total number of subjects   | 350                    |
| EEA total number of subjects         | 78                     |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 168 |
| From 65 to 84 years                       | 179 |
| 85 years and over                         | 3   |

## Subject disposition

### Recruitment

Recruitment details:

Study participants were involved in the study from 11 May 2010 at 59 centers in 18 countries. A total of 418 participants were screened, of which 351 participants were enrolled. A total of 67 participants had screen failures due to failure to meet inclusion criteria. 1 participant was enrolled but not treated.

### Pre-assignment

Screening details:

Study consisted 2 phases; Phase 1=dose escalation part of isatuximab to determine MTD. Phase 2=for efficacy and safety evaluation of isatuximab with or without dexamethasone. It consisted of 2 stages: Stage 1 (comprised of 1a and 1b) and Stage 2. Here Completed'=Participants with end of treatment or death from any cause forms completed.

### Period 1

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

### Arms

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes   |
| <b>Arm title</b>             | Phase1: Isatuximab $\leq$ 1 mg/kg every 2 weeks (Q2W) |

Arm description:

Participants with CD38+ hematological malignancies (HM), received Isatuximab at any one of the dose less than or equal to ( $\leq$ ) 1 milligram per kilogram (mg/kg) (i.e. either 0.0001 mg/kg or 0.001 mg/kg or 0.01 mg/kg or 0.03 mg/kg, or 0.1 mg/kg or 0.3 mg/kg or 1 mg/kg) as intravenous (IV) infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal by participant, investigator's decision, and/or availability of study drug.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

Isatuximab  $\leq$  1 mg/kg was administered by IV infusion every week or Q2W in 14-day cycles until protocol defined discontinuation criteria was met.

|                  |                                |
|------------------|--------------------------------|
| <b>Arm title</b> | Phase 1: Isatuximab 3mg/kg Q2W |
|------------------|--------------------------------|

Arm description:

Participants with CD38+ HM, received Isatuximab 3 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

Isatuximab 3 mg/kg was administered by IV infusion every week or Q2W in 14-day cycles until protocol defined discontinuation criteria was met.

|                  |                                 |
|------------------|---------------------------------|
| <b>Arm title</b> | Phase 1: Isatuximab 5 mg/kg Q2W |
|------------------|---------------------------------|

**Arm description:**

Participants with CD38+ HM, received Isatuximab 5 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Isatuximab 5 mg/kg was administered by IV infusion every week or Q2W in 14-day cycles until protocol defined discontinuation criteria was met.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase1:Isatuximab (CD38+HM and Standard Risk Multiple Myeloma) |
|------------------|--|

**Arm description:**

Participants with CD38+ HM along with participants with standard risk multiple myeloma were included in this arm and, received Isatuximab 10 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Isatuximab 10 mg/kg was administered by IV infusion on Day 1 of each 14-day cycle until protocol defined discontinuation criteria was met.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase 1: Isatuximab (CD38 + HM and High Risk Multiple Myeloma) |
|------------------|--|

**Arm description:**

Participants with CD38+ HM along with participants with high risk multiple myeloma were included in this arm and, received Isatuximab 10 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Isatuximab 10 mg/kg was administered by IV infusion on Day 1 of each 14-day cycle until protocol defined discontinuation criteria was met.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase 1: Isatuximab 10 mg/kg Every Week (QW) |
|------------------|--|

**Arm description:**

Participants with CD38+ HM, received Isatuximab 10 mg/kg, as IV infusion QW, i.e. on Day 1 and 8 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Isatuximab 10 mg/kg was administered by IV infusion on Day 1 and 8 of each 14-day cycle until protocol defined discontinuation criteria was met.

|                  |                                  |
|------------------|----------------------------------|
| <b>Arm title</b> | Phase 1: Isatuximab 20 mg/kg Q2W |
|------------------|----------------------------------|

**Arm description:**

Participants with CD38+ HM, received Isatuximab 20 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Isatuximab 20 mg/kg was administered by IV infusion on Day 1 of each 14-day cycle until protocol defined discontinuation criteria was met.

|                  |                                 |
|------------------|---------------------------------|
| <b>Arm title</b> | Phase 1: Isatuximab 20 mg/kg QW |
|------------------|---------------------------------|

**Arm description:**

Participants with CD38+ HM, received Isatuximab 20 mg/kg, as IV infusion QW, i.e. on Day 1 and 8 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Isatuximab 20 mg/kg was administered by IV infusion on Day 1 and 8 of each 14-day cycle until protocol defined discontinuation criteria was met.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase 2 Stage 1a: Isatuximab 3 mg/kg Q2W |
|------------------|--|

**Arm description:**

Participants with multiple Myeloma received Isatuximab 3 mg/kg, as IV infusion on Day 1 and Day 15 of each 28-day cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Isatuximab 3 mg/kg was administered by IV infusion on Day 1 and 15 of each 28-day cycle until protocol defined discontinuation criteria was met.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Phase 2 Stage 1a: Isatuximab 10 mg/kg Q2W |
|------------------|---|

**Arm description:**

Participants with multiple Myeloma received Isatuximab 10 mg/kg, as IV infusion on Day 1 and Day 15 of each 28-day cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

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

|  |                                       |
|--|---------------------------------------|
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Isatuximab 10 mg/kg was administered by IV infusion on Day 1 and 15 of each 28-day cycle until protocol defined discontinuation criteria was met.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W |
|------------------|--|

**Arm description:**

Participants with multiple Myeloma received Isatuximab 10 mg/kg, as IV infusion Q2W, i.e. on Day 1 and Day 15 of Cycle 1 and 2 (each cycle 28 days), then every 4 weeks (Q4W), i.e. on Day 1 of each 28-days cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Isatuximab 10 mg/kg was administered by IV infusion on Day 1 and 15 of Cycle 1 and 2 (each cycle 28 days) then Q4W on Day 1 of each 28-day cycle until protocol defined discontinuation criteria was met.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
|------------------|--|

**Arm description:**

Participants with multiple Myeloma received Isatuximab 20 mg/kg, as IV infusion QW, i.e. on Day 1, 8, 15 and 22 of Cycle 1 and 2 (each cycle 28 days), then Q2W, i.e. on Day 1 and Day 15 of each 28-days cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Isatuximab 20 mg/kg was administered by IV infusion on Days 1, 8, 15 and 22 of Cycle 1 and 2 (each cycle 28 days) then Q2W on Days 1 and 15 of each 28-day cycle until protocol defined discontinuation criteria was met.

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | Phase 2 Stage 2: Isatuximab alone |
|------------------|-----------------------------------|

**Arm description:**

Participants with relapsed or RRMM, received Isatuximab 20 mg/kg, as IV infusion on Day 1, 8, 15 and Day 22 of Cycle 1 (28 days) and then on Day 1 and 15 of each subsequent 28-day cycles until unacceptable AE, disease progression, poor compliance to the study protocol, study termination, lost to follow up or investigator's decision.

|  |                                       |
|--|---------------------------------------|
| Arm type                               | Experimental                          |
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

**Dosage and administration details:**

Isatuximab 20 mg/kg was administered by IV infusion on Days 1, 8, 15 and 22 of Cycle 1 (28 days) then on Days 1 and 15 of each subsequent 28-day cycle until protocol defined discontinuation criteria was met.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Phase 2 Stage 2: Isatuximab + Dexamethasone |
|------------------|---|

Arm description:

Participants with relapsed or RRMM, received Isatuximab 20 mg/kg, as IV infusion on Day 1, 8, 15 and Day 22 of Cycle 1 (28 days) and then on Day 1 and 15 of each subsequent 28-day cycles along with dexamethasone: tablet or as IV infusion (40 mg/day for less than [ $<$ ] 75 years of age; 20 mg/day for greater than or equal to [ $\geq$ ] 75 years of age) on Days 1, 8, 15 and 22 of each 28 days cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination, lost to follow up or investigator's decision.

|  |                               |
|--|-------------------------------|
| Arm type                               | Experimental                  |
| Investigational medicinal product name | Dexamethasone                 |
| Investigational medicinal product code |                               |
| Other name                             |                               |
| Pharmaceutical forms                   | Solution for infusion, Tablet |
| Routes of administration               | Oral use, Intravenous use     |

Dosage and administration details:

Dexamethasone was administered (40 mg/day for  $<75$  years of age; 20 mg/day for  $\geq 75$  years of age) on Days 1, 8, 15 and 22 of each 28-day cycle until protocol defined discontinuation criteria was met.

|  |                                       |
|--|---------------------------------------|
| Investigational medicinal product name | Isatuximab                            |
| Investigational medicinal product code | SAR650984                             |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

Isatuximab 20 mg/kg was administered by IV infusion on Days 1, 8, 15 and 22 of Cycle 1 (28 days) then on Days 1 and 15 of each subsequent 28-day cycle until protocol defined discontinuation criteria was met.

| <b>Number of subjects in period 1</b> | Phase1: Isatuximab<br>$\leq 1$ mg/kg every 2<br>weeks (Q2W) | Phase 1: Isatuximab<br>3mg/kg Q2W | Phase 1: Isatuximab<br>5 mg/kg Q2W |
|---------------------------------------|---|-----------------------------------|------------------------------------|
| Started                               | 16  | 6                                 | 3                                  |
| All Treated (AT) population           | 16  | 6                                 | 3                                  |
| Completed                             | 16  | 6                                 | 3                                  |

| <b>Number of subjects in period 1</b> | Phase1:Isatuximab<br>(CD38+HM and<br>Standard Risk<br>Multiple Myeloma) | Phase 1: Isatuximab<br>(CD38 + HM and<br>High Risk Multiple<br>Myeloma) | Phase 1: Isatuximab<br>10 mg/kg Every<br>Week (QW) |
|---------------------------------------|---|---|--|
| Started                               | 26  | 18  | 6  |
| All Treated (AT) population           | 26  | 18  | 6  |
| Completed                             | 26  | 18  | 6  |

| <b>Number of subjects in period 1</b> | Phase 1: Isatuximab<br>20 mg/kg Q2W | Phase 1: Isatuximab<br>20 mg/kg QW | Phase 2 Stage 1a:<br>Isatuximab 3 mg/kg<br>Q2W |
|---------------------------------------|-------------------------------------|------------------------------------|--|
| Started                               | 7                                   | 7                                  | 23   |
| All Treated (AT) population           | 7                                   | 7                                  | 23   |
| Completed                             | 7                                   | 7                                  | 23   |



| <b>Number of subjects in period 1</b> | Phase 2 Stage 1a:<br>Isatuximab 10<br>mg/kg Q2W | Phase 2 Stage 1a:<br>Isatuximab 10mg/kg<br>Q2W; Then Q4W | Phase 2 Stage 1b:<br>Isatuximab 20mg/kg<br>QW and Then Q2W |
|---------------------------------------|---|--|--|
| Started                               | 24  | 25   | 25   |
| All Treated (AT) population           | 24  | 25   | 25   |
| Completed                             | 24  | 25   | 25   |

| <b>Number of subjects in period 1</b> | Phase 2 Stage 2:<br>Isatuximab alone | Phase 2 Stage 2:<br>Isatuximab +<br>Dexamethasone |
|---------------------------------------|--------------------------------------|---|
|                                       |                                      |   |
| Started                               | 109                                  | 55  |
| All Treated (AT) population           | 109                                  | 55  |
| Completed                             | 109                                  | 55  |

## Baseline characteristics

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Phase1: Isatuximab <=1 mg/kg every 2 weeks (Q2W) |
|-----------------------|--|

Reporting group description:

Participants with CD38+ hematological malignancies (HM), received Isatuximab at any one of the dose less than or equal to ( $\leq$ ) 1 milligram per kilogram (mg/kg) (i.e. either 0.0001 mg/kg or 0.001 mg/kg or 0.01 mg/kg or 0.03 mg/kg, or 0.1 mg/kg or 0.3 mg/kg or 1 mg/kg) as intravenous (IV) infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal by participant, investigator's decision, and/or availability of study drug.

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Phase 1: Isatuximab 3mg/kg Q2W |
|-----------------------|--------------------------------|

Reporting group description:

Participants with CD38+ HM, received Isatuximab 3 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | Phase 1: Isatuximab 5 mg/kg Q2W |
|-----------------------|---------------------------------|

Reporting group description:

Participants with CD38+ HM, received Isatuximab 5 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase1:Isatuximab (CD38+HM and Standard Risk Multiple Myeloma) |
|-----------------------|--|

Reporting group description:

Participants with CD38+ HM along with participants with standard risk multiple myeloma were included in this arm and, received Isatuximab 10 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 1: Isatuximab (CD38 + HM and High Risk Multiple Myeloma) |
|-----------------------|--|

Reporting group description:

Participants with CD38+ HM along with participants with high risk multiple myeloma were included in this arm and, received Isatuximab 10 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 1: Isatuximab 10 mg/kg Every Week (QW) |
|-----------------------|--|

Reporting group description:

Participants with CD38+ HM, received Isatuximab 10 mg/kg, as IV infusion QW, i.e. on Day 1 and 8 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |                                  |
|-----------------------|----------------------------------|
| Reporting group title | Phase 1: Isatuximab 20 mg/kg Q2W |
|-----------------------|----------------------------------|

Reporting group description:

Participants with CD38+ HM, received Isatuximab 20 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | Phase 1: Isatuximab 20 mg/kg QW |
|-----------------------|---------------------------------|

Reporting group description:

Participants with CD38+ HM, received Isatuximab 20 mg/kg, as IV infusion QW, i.e. on Day 1 and 8 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 2 Stage 1a: Isatuximab 3 mg/kg Q2W |
|-----------------------|--|

Reporting group description:

Participants with multiple Myeloma received Isatuximab 3 mg/kg, as IV infusion on Day 1 and Day 15 of each 28-day cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase 2 Stage 1a: Isatuximab 10 mg/kg Q2W |
|-----------------------|---|

Reporting group description:

Participants with multiple Myeloma received Isatuximab 10 mg/kg, as IV infusion on Day 1 and Day 15 of each 28-day cycle until unacceptable AE, disease progression, poor compliance to the study protocol,

study termination or lost to follow up.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W |
|-----------------------|--|

Reporting group description:

Participants with multiple Myeloma received Isatuximab 10 mg/kg, as IV infusion Q2W, i.e. on Day 1 and Day 15 of Cycle 1 and 2 (each cycle 28 days), then every 4 weeks (Q4W), i.e. on Day 1 of each 28-days cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
|-----------------------|--|

Reporting group description:

Participants with multiple Myeloma received Isatuximab 20 mg/kg, as IV infusion QW, i.e. on Day 1, 8, 15 and 22 of Cycle 1 and 2 (each cycle 28 days), then Q2W, i.e. on Day 1 and Day 15 of each 28-days cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Phase 2 Stage 2: Isatuximab alone |
|-----------------------|-----------------------------------|

Reporting group description:

Participants with relapsed or RRMM, received Isatuximab 20 mg/kg, as IV infusion on Day 1, 8, 15 and Day 22 of Cycle 1 (28 days) and then on Day 1 and 15 of each subsequent 28-day cycles until unacceptable AE, disease progression, poor compliance to the study protocol, study termination, lost to follow up or investigator's decision.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase 2 Stage 2: Isatuximab + Dexamethasone |
|-----------------------|---|

Reporting group description:

Participants with relapsed or RRMM, received Isatuximab 20 mg/kg, as IV infusion on Day 1, 8, 15 and Day 22 of Cycle 1 (28 days) and then on Day 1 and 15 of each subsequent 28-day cycles along with dexamethasone: tablet or as IV infusion (40 mg/day for less than [ $<$ ] 75 years of age; 20 mg/day for greater than or equal to [ $\geq$ ] 75 years of age) on Days 1, 8, 15 and 22 of each 28 days cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination, lost to follow up or investigator's decision.

| Reporting group values             | Phase1: Isatuximab<br>$\leq 1$ mg/kg every 2<br>weeks (Q2W) | Phase 1: Isatuximab<br>3mg/kg Q2W | Phase 1: Isatuximab<br>5 mg/kg Q2W |
|------------------------------------|---|-----------------------------------|------------------------------------|
| Number of subjects                 | 16  | 6                                 | 3                                  |
| Age categorical<br>Units: Subjects |   |                                   |                                    |

|   |                    |                   |                   |
|---|--------------------|-------------------|-------------------|
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 64.9<br>$\pm 11.6$ | 63.5<br>$\pm 6.2$ | 62.0<br>$\pm 3.5$ |
| Sex: Female, Male<br>Units: participants                                |                    |                   |                   |
| Female  | 5                  | 3                 | 1                 |
| Male  | 11                 | 3                 | 2                 |
| Race (NIH/OMB)<br>Units: Subjects                                       |                    |                   |                   |
| American Indian or Alaska Native  | 0                  | 0                 | 0                 |
| Asian   | 0                  | 0                 | 0                 |
| Native Hawaiian or Other Pacific<br>Islander                            | 0                  | 0                 | 0                 |
| Black or African American   | 0                  | 1                 | 0                 |
| White   | 14                 | 4                 | 3                 |
| More than one race  | 0                  | 0                 | 0                 |
| Unknown or Not Reported   | 2                  | 1                 | 0                 |

| Reporting group values | Phase1:Isatuximab | Phase 1: Isatuximab | Phase 1: Isatuximab |
|------------------------|-------------------|---------------------|---------------------|
|------------------------|-------------------|---------------------|---------------------|

|                    | (CD38+HM and<br>Standard Risk<br>Multiple Myeloma) | (CD38 + HM and<br>High Risk Multiple<br>Myeloma) | 10 mg/kg Every<br>Week (QW) |
|--------------------|--|--|-----------------------------|
| Number of subjects | 26   | 18   | 6                           |
| Age categorical    |  |  |                             |
| Units: Subjects    |  |  |                             |

|   |       |        |        |
|---|-------|--------|--------|
| Age Continuous                            |       |        |        |
| Units: years                              |       |        |        |
| arithmetic mean                           | 65.0  | 60.8   | 61.7   |
| standard deviation                        | ± 7.2 | ± 12.6 | ± 12.7 |
| Sex: Female, Male                         |       |        |        |
| Units: participants                       |       |        |        |
| Female                                    | 11    | 9      | 2      |
| Male                                      | 15    | 9      | 4      |
| Race (NIH/OMB)                            |       |        |        |
| Units: Subjects                           |       |        |        |
| American Indian or Alaska Native          | 0     | 0      | 0      |
| Asian                                     | 0     | 2      | 0      |
| Native Hawaiian or Other Pacific Islander | 0     | 0      | 0      |
| Black or African American                 | 0     | 1      | 0      |
| White                                     | 20    | 13     | 4      |
| More than one race                        | 0     | 0      | 0      |
| Unknown or Not Reported                   | 6     | 2      | 2      |

| <b>Reporting group values</b> | Phase 1: Isatuximab<br>20 mg/kg Q2W | Phase 1: Isatuximab<br>20 mg/kg QW | Phase 2 Stage 1a:<br>Isatuximab 3 mg/kg<br>Q2W |
|-------------------------------|-------------------------------------|------------------------------------|--|
| Number of subjects            | 7                                   | 7                                  | 23   |
| Age categorical               |                                     |                                    |  |
| Units: Subjects               |                                     |                                    |  |

|   |        |       |       |
|---|--------|-------|-------|
| Age Continuous                            |        |       |       |
| Units: years                              |        |       |       |
| arithmetic mean                           | 63.3   | 60.0  | 63.2  |
| standard deviation                        | ± 10.0 | ± 8.3 | ± 8.9 |
| Sex: Female, Male                         |        |       |       |
| Units: participants                       |        |       |       |
| Female                                    | 2      | 3     | 11    |
| Male                                      | 5      | 4     | 12    |
| Race (NIH/OMB)                            |        |       |       |
| Units: Subjects                           |        |       |       |
| American Indian or Alaska Native          | 0      | 0     | 0     |
| Asian                                     | 0      | 0     | 0     |
| Native Hawaiian or Other Pacific Islander | 0      | 0     | 0     |
| Black or African American                 | 0      | 0     | 1     |
| White                                     | 6      | 7     | 21    |
| More than one race                        | 0      | 0     | 0     |
| Unknown or Not Reported                   | 1      | 0     | 1     |

| <b>Reporting group values</b> | Phase 2 Stage 1a:<br>Isatuximab 10 | Phase 2 Stage 1a:<br>Isatuximab 10mg/kg | Phase 2 Stage 1b:<br>Isatuximab 20mg/kg |
|-------------------------------|------------------------------------|---|---|
|-------------------------------|------------------------------------|---|---|

|   | mg/kg Q2W                            | Q2W; Then Q4W                                     | QW and Then Q2W |
|---|--------------------------------------|---|-----------------|
| Number of subjects                        | 24                                   | 25  | 25              |
| Age categorical                           |                                      |   |                 |
| Units: Subjects                           |                                      |   |                 |
| Age Continuous                            |                                      |   |                 |
| Units: years                              |                                      |   |                 |
| arithmetic mean                           | 63.9                                 | 61.0  | 61.1            |
| standard deviation                        | ± 8.8                                | ± 7.3   | ± 10.3          |
| Sex: Female, Male                         |                                      |   |                 |
| Units: participants                       |                                      |   |                 |
| Female                                    | 11                                   | 7   | 13              |
| Male                                      | 13                                   | 18  | 12              |
| Race (NIH/OMB)                            |                                      |   |                 |
| Units: Subjects                           |                                      |   |                 |
| American Indian or Alaska Native          | 0                                    | 1   | 0               |
| Asian                                     | 0                                    | 0   | 1               |
| Native Hawaiian or Other Pacific Islander | 1                                    | 0   | 0               |
| Black or African American                 | 2                                    | 4   | 3               |
| White                                     | 19                                   | 19  | 21              |
| More than one race                        | 0                                    | 0   | 0               |
| Unknown or Not Reported                   | 2                                    | 1   | 0               |
|   |                                      |   |                 |
| <b>Reporting group values</b>             | Phase 2 Stage 2:<br>Isatuximab alone | Phase 2 Stage 2:<br>Isatuximab +<br>Dexamethasone | Total           |
| Number of subjects                        | 109                                  | 55  | 350             |
| Age categorical                           |                                      |   |                 |
| Units: Subjects                           |                                      |   |                 |
| Age Continuous                            |                                      |   |                 |
| Units: years                              |                                      |   |                 |
| arithmetic mean                           | 66.6                                 | 66.3  |                 |
| standard deviation                        | ± 8.8                                | ± 8.9   | -               |
| Sex: Female, Male                         |                                      |   |                 |
| Units: participants                       |                                      |   |                 |
| Female                                    | 58                                   | 26  | 162             |
| Male                                      | 51                                   | 29  | 188             |
| Race (NIH/OMB)                            |                                      |   |                 |
| Units: Subjects                           |                                      |   |                 |
| American Indian or Alaska Native          | 2                                    | 0   | 3               |
| Asian                                     | 0                                    | 1   | 4               |
| Native Hawaiian or Other Pacific Islander | 0                                    | 0   | 1               |
| Black or African American                 | 5                                    | 3   | 20              |
| White                                     | 91                                   | 45  | 287             |
| More than one race                        | 0                                    | 0   | 0               |
| Unknown or Not Reported                   | 11                                   | 6   | 35              |

## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | Phase1: Isatuximab $\leq$ 1 mg/kg every 2 weeks (Q2W)          |
| Reporting group description:<br>Participants with CD38+ hematological malignancies (HM), received Isatuximab at any one of the dose less than or equal to ( $\leq$ ) 1 milligram per kilogram (mg/kg) (i.e. either 0.0001 mg/kg or 0.001 mg/kg or 0.01 mg/kg or 0.03 mg/kg, or 0.1 mg/kg or 0.3 mg/kg or 1 mg/kg) as intravenous (IV) infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal by participant, investigator's decision, and/or availability of study drug. |  |
| Reporting group title  | Phase 1: Isatuximab 3mg/kg Q2W                                 |
| Reporting group description:<br>Participants with CD38+ HM, received Isatuximab 3 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.   |  |
| Reporting group title  | Phase 1: Isatuximab 5 mg/kg Q2W                                |
| Reporting group description:<br>Participants with CD38+ HM, received Isatuximab 5 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.   |  |
| Reporting group title  | Phase1:Isatuximab (CD38+HM and Standard Risk Multiple Myeloma) |
| Reporting group description:<br>Participants with CD38+ HM along with participants with standard risk multiple myeloma were included in this arm and, received Isatuximab 10 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.  |  |
| Reporting group title  | Phase 1: Isatuximab (CD38 + HM and High Risk Multiple Myeloma) |
| Reporting group description:<br>Participants with CD38+ HM along with participants with high risk multiple myeloma were included in this arm and, received Isatuximab 10 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.  |  |
| Reporting group title  | Phase 1: Isatuximab 10 mg/kg Every Week (QW)                   |
| Reporting group description:<br>Participants with CD38+ HM, received Isatuximab 10 mg/kg, as IV infusion QW, i.e. on Day 1 and 8 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.   |  |
| Reporting group title  | Phase 1: Isatuximab 20 mg/kg Q2W                               |
| Reporting group description:<br>Participants with CD38+ HM, received Isatuximab 20 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.  |  |
| Reporting group title  | Phase 1: Isatuximab 20 mg/kg QW                                |
| Reporting group description:<br>Participants with CD38+ HM, received Isatuximab 20 mg/kg, as IV infusion QW, i.e. on Day 1 and 8 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.   |  |
| Reporting group title  | Phase 2 Stage 1a: Isatuximab 3 mg/kg Q2W                       |
| Reporting group description:<br>Participants with multiple Myeloma received Isatuximab 3 mg/kg, as IV infusion on Day 1 and Day 15 of each 28-day cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.   |  |
| Reporting group title  | Phase 2 Stage 1a: Isatuximab 10 mg/kg Q2W                      |
| Reporting group description:<br>Participants with multiple Myeloma received Isatuximab 10 mg/kg, as IV infusion on Day 1 and Day 15 of each 28-day cycle until unacceptable AE, disease progression, poor compliance to the study protocol,  |  |

study termination or lost to follow up.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W |
|-----------------------|--|

Reporting group description:

Participants with multiple Myeloma received Isatuximab 10 mg/kg, as IV infusion Q2W, i.e. on Day 1 and Day 15 of Cycle 1 and 2 (each cycle 28 days), then every 4 weeks (Q4W), i.e. on Day 1 of each 28-days cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
|-----------------------|--|

Reporting group description:

Participants with multiple Myeloma received Isatuximab 20 mg/kg, as IV infusion QW, i.e. on Day 1, 8, 15 and 22 of Cycle 1 and 2 (each cycle 28 days), then Q2W, i.e. on Day 1 and Day 15 of each 28-days cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Phase 2 Stage 2: Isatuximab alone |
|-----------------------|-----------------------------------|

Reporting group description:

Participants with relapsed or RRMM, received Isatuximab 20 mg/kg, as IV infusion on Day 1, 8, 15 and Day 22 of Cycle 1 (28 days) and then on Day 1 and 15 of each subsequent 28-day cycles until unacceptable AE, disease progression, poor compliance to the study protocol, study termination, lost to follow up or investigator's decision.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase 2 Stage 2: Isatuximab + Dexamethasone |
|-----------------------|---|

Reporting group description:

Participants with relapsed or RRMM, received Isatuximab 20 mg/kg, as IV infusion on Day 1, 8, 15 and Day 22 of Cycle 1 (28 days) and then on Day 1 and 15 of each subsequent 28-day cycles along with dexamethasone: tablet or as IV infusion (40 mg/day for less than [ $<$ ] 75 years of age; 20 mg/day for greater than or equal to [ $\geq$ ] 75 years of age) on Days 1, 8, 15 and 22 of each 28 days cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination, lost to follow up or investigator's decision.

|                            |                                   |
|----------------------------|-----------------------------------|
| Subject analysis set title | Phase 1: Isatuximab 0.3 mg/kg Q2W |
|----------------------------|-----------------------------------|

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

Subject analysis set description:

Participants with CD38+ HM, received Isatuximab 0.3 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                            |                                 |
|----------------------------|---------------------------------|
| Subject analysis set title | Phase 1: Isatuximab 1 mg/kg Q2W |
|----------------------------|---------------------------------|

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

Subject analysis set description:

Participants with CD38+ HM, received Isatuximab 1 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal by participant, investigator's decision, and/or availability of study drug

|                            |                     |
|----------------------------|---------------------|
| Subject analysis set title | Phase 1: Isatuximab |
|----------------------------|---------------------|

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

Subject analysis set description:

All participants who were enrolled in Phase 1 and received Isatuximab.

### **Primary: Phase 1: Number of Participants With Dose Limiting Toxicities (DLTs)**

|                 |  |
|-----------------|--|
| End point title | Phase 1: Number of Participants With Dose Limiting Toxicities (DLTs) <sup>[1][2]</sup> |
|-----------------|--|

End point description:

DLTs were assessed using the national cancer institute common terminology criteria for adverse events (NCI-CTCAE) version 4.03. DLTs were defined as any Grade 3 or higher non-hematological toxicity (with the exception of allergic reaction/hypersensitivity), Grade 4 neutropenia and/or Grade 4 thrombocytopenia lasting longer than 5 days, attributed to isatuximab. Any other toxicity that the Investigator and the Sponsor deemed to be dose-limiting, regardless of the grade, was also considered as DLT. DLT evaluable population included participants who gave their informed consent, received at least 1 dose of isatuximab during Phase 1 and had a DLT assessment at the end of Cycle 2. Data was planned not to be collected and analyzed for the arm: Phase 1: Isatuximab (CD38 + HM and High Risk Multiple Myeloma).

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

End point timeframe:

Day 1 of Cycle 1 up to Day 14 of Cycle 2

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

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

Justification: Only Phase 1 participants were analyzed in this endpoint.

| End point values            | Phase1:<br>Isatuximab<br><=1 mg/kg<br>every 2 weeks<br>(Q2W) | Phase 1:<br>Isatuximab<br>3mg/kg Q2W | Phase 1:<br>Isatuximab 5<br>mg/kg Q2W | Phase1:Isatuxi<br>mab<br>(CD38+HM and<br>Standard Risk<br>Multiple<br>Myeloma) |
|-----------------------------|--|--------------------------------------|---------------------------------------|--|
| Subject group type          | Reporting group  | Reporting group                      | Reporting group                       | Reporting group  |
| Number of subjects analysed | 14   | 6                                    | 3                                     | 6  |
| Units: participants         | 1  | 1                                    | 0                                     | 0  |

| End point values            | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW |  |
|-----------------------------|---|--|---------------------------------------|--|
| Subject group type          | Reporting group                                       | Reporting group                        | Reporting group                       |  |
| Number of subjects analysed | 6   | 6                                      | 6                                     |  |
| Units: participants         | 0   | 0                                      | 0                                     |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Phase 1: Number of Participants With Treatment Emergent Adverse Events (TEAEs)

|                 |  |
|-----------------|--|
| End point title | Phase 1: Number of Participants With Treatment Emergent Adverse Events (TEAEs) <sup>[3][4]</sup> |
|-----------------|--|

End point description:

Adverse event (AE) was defined as any untoward medical occurrence in a participant who received study drug and did not necessarily have to have a causal relationship with the treatment. TEAEs were defined as AEs that developed or worsened during the on-treatment period which was defined as the period from the time of first dose of study treatment until 30 days after the last dose of study treatment. Analysis was performed on AT population which included participants who signed informed consent and received at least 1 dose/even incomplete of isatuximab.

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

End point timeframe:

From Baseline up to 30 days after the last dose (maximum duration: 120 weeks )

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: As the endpoint was descriptive in nature, no statistical analysis was reported.

[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: Only Phase 1 participants were analyzed in this endpoint.

| End point values            | Phase1:<br>Isatuximab<br><=1 mg/kg<br>every 2 weeks<br>(Q2W) | Phase 1:<br>Isatuximab<br>3mg/kg Q2W | Phase 1:<br>Isatuximab 5<br>mg/kg Q2W | Phase1:Isatuxi<br>mab<br>(CD38+HM and<br>Standard Risk<br>Multiple<br>Myeloma) |
|-----------------------------|--|--------------------------------------|---------------------------------------|--|
| Subject group type          | Reporting group  | Reporting group                      | Reporting group                       | Reporting group  |
| Number of subjects analysed | 16   | 6                                    | 3                                     | 26   |
| Units: participants         | 16   | 6                                    | 3                                     | 26   |

| End point values            | Phase 1:<br>Isatuximab<br>(CD38 + HM<br>and High Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW |
|-----------------------------|---|---|--|---------------------------------------|
| Subject group type          | Reporting group   | Reporting group                                       | Reporting group                        | Reporting group                       |
| Number of subjects analysed | 18  | 6   | 7                                      | 7                                     |
| Units: participants         | 18  | 6   | 7                                      | 6                                     |

## Statistical analyses

No statistical analyses for this end point

## Primary: Phase 2 Stage 1: Percentage of Participants With Overall Response (OR) According to International Myeloma Working Group (IMWG) Uniform Response Criteria

|                 |  |
|-----------------|--|
| End point title | Phase 2 Stage 1: Percentage of Participants With Overall Response (OR) According to International Myeloma Working Group (IMWG) Uniform Response Criteria <sup>[5][6]</sup> |
|-----------------|--|

End point description:

OR defined as participants with stringent complete response (sCR) or complete response (CR) or very good partial response (VGPR) or partial response (PR).Based on IMWG, CR: Negative serum and urine on immunofixation, disappearance of any soft tissue plasmacytomas (STP) and <=5% plasma cells in bone marrow; sCR:CR and normal free light chain (FLC) ratio and no clonal cells in bone marrow; VGPR: Serum and urine M-protein detectable by immunofixation but not on electrophoresis or >=90% reduction in serum M-protein and urine M-protein level <100 mg/24 hours;PR: >=50% reduction of serum M-Protein and reduction in urinary M-protein by >=90% or to <200 mg/24 hours;>=50% decrease in difference between involved and uninvolved FLC levels in place of M-protein criteria or >=50% reduction in plasma cells in place of M-protein if present at baseline.Analysis on AT population which included participants who signed informed consent and received at least 1 dose/even incomplete of isatuximab.

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

End point timeframe:

From the date of randomization until disease progression or death or data cut-off (maximum duration: 77 weeks for Stage 1a arms and 53 weeks for Stage 1b arm)

Notes:

[5] - 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: As the endpoint was descriptive in nature, no statistical analysis was reported.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Only Phase 2 Stage 1 participants were analyzed in this endpoint.

| End point values                  | Phase 2 Stage 1a: Isatuximab 3 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
|-----------------------------------|--|---|--|--|
| Subject group type                | Reporting group                          | Reporting group                           | Reporting group                                    | Reporting group                                      |
| Number of subjects analysed       | 23                                       | 24  | 25   | 25   |
| Units: percentage of participants |  |   |  |  |
| number (not applicable)           | 4.3                                      | 29.2                                      | 20.0   | 24.0   |

## Statistical analyses

No statistical analyses for this end point

## Primary: Phase 2 Stage 2: Percentage of Participants With Overall Response According to Updated IMWG Response Criteria

|                 |   |
|-----------------|---|
| End point title | Phase 2 Stage 2: Percentage of Participants With Overall Response According to Updated IMWG Response Criteria <sup>[7][8]</sup> |
|-----------------|---|

End point description:

OR: participants with sCR or CR or VGPR or PR. As per updated IMWG, CR: Negative immunofixation on serum and urine, disappearance of any STP and  $\leq 5\%$  plasma cells in bone marrow; normal FLC ratio of 0.26-1.65 in participants with only FLC disease; sCR: CR and normal FLC ratio and no clonal cells in bone marrow; VGPR: Serum and urine M-protein detectable by immunofixation but not on electrophoresis or  $\geq 90\%$  reduction in serum M-protein and urine M-protein level  $< 100$  mg/24 hours,  $> 90\%$  decrease in the difference between involved and uninvolved FLC levels; PR:  $\geq 50\%$  reduction of serum M-Protein and reduction in urinary M-protein by  $\geq 90\%$  or to  $< 200$  mg/24 hours;  $\geq 50\%$  decrease in the difference between involved and uninvolved FLC levels in place of M-protein criteria or  $\geq 50\%$  reduction in plasma cells in place of M-protein if present at baseline. Analysis was performed on AT population.

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

End point timeframe:

From the date of randomization to date of death from any cause (maximum duration: 97 weeks)

Notes:

[7] - 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: As the endpoint was descriptive in nature, no statistical analysis was reported.

[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: Only Phase 2 Stage 2 participants were analyzed in this endpoint.

| End point values                  | Phase 2 Stage 2: Isatuximab alone | Phase 2 Stage 2: Isatuximab + Dexamethasone |  |  |
|-----------------------------------|-----------------------------------|---|--|--|
| Subject group type                | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed       | 109                               | 55  |  |  |
| Units: percentage of participants |                                   |   |  |  |
| number (not applicable)           | 23.9                              | 43.6  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetic (PK) assessment: Phase 1: Plasma Concentration of Isatuximab observed at the end of an Intravenous infusion (Ceoi)

|                 |   |
|-----------------|---|
| End point title | Pharmacokinetic (PK) assessment: Phase 1: Plasma Concentration of Isatuximab observed at the end of an Intravenous infusion (Ceoi) <sup>[9]</sup> |
|-----------------|---|

End point description:

Ceoi was defined as the plasma concentration of Isatuximab at end of infusion. Data for this outcome measure was planned to be collected and analyzed separately for dose 0.3 mg/kg, 1 mg/kg and not for 0.0001, 0.001, 0.01, 0.03 and 0.1 dose levels (reported under one arm, i.e. Phase 1: Isatuximab <=1mg/kg in participant flow). Analysis was performed on PK population: participants who gave informed consent, received at least one dose (even if incomplete) of isatuximab, had an assessable PK parameter. Here, "Number of Participants analyzed"=participants evaluable for this outcome measure and "99999" signifies none of the participant were evaluable because at Cycle 3, Day 1, only data for reporting arms "Phase 1: Isatuximab 10mg/kg QW" and "Phase 1: Isatuximab 20mg/kg QW" was planned to be collected and analyzed. Analysis was performed on AT population. Here, n= number of participants with data collected for each category.

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

End point timeframe:

Cycle 1 Day 1 and Cycle 3 Day 1: At the end of infusion

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only Phase 1 participants were analyzed in this endpoint.

| End point values                              | Phase 1:<br>Isatuximab<br>3mg/kg Q2W | Phase 1:<br>Isatuximab 5<br>mg/kg Q2W | Phase1:Isatuxi<br>mab<br>(CD38+HM and<br>Standard Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab<br>(CD38 + HM<br>and High Risk<br>Multiple<br>Myeloma) |
|---|--------------------------------------|---------------------------------------|--|---|
| Subject group type                            | Reporting group                      | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed                   | 4                                    | 2                                     | 15   | 5   |
| Units: microgram per milliliter (mcg/mL)      |                                      |                                       |  |   |
| arithmetic mean (standard deviation)          |                                      |                                       |  |   |
| Cycle 1 Day 1 (n= 4, 2, 15, 5, 3, 3, 6, 6, 3) | 44.22500 (± 15.30651)                | 125.50000 (± 53.03301)                | 171.43333 (± 50.18853)   | 148.80000 (± 18.48513)  |
| Cycle 3 Day 1 (n= 0, 0, 0, 0, 4, 0, 6, 0, 0)  | 99999 (± 99999)                      | 99999 (± 99999)                       | 99999 (± 99999)  | 99999 (± 99999)   |

| End point values                              | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW | Phase 1:<br>Isatuximab 0.3<br>mg/kg Q2W |
|---|---|--|---------------------------------------|---|
| Subject group type                            | Reporting group                                       | Reporting group                        | Reporting group                       | Subject analysis set                    |
| Number of subjects analysed                   | 4   | 3                                      | 6                                     | 6                                       |
| Units: microgram per milliliter (mcg/mL)      |   |  |                                       |   |
| arithmetic mean (standard deviation)          |   |  |                                       |   |
| Cycle 1 Day 1 (n= 4, 2, 15, 5, 3, 3, 6, 6, 3) | 173.33333 (± 20.64784)                                | 400.33333 (± 52.51984)                 | 334.33333 (± 98.28462)                | 2.08667 (± 0.65567)                     |
| Cycle 3 Day 1 (n= 0, 0, 0, 0, 4, 0, 6, 0, 0)  | 299.82500 (± 220.83898)                               | 99999 (± 99999)                        | 715.33333 (± 188.01241)               | 99999 (± 99999)                         |

|   |                                       |  |  |  |
|---|---------------------------------------|--|--|--|
| <b>End point values</b>                       | Phase 1:<br>Isatuximab 1<br>mg/kg Q2W |  |  |  |
| Subject group type                            | Subject analysis set                  |  |  |  |
| Number of subjects analysed                   | 3                                     |  |  |  |
| Units: microgram per milliliter (mcg/mL)      |                                       |  |  |  |
| arithmetic mean (standard deviation)          |                                       |  |  |  |
| Cycle 1 Day 1 (n= 4, 2, 15, 5, 3, 3, 6, 6, 3) | 13.18333 (± 5.74464)                  |  |  |  |
| Cycle 3 Day 1 (n= 0, 0, 0, 0, 4, 0, 6, 0, 0)  | 99999 (± 99999)                       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: PK Assessment: Phase 1: Maximum Observed Plasma Concentration (Cmax) of Isatuximab

|                 |  |
|-----------------|--|
| End point title | PK Assessment: Phase 1: Maximum Observed Plasma Concentration (Cmax) of Isatuximab <sup>[10]</sup> |
|-----------------|--|

End point description:

Data for this outcome measure was planned to be collected and analyzed separately for dose 0.3 mg/kg, 1 mg/kg and not for 0.0001, 0.001, 0.01, 0.03 and 0.1 dose levels (reported under one arm, i.e. Phase 1: Isatuximab ≤1mg/kg in participant flow). Analysis was performed on PK population. Here, "Number of Participants analyzed"=participants evaluable for this outcome measure and "99999" signifies none of the participant were evaluable because at Cycle 3, Day 1, only data for reporting arms "Phase 1: Isatuximab 10mg/kg QW" and "Phase 1: Isatuximab 20mg/kg QW" was planned to be collected and analyzed. 9999=pre-specified not to calculate if n≤2. Here, n= number of participants with data collected for each category.

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

End point timeframe:

For Q2W: Cycle 1, Day 1: pre-dose, 15 min after start of infusion, at the end of infusion, 3, 7, 24, 48 and 168 hr post-infusion; For QW: Cycle 1, Day 1: pre-dose, 15 min after start of infusion, at the end of infusion, 4, 24, 48, 72 and 168 hr post-infusion

Notes:

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

Justification: Only Phase 1 participants were analyzed in this endpoint.

|   |                                      |                                       |  |   |
|---|--------------------------------------|---------------------------------------|--|---|
| <b>End point values</b>                             | Phase 1:<br>Isatuximab<br>3mg/kg Q2W | Phase 1:<br>Isatuximab 5<br>mg/kg Q2W | Phase1:Isatuxi<br>mab<br>(CD38+HM and<br>Standard Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab<br>(CD38 + HM<br>and High Risk<br>Multiple<br>Myeloma) |
| Subject group type                                  | Reporting group                      | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed                         | 4                                    | 2                                     | 11   | 5   |
| Units: mcg/mL                                       |                                      |                                       |  |   |
| geometric mean (geometric coefficient of variation) |                                      |                                       |  |   |

|   |                 |                 |                 |                 |
|---|-----------------|-----------------|-----------------|-----------------|
| Cycle 1 Day 1 (n= 4, 2, 11, 5, 3, 3, 6, 6, 3)     | 53.7 (± 28)     | 126 (± 9999)    | 181 (± 48)      | 154 (± 13)      |
| Cycle 3 Day 1 1 (n= n= 0, 0, 0, 0, 4, 0, 6, 0, 0) | 99999 (± 99999) | 99999 (± 99999) | 99999 (± 99999) | 99999 (± 99999) |

| End point values                                    | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW | Phase 1:<br>Isatuximab 0.3<br>mg/kg Q2W |
|---|---|--|---------------------------------------|---|
| Subject group type                                  | Reporting group                                       | Reporting group                        | Reporting group                       | Subject analysis set                    |
| Number of subjects analysed                         | 4   | 3                                      | 6                                     | 6                                       |
| Units: mcg/mL                                       |   |  |                                       |   |
| geometric mean (geometric coefficient of variation) |   |  |                                       |   |
| Cycle 1 Day 1 (n= 4, 2, 11, 5, 3, 3, 6, 6, 3)       | 181 (± 20)  | 457 (± 28)                             | 343 (± 29)                            | 2.00 (± 31)                             |
| Cycle 3 Day 1 1 (n= n= 0, 0, 0, 0, 4, 0, 6, 0, 0)   | 265 (± 67)  | 99999 (± 9999)                         | 712 (± 27)                            | 99999 (± 99999)                         |

| End point values                                    | Phase 1:<br>Isatuximab 1<br>mg/kg Q2W |  |  |  |
|---|---------------------------------------|--|--|--|
| Subject group type                                  | Subject analysis set                  |  |  |  |
| Number of subjects analysed                         | 3                                     |  |  |  |
| Units: mcg/mL                                       |                                       |  |  |  |
| geometric mean (geometric coefficient of variation) |                                       |  |  |  |
| Cycle 1 Day 1 (n= 4, 2, 11, 5, 3, 3, 6, 6, 3)       | 12.4 (± 45)                           |  |  |  |
| Cycle 3 Day 1 1 (n= n= 0, 0, 0, 0, 4, 0, 6, 0, 0)   | 99999 (± 99999)                       |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: PK Assessment: Phase 1: Time to reach maximum plasma concentration observed (tmax) of Isatuximab

|                 |  |
|-----------------|--|
| End point title | PK Assessment: Phase 1: Time to reach maximum plasma concentration observed (tmax) of Isatuximab <sup>[11]</sup> |
|-----------------|--|

End point description:

Data for this outcome measure was planned to be collected and analyzed separately for dose 0.3 mg/kg, 1 mg/kg and not for 0.0001, 0.001, 0.01, 0.03 and 0.1 dose levels (reported under one arm, i.e. Phase 1: Isatuximab ≤1mg/kg in participant flow). Analysis was performed on PK population. Here, "Number of Participants analyzed"=participants evaluable for this outcome measure and "99999" signifies none of the participant were evaluable because at Cycle 3, Day 1, only data for reporting arms "Phase 1: Isatuximab 10mg/kg QW" and "Phase 1: Isatuximab 20mg/kg QW" was planned to be collected and analyzed. Here, n= number of participants with data collected for each category.

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

End point timeframe:

For Q2W: Cycle 1, Day 1: pre-dose, 15 min after start of infusion, at the end of infusion, 3, 7, 24, 48 and 168 hr post-infusion; For QW: Cycle 1, Day 1: pre-dose, 15 min after start of infusion, at the end of infusion, 4, 24, 48, 72 and 168 hr post-infusion

Notes:

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

Justification: Only Phase 1 participants were analyzed in this endpoint.

| End point values                              | Phase 1:<br>Isatuximab<br>3mg/kg Q2W | Phase 1:<br>Isatuximab 5<br>mg/kg Q2W | Phase1:Isatuxi<br>mab<br>(CD38+HM and<br>Standard Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab<br>(CD38 + HM<br>and High Risk<br>Multiple<br>Myeloma) |
|---|--------------------------------------|---------------------------------------|--|---|
| Subject group type                            | Reporting group                      | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed                   | 4                                    | 2                                     | 11   | 5   |
| Units: hours                                  |                                      |                                       |  |   |
| median (full range (min-max))                 |                                      |                                       |  |   |
| Cycle 1 Day 1 (n= 4, 2, 11, 5, 3, 3, 6, 6, 3) | 6.99 (4.58 to 8.00)                  | 7.65 (5.13 to 10.17)                  | 4.28 (2.15 to 9.37)  | 4.92 (2.60 to 30.08)  |
| Cycle 3 Day 1 (n= 0, 0, 0, 0, 4, 0, 6, 0, 0)  | 99999 (99999 to 99999)               | 99999 (99999 to 99999)                | 99999 (99999 to 99999)   | 99999 (99999 to 99999)  |

| End point values                              | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW | Phase 1:<br>Isatuximab 0.3<br>mg/kg Q2W |
|---|---|--|---------------------------------------|---|
| Subject group type                            | Reporting group                                       | Reporting group                        | Reporting group                       | Subject analysis set                    |
| Number of subjects analysed                   | 4   | 3                                      | 6                                     | 6                                       |
| Units: hours                                  |   |  |                                       |   |
| median (full range (min-max))                 |   |  |                                       |   |
| Cycle 1 Day 1 (n= 4, 2, 11, 5, 3, 3, 6, 6, 3) | 2.25 (2.20 to 7.50)                                   | 5.87 (5.78 to 9.90)                    | 6.83 (3.98 to 10.53)                  | 2.49 (1.42 to 3.43)                     |
| Cycle 3 Day 1 (n= 0, 0, 0, 0, 4, 0, 6, 0, 0)  | 4.30 (2.57 to 27.48)                                  | 99999 (99999 to 99999)                 | 8.07 (2.87 to 29.03)                  | 99999 (99999 to 99999)                  |

| End point values                              | Phase 1:<br>Isatuximab 1<br>mg/kg Q2W |  |  |  |
|---|---------------------------------------|--|--|--|
| Subject group type                            | Subject analysis set                  |  |  |  |
| Number of subjects analysed                   | 3                                     |  |  |  |
| Units: hours                                  |                                       |  |  |  |
| median (full range (min-max))                 |                                       |  |  |  |
| Cycle 1 Day 1 (n= 4, 2, 11, 5, 3, 3, 6, 6, 3) | 4.35 (3.13 to 6.33)                   |  |  |  |
| Cycle 3 Day 1 (n= 0, 0, 0, 0, 4, 0, 6, 0, 0)  | 99999 (99999 to 99999)                |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: PK Assessment: Phase 1: Plasma Concentration of Isatuximab at Week 1, 2 and 3

|                 |   |
|-----------------|---|
| End point title | PK Assessment: Phase 1: Plasma Concentration of Isatuximab at Week 1, 2 and 3 <sup>[12]</sup> |
|-----------------|---|

End point description:

Data for this outcome measure was planned to be collected and analyzed only for dose 1 mg/kg and not for 0.0001, 0.001, 0.01, 0.03, 0.1 and 0.3 mg/kg dose levels (reported under one arm, i.e. Phase 1: Isatuximab ≤1mg/kg in participant flow). Analysis was performed on PK population. Here, 'number analyzed' = number of participants with available data for each category. Here, n= number of participants with data collected for each category.

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

End point timeframe:

Week 1, 2 and 3

Notes:

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

Justification: Only Phase 1 participants were analyzed in this endpoint.

| End point values                                    | Phase 1:<br>Isatuximab<br>3mg/kg Q2W | Phase 1:<br>Isatuximab 5<br>mg/kg Q2W | Phase1:Isatuxi<br>mab<br>(CD38+HM and<br>Standard Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab<br>(CD38 + HM<br>and High Risk<br>Multiple<br>Myeloma) |
|---|--------------------------------------|---------------------------------------|--|---|
| Subject group type                                  | Reporting group                      | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed                         | 6                                    | 3                                     | 18   | 16  |
| Units: mcg/mL                                       |                                      |                                       |  |   |
| geometric mean (geometric coefficient of variation) |                                      |                                       |  |   |
| Week 1 (n= 6, 3, 18, 16 6, 6, 7, 3)                 | 1.44 (± 85)                          | 15.3 (± 90)                           | 27.6 (± 81)  | 44.2 (± 52)   |
| Week 2 (n= 6, 3, 18, 16 6, 6, 7, 3)                 | 0.181 (± 136)                        | 1.39 (± 116)                          | 1.97 (± 145)   | 8.31 (± 77)   |
| Week 3 (n= 6, 2, 17, 14, 6, 5, 6, 3)                | 0.460 (± 121)                        | 42.7 (± 73)                           | 4.18 (± 133)   | 18.6 (± 71)   |

| End point values                                    | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW | Phase 1:<br>Isatuximab 1<br>mg/kg Q2W |
|---|---|--|---------------------------------------|---------------------------------------|
| Subject group type                                  | Reporting group                                       | Reporting group                        | Reporting group                       | Subject analysis set                  |
| Number of subjects analysed                         | 6   | 6                                      | 7                                     | 3                                     |
| Units: mcg/mL                                       |   |  |                                       |                                       |
| geometric mean (geometric coefficient of variation) |   |  |                                       |                                       |
| Week 1 (n= 6, 3, 18, 16 6, 6, 7, 3)                 | 20.7 (± 63)   | 113 (± 37)                             | 108 (± 33)                            | 0.00223 (± 86)                        |
| Week 2 (n= 6, 3, 18, 16 6, 6, 7, 3)                 | 55.1 (± 63)   | 63.9 (± 46)                            | 194.8 (± 36)                          | 0.000800 (± 173)                      |
| Week 3 (n= 6, 2, 17, 14, 6, 5, 6, 3)                | 75.9 (± 78)   | 91.0 (± 52)                            | 347.3 (± 36)                          | 0.000283 (± 145)                      |

## Statistical analyses

No statistical analyses for this end point

### Secondary: PK Assessment: Phase 1: Predicted Cumulative Area under the plasma concentration Curve (AUC) of Isatuximab Over the First Week (0-168 hours) (AUC1W)

|                 |  |
|-----------------|--|
| End point title | PK Assessment: Phase 1: Predicted Cumulative Area under the plasma concentration Curve (AUC) of Isatuximab Over the First Week (0-168 hours) (AUC1W) <sup>[13]</sup> |
|-----------------|--|

#### End point description:

Data for this outcome measure was planned to be collected and analyzed only for dose 1 mg/kg and not for 0.0001, 0.001, 0.01, 0.03, 0.1 and 0.3 mg/kg dose levels (reported under one arm, i.e. Phase 1: Isatuximab ≤1mg/kg in participant flow). Analysis was performed on PK population. Here, "Number of Participants Analyzed" = participants evaluable for this outcome measure.

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

#### End point timeframe:

For Q2W: Cycle 1, Day 1: pre-dose, 15 min after start of infusion, at the end of infusion, 3, 7, 24, 48 and 168 hr post-infusion; For QW: Cycle 1, Day 1: pre-dose, 15 min after start of infusion, at the end of infusion, 4, 24, 48, 72 and 168 hr post-infusion

#### Notes:

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

Justification: Only Phase 1 participants were analyzed in this endpoint.

| End point values                                    | Phase 1:<br>Isatuximab<br>3mg/kg Q2W | Phase 1:<br>Isatuximab 5<br>mg/kg Q2W | Phase1:Isatuxi<br>mab<br>(CD38+HM and<br>Standard Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab<br>(CD38 + HM<br>and High Risk<br>Multiple<br>Myeloma) |
|---|--------------------------------------|---------------------------------------|--|---|
| Subject group type                                  | Reporting group                      | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed                         | 6                                    | 3                                     | 18   | 16  |
| Units: mcg*hour/mL                                  |                                      |                                       |  |   |
| geometric mean (geometric coefficient of variation) | 2624 (± 24)                          | 7174 (± 54)                           | 11566 (± 48)   | 13480 (± 38)  |

| End point values                                    | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW | Phase 1:<br>Isatuximab 1<br>mg/kg Q2W |
|---|---|--|---------------------------------------|---------------------------------------|
| Subject group type                                  | Reporting group                                       | Reporting group                        | Reporting group                       | Subject analysis set                  |
| Number of subjects analysed                         | 6   | 6                                      | 7                                     | 3                                     |
| Units: mcg*hour/mL                                  |   |  |                                       |                                       |
| geometric mean (geometric coefficient of variation) | 12680 (± 35)  | 32739 (± 28)                           | 28405 (± 27)                          | 222 (± 80)                            |



## Statistical analyses

No statistical analyses for this end point

### Secondary: PK Assessment: Phase 1: Predicted Cumulative Area Under the Plasma Concentration Curve (AUC) of Isatuximab Over the First 2 Weeks (0-336 hours) (AUC2W)

|                 |   |
|-----------------|---|
| End point title | PK Assessment: Phase 1: Predicted Cumulative Area Under the Plasma Concentration Curve (AUC) of Isatuximab Over the First 2 Weeks (0-336 hours) (AUC2W) <sup>[14]</sup> |
|-----------------|---|

#### End point description:

Data for this outcome measure was planned to be collected and analyzed only for dose 1 mg/kg and not for 0.0001, 0.001, 0.01, 0.03, 0.1 and 0.3 mg/kg dose levels (reported under one arm, i.e. Phase 1: Isatuximab ≤1mg/kg in participant flow). Analysis was performed on PK population. Here, "Number of Participants Analyzed" = participants evaluable for this outcome measure

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

#### End point timeframe:

For Q2W: Cycle 1, Day 1: pre-dose, 15 min after start of infusion, at the end of infusion, 3, 7, 24, 48 and 336 hr post-infusion; For QW: Cycle 1, Day 1: pre-dose, 15 min after start of infusion, at the end of infusion, 4, 24, 48, 72 and 336 hr post-infusion

#### Notes:

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

Justification: Only Phase 1 participants were analyzed in this endpoint.

| End point values                                    | Phase 1:<br>Isatuximab<br>3mg/kg Q2W | Phase 1:<br>Isatuximab 5<br>mg/kg Q2W | Phase1:Isatuxi<br>mab<br>(CD38+HM and<br>Standard Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab<br>(CD38 + HM<br>and High Risk<br>Multiple<br>Myeloma) |
|---|--------------------------------------|---------------------------------------|--|---|
| Subject group type                                  | Reporting group                      | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed                         | 6                                    | 3                                     | 18   | 16  |
| Units: mcg*hour/mL                                  |                                      |                                       |  |   |
| geometric mean (geometric coefficient of variation) | 3076 (± 35)                          | 9546 (± 70)                           | 14876 (± 64)   | 18967 (± 44)  |

| End point values                                    | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW | Phase 1:<br>Isatuximab 1<br>mg/kg Q2W |
|---|---|--|---------------------------------------|---------------------------------------|
| Subject group type                                  | Reporting group                                       | Reporting group                        | Reporting group                       | Subject analysis set                  |
| Number of subjects analysed                         | 6   | 6                                      | 7                                     | 3                                     |
| Units: mcg*hour/mL                                  |   |  |                                       |                                       |
| geometric mean (geometric coefficient of variation) | 30187 (± 40)  | 48003 (± 31)                           | 71174 (± 29)                          | 222 (± 80)                            |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacodynamic (PD) assessment: Phase 1: Change From Baseline in Serum/Plasma Markers

|                 |  |
|-----------------|--|
| End point title | Pharmacodynamic (PD) assessment: Phase 1: Change From Baseline in Serum/Plasma Markers <sup>[15]</sup> |
|-----------------|--|

End point description:

Serum/plasma markers included: tumor necrosis factor alpha (TNF- $\alpha$ ), interleukin-1 $\beta$  (IL-1- $\beta$ ), interleukin 6 (IL-6) and interferon-gamma (IFN-Gamma). Due to change in planned analysis, data for high-sensitivity C-reactive protein (hs-CRP) and CD38 was not collected and analyzed. Analysis was performed on all randomized participants who gave their informed consent, had received at least 1 dose (even incomplete) of isatuximab and had an assessable PD parameter. Here, 'n' = number of participants with available data for each category. Here, n= number of participants with data collected for each category.

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

End point timeframe:

Cycle 1 Day 1

Notes:

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

Justification: Only Phase 1 participants were analyzed in this endpoint.

| End point values                        | Phase1:<br>Isatuximab<br><=1 mg/kg<br>every 2 weeks<br>(Q2W) | Phase 1:<br>Isatuximab<br>3mg/kg Q2W | Phase 1:<br>Isatuximab 5<br>mg/kg Q2W | Phase1:Isatuxi<br>mab<br>(CD38+HM and<br>Standard Risk<br>Multiple<br>Myeloma) |
|---|--|--------------------------------------|---------------------------------------|--|
| Subject group type                      | Reporting group  | Reporting group                      | Reporting group                       | Reporting group  |
| Number of subjects analysed             | 16   | 6                                    | 3                                     | 26   |
| Units: picogram/milliliter (pg/mL)      |  |                                      |                                       |  |
| arithmetic mean (standard deviation)    |  |                                      |                                       |  |
| TNF alpha (n=16, 5, 3, 23, 16, 6, 6, 5) | 163.181 ( $\pm$ 253.373)                                     | 179.783 ( $\pm$ 191.455)             | 352.974 ( $\pm$ 220.394)              | 340.799 ( $\pm$ 341.100)   |
| IL-1 Beta (n=15, 4, 3, 21, 16, 6, 6, 5) | 64.577 ( $\pm$ 227.399)                                      | 29.741 ( $\pm$ 55.515)               | 7.527 ( $\pm$ 8.118)                  | 299.058 ( $\pm$ 572.260)   |
| IL-6 (n=16, 5, 3, 23, 16, 6, 6, 5)      | 139.234 ( $\pm$ 212.385)                                     | 261.732 ( $\pm$ 270.119)             | 73.899 ( $\pm$ 53.211)                | 148.594 ( $\pm$ 175.719)   |
| IFN Gamma (n=15, 3, 3, 23, 16, 6, 6, 5) | 477.116 ( $\pm$ 1673.063)                                    | 5.376 ( $\pm$ 9.312)                 | 25.806 ( $\pm$ 44.698)                | 445.772 ( $\pm$ 1043.982)  |

| End point values | Phase 1:<br>Isatuximab<br>(CD38 + HM<br>and High Risk<br>Multiple | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW |
|------------------|---|---|--|---------------------------------------|
|------------------|---|---|--|---------------------------------------|

|   | Myeloma)             |                      |                     |                       |
|---|----------------------|----------------------|---------------------|-----------------------|
| Subject group type                      | Reporting group      | Reporting group      | Reporting group     | Reporting group       |
| Number of subjects analysed             | 18                   | 6                    | 7                   | 7                     |
| Units: picogram/milliliter (pg/mL)      |                      |                      |                     |                       |
| arithmetic mean (standard deviation)    |                      |                      |                     |                       |
| TNF alpha (n=16, 5, 3, 23, 16, 6, 6, 5) | 503.462 (± 479.813)  | 342.664 (± 410.245)  | 307.319 (± 398.025) | 412.541 (± 243.169)   |
| IL-1 Beta (n=15, 4, 3, 21, 16, 6, 6, 5) | 547.770 (± 1454.175) | 327.957 (± 759.305)  | 305.914 (± 621.754) | 293.307 (± 612.746)   |
| IL-6 (n=16, 5, 3, 23, 16, 6, 6, 5)      | 173.004 (± 433.297)  | -8.109 (± 45.845)    | 274.616 (± 234.752) | 165.295 (± 203.451)   |
| IFN Gamma (n=15, 3, 3, 23, 16, 6, 6, 5) | 568.806 (± 1022.000) | 627.089 (± 1527.647) | 448.387 (± 569.499) | 1487.097 (± 2693.826) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Immunogenicity Assessment: Phase 1: Number of Participants With Treatment-Emergent And Treatment-Boosted Anti-drug Antibodies (ADA) Response

|                 |  |
|-----------------|--|
| End point title | Immunogenicity Assessment: Phase 1: Number of Participants With Treatment-Emergent And Treatment-Boosted Anti-drug Antibodies (ADA) Response <sup>[16]</sup> |
|-----------------|--|

End point description:

ADA response was categorized as: treatment induced and treatment boosted response. Treatment-induced ADA was defined as ADA that developed at any time during the ADA on-study observation period (defined as the time from the first isatuximab administration until end of Phase 1) in participants without preexisting ADA (defined as: ADA that were present in samples drawn before treatment), including participants without pre-treatment (before treatment) samples. Treatment boosted ADA was defined as pre-existing ADA that increased at least 2 titer steps between pre-treatment (before treatment) and post-treatment. Analysis was performed on ADA evaluable population which included all treated participants with at least one ADA assessment with a reportable result during the ADA on-study observation period.

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

End point timeframe:

Up to 120 weeks

Notes:

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

Justification: Only Phase 1 participants were analyzed in this endpoint.

| End point values            | Phase1: Isatuximab ≤1 mg/kg every 2 weeks (Q2W) | Phase 1: Isatuximab 3mg/kg Q2W | Phase 1: Isatuximab 5 mg/kg Q2W | Phase1:Isatuximab (CD38+HM and Standard Risk Multiple Myeloma) |
|-----------------------------|---|--------------------------------|---------------------------------|--|
| Subject group type          | Reporting group                                 | Reporting group                | Reporting group                 | Reporting group  |
| Number of subjects analysed | 16  | 6                              | 3                               | 26   |
| Units: participants         |   |                                |                                 |  |
| Treatment-induced ADA       | 2   | 0                              | 0                               | 1  |
| Treatment boosted ADA       | 0   | 0                              | 0                               | 0  |

| End point values            | Phase 1:<br>Isatuximab<br>(CD38 + HM<br>and High Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW |
|-----------------------------|---|---|--|---------------------------------------|
| Subject group type          | Reporting group   | Reporting group                                       | Reporting group                        | Reporting group                       |
| Number of subjects analysed | 18  | 6   | 6                                      | 7                                     |
| Units: participants         |   |   |  |                                       |
| Treatment-induced ADA       | 1   | 1   | 1                                      | 1                                     |
| Treatment boosted ADA       | 0   | 0   | 0                                      | 0                                     |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Clinical assessment: Phase 1: Percentage of Participants With Overall Response and Clinical Benefit: Assessed Using European Society for Blood and Marrow Transplantation (EBMT) criteria

|                 |   |
|-----------------|---|
| End point title | Clinical assessment: Phase 1: Percentage of Participants With Overall Response and Clinical Benefit: Assessed Using European Society for Blood and Marrow Transplantation (EBMT) criteria <sup>[17]</sup> |
|-----------------|---|

End point description:

OR: Participants with CR or PR as best overall response (BOR). Clinical benefit: participants with minimal response (MR) or better as BOR. BOR: best sequential response from start of treatment through the entire study excluding any time point following start of other treatment. CR: negative immunofixation on serum and urine, disappearance of any STP, <5% plasma cells in bone marrow aspirates, no increase in size or number of lytic bone lesions. PR: ≥50% reduction of serum M-protein, reduction in 24 h urinary M-protein by ≥90% or <200mg, ≥50% reduction in size/number of STP, no increase in size or number of lytic bone lesions. MR: 25 to 49% reduction in serum M-protein, 50-89% reduction in 24h urine M-protein, 25-49% reduction in size of STP, no increase in size or number of lytic bone lesions. Analysis was performed on AT population. Here, 'number of participants analyzed' = participants evaluable for this outcome measure.

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

End point timeframe:

From the date of randomization to the date of first documentation of progression or death (due to any cause) (maximum duration: 120 weeks)

Notes:

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

Justification: Only Phase 1 participants were analyzed in this endpoint.

| End point values                  | Phase 1:<br>Isatuximab<br>3mg/kg Q2W | Phase 1:<br>Isatuximab 5<br>mg/kg Q2W | Phase1:Isatuxi<br>mab<br>(CD38+HM and<br>Standard Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab<br>(CD38 + HM<br>and High Risk<br>Multiple<br>Myeloma) |
|-----------------------------------|--------------------------------------|---------------------------------------|--|---|
| Subject group type                | Reporting group                      | Reporting group                       | Reporting group  | Reporting group   |
| Number of subjects analysed       | 5                                    | 3                                     | 25   | 18  |
| Units: percentage of participants |                                      |                                       |  |   |

|                         |      |      |      |      |
|-------------------------|------|------|------|------|
| number (not applicable) |      |      |      |      |
| OR                      | 0    | 33.3 | 28.0 | 16.7 |
| Clinical benefit        | 20.0 | 33.3 | 28.0 | 27.8 |

| End point values                  | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW | Phase 1:<br>Isatuximab 1<br>mg/kg Q2W |
|-----------------------------------|---|--|---------------------------------------|---------------------------------------|
| Subject group type                | Reporting group                                       | Reporting group                        | Reporting group                       | Subject analysis set                  |
| Number of subjects analysed       | 6   | 7                                      | 7                                     | 3                                     |
| Units: percentage of participants |   |  |                                       |                                       |
| number (not applicable)           |   |  |                                       |                                       |
| OR                                | 33.3  | 14.3                                   | 28.6                                  | 33.3                                  |
| Clinical benefit                  | 33.3  | 28.6                                   | 42.9                                  | 33.3                                  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Clinical assessment: Phase 1: Duration of response (DOR)

|                 |  |
|-----------------|--|
| End point title | Clinical assessment: Phase 1: Duration of response (DOR) <sup>[18]</sup> |
|-----------------|--|

End point description:

DOR: time from first response (PR or better) to first documented tumor progression/death. Progression (EBMT): >25% increase in serum monoclonal paraprotein level also absolute increase of  $\geq 5$  g/l; >25% increase in 24h urinary light chain excretion also absolute increase of  $\geq 200$  mg/24 h; >25% increase in plasma cells in a bone marrow aspirate/on trephine biopsy also absolute increase of  $\geq 10\%$ ; definite increase in size of existing bone lesions/STP; development of new bone lesions/STP or hypercalcemia (corrected serum calcium  $>11.5$  mg/dl) not attributable to any other cause. PR:  $\geq 50\%$  reduction of serum M-protein, reduction in 24h urinary M-protein by  $\geq 90\%$  or  $<200$ mg,  $\geq 50\%$  reduction in size/number of STP, no increase in size/number of lytic bone lesions. Analysis only on subset of participants who had response in Phase 1; not for reporting group with no response. 22222=standard deviation cannot be calculated for single participant.

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

End point timeframe:

From the date of first response to the date of first documentation of progression or death (due to any cause) (maximum duration: 120 weeks)

Notes:

[18] - 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: Only Phase 1 participants were analyzed in this endpoint.

| End point values                     | Phase 1:<br>Isatuximab 5<br>mg/kg Q2W | Phase1:Isatuxi<br>mab<br>(CD38+HM and<br>Standard Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab<br>(CD38 + HM<br>and High Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) |
|--------------------------------------|---------------------------------------|--|---|---|
| Subject group type                   | Reporting group                       | Reporting group  | Reporting group   | Reporting group                                       |
| Number of subjects analysed          | 1                                     | 7  | 3   | 2   |
| Units: months                        |                                       |  |   |   |
| arithmetic mean (standard deviation) | 7.16 ( $\pm$ 22222)                   | 5.76 ( $\pm$ 4.62)   | 10.70 ( $\pm$   | 14.31 ( $\pm$ 7.50)                                   |

| End point values                     | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW | Phase 1:<br>Isatuximab 1<br>mg/kg Q2W |  |
|--------------------------------------|--|---------------------------------------|---------------------------------------|--|
| Subject group type                   | Reporting group                        | Reporting group                       | Subject analysis set                  |  |
| Number of subjects analysed          | 1                                      | 2                                     | 1                                     |  |
| Units: months                        |  |                                       |                                       |  |
| arithmetic mean (standard deviation) | 3.94 (± 22222)                         | 8.82 (± 7.83)                         | 20.21 (± 22222)                       |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical assessment: Phase 1: Time to First Response (TTR)

|                 |  |
|-----------------|--|
| End point title | Clinical assessment: Phase 1: Time to First Response (TTR) <sup>[19]</sup> |
|-----------------|--|

End point description:

TTR was defined as the time from first dose of isatuximab to first response (PR or better). PR:  $\geq 50\%$  reduction of serum M-protein, reduction in 24 h urinary M-protein by  $\geq 90\%$  or  $< 200\text{mg}$ ,  $\geq 50\%$  reduction in size/number of STP, no increase in size or number of lytic bone lesions. Analysis was performed only on subset of participants who had response in Phase 1 and not for the reporting group with no response. 22222=standard deviation cannot be calculated for a single participant.

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

End point timeframe:

From the date of first dose administration to the date of first response or death (due to any cause) (maximum duration: 120 weeks)

Notes:

[19] - 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: Only Phase 1 participants were analyzed in this endpoint.

| End point values                     | Phase 1:<br>Isatuximab 5<br>mg/kg Q2W | Phase1:Isatuxi<br>mab<br>(CD38+HM and<br>Standard Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab<br>(CD38 + HM<br>and High Risk<br>Multiple<br>Myeloma) | Phase 1:<br>Isatuximab 10<br>mg/kg Every<br>Week (QW) |
|--------------------------------------|---------------------------------------|--|---|---|
| Subject group type                   | Reporting group                       | Reporting group  | Reporting group   | Reporting group                                       |
| Number of subjects analysed          | 1                                     | 7  | 3   | 2   |
| Units: months                        |                                       |  |   |   |
| arithmetic mean (standard deviation) | 6.41 (± 22222)                        | 2.52 (± 3.77)  | 1.96 (± 1.72)   | 1.38 (± 0.65)   |

| End point values            | Phase 1:<br>Isatuximab 20<br>mg/kg Q2W | Phase 1:<br>Isatuximab 20<br>mg/kg QW | Phase 1:<br>Isatuximab 1<br>mg/kg Q2W |  |
|-----------------------------|--|---------------------------------------|---------------------------------------|--|
| Subject group type          | Reporting group                        | Reporting group                       | Subject analysis set                  |  |
| Number of subjects analysed | 1                                      | 2                                     | 1                                     |  |

|                                      |                |               |                |  |
|--------------------------------------|----------------|---------------|----------------|--|
| Units: months                        |                |               |                |  |
| arithmetic mean (standard deviation) | 1.18 (± 22222) | 1.46 (± 0.77) | 0.95 (± 22222) |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical assessment: Phase 1: Number of Participants With Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) (Karnofsky performance status)-Shift From Baseline Value to Best Value During Treatment

|   |   |
|---|---|
| End point title   | Clinical assessment: Phase 1: Number of Participants With Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) (Karnofsky performance status)-Shift From Baseline Value to Best Value During Treatment |
| End point description:  |   |
| ECOG performance status was measured on a 4 point scale to assess participant's performance status. 0=Normal, fully functional; 1=Fatigue without significant decrease in daily activity; 2=Fatigue with significant impairment of daily activities or bed rest <50% of waking hours; 3=Bed rest/sitting >50% of waking hours; 4=Bedridden or unable to care for self, where lower score indicated good performance status. Number of participants with Baseline ECOG PS score and corresponding changes to the best values (categorized as: Baseline ECOG 1, During Treatment ECOG 0; Baseline ECOG 2, During Treatment ECOG 0; Baseline ECOG 2, During Treatment ECOG 1) are reported. Analysis was performed on AT population. Data for this outcome measure was planned to be collected and analyzed for a combined arm of overall Phase 1 AT population. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| At baseline, during treatment (Day 1 up to 120 weeks)   |   |

| End point values                         | Phase 1:<br>Isatuximab |  |  |  |
|--|------------------------|--|--|--|
| Subject group type                       | Subject analysis set   |  |  |  |
| Number of subjects analysed              | 89                     |  |  |  |
| Units: participants                      |                        |  |  |  |
| Baseline ECOG 1, During Treatment ECOG 0 | 11                     |  |  |  |
| Baseline ECOG 2, During Treatment ECOG 0 | 2                      |  |  |  |
| Baseline ECOG 2, During Treatment ECOG 1 | 11                     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Clinical assessment: Phase 1: Number of Participants With Eastern Cooperative Oncology Group Performance Status (Karnofsky performance status)-Shift From Baseline Value to Worst Value During Treatment

|                 |   |
|-----------------|---|
| End point title | Clinical assessment: Phase 1: Number of Participants With |
|-----------------|---|

End point description:

ECOG performance status was measured on a 4 point scale to assess participant's performance status. 0=Normal, fully functional; 1=Fatigue without significant decrease in daily activity; 2=Fatigue with significant impairment of daily activities or bed rest <50% of waking hours; 3=Bed rest/sitting>50% of waking hours; 4=Bedridden or unable to care for self, where higher score indicated worst performance status. Number of participants with Baseline ECOG PS score and corresponding changes to the worst values (categorized as: Baseline ECOG 0, During Treatment ECOG 1; Baseline ECOG 2, During Treatment ECOG 1; Baseline ECOG 0, During Treatment ECOG 2; Baseline ECOG 1, During Treatment ECOG 2; Baseline ECOG 0, During Treatment ECOG 3; Baseline ECOG 1, During Treatment ECOG 3; Baseline ECOG 2, During Treatment ECOG 3) are reported. Analysis was performed on AT population. Data for this outcome measure was planned to be collected and analyzed for a combined arm of overall Phase 1 AT population.

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

End point timeframe:

At baseline, during treatment (up to 120 weeks)

| End point values                         | Phase 1:<br>Isatuximab |  |  |  |
|--|------------------------|--|--|--|
| Subject group type                       | Subject analysis set   |  |  |  |
| Number of subjects analysed              | 89                     |  |  |  |
| Units: participants                      |                        |  |  |  |
| Baseline ECOG 0, During Treatment ECOG 1 | 8                      |  |  |  |
| Baseline ECOG 2, During Treatment ECOG 1 | 1                      |  |  |  |
| Baseline ECOG 0, During Treatment ECOG 2 | 3                      |  |  |  |
| Baseline ECOG 1, During Treatment ECOG 2 | 20                     |  |  |  |
| Baseline ECOG 0, During Treatment ECOG 3 | 1                      |  |  |  |
| Baseline ECOG 1, During Treatment ECOG 3 | 2                      |  |  |  |
| Baseline ECOG 2, During Treatment ECOG 3 | 1                      |  |  |  |

Statistical analyses

No statistical analyses for this end point

**Secondary: Phase 2 Stage 1: Number of Participants With Treatment Emergent Adverse Events (TEAEs)**

|                 |  |
|-----------------|--|
| End point title | Phase 2 Stage 1: Number of Participants With Treatment Emergent Adverse Events (TEAEs) <sup>[20]</sup> |
|-----------------|--|

End point description:

Adverse event (AE) was defined as any untoward medical occurrence in a participant who received study drug and did not necessarily have to have a causal relationship with the treatment. TEAEs were defined as AEs that developed or worsened during the on-treatment period which was defined as the period from the time of first dose of study treatment until 30 days after the last dose of study treatment. Analysis was performed on AT population which included participants who signed informed consent & received at least 1 dose/even incomplete of isatuximab.



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

End point timeframe:

From Baseline up to 30 days after the last dose (maximum duration: 414 weeks for Stage 1a and 92 weeks for Stage 1b)

Notes:

[20] - 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: Only Phase 2 Stage 1 participants were analyzed in this endpoint.

| End point values            | Phase 2 Stage 1a: Isatuximab 3 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
|-----------------------------|--|---|--|--|
| Subject group type          | Reporting group                          | Reporting group                           | Reporting group                                    | Reporting group                                      |
| Number of subjects analysed | 23                                       | 24  | 25   | 25   |
| Units: participants         | 22                                       | 24  | 25   | 25   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Stage 1: Duration of Response

|                 |   |
|-----------------|---|
| End point title | Phase 2 Stage 1: Duration of Response <sup>[21]</sup> |
|-----------------|---|

End point description:

DOR: Time from date of 1st IAC determined response ( $\geq$  PR) that was subsequently confirmed, to date of first IAC determined PD/death, whichever happened earlier. updated IMWG criteria- PR:  $\geq$ 50% decrease in difference between involved and uninvolved FLC levels in place of M-protein criteria or a  $\geq$ 50% reduction in plasma cells in place of M-protein if baseline was  $\geq$ 30%. If present at baseline a  $\geq$ 50% reduction in size of STP; PD: Increase of 25% from lowest response value in any of following: Serum M-protein  $\geq$ 0.5 g/dL absolute increase and/or urine M-protein  $\geq$ 200 mg/24 hours absolute increase and/or  $>10$  mg/dL absolute increase in difference between involved and uninvolved FLC levels  $\geq$ 10% bone marrow plasma cells (PC), development of new or increase in size of bone lesions/STP, development of hypercalcemia. Analysis was only on subset of population who had response in Phase 2 stage 1. 2222=Standard deviation cannot be calculated for single participant.

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

End point timeframe:

From the date of first response until disease progression or death or data cut-off (maximum duration: 77 weeks for Stage 1a arms and 53 weeks for stage 1b arm)

Notes:

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

Justification: Only Phase 2 Stage 1 participants were analyzed in this endpoint.

| End point values                     | Phase 2 Stage 1a: Isatuximab 3 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                          | Reporting group                           | Reporting group                                    | Reporting group                                      |
| Number of subjects analysed          | 1  | 7   | 5  | 6  |
| Units: months                        |  |   |  |  |
| arithmetic mean (standard deviation) | 1.91 ( $\pm$ 2222)                       | 11.17 ( $\pm$ 5.77)                       | 7.31 ( $\pm$ 3.65)                                 | 8.11 ( $\pm$ 2.33)                                   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2 Stage 2: Number of Participants With Treatment Emergent Adverse Events (TEAEs)

|                 |  |
|-----------------|--|
| End point title | Phase 2 Stage 2: Number of Participants With Treatment Emergent Adverse Events (TEAEs) <sup>[22]</sup> |
|-----------------|--|

End point description:

AE was defined as any untoward medical occurrence in a participant who received study drug and did not necessarily have to have a causal relationship with the treatment. TEAEs were defined as AEs that developed or worsened during the on-treatment period which was defined as the period from the time of first dose of study treatment until 30 days after the last dose of study treatment. Analysis was performed on AT population which included participants who signed informed consent & received at least 1 dose/even incomplete of isatuximab.

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

End point timeframe:

From Baseline up to 30 days after the last dose (maximum duration: 301 weeks)

Notes:

[22] - 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: Only Phase 2 Stage 2 participants were analyzed in this endpoint.

| End point values            | Phase 2 Stage 2: Isatuximab alone | Phase 2 Stage 2: Isatuximab + Dexamethasone |  |  |
|-----------------------------|-----------------------------------|---|--|--|
| Subject group type          | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed | 109                               | 55  |  |  |
| Units: participants         | 101                               | 51  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2 Stage 2: Percentage of Participants With Clinical Benefit

|                 |   |
|-----------------|---|
| End point title | Phase 2 Stage 2: Percentage of Participants With Clinical Benefit <sup>[23]</sup> |
|-----------------|---|

End point description:

Clinical benefit: participants with sCR, CR, VGPR, PR or MR, per IMWG criteria, determined by IAC. CR: negative immunofixation on serum & urine, disappearance of any STP, <5% plasma cells in bone marrow aspirates, normal FLC ratio (0.26-1.65) in participants with only FLC disease. sCR: CR + normal FLC ratio, absence of clonal cells in bone marrow biopsy. VGPR: serum & urine M-component detectable by immunofixation, not on electrophoresis, >=90% reduction in serum M-component plus urine M-component level <100mg/24h, >=90% decrease in difference between involved and uninvolved FLC levels; PR: >=50% reduction of serum M-protein, reduction in 24h urinary M-protein by >=90%

/<200mg/24h,>50% decrease in difference between involved and uninvolved FLC in place of M-protein criteria, >=50% reduction in size/number of STP. MR:>=25 but <49% reduction in serum M-protein, reduction in 24h urine M-protein by 50-89%, 25-49% reduction in size of STP. Analysis was on AT population.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| From the date of randomization to the date of first documentation of progression or death (maximum duration: 97 weeks ) |           |

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: Only Phase 2 Stage 2 participants were analyzed in this endpoint.

| End point values                  | Phase 2 Stage 2: Isatuximab alone | Phase 2 Stage 2: Isatuximab + Dexamethasone |  |  |
|-----------------------------------|-----------------------------------|---|--|--|
| Subject group type                | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed       | 109                               | 55  |  |  |
| Units: percentage of participants |                                   |   |  |  |
| number (not applicable)           | 43.1                              | 54.5  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Stage 1: Percentage of Participants With Clinical Benefit

|                 |   |
|-----------------|---|
| End point title | Phase 2 Stage 1: Percentage of Participants With Clinical Benefit <sup>[24]</sup> |
|-----------------|---|

End point description:

Clinical benefit: participants with sCR, CR, VGPR, PR or MR as per IMWG criteria by IAC. CR: negative immunofixation on serum & urine, disappearance of any STP, <5% PCs in bone marrow aspirates. sCR: CR + normal FLC ratio (0.26-1.65), absence of clonal cells in bone marrow biopsy. VGPR: serum & urine M-component detectable by immunofixation, not on electrophoresis, >=90% reduction in serum M-component plus urine M-component level <100mg/24hours; PR: >=50% reduction of serum M-Protein and reduction in urinary M-protein by >=90% or to <200 mg/24 hours, >=50% decrease in difference between involved and uninvolved FLC levels in place of M-protein criteria or >=50% reduction in plasma cells in place of M-protein if baseline >=30%. If present at baseline, >=50% size reduction in STP. MR: >=25 but <49% reduction in serum M-protein, reduction in 24h urine M-protein by 50-89%, 25-49% size reduction in STP. Analysis was on AT population.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| From Baseline up to 30 days after the last dose (maximum duration: 77 weeks for Stage 1a arms and 53 weeks for stage 1b arm) |           |

Notes:

[24] - 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: Only Phase 2 Stage 1 participants were analyzed in this endpoint.

| End point values                  | Phase 2 Stage 1a: Isatuximab 3 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
|-----------------------------------|--|---|--|--|
| Subject group type                | Reporting group                          | Reporting group                           | Reporting group                                    | Reporting group                                      |
| Number of subjects analysed       | 23                                       | 24  | 25   | 25   |
| Units: percentage of participants |  |   |  |  |
| number (not applicable)           | 4.3                                      | 41.7                                      | 32.0   | 36.0   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Stage 2: Duration of Response

|                 |   |
|-----------------|---|
| End point title | Phase 2 Stage 2: Duration of Response <sup>[25]</sup> |
|-----------------|---|

End point description:

DOR: Time from date of 1st IAC determined response ( $\geq$  PR) subsequently confirmed, to date of 1st IAC determined PD or death, whichever happened earlier. As per updated IMWG criteria-PR:  $\geq$ 50% reduction of serum M-Protein and reduction in urinary M-protein by  $\geq$ 90% or to  $<200$  mg/24 hours.  $\geq$ 50% decrease in difference between involved and uninvolved FLC levels in place of M-protein criteria or  $\geq$ 50% reduction in plasma cells in place of M-protein if baseline  $\geq$ 30%. If present at baseline  $\geq$ 50% reduction in size of STP; PD: Increase of  $>25\%$  from lowest response value in any 1 of following: Serum M-component (absolute increase  $>0.5$  g/dL)4 and/or Urine M-component (absolute increase 200 mg/24 h) and/or  $>10$  mg/dL absolute increase in difference between involved and uninvolved FLC levels,  $\geq$ 10% bone marrow plasma cell, development of hypercalcemia attributed solely to PC proliferative disorder. Analysis was only on subset of population who had response in Phase 2 stage 2.

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

End point timeframe:

From the date of first response until disease progression or death or data cut-off (maximum duration: 97 weeks)

Notes:

[25] - 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: Only Phase 2 Stage 2 participants were analyzed in this endpoint.

| End point values                     | Phase 2 Stage 2: Isatuximab alone | Phase 2 Stage 2: Isatuximab + Dexamethasone |  |  |
|--------------------------------------|-----------------------------------|---|--|--|
| Subject group type                   | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed          | 26                                | 24  |  |  |
| Units: months                        |                                   |   |  |  |
| arithmetic mean (standard deviation) | 8.6 ( $\pm$ 5.2)                  | 10.9 ( $\pm$ 4.6)                           |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Stage 1: Progression free survival (PFS)

|  |  |
|--|--|
| End point title  | Phase 2 Stage 1: Progression free survival (PFS) <sup>[26]</sup> |
| End point description:   |  |
| PFS:Time interval from date of first isatuximab administration to date of first IAC-confirmed disease progression (PD) or date of death due to any cause, whichever came first. As per IMWG criteria, PD: Increase of > 25% from lowest response value in any 1 or more of following: Serum M-component and/or (absolute increase> 0.5 g/dL),Urine M-component and/or (absolute increase> 200 mg/24 h), > 10mg/dL decrease in difference between involved and uninvolved FLC levels in place of M-protein criteria,>10% absolute percentage of bone marrow plasma cell, definite development of new bone lesions or STP or definite increase in the size of existing bone lesions or STP, development of hypercalcemia (corrected serum calcium > 11.5 mg/dL or 2.65 mmol/L) attributed solely to PC proliferative disorder. Analysis was performed by Kaplan-Meier method. Analysis was performed on AT population. 55555=Upper limit of confidence interval was not estimable due to less number of participants with event. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| From the date of the first dose administration until progression or death, whichever occurred first (maximum duration: 77 weeks for Stage 1a arms and 53 weeks for stage 1b arm)   |  |
| Notes:   |  |
| [26] - 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: Only Phase 2 Stage 1 participants were analyzed in this endpoint.   |  |

| End point values                 | Phase 2 Stage 1a: Isatuximab 3 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                          | Reporting group                           | Reporting group                                    | Reporting group                                      |
| Number of subjects analysed      | 23                                       | 24  | 25   | 25   |
| Units: months                    |  |   |  |  |
| median (confidence interval 95%) | 2.1 (1.02 to 5.49)                       | 9.6 (2.23 to 55555)                       | 4.4 (1.84 to 5.82)                                 | 3.6 (1.91 to 9.20)                                   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Stage 2: Overall survival

|   |   |
|---|---|
| End point title   | Phase 2 Stage 2: Overall survival <sup>[27]</sup> |
| End point description:  |   |
| OS was defined as the time interval from the date of first Isatuximab administration to death from any cause. Analysis was performed by Kaplan-Meier method. Analysis was performed on AT population. 55555=Not estimable, due to less number of participants with event. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| From the date of randomization to date of death from any cause (maximum duration: 97 weeks)   |   |
| 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: Only Phase 2 Stage 2 participants were analyzed in this endpoint.  |   |

|                                  |                                   |   |  |  |
|----------------------------------|-----------------------------------|---|--|--|
| <b>End point values</b>          | Phase 2 Stage 2: Isatuximab alone | Phase 2 Stage 2: Isatuximab + Dexamethasone |  |  |
| Subject group type               | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed      | 109                               | 55  |  |  |
| Units: months                    |                                   |   |  |  |
| median (confidence interval 95%) | 18.92 (13.602 to 23.064)          | 17.25 (15.409 to 55555)                     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2 Stage 1: Overall survival (OS)

|                 |  |
|-----------------|--|
| End point title | Phase 2 Stage 1: Overall survival (OS) <sup>[28]</sup> |
|-----------------|--|

End point description:

OS was defined as the time interval from the date of first Isatuximab administration to death from any cause. Analysis was performed by Kaplan-Meier method. Analysis was performed on AT population. 55555= Not estimable, due to less number of participants with event.

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

End point timeframe:

From the date of randomization to date of death from any cause (maximum duration 77 weeks for Stage 1a arms and 53 weeks for stage 1b arm)

Notes:

[28] - 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: Only Phase 2 Stage 1 participants were analyzed in this endpoint.

|                                  |  |   |  |  |
|----------------------------------|--|---|--|--|
| <b>End point values</b>          | Phase 2 Stage 1a: Isatuximab 3 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
| Subject group type               | Reporting group                          | Reporting group                           | Reporting group                                    | Reporting group                                      |
| Number of subjects analysed      | 23                                       | 24  | 25   | 25   |
| Units: months                    |  |   |  |  |
| median (confidence interval 95%) | 15.277 (4.7310 to 55555)                 | 18.628 (7.7536 to 20.1068)                | 55555 (8.4435 to 55555)                            | 55555 (8.3450 to 55555)                              |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2 Stage 2: Progression free survival

|                 |  |
|-----------------|--|
| End point title | Phase 2 Stage 2: Progression free survival <sup>[29]</sup> |
|-----------------|--|

End point description:

PFS was defined as the time interval from the date of first isatuximab administration to the date of the first IAC-confirmed disease progression or the date of death due to any cause, whichever came first. As per IMWG criteria, PD: Increase of >25% from lowest response value in any one of the following: Serum

M-component (the absolute increase must be >0.5 g/dL)4 and/or Urine M-component (the absolute increase must be >200 mg/24 h) and/or >10 mg/dL decrease in the difference between involved and uninvolved FLC levels in place of the M-protein criteria, ≥10% bone marrow plasma cell, development of hypercalcemia (corrected serum calcium >11.5 mg/dL) attributed solely to the plasma cell proliferative disorder. Analysis was performed by Kaplan-Meier method. Analysis was performed on AT population.

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

End point timeframe:

From the date of the first dose administration until progression or death, whichever occurred first (maximum duration: 97 weeks)

Notes:

[29] - 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: Only Phase 2 Stage 2 participants were analyzed in this endpoint.

| End point values                 | Phase 2 Stage 2: Isatuximab alone | Phase 2 Stage 2: Isatuximab + Dexamethasone |  |  |
|----------------------------------|-----------------------------------|---|--|--|
| Subject group type               | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed      | 109                               | 55  |  |  |
| Units: months                    |                                   |   |  |  |
| median (confidence interval 95%) | 4.86 (3.877 to 7.688)             | 10.15 (4.862 to 17.347)                     |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Stage 1: Change From Baseline in Health Related Quality of Life (HRQL) European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) Scores: Global Health Status

|                 |  |
|-----------------|--|
| End point title | Phase 2 Stage 1: Change From Baseline in Health Related Quality of Life (HRQL) European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) Scores: Global Health Status <sup>[30]</sup> |
|-----------------|--|

End point description:

EORTC-QLQ-C30: Cancer-specific instrument with 30 questions for evaluation of new chemotherapy; provides an assessment of participant reported outcome dimensions. 1st 28 questions used 4-point scale (1=not at all, 2=a little, 3=quite a bit, 4=very much) for evaluating 5 functional scales (physical, role, emotional, cognitive, social), 3 symptom scales (fatigue, nausea/vomiting, pain); other single items. For each item, high score=high level of problem. Last 2 questions were participant's assessment of overall health+quality of life (QoL), coded on 7-point scale (1=very poor to 7=excellent). It observed values and change from baseline for global health status (scoring of questions 29 & 30) and 5 functional scales, 3 symptom scales and other single items (scoring of questions 1 to 28). Answers were converted into grading scale, values between 0 and 100. High score: favorable outcome with best QoL. Analysis: AT population. Only those participants with data available for each specified category are reported.

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

End point timeframe:

Baseline, Day 1 of Cycles 2, 3, 4, 5, 6, 7, 8, 9, 10 and End of Treatment (EOT: anytime up to 77 weeks for Stage 1a arms and 53 weeks for stage 1b arm)

Notes:

[30] - 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: Only Phase 2 Stage 1 participants were analyzed in this endpoint.

| End point values                     | Phase 2 Stage 1a: Isatuximab 3 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                          | Reporting group                           | Reporting group                                    | Reporting group                                      |
| Number of subjects analysed          | 22                                       | 21  | 24   | 22   |
| Units: score on a scale              |  |   |  |  |
| arithmetic mean (standard deviation) |  |   |  |  |
| Cycle 2 day 1 (n=14, 15, 19, 18)     | -8.33 (± 20.15)                          | 2.22 (± 16.51)                            | -3.95 (± 20.67)                                    | 0.00 (± 15.39)                                       |
| Cycle 3 day 1 (n=7, 11, 14, 12)      | 0.00 (± 19.25)                           | -0.76 (± 16.44)                           | 6.55 (± 19.66)                                     | -2.08 (± 15.54)                                      |
| Cycle 4 day 1 (n=4, 11, 11, 9)       | 0.00 (± 24.53)                           | -5.30 (± 21.50)                           | 6.06 (± 21.11)                                     | 7.41 (± 8.78)  |
| Cycle 5 day 1 (n=4, 12, 9, 5)        | 0.00 (± 24.53)                           | 0.69 (± 15.27)                            | 6.48 (± 21.15)                                     | 5.00 (± 4.56)  |
| Cycle 6 day 1 (n=4, 9, 7, 4)         | 12.50 (± 14.43)                          | -10.19 (± 25.27)                          | 5.95 (± 13.36)                                     | 10.42 (± 7.98)                                       |
| Cycle 7 day 1 (n=2, 7, 4, 5)         | 12.50 (± 5.89)                           | -3.57 (± 15.85)                           | 8.33 (± 11.79)                                     | 6.67 (± 6.97)  |
| Cycle 8 day 1 (n=2, 6, 4, 4)         | 0.00 (± 35.36)                           | -11.11 (± 18.76)                          | 4.17 (± 15.96)                                     | 6.25 (± 10.49)                                       |
| Cycle 9 day 1 (n=2, 5, 4, 4)         | -8.33 (± 11.79)                          | -10.00 (± 19.90)                          | 4.17 (± 14.43)                                     | 6.25 (± 10.49)                                       |
| Cycle 10 day 1 (n=2, 3, 4, 5)        | -8.33 (± 35.36)                          | -16.67 (± 22.05)                          | 8.33 (± 11.79)                                     | 3.33 (± 7.45)  |
| End of treatment (n=5, 5, 3, 2)      | 3.33 (± 33.64)                           | -11.67 (± 13.94)                          | -11.11 (± 20.97)                                   | -12.50 (± 5.89)                                      |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Stage 1: Change From Baseline in European Organization for Research and Treatment of Cancer Quality of Life Multiple Myeloma Specific Module With 20 Items (EORTC QLQ-MY20) Scores: Disease Symptom Subscale Score

|                 |  |
|-----------------|--|
| End point title | Phase 2 Stage 1: Change From Baseline in European Organization for Research and Treatment of Cancer Quality of Life Multiple Myeloma Specific Module With 20 Items (EORTC QLQ-MY20) Scores: Disease Symptom Subscale Score <sup>[31]</sup> |
|-----------------|--|

### End point description:

EORTC QLQ-MY20 is a validated questionnaire to assess the overall quality of life in participants with MM. It has 4 subscales: body image, future perspective), and 2 symptoms scales (disease symptoms and side-effects of treatment). Disease symptoms subscale used 4-point scale ranged from 1= 'Not at All' to 4= 'Very Much'. Scores were averaged, and transformed to 0 -100 scale, where higher scores = more symptoms and lower health-related quality of life (HRQL) and lower score = less symptoms and more HRQL. Analysis was performed on AT population. Here, "Number of Participants Analyzed" = participants evaluable for this outcome measure and 'n' = number of participants with data collected for each category.

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

### End point timeframe:

Baseline, Day 1 of Cycles 2, 3, 4, 5, 6, 7, 8, 9, 10 and EOT (anytime up to 77 weeks for Stage 1a arms and 53 weeks for stage 1b arm)

### 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: Only Phase 2 Stage 1 participants were analyzed in this endpoint.



| End point values                     | Phase 2 Stage 1a: Isatuximab 3 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                          | Reporting group                           | Reporting group                                    | Reporting group                                      |
| Number of subjects analysed          | 22                                       | 21  | 23   | 22   |
| Units: score on a scale              |  |   |  |  |
| arithmetic mean (standard deviation) |  |   |  |  |
| Cycle 2 day 1 (n=14, 13, 18, 17)     | 5.56 (± 18.36)                           | -3.42 (± 11.24)                           | 0.93 (± 13.91)                                     | 2.61 (± 18.75)                                       |
| Cycle 3 day 1 (n=7, 11, 13, 11)      | 7.94 (± 11.94)                           | -5.05 (± 14.15)                           | -5.98 (± 16.89)                                    | -1.52 (± 13.17)                                      |
| Cycle 4 day 1 (n=4, 10, 10, 9)       | 8.33 (± 13.22)                           | -3.89 (± 16.98)                           | -10.00 (± 16.93)                                   | 0.62 (± 30.10)                                       |
| Cycle 5 day 1 (n=4, 11, 8, 5)        | -6.94 (± 10.52)                          | 0.51 (± 19.95)                            | -9.03 (± 17.04)                                    | -6.67 (± 17.74)                                      |
| Cycle 6 day 1 (n=4, 9, 7, 4)         | 8.33 (± 7.17)                            | 1.23 (± 23.53)                            | -15.08 (± 20.96)                                   | -6.94 (± 10.52)                                      |
| Cycle 7 day 1 (n=2, 6, 4, 5)         | 2.78 (± 3.93)                            | -3.70 (± 22.95)                           | -18.06 (± 21.93)                                   | -11.11 (± 11.79)                                     |
| Cycle 8 day 1 (n=2, 6, 4, 4)         | -5.56 (± 7.86)                           | -2.78 (± 23.50)                           | -15.28 (± 23.30)                                   | -4.17 (± 5.32)                                       |
| Cycle 9 day 1 (n=2, 5, 4, 4)         | 5.56 (± 7.86)                            | -10.00 (± 10.69)                          | -16.67 (± 29.75)                                   | -6.94 (± 12.32)                                      |
| Cycle 10 day 1 (n=2, 3, 4, 5)        | 0.00 (± 0.00)                            | 0.00 (± 19.25)                            | -15.28 (± 30.56)                                   | -6.67 (± 17.30)                                      |
| End of treatment (n=4, 5, 3, 2)      | -9.72 (± 19.44)                          | 7.78 (± 24.41)                            | 24.07 (± 22.45)                                    | 25.00 (± 35.36)                                      |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Stage 1: Change From Baseline in Euro Quality of Life 5 Dimension (EQ-5D) Generic Health Status - Visual Analogue Scale Scores

|                 |  |
|-----------------|--|
| End point title | Phase 2 Stage 1: Change From Baseline in Euro Quality of Life 5 Dimension (EQ-5D) Generic Health Status - Visual Analogue Scale Scores <sup>[32]</sup> |
|-----------------|--|

End point description:

EQ-5D was a standardized HRQL questionnaire consisting of EQ-5D descriptive system and Visual Analogue Scale (VAS). EQ-5D VAS was used to record a participant's rating for his/her current health-related quality of life state and captured on a vertical VAS (0-100), where 0 = worst imaginable health state and 100 = best imaginable health state. Analysis was performed on AT population. Here, "Number of Participants Analyzed" = participants evaluable for this outcome measure and 'n' = number of participants with available data for each category. 22222=Standard deviation cannot be calculated for a single participant. 99999=no evaluable participants

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

End point timeframe:

Baseline, Day 1 of Cycles 4, 7, 10, 13, 16, 19, and EOT (anytime up to 77 weeks for Stage 1a arms and 53 weeks for stage 1b arm)

Notes:

[32] - 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: Only Phase 2 Stage 1 participants were analyzed in this endpoint.

| End point values                     | Phase 2 Stage 1a: Isatuximab 3 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10 mg/kg Q2W | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                          | Reporting group                           | Reporting group                                    | Reporting group                                      |
| Number of subjects analysed          | 22                                       | 21  | 22   | 22   |
| Units: score on a scale              |  |   |  |  |
| arithmetic mean (standard deviation) |  |   |  |  |
| Cycle 4 day 1 (n=4, 9, 9, 9)         | -5.75 (± 18.55)                          | 2.00 (± 16.88)                            | -4.78 (± 15.71)                                    | 4.89 (± 16.02)                                       |
| Cycle 7 day 1 (n=2, 6, 3, 5)         | -2.50 (± 0.71)                           | -6.00 (± 27.39)                           | 9.00 (± 18.25)                                     | 1.00 (± 7.94)  |
| Cycle 10 day 1 (n=2, 3, 3, 5)        | 0.50 (± 2.12)                            | -10.33 (± 9.29)                           | 10.33 (± 24.38)                                    | -2.60 (± 8.11)                                       |
| Cycle 13 day 1 (n=2, 3, 1, 1)        | 14.00 (± 19.80)                          | -5.00 (± 4.00)                            | -9.00 (± 22222)                                    | -5.00 (± 22222)                                      |
| Cycle 16 day 1 (n=2, 3, 0, 0)        | 5.00 (± 5.66)                            | 0.67 (± 23.71)                            | 99999 (± 99999)                                    | 99999 (± 99999)                                      |
| Cycle 19 day 1 (n=0, 2, 0, 0)        | 99999 (± 99999)                          | -5.50 (± 4.95)                            | 99999 (± 99999)                                    | 99999 (± 99999)                                      |
| End of treatment (n=4, 5, 3, 2)      | -18.50 (± 16.98)                         | -11.60 (± 11.37)                          | -10.00 (± 9.54)                                    | -9.00 (± 0.00)                                       |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetic assessment: Phase 2 Stage 2: Area under the plasma concentration versus time curve of Isatuximab over 1 week interval

|                 |   |
|-----------------|---|
| End point title | Pharmacokinetic assessment: Phase 2 Stage 2: Area under the plasma concentration versus time curve of Isatuximab over 1 week interval <sup>[33]</sup> |
|-----------------|---|

End point description:

Analysis was performed on PK population which included participants who gave informed consent, received at least one dose (even if incomplete) of isatuximab, had an assessable PK parameter.

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

End point timeframe:

Pre-dose, at the end of infusion, 1 hour and 168 hours post dose on Day 1 of Cycle 1

Notes:

[33] - 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: Only Phase 2 Stage 2 participants were analyzed in this endpoint.

| End point values                                    | Phase 2 Stage 2: Isatuximab alone | Phase 2 Stage 2: Isatuximab + Dexamethasone |  |  |
|---|-----------------------------------|---|--|--|
| Subject group type                                  | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed                         | 102                               | 52  |  |  |
| Units: mcg*hour/mL                                  |                                   |   |  |  |
| geometric mean (geometric coefficient of variation) | 37096 (± 80)                      | 35423 (± 88)                                |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetic assessment: Phase 2 Stage 2: Area under the plasma concentration versus time curve of Isatuximab over 2 weeks interval

|                 |  |
|-----------------|--|
| End point title | Pharmacokinetic assessment: Phase 2 Stage 2: Area under the plasma concentration versus time curve of Isatuximab over 2 weeks interval <sup>[34]</sup> |
|-----------------|--|

End point description:

Analysis was performed on PK population.

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

End point timeframe:

Cycle 1, Day 1: pre-dose, at the end of infusion, 168 and 336 hours post-infusion

Notes:

[34] - 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: Only Phase 2 Stage 2 participants were analyzed in this endpoint.

| End point values                                    | Phase 2 Stage 2: Isatuximab alone | Phase 2 Stage 2: Isatuximab + Dexamethasone |  |  |
|---|-----------------------------------|---|--|--|
| Subject group type                                  | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed                         | 102                               | 52  |  |  |
| Units: mcg*hour/mL                                  |                                   |   |  |  |
| geometric mean (geometric coefficient of variation) | 91271 ( $\pm$ 78)                 | 86761 ( $\pm$ 77)                           |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetic assessment: Phase 2 Stage 2: Area under the plasma concentration versus time curve of Isatuximab over 4 weeks interval

|                 |  |
|-----------------|--|
| End point title | Pharmacokinetic assessment: Phase 2 Stage 2: Area under the plasma concentration versus time curve of Isatuximab over 4 weeks interval <sup>[35]</sup> |
|-----------------|--|

End point description:

Analysis was performed on PK population.

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

End point timeframe:

Cycle 1, Day 1: pre-dose, at the end of infusion, 168, 336, and 672 hours post-infusion

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: Only Phase 2 Stage 2 participants were analyzed in this endpoint.

| End point values                                    | Phase 2 Stage 2: Isatuximab alone | Phase 2 Stage 2: Isatuximab + Dexamethasone |  |  |
|---|-----------------------------------|---|--|--|
| Subject group type                                  | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed                         | 102                               | 52  |  |  |
| Units: mcg*hour/mL                                  |                                   |   |  |  |
| geometric mean (geometric coefficient of variation) | 236360 ( $\pm$ 72)                | 226372 ( $\pm$ 66)                          |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetic assessment: Phase 2 Stage 2: Accumulation ratio of Isatuximab based on Ctrough

|                 |  |
|-----------------|--|
| End point title | Pharmacokinetic assessment: Phase 2 Stage 2: Accumulation ratio of Isatuximab based on Ctrough <sup>[36]</sup> |
|-----------------|--|

End point description:

Ctrough is the plasma concentration observed before treatment administration. For 1st category, the accumulation ratio was calculated by dividing Ctrough value of Cycle 2 Day 1 by Cycle 1 Day 8 and for second category, accumulation ratio was calculated by dividing Ctrough value of Cycle 4 Day 1 by Cycle 1 Day 8. Analysis was performed on PK population. Here, 'number of participants analyzed' = participants evaluable for this outcome measure.

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

End point timeframe:

Cycle 2, Day 1; Cycle 1, Day 8; Cycle 4, Day 1

Notes:

[36] - 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: Only Phase 2 Stage 2 participants were analyzed in this endpoint.

| End point values                     | Phase 2 Stage 2: Isatuximab alone | Phase 2 Stage 2: Isatuximab + Dexamethasone |  |  |
|--------------------------------------|-----------------------------------|---|--|--|
| Subject group type                   | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed          | 95                                | 48  |  |  |
| Units: ratio                         |                                   |   |  |  |
| arithmetic mean (standard deviation) |                                   |   |  |  |
| Cycle 2 Day 1/Cycle 1 Day 8          | 521.38338 ( $\pm$ 4891.63390)     | 3.24370 ( $\pm$ 1.73860)                    |  |  |
| Cycle 4 Day 1/Cycle 1 Day 8          | 3.58378 ( $\pm$ 2.77398)          | 3.95950 ( $\pm$ 3.19310)                    |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetic assessment: Phase 2 Stage 2: plasma concentration of Isatuximab before treatment administration (Ctough)

|                 |  |
|-----------------|--|
| End point title | Pharmacokinetic assessment: Phase 2 Stage 2: plasma concentration of Isatuximab before treatment administration (Ctough) <sup>[37]</sup> |
|-----------------|--|

End point description:

Analysis was performed on PK population.

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

End point timeframe:

At Days 7, 14, 28

Notes:

[37] - 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: Only Phase 2 Stage 2 participants were analyzed in this endpoint.

| End point values                                    | Phase 2 Stage 2: Isatuximab alone | Phase 2 Stage 2: Isatuximab + Dexamethasone |  |  |
|---|-----------------------------------|---|--|--|
| Subject group type                                  | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed                         | 102                               | 52  |  |  |
| Units: mcg/mL                                       |                                   |   |  |  |
| geometric mean (geometric coefficient of variation) |                                   |   |  |  |
| Day 7   | 137 (± 75)                        | 128 (± 54)                                  |  |  |
| Day 14  | 230 (± 70)                        | 214 (± 57)                                  |  |  |
| Day 28  | 360 (± 63)                        | 305 (± 66)                                  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Immunogenicity assessment: Phase 2 Stage 2: Number of participants with anti-drug antibodies to Isatuximab

|                 |  |
|-----------------|--|
| End point title | Immunogenicity assessment: Phase 2 Stage 2: Number of participants with anti-drug antibodies to Isatuximab <sup>[38]</sup> |
|-----------------|--|

End point description:

ADA response was categorized as: treatment induced and treatment boosted response. Treatment-induced ADA was defined as ADA that developed at any time during the ADA on-study observation period (defined as the time from the first isatuximab administration until end of Phase 2 Stage 2) in participants without preexisting ADA (defined as: ADA that were present in samples drawn before

treatment), including participants without pre-treatment (before treatment) samples. Treatment boosted ADA was defined as pre-existing ADA that increased at least 2 titer steps between pre-treatment (before treatment) and post-treatment. Analysis was performed on ADA evaluable population which included all treated participants with at least one ADA assessment with a reportable result during the ADA on-study observation period.

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

End point timeframe:

Up to 97 weeks

Notes:

[38] - 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: Only Phase 2 Stage 2 participants were analyzed in this endpoint.

| End point values            | Phase 2 Stage 2: Isatuximab alone | Phase 2 Stage 2: Isatuximab + Dexamethasone |  |  |
|-----------------------------|-----------------------------------|---|--|--|
| Subject group type          | Reporting group                   | Reporting group                             |  |  |
| Number of subjects analysed | 107                               | 53  |  |  |
| Units: participants         |                                   |   |  |  |
| Treatment induced ADA       | 1                                 | 0   |  |  |
| Treatment boosted ADA       | 0                                 | 0   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All AEs=from signing of informed consent up to 30 days from last administration of IP(maximum exposure:up to 120 weeks-Phase 1, 414 weeks-Phase 2 Stage 1a,92 weeks-Phase 2 Stage 1b, 301 weeks-Phase 2 Stage 2).Deaths=for entire study duration, 683 weeks

Adverse event reporting additional description:

Reported AEs and deaths were TEAEs which was defined as an AE that developed or worsened during the 'on treatment period' (time from the first dose of any study treatment up to 30 days after the last administration of the study treatment). Analysis was performed on AT population. Phase 1 MedDRA version was 19.1. Phase 2 MedDRA version was 26.0.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 26.0   |

### Reporting groups

|                       |                                  |
|-----------------------|----------------------------------|
| Reporting group title | Phase 1: Isatuximab <=1mg/kg Q2W |
|-----------------------|----------------------------------|

Reporting group description:

Participants with CD38+ HM, received Isatuximab at any one of the dose <=1 mg/kg (i.e. either 0.0001 mg/kg or 0.001 mg/kg or 0.01 mg/kg or 0.03 mg/kg, or 0.1 mg/kg or 0.3 mg/kg or 1 mg/kg) as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal by participant, investigator's decision, and/or availability of study drug.

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Phase 1: Isatuximab 3mg/kg Q2W |
|-----------------------|--------------------------------|

Reporting group description:

Participants with CD38+ HM, received Isatuximab 3 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Phase 1: Isatuximab 5mg/kg Q2W |
|-----------------------|--------------------------------|

Reporting group description:

Participants with CD38+ HM, received Isatuximab 5 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase1:Isatuximab (CD38+HM and Standard Risk Multiple Myeloma) |
|-----------------------|--|

Reporting group description:

Participants with CD38+ HM along with participants with standard risk multiple myeloma were included in this arm and, received Isatuximab 10 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 1: Isatuximab (CD38 + HM and High Risk Multiple Myeloma) |
|-----------------------|--|

Reporting group description:

Participants with CD38+ HM along with participants with high risk multiple myeloma were included in this arm and, received Isatuximab 10 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Phase 1: Isatuximab 10mg/kg QW |
|-----------------------|--------------------------------|

Reporting group description:

Participants with CD38+ HM, received Isatuximab 10 mg/kg, as IV infusion QW, i.e. on Day 1 and 8 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | Phase 1: Isatuximab 20mg/kg Q2W |
|-----------------------|---------------------------------|

Reporting group description:

Participants with CD38+ HM, received Isatuximab 20 mg/kg, as IV infusion on Day 1 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent

withdrawal, investigator's decision, and/or availability of study drug.

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Phase 1: Isatuximab 20mg/kg QW |
|-----------------------|--------------------------------|

Reporting group description:

Participants with CD38+ HM, received Isatuximab 20 mg/kg, as IV infusion QW, i.e. on Day 1 and 8 of each 14-day treatment cycle until occurrence of unacceptable toxicity, disease progression, death, consent withdrawal, investigator's decision, and/or availability of study drug.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase 2 Stage 1a: Isatuximab 3mg/kg Q2W |
|-----------------------|---|

Reporting group description:

Participants with multiple Myeloma received Isatuximab 3 mg/kg, as IV infusion on Day 1 and Day 15 of each 28-day cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W |
|-----------------------|--|

Reporting group description:

Participants with multiple Myeloma received Isatuximab 10 mg/kg, as IV infusion on Day 1 and Day 15 of each 28-day cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 2 Stage 1a: Isatuximab 10mg/kg Q2W; Then Q4W |
|-----------------------|--|

Reporting group description:

Participants with multiple Myeloma received Isatuximab 10 mg/kg, as IV infusion Q2W, i.e. on Day 1 and Day 15 of Cycle 1 and 2 (each cycle 28 days), then every 4 weeks (Q4W), i.e. on Day 1 of each 28-days cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 2 Stage 1b: Isatuximab 20mg/kg QW and Then Q2W |
|-----------------------|--|

Reporting group description:

Participants with multiple Myeloma received Isatuximab 20 mg/kg, as IV infusion QW, i.e. on Day 1, 8, 15 and 22 of Cycle 1 and 2 (each cycle 28 days), then Q2W, i.e. on Day 1 and Day 15 of each 28-days cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination or lost to follow up.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Phase 2 Stage 2: Isatuximab Alone |
|-----------------------|-----------------------------------|

Reporting group description:

Participants with relapsed or relapsed/refractory multiple myeloma (RRMM), received Isatuximab 20 mg/kg, as IV infusion on Day 1, 8, 15 and Day 22 of Cycle 1 (28 days) and then on Day 1 and 15 of each subsequent 28-day cycles until unacceptable AE, disease progression, poor compliance to the study protocol, study termination, lost to follow up or investigator's decision.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase 2 Stage 2: Isatuximab + Dexamethasone |
|-----------------------|---|

Reporting group description:

Participants with relapsed or RRMM, received Isatuximab 20 mg/kg, as IV infusion on Day 1, 8, 15 and Day 22 of Cycle 1 (28 days) and then on Day 1 and 15 of each subsequent 28-day cycles along with dexamethasone: tablet or as IV infusion (40 mg/day for <75 years of age; 20 mg/day for ≥75 years of age) on Days 1, 8, 15 and 22 of each 28 days cycle until unacceptable AE, disease progression, poor compliance to the study protocol, study termination, lost to follow up or investigator's decision.

| <b>Serious adverse events</b>                                       | Phase 1: Isatuximab<br><=1mg/kg Q2W | Phase 1: Isatuximab<br>3mg/kg Q2W | Phase 1: Isatuximab<br>5mg/kg Q2W |
|---|-------------------------------------|-----------------------------------|-----------------------------------|
| Total subjects affected by serious adverse events                   |                                     |                                   |                                   |
| subjects affected / exposed   | 3 / 16 (18.75%)                     | 3 / 6 (50.00%)                    | 1 / 3 (33.33%)                    |
| number of deaths (all causes)                                       | 5                                   | 1                                 | 0                                 |
| number of deaths resulting from adverse events                      |                                     |                                   |                                   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                     |                                   |                                   |
| Basal Cell Carcinoma  |                                     |                                   |                                   |



|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Colon Cancer                                    |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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                     | 1 / 16 (6.25%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Malignant Melanoma                              |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Plasma Cell Leukaemia                           |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 The Oral Cavity      |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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                              |                |               |               |
| Aortic Aneurysm                                 |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Extrinsic Iliac Vein Compression                |                |               |               |

|  |                |               |               |
|--|----------------|---------------|---------------|
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0         |
| Hypertensive Crisis                                  |                |               |               |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0         |
| Hypotension  |                |               |               |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 |                |               |               |
| Chills   |                |               |               |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0         |
| Asthenia   |                |               |               |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0         |
| Disease Progression                                  |                |               |               |
| subjects affected / exposed                          | 1 / 16 (6.25%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0         |
| Fatigue  |                |               |               |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0         |
| Feeling Cold   |                |               |               |
| subjects affected / exposed                          | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0         |
| Hyperpyrexia   |                |               |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| General Physical Health Deterioration           |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Non-Cardiac Chest Pain                          |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Malaise   |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pain  |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 1 / 6 (16.67%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Physical Deconditioning                         |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Performance Status Decreased                    |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Sudden Death                                    |                |                |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                       | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0         | 0 / 0         |
| Social circumstances                              |                |               |               |
| Loss Of Personal Independence In Daily Activities |                |               |               |
| subjects affected / exposed                       | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0         | 0 / 0         |
| Reproductive system and breast disorders          |                |               |               |
| Prostatitis                                       |                |               |               |
| subjects affected / exposed                       | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0         | 0 / 0         |
| Pelvic Pain                                       |                |               |               |
| subjects affected / exposed                       | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0         | 0 / 0         |
| Dyspnoea  |                |               |               |
| subjects affected / exposed                       | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0         | 0 / 0         |
| Bronchospasm                                      |                |               |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Apnoea  |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Dyspnoea At Rest                                |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Dyspnoea Exertional                             |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Haemoptysis                                     |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Laryngeal Oedema                                |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Laryngospasm                                    |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Pharyngeal Swelling                             |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Pleural Effusion                                |                |               |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Respiratory Tract Haemorrhage                   |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 Alkalosis                           |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 Fibrosis                              |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Product issues                                  |                |               |               |
| Device Malfunction                              |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Device Occlusion                                |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Investigations                                  |                |               |               |
| Blood Creatinine Increased                      |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 Pressure Increased                        |                |               |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                           | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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>Injury, poisoning and procedural complications</b> |                |               |               |
| Fall  |                |               |               |
| subjects affected / exposed                           | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         | 0 / 0         |
| Infusion Related Reaction                             |                |               |               |
| subjects affected / exposed                           | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         | 0 / 0         |
| Joint Injury  |                |               |               |
| subjects affected / exposed                           | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         | 0 / 0         |
| Road Traffic Accident                                 |                |               |               |
| subjects affected / exposed                           | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         | 0 / 0         |
| Post Procedural Complication                          |                |               |               |
| subjects affected / exposed                           | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         | 0 / 0         |
| Traumatic Fracture                                    |                |               |               |
| subjects affected / exposed                           | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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>Cardiac disorders</b>                              |                |               |               |
| Acute Coronary Syndrome                               |                |               |               |
| subjects affected / exposed                           | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         | 0 / 0         |

|   |                |               |               |
|---|----------------|---------------|---------------|
| Acute Myocardial Infarction                     |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Stress Cardiomyopathy                           |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Cardiac Failure                                 |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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                        |                |               |               |
| Cerebral Haemorrhage                            |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Dizziness                                       |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Headache  |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Sciatica  |                |               |               |



|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Ischaemic Stroke                                |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Seizure   |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Spinal Cord Compression                         |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Somnolence                                      |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Blood and lymphatic system disorders            |                |               |               |
| Anaemia   |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Febrile Neutropenia                             |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Hyperviscosity Syndrome                         |                |               |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Thrombocytopenia                                |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Eye disorders                                   |                |               |               |
| Eye Pain  |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Cataract  |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Visual Impairment                               |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Gastrointestinal disorders                      |                |               |               |
| Diarrhoea                                       |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Diverticular Perforation                        |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Gastrointestinal Haemorrhage                    |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Gastrointestinal Amyloidosis                    |                |               |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Intussusception                                 |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Ileus   |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Mechanical Ileus                                |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Nausea  |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Small Intestinal Obstruction                    |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Obstruction Gastric                             |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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                         |                |               |               |
| Hyperbilirubinaemia                             |                |               |               |

|   |                |               |                |
|---|----------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Cholestasis                                     |                |               |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Renal and urinary disorders                     |                |               |                |
| Acute Kidney Injury                             |                |               |                |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Chronic Kidney Disease                          |                |               |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Endocrine disorders                             |                |               |                |
| Hypercalcaemia Of Malignancy                    |                |               |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| 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 |                |               |                |
| Musculoskeletal Chest Pain                      |                |               |                |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Back Pain                                       |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pathological Fracture                           |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Spinal Stenosis                                 |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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                     |                |                |               |
| Acute Sinusitis                                 |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Abdominal Sepsis                                |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 1 / 6 (16.67%) | 0 / 3 (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         |
| Atypical Pneumonia                              |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Bronchiolitis                                   |                |                |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Bronchitis                                      |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Campylobacter Gastroenteritis                   |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Covid-19 Pneumonia                              |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Device Related Infection                        |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Escherichia Sepsis                              |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Gastroenteritis                                 |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Gastroenteritis Rotavirus                       |                |               |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Haemophilus Sepsis                              |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Infectious Colitis                              |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Infective Aortitis                              |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Intervertebral Discitis                         |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Lower Respiratory Tract Infection               |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Lower Respiratory Tract Infection Viral         |                |               |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 Bacterial                            |                |               |               |
| subjects affected / exposed                     | 1 / 16 (6.25%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 0         |
| Meningococcal Sepsis                            |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Otitis Media                                    |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Parainfluenzae Virus Infection                  |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Pneumococcal Bacteraemia                        |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Pneumocystis Jirovecii Pneumonia                |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Pneumonia Aspiration                            |                |               |               |



|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 1 / 6 (16.67%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pneumonia Bacterial                             |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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 Mycoplasmal                           |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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 Respiratory Syncytial Viral           |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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 Streptococcal                         |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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 Sepsis                                |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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 Syncytial Virus Infection           |                |                |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Respiratory Tract Infection                     |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Septic Shock                                    |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| 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 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Sinusitis                                       |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Tracheobronchitis                               |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Upper Respiratory Tract Infection               |                |               |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Urinary Tract Infection                         |                |               |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 1 / 6 (16.67%) | 0 / 3 (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         |
| Varicella                                       |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Varicella Zoster Virus Infection                |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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              |                |                |               |
| Decreased Appetite                              |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Dehydration                                     |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Electrolyte Imbalance                           |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| 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                     | 1 / 16 (6.25%) | 1 / 6 (16.67%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Tumour Lysis Syndrome                           |                |                |               |
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Hyperuricaemia                                  |                |                |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 16 (0.00%) | 0 / 6 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |

| <b>Serious adverse events</b>                                       | Phase1:Isatuximab<br>(CD38+HM and<br>Standard Risk<br>Multiple Myeloma) | Phase 1: Isatuximab<br>(CD38 + HM and<br>High Risk Multiple<br>Myeloma) | Phase 1: Isatuximab<br>10mg/kg QW |
|---|---|---|-----------------------------------|
| Total subjects affected by serious adverse events                   |   |   |                                   |
| subjects affected / exposed   | 10 / 26 (38.46%)  | 10 / 18 (55.56%)  | 3 / 6 (50.00%)                    |
| number of deaths (all causes)                                       | 0   | 2   | 2                                 |
| number of deaths resulting from adverse events                      |   |   |                                   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |   |                                   |
| Basal Cell Carcinoma  |   |   |                                   |
| subjects affected / exposed   | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 1 / 6 (16.67%)                    |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0   | 0 / 1                             |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0                             |
| Colon Cancer  |   |   |                                   |
| subjects affected / exposed   | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)                     |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0   | 0 / 0                             |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0                             |
| Myelodysplastic Syndrome  |   |   |                                   |
| subjects affected / exposed   | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)                     |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0   | 0 / 0                             |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0                             |
| Malignant Melanoma  |   |   |                                   |
| subjects affected / exposed   | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)                     |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0   | 0 / 0                             |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0                             |
| Plasma Cell Leukaemia   |   |   |                                   |
| subjects affected / exposed   | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)                     |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0   | 0 / 0                             |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0                             |
| Prostate Cancer   |   |   |                                   |

|  |                |                |               |
|--|----------------|----------------|---------------|
| subjects affected / exposed                          | 0 / 26 (0.00%) | 1 / 18 (5.56%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Squamous Cell Carcinoma Of The Oral Cavity           |                |                |               |
| subjects affected / exposed                          | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Vascular disorders                                   |                |                |               |
| Aortic Aneurysm                                      |                |                |               |
| subjects affected / exposed                          | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Extrinsic Iliac Vein Compression                     |                |                |               |
| subjects affected / exposed                          | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Hypertensive Crisis                                  |                |                |               |
| subjects affected / exposed                          | 1 / 26 (3.85%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Hypotension  |                |                |               |
| subjects affected / exposed                          | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| General disorders and administration site conditions |                |                |               |
| Chills   |                |                |               |
| subjects affected / exposed                          | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |
| Asthenia   |                |                |               |
| subjects affected / exposed                          | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0         |

|   |                |                |               |  |
|---|----------------|----------------|---------------|--|
| Disease Progression                             |                |                |               |  |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |  |
| Fatigue   |                |                |               |  |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |  |
| Feeling Cold                                    |                |                |               |  |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |  |
| Hyperpyrexia                                    |                |                |               |  |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |  |
| General Physical Health Deterioration           |                |                |               |  |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |  |
| Non-Cardiac Chest Pain                          |                |                |               |  |
| subjects affected / exposed                     | 1 / 26 (3.85%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |  |
| Malaise   |                |                |               |  |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |  |
| Pain  |                |                |               |  |
| subjects affected / exposed                     | 1 / 26 (3.85%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |  |
| Pyrexia   |                |                |               |  |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                       | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0         |
| Physical Deconditioning                           |                |                |               |
| subjects affected / exposed                       | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0         |
| Performance Status Decreased                      |                |                |               |
| subjects affected / exposed                       | 1 / 26 (3.85%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0         |
| Sudden Death                                      |                |                |               |
| subjects affected / exposed                       | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0         |
| Immune system disorders                           |                |                |               |
| Anaphylactic Reaction                             |                |                |               |
| subjects affected / exposed                       | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0         |
| Social circumstances                              |                |                |               |
| Loss Of Personal Independence In Daily Activities |                |                |               |
| subjects affected / exposed                       | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0         |
| Reproductive system and breast disorders          |                |                |               |
| Prostatitis                                       |                |                |               |
| subjects affected / exposed                       | 0 / 26 (0.00%) | 1 / 18 (5.56%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0         |
| Pelvic Pain                                       |                |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders |                |                |               |
| Acute Respiratory Failure                       |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Dyspnoea  |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Bronchospasm                                    |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Apnoea  |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Dyspnoea At Rest                                |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Dyspnoea Exertional                             |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Haemoptysis                                     |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Laryngeal Oedema                                |                |                |               |



|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Laryngospasm                                    |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pharyngeal Swelling                             |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pleural Effusion                                |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pulmonary Embolism                              |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Respiratory Tract Haemorrhage                   |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Respiratory Alkalosis                           |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pulmonary Fibrosis                              |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Product issues                                  |                |                |               |
| Device Malfunction                              |                |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Device Occlusion                                |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Investigations                                  |                |                |               |
| Blood Creatinine Increased                      |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 1 / 18 (5.56%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Blood Pressure Increased                        |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Injury, poisoning and procedural complications  |                |                |               |
| Fall  |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Infusion Related Reaction                       |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Joint Injury                                    |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 1 / 18 (5.56%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Road Traffic Accident                           |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Post Procedural Complication                    |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Traumatic Fracture                              |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Acute Coronary Syndrome                         |                |                |                |
| subjects affected / exposed                     | 1 / 26 (3.85%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Acute Myocardial Infarction                     |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Atrial Fibrillation                             |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Stress Cardiomyopathy                           |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tachycardia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Cerebral Haemorrhage                            |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Dizziness                                       |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Headache  |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Sciatica  |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Ischaemic Stroke                                |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Seizure   |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Spinal Cord Compression                         |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Somnolence                                      |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Syncope   |                |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| <b>Blood and lymphatic system disorders</b>     |                |                |               |
| <b>Anaemia</b>                                  |                |                |               |
| subjects affected / exposed                     | 1 / 26 (3.85%) | 1 / 18 (5.56%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| <b>Febrile Neutropenia</b>                      |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 1 / 18 (5.56%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| <b>Hyperviscosity Syndrome</b>                  |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| <b>Thrombocytopenia</b>                         |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| <b>Eye disorders</b>                            |                |                |               |
| <b>Eye Pain</b>                                 |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| <b>Cataract</b>                                 |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| <b>Visual Impairment</b>                        |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| <b>Gastrointestinal disorders</b>               |                |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Diarrhoea                                       |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Diverticular Perforation                        |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Gastrointestinal Haemorrhage                    |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Gastrointestinal Amyloidosis                    |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Intussusception                                 |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Ileus   |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Mechanical Ileus                                |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Nausea  |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Vomiting  |                |                |               |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Small Intestinal Obstruction                    |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Obstruction Gastric                             |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Hyperbilirubinaemia                             |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cholestasis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Acute Kidney Injury                             |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 1 / 18 (5.56%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 1 / 1          | 0 / 0          |
| Chronic Kidney Disease                          |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal Failure                                   |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Endocrine disorders                             |                |                |                |

|   |                |                 |               |
|---|----------------|-----------------|---------------|
| Hypercalcaemia Of Malignancy<br>subjects affected / exposed | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 0           | 0 / 0         |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0           | 0 / 0         |
| Musculoskeletal and connective tissue<br>disorders          |                |                 |               |
| Musculoskeletal Chest Pain<br>subjects affected / exposed   | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 0           | 0 / 0         |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0           | 0 / 0         |
| Bone Pain<br>subjects affected / exposed                    | 0 / 26 (0.00%) | 1 / 18 (5.56%)  | 0 / 6 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 1           | 0 / 0         |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0           | 0 / 0         |
| Back Pain<br>subjects affected / exposed                    | 0 / 26 (0.00%) | 2 / 18 (11.11%) | 0 / 6 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 2           | 0 / 0         |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0           | 0 / 0         |
| Musculoskeletal Pain<br>subjects affected / exposed         | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 0           | 0 / 0         |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0           | 0 / 0         |
| Pathological Fracture<br>subjects affected / exposed        | 0 / 26 (0.00%) | 1 / 18 (5.56%)  | 0 / 6 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 1           | 0 / 0         |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0           | 0 / 0         |
| Pain In Extremity<br>subjects affected / exposed            | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 0           | 0 / 0         |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0           | 0 / 0         |
| Spinal Stenosis<br>subjects affected / exposed              | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 0           | 0 / 0         |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0           | 0 / 0         |



|  |                                  |                                  |                                 |
|--|----------------------------------|----------------------------------|---------------------------------|
| Infections and infestations<br>Acute Sinusitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | 0 / 26 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 18 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0 |
| Abdominal Sepsis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                               | 0 / 26 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 18 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0 |
| Atypical Pneumonia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                             | 0 / 26 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 18 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0 |
| Bronchiolitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                  | 0 / 26 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 18 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0 |
| Bronchitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                     | 1 / 26 (3.85%)<br>0 / 1<br>0 / 0 | 0 / 18 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0 |
| Campylobacter Gastroenteritis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                  | 0 / 26 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 18 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0 |
| Covid-19 Pneumonia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                             | 0 / 26 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 18 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0 |
| Cellulitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                     | 0 / 26 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 18 (0.00%)<br>0 / 0<br>0 / 0 | 0 / 6 (0.00%)<br>0 / 0<br>0 / 0 |
| Device Related Infection   |                                  |                                  |                                 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Escherichia Sepsis                              |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis Rotavirus                       |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Haemophilus Sepsis                              |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infectious Colitis                              |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 1 / 18 (5.56%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Herpes Zoster                                   |                |                |                |
| subjects affected / exposed                     | 1 / 26 (3.85%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infective Aortitis                              |                |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Influenza                                       |                |                |                |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Intervertebral Discitis                         |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Lower Respiratory Tract Infection               |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Lower Respiratory Tract Infection Viral         |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Lung Infection                                  |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 1 / 18 (5.56%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Meningitis Bacterial                            |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Meningococcal Sepsis                            |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Otitis Media                                    |                |                |               |
| subjects affected / exposed                     | 1 / 26 (3.85%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Parainfluenzae Virus Infection                  |                |                |               |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 26 (0.00%)  | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumococcal Bacteraemia                        |                 |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%)  | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumocystis Jirovecii Pneumonia                |                 |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%)  | 1 / 18 (5.56%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia Aspiration                            |                 |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%)  | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                 |                |                |
| subjects affected / exposed                     | 4 / 26 (15.38%) | 0 / 18 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 2 / 4           | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia Bacterial                             |                 |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%)  | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia Mycoplasmal                           |                 |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%)  | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia Respiratory Syncytial Viral           |                 |                |                |
| subjects affected / exposed                     | 0 / 26 (0.00%)  | 0 / 18 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia Streptococcal                         |                 |                |                |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pulmonary Sepsis                                |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pneumonia Viral                                 |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Respiratory Syncytial Virus Infection           |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pyelonephritis                                  |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Respiratory Tract Infection                     |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Septic Shock                                    |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Sepsis  |                |                |               |
| subjects affected / exposed                     | 2 / 26 (7.69%) | 1 / 18 (5.56%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Sinusitis                                       |                |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Tracheobronchitis                               |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Upper Respiratory Tract Infection               |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Urinary Tract Infection                         |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Varicella                                       |                |                |               |
| subjects affected / exposed                     | 1 / 26 (3.85%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Varicella Zoster Virus Infection                |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Metabolism and nutrition disorders              |                |                |               |
| Decreased Appetite                              |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Dehydration                                     |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Electrolyte Imbalance                           |                |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Hypercalcaemia                                  |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Tumour Lysis Syndrome                           |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 1 / 18 (5.56%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Hyperuricaemia                                  |                |                |               |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |

| Serious adverse events  | Phase 1: Isatuximab 20mg/kg Q2W | Phase 1: Isatuximab 20mg/kg QW | Phase 2 Stage 1a: Isatuximab 3mg/kg Q2W |
|---|---------------------------------|--------------------------------|---|
| Total subjects affected by serious adverse events                   |                                 |                                |   |
| subjects affected / exposed   | 3 / 7 (42.86%)                  | 3 / 7 (42.86%)                 | 13 / 23 (56.52%)                        |
| number of deaths (all causes)                                       | 2                               | 0                              | 11                                      |
| number of deaths resulting from adverse events                      |                                 |                                |   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                 |                                |   |
| Basal Cell Carcinoma  |                                 |                                |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                   | 0 / 7 (0.00%)                  | 0 / 23 (0.00%)                          |
| occurrences causally related to treatment / all                     | 0 / 0                           | 0 / 0                          | 0 / 0                                   |
| deaths causally related to treatment / all                          | 0 / 0                           | 0 / 0                          | 0 / 0                                   |
| Colon Cancer  |                                 |                                |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                   | 0 / 7 (0.00%)                  | 0 / 23 (0.00%)                          |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Plasma Cell Leukaemia                           |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 The Oral Cavity      |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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                              |               |               |                |
| Aortic Aneurysm                                 |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Extrinsic Iliac Vein Compression                |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hypertensive Crisis                             |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hypotension                                     |               |               |                |



|  |                |               |                 |
|--|----------------|---------------|-----------------|
| subjects affected / exposed                          | 1 / 7 (14.29%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| General disorders and administration site conditions |                |               |                 |
| Chills   |                |               |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| Asthenia   |                |               |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 1 / 23 (4.35%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| Disease Progression                                  |                |               |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 4 / 23 (17.39%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 4           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 4 / 4           |
| Fatigue  |                |               |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| Feeling Cold   |                |               |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| Hyperpyrexia   |                |               |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| General Physical Health Deterioration                |                |               |                 |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0           |
| Non-Cardiac Chest Pain                               |                |               |                 |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Malaise   |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pain  |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Physical Deconditioning                         |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Performance Status Decreased                    |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Sudden Death                                    |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Social circumstances                            |               |               |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Loss Of Personal Independence In Daily Activities |                |                |                |
| subjects affected / exposed                       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders          |                |                |                |
| Prostatitis                                       |                |                |                |
| subjects affected / exposed                       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Pelvic Pain                                       |                |                |                |
| subjects affected / exposed                       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| 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 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Dyspnoea  |                |                |                |
| subjects affected / exposed                       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Bronchospasm                                      |                |                |                |
| subjects affected / exposed                       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Apnoea  |                |                |                |
| subjects affected / exposed                       | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all   | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Dyspnoea At Rest                                  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dyspnoea Exertional                             |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Haemoptysis                                     |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Laryngeal Oedema                                |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (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          |
| Laryngospasm                                    |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (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          |
| Pharyngeal Swelling                             |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pleural Effusion                                |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary Embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory Tract Haemorrhage                   |                |                |                |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 Alkalosis                           |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pulmonary Fibrosis                              |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Product issues                                  |               |               |                |
| Device Malfunction                              |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Device Occlusion                                |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Investigations                                  |               |               |                |
| Blood Creatinine Increased                      |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 Pressure Increased                        |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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  |               |               |                |
| Fall  |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |

|   |                |               |                |
|---|----------------|---------------|----------------|
| Infusion Related Reaction                       |                |               |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Joint Injury                                    |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Road Traffic Accident                           |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Post Procedural Complication                    |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Traumatic Fracture                              |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Cardiac disorders                               |                |               |                |
| Acute Coronary Syndrome                         |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Acute Myocardial Infarction                     |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Stress Cardiomyopathy                           |                |               |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 7 (14.29%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cardiac Failure                                 |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| 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                        |               |                |                |
| Cerebral Haemorrhage                            |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Dizziness                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Headache  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Sciatica  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Ischaemic Stroke                                |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Seizure   |               |                |                |

|   |                |               |                |
|---|----------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Spinal Cord Compression                         |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Somnolence                                      |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Blood and lymphatic system disorders            |                |               |                |
| Anaemia   |                |               |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Febrile Neutropenia                             |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Hyperviscosity Syndrome                         |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Thrombocytopenia                                |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Eye disorders                                   |                |               |                |



|   |                |               |                |
|---|----------------|---------------|----------------|
| Eye Pain  |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Cataract  |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Visual Impairment                               |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Gastrointestinal disorders                      |                |               |                |
| Diarrhoea                                       |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Diverticular Perforation                        |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Gastrointestinal Haemorrhage                    |                |               |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Gastrointestinal Amyloidosis                    |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Intussusception                                 |                |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Ileus   |                |               |                |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Mechanical Ileus                                |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Nausea  |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Small Intestinal Obstruction                    |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Obstruction Gastric                             |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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                         |               |               |                |
| Hyperbilirubinaemia                             |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Cholestasis                                     |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Chronic Kidney Disease                          |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Endocrine disorders                             |               |               |                |
| Hypercalcaemia Of Malignancy                    |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 |               |               |                |
| Musculoskeletal Chest Pain                      |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Back Pain                                       |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Musculoskeletal Pain                            |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Pathological Fracture                           |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Spinal Stenosis                                 |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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                     |               |               |                |
| Acute Sinusitis                                 |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Abdominal Sepsis                                |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Atypical Pneumonia                              |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Bronchiolitis                                   |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Bronchitis                                      |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Campylobacter Gastroenteritis                   |               |               |                |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Covid-19 Pneumonia                              |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Device Related Infection                        |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Escherichia Sepsis                              |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Gastroenteritis                                 |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Gastroenteritis Rotavirus                       |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Haemophilus Sepsis                              |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Infectious Colitis                              |               |               |                |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Infective Aortitis                              |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Intervertebral Discitis                         |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Lower Respiratory Tract Infection               |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Lower Respiratory Tract Infection Viral         |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 Bacterial                            |               |               |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Meningococcal Sepsis                            |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Otitis Media                                    |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Parainfluenzae Virus Infection                  |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (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          |
| Pneumococcal Bacteraemia                        |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumocystis Jirovecii Pneumonia                |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia Aspiration                            |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| 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 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%) |
| 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 Bacterial                             |                |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| 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 Mycoplasmal                           |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| 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 Respiratory Syncytial Viral           |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| 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 Streptococcal                         |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 7 (14.29%) | 0 / 23 (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          |
| Pulmonary Sepsis                                |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| 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 Syncytial Virus Infection           |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Respiratory Tract Infection                     |               |                |                |



|   |               |               |                 |
|---|---------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0           |
| Septic Shock                                    |               |               |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 4 / 23 (17.39%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 4           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0           |
| Sinusitis                                       |               |               |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0           |
| Tracheobronchitis                               |               |               |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0           |
| Upper Respiratory Tract Infection               |               |               |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 2 / 23 (8.70%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0           |
| Urinary Tract Infection                         |               |               |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0           |
| Varicella                                       |               |               |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0           |
| Varicella Zoster Virus Infection                |               |               |                 |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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              |               |               |                |
| Decreased Appetite                              |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Dehydration                                     |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Electrolyte Imbalance                           |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| 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 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Tumour Lysis Syndrome                           |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hyperuricaemia                                  |               |               |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |

| Serious adverse events                            | Phase 2 Stage 1a:<br>Isatuximab 10mg/kg<br>Q2W | Phase 2 Stage 1a:<br>Isatuximab 10mg/kg<br>Q2W; Then Q4W | Phase 2 Stage 1b:<br>Isatuximab 20mg/kg<br>QW and Then Q2W |
|---|--|--|--|
| Total subjects affected by serious adverse events |  |  |  |
| subjects affected / exposed                       | 11 / 24 (45.83%)                               | 10 / 25 (40.00%)   | 9 / 25 (36.00%)  |
| number of deaths (all causes)                     | 13   | 11   | 11   |
| number of deaths resulting from                   |  |  |  |

|   |                |                |                |
|---|----------------|----------------|----------------|
| adverse events  |                |                |                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |                |
| Basal Cell Carcinoma  |                |                |                |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Colon Cancer  |                |                |                |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Myelodysplastic Syndrome  |                |                |                |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Malignant Melanoma  |                |                |                |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Plasma Cell Leukaemia   |                |                |                |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Prostate Cancer   |                |                |                |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Squamous Cell Carcinoma Of The Oral Cavity                          |                |                |                |
| subjects affected / exposed   | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders  |                |                |                |
| Aortic Aneurysm   |                |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                          | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Extrinsic Iliac Vein Compression                     |                |                |                |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypertensive Crisis                                  |                |                |                |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypotension  |                |                |                |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Chills   |                |                |                |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Asthenia   |                |                |                |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Disease Progression                                  |                |                |                |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 1 / 1          | 0 / 1          |
| Fatigue  |                |                |                |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Feeling Cold   |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hyperpyrexia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| General Physical Health Deterioration           |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Non-Cardiac Chest Pain                          |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Malaise   |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pain  |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pyrexia   |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Physical Deconditioning                         |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Performance Status Decreased                    |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                       | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Sudden Death                                      |                |                |                |
| subjects affected / exposed                       | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 1 / 1          | 0 / 0          |
| Immune system disorders                           |                |                |                |
| Anaphylactic Reaction                             |                |                |                |
| subjects affected / exposed                       | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all   | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Social circumstances                              |                |                |                |
| Loss Of Personal Independence In Daily Activities |                |                |                |
| subjects affected / exposed                       | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Reproductive system and breast disorders          |                |                |                |
| Prostatitis                                       |                |                |                |
| subjects affected / exposed                       | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Pelvic Pain                                       |                |                |                |
| subjects affected / exposed                       | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders   |                |                |                |
| Acute Respiratory Failure                         |                |                |                |
| subjects affected / exposed                       | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| Dyspnoea  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bronchospasm                                    |                |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Apnoea  |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dyspnoea At Rest                                |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dyspnoea Exertional                             |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Haemoptysis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Laryngeal Oedema                                |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Laryngospasm                                    |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pharyngeal Swelling                             |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pleural Effusion                                |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary Embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory Tract Haemorrhage                   |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory Alkalosis                           |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary Fibrosis                              |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Product issues                                  |                |                |                |
| Device Malfunction                              |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Device Occlusion                                |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| Blood Creatinine Increased<br>subjects affected / exposed | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to<br>treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood Pressure Increased<br>subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to<br>treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural<br>complications         |                |                |                |
| Fall  |                |                |                |
| subjects affected / exposed                               | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to<br>treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| Infusion Related Reaction                                 |                |                |                |
| subjects affected / exposed                               | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to<br>treatment / all        | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| Joint Injury  |                |                |                |
| subjects affected / exposed                               | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to<br>treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| Road Traffic Accident                                     |                |                |                |
| subjects affected / exposed                               | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to<br>treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| Post Procedural Complication                              |                |                |                |
| subjects affected / exposed                               | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to<br>treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| Traumatic Fracture  |                |                |                |
| subjects affected / exposed                               | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to<br>treatment / all        | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to<br>treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Cardiac disorders                               |                |                |                |
| Acute Coronary Syndrome                         |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Acute Myocardial Infarction                     |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Atrial Fibrillation                             |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1          |
| Stress Cardiomyopathy                           |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac Failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tachycardia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Cerebral Haemorrhage                            |                |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0          |
| Dizziness                                       |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Headache  |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sciatica  |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ischaemic Stroke                                |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Seizure   |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spinal Cord Compression                         |                |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Somnolence                                      |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Syncope   |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| Anaemia   |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Febrile Neutropenia                             |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hyperviscosity Syndrome                         |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Thrombocytopenia                                |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Eye disorders                                   |                |                |                |
| Eye Pain  |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cataract  |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Visual Impairment                               |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |
| Diarrhoea                                       |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Diverticular Perforation                        |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal Haemorrhage                    |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal Amyloidosis                    |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intussusception                                 |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ileus   |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Mechanical Ileus                                |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nausea  |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Vomiting  |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Small Intestinal Obstruction                    |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Obstruction Gastric                             |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |                |                |                |
| Hyperbilirubinaemia                             |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cholestasis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |                |                |                |
| Acute Kidney Injury                             |                |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 2 / 25 (8.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 3          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Chronic Kidney Disease                          |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal Failure                                   |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Endocrine disorders                             |                |                |                |
| Hypercalcaemia Of Malignancy                    |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Musculoskeletal Chest Pain                      |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bone Pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Back Pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal Pain                            |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pathological Fracture                           |                |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 2 / 25 (8.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pain In Extremity                               |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spinal Stenosis                                 |                |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Acute Sinusitis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Abdominal Sepsis                                |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Atypical Pneumonia                              |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bronchiolitis                                   |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bronchitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Campylobacter Gastroenteritis                   |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Covid-19 Pneumonia                              |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Device Related Infection                        |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Escherichia Sepsis                              |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastroenteritis Rotavirus                       |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Haemophilus Sepsis                              |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infectious Colitis                              |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Herpes Zoster                                   |                |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infective Aortitis                              |                |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Influenza                                       |                |                |                |
| subjects affected / exposed                     | 2 / 24 (8.33%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intervertebral Discitis                         |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lower Respiratory Tract Infection               |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lower Respiratory Tract Infection Viral         |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lung Infection                                  |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Meningitis Bacterial                            |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Meningococcal Sepsis                            |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Otitis Media                                    |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Parainfluenzae Virus Infection                  |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumococcal Bacteraemia                        |                |                |                |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumocystis Jirovecii Pneumonia                |                 |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia Aspiration                            |                 |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                 |                |                |
| subjects affected / exposed                     | 4 / 24 (16.67%) | 2 / 25 (8.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia Bacterial                             |                 |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia Mycoplasmal                           |                 |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia Respiratory Syncytial Viral           |                 |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pneumonia Streptococcal                         |                 |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Pulmonary Sepsis                                |                 |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia Viral                                 |                |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory Syncytial Virus Infection           |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pyelonephritis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory Tract Infection                     |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Septic Shock                                    |                |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sepsis  |                |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sinusitis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tracheobronchitis                               |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Upper Respiratory Tract Infection               |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary Tract Infection                         |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Varicella                                       |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Varicella Zoster Virus Infection                |                |                |                |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Decreased Appetite                              |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dehydration                                     |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Electrolyte Imbalance                           |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypercalcaemia                                  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Tumour Lysis Syndrome</b>                    |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Hyperuricaemia</b>                           |                |                |                |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>  | Phase 2 Stage 2:<br>Isatuximab Alone | Phase 2 Stage 2:<br>Isatuximab +<br>Dexamethasone |  |
|--|--------------------------------------|---|--|
| <b>Total subjects affected by serious adverse events</b>                   |                                      |   |  |
| subjects affected / exposed  | 52 / 109 (47.71%)                    | 27 / 55 (49.09%)                                  |  |
| number of deaths (all causes)  | 56                                   | 25  |  |
| number of deaths resulting from adverse events                             |                                      |   |  |
| <b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b> |                                      |   |  |
| <b>Basal Cell Carcinoma</b>  |                                      |   |  |
| subjects affected / exposed  | 1 / 109 (0.92%)                      | 0 / 55 (0.00%)                                    |  |
| occurrences causally related to treatment / all                            | 0 / 1                                | 0 / 0   |  |
| deaths causally related to treatment / all                                 | 0 / 0                                | 0 / 0   |  |
| <b>Colon Cancer</b>  |                                      |   |  |
| subjects affected / exposed  | 0 / 109 (0.00%)                      | 1 / 55 (1.82%)                                    |  |
| occurrences causally related to treatment / all                            | 0 / 0                                | 0 / 1   |  |
| deaths causally related to treatment / all                                 | 0 / 0                                | 0 / 0   |  |
| <b>Myelodysplastic Syndrome</b>  |                                      |   |  |
| subjects affected / exposed  | 0 / 109 (0.00%)                      | 0 / 55 (0.00%)                                    |  |
| occurrences causally related to treatment / all                            | 0 / 0                                | 0 / 0   |  |
| deaths causally related to treatment / all                                 | 0 / 0                                | 0 / 0   |  |
| <b>Malignant Melanoma</b>  |                                      |   |  |

|  |                 |                |  |
|--|-----------------|----------------|--|
| subjects affected / exposed                          | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Plasma Cell Leukaemia                                |                 |                |  |
| subjects affected / exposed                          | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Prostate Cancer                                      |                 |                |  |
| subjects affected / exposed                          | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Squamous Cell Carcinoma Of The Oral Cavity           |                 |                |  |
| subjects affected / exposed                          | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Vascular disorders                                   |                 |                |  |
| Aortic Aneurysm                                      |                 |                |  |
| subjects affected / exposed                          | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Extrinsic Iliac Vein Compression                     |                 |                |  |
| subjects affected / exposed                          | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Hypertensive Crisis                                  |                 |                |  |
| subjects affected / exposed                          | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| Hypotension  |                 |                |  |
| subjects affected / exposed                          | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          |  |
| General disorders and administration site conditions |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Chills  |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Asthenia  |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Disease Progression                             |                 |                |  |
| subjects affected / exposed                     | 7 / 109 (6.42%) | 2 / 55 (3.64%) |  |
| occurrences causally related to treatment / all | 0 / 7           | 0 / 2          |  |
| deaths causally related to treatment / all      | 6 / 7           | 2 / 2          |  |
| Fatigue   |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Feeling Cold                                    |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hyperpyrexia                                    |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| General Physical Health Deterioration           |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          |  |
| Non-Cardiac Chest Pain                          |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Malaise   |                 |                |  |



|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                       | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0          |  |
| Pain  |                 |                |  |
| subjects affected / exposed                       | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all   | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0          |  |
| Pyrexia   |                 |                |  |
| subjects affected / exposed                       | 1 / 109 (0.92%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all   | 0 / 1           | 0 / 1          |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0          |  |
| Physical Deconditioning                           |                 |                |  |
| subjects affected / exposed                       | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0          |  |
| Performance Status Decreased                      |                 |                |  |
| subjects affected / exposed                       | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0          |  |
| Sudden Death                                      |                 |                |  |
| subjects affected / exposed                       | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0          |  |
| Immune system disorders                           |                 |                |  |
| Anaphylactic Reaction                             |                 |                |  |
| subjects affected / exposed                       | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0          |  |
| Social circumstances                              |                 |                |  |
| Loss Of Personal Independence In Daily Activities |                 |                |  |
| subjects affected / exposed                       | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all   | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0          |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Reproductive system and breast disorders        |                 |                |  |
| Prostatitis                                     |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pelvic Pain                                     |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders |                 |                |  |
| Acute Respiratory Failure                       |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Dyspnoea  |                 |                |  |
| subjects affected / exposed                     | 2 / 109 (1.83%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 2 / 2           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Bronchospasm                                    |                 |                |  |
| subjects affected / exposed                     | 2 / 109 (1.83%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Apnoea  |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Dyspnoea At Rest                                |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Dyspnoea Exertional                             |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Haemoptysis                                     |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Laryngeal Oedema                                |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Laryngospasm                                    |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pharyngeal Swelling                             |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pleural Effusion                                |                 |                |  |
| subjects affected / exposed                     | 2 / 109 (1.83%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pulmonary Embolism                              |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 1 / 1          |  |
| Respiratory Tract Haemorrhage                   |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0          |  |
| Respiratory Alkalosis                           |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pulmonary Fibrosis                              |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Product issues                                  |                 |                |  |
| Device Malfunction                              |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Device Occlusion                                |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Investigations                                  |                 |                |  |
| Blood Creatinine Increased                      |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Blood Pressure Increased                        |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Injury, poisoning and procedural complications  |                 |                |  |
| Fall  |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Infusion Related Reaction                       |                 |                |  |
| subjects affected / exposed                     | 6 / 109 (5.50%) | 2 / 55 (3.64%) |  |
| occurrences causally related to treatment / all | 6 / 6           | 2 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Joint Injury                                    |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Road Traffic Accident                           |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Post Procedural Complication                    |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Traumatic Fracture                              |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cardiac disorders                               |                 |                |  |
| Acute Coronary Syndrome                         |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Acute Myocardial Infarction                     |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Atrial Fibrillation                             |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Stress Cardiomyopathy                           |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cardiac Failure                                 |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (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 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Nervous system disorders                        |                 |                |  |
| Cerebral Haemorrhage                            |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Dizziness                                       |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Headache  |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Sciatica  |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Ischaemic Stroke                                |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0          |  |
| Seizure   |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Spinal Cord Compression                         |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 2 / 109 (1.83%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Somnolence                                      |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (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                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Blood and lymphatic system disorders            |                 |                |  |
| Anaemia   |                 |                |  |
| subjects affected / exposed                     | 4 / 109 (3.67%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 4           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Febrile Neutropenia                             |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hyperviscosity Syndrome                         |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Thrombocytopenia                                |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Eye disorders                                   |                 |                |  |
| Eye Pain  |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cataract  |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Visual Impairment                               |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Gastrointestinal disorders                      |                 |                |  |
| Diarrhoea                                       |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Diverticular Perforation                        |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Gastrointestinal Haemorrhage                    |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Gastrointestinal Amyloidosis                    |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Intussusception                                 |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Ileus   |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Mechanical Ileus                                |                 |                |  |



|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Nausea  |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Vomiting  |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Small Intestinal Obstruction                    |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 2 / 55 (3.64%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Obstruction Gastric                             |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hepatobiliary disorders                         |                 |                |  |
| Hyperbilirubinaemia                             |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cholestasis                                     |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (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                     | 4 / 109 (3.67%) | 3 / 55 (5.45%) |  |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 3          |  |
| deaths causally related to treatment / all      | 1 / 1           | 1 / 2          |  |
| Chronic Kidney Disease                          |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (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 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Endocrine disorders                             |                 |                |  |
| Hypercalcaemia Of Malignancy                    |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                 |                |  |
| Musculoskeletal Chest Pain                      |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Bone Pain                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Back Pain                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (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 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pathological Fracture                           |                 |                |  |
| subjects affected / exposed                     | 3 / 109 (2.75%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| Pain In Extremity                               |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 2 / 55 (3.64%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Spinal Stenosis                                 |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Infections and infestations                     |                 |                |  |
| Acute Sinusitis                                 |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Abdominal Sepsis                                |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Atypical Pneumonia                              |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Bronchiolitis                                   |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Bronchitis                                      |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 3 / 55 (5.45%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 3          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Campylobacter Gastroenteritis                   |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Covid-19 Pneumonia                              |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Cellulitis                                      |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Device Related Infection                        |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Escherichia Sepsis                              |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Gastroenteritis                                 |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Gastroenteritis Rotavirus                       |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Haemophilus Sepsis                              |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Infectious Colitis                              |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Herpes Zoster                                   |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Infective Aortitis                              |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Influenza                                       |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Intervertebral Discitis                         |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Lower Respiratory Tract Infection               |                 |                |  |
| subjects affected / exposed                     | 2 / 109 (1.83%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Lower Respiratory Tract Infection Viral         |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (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 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Meningitis Bacterial                            |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Meningococcal Sepsis                            |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Otitis Media                                    |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Parainfluenzae Virus Infection                  |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumococcal Bacteraemia                        |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumocystis Jirovecii Pneumonia                |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumonia Aspiration                            |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumonia                                       |                 |                |  |
| subjects affected / exposed                     | 8 / 109 (7.34%) | 5 / 55 (9.09%) |  |
| occurrences causally related to treatment / all | 4 / 10          | 1 / 5          |  |
| deaths causally related to treatment / all      | 0 / 1           | 1 / 1          |  |
| Pneumonia Bacterial                             |                 |                |  |
| subjects affected / exposed                     | 2 / 109 (1.83%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumonia Mycoplasmal                           |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumonia Respiratory Syncytial Viral           |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pneumonia Streptococcal                         |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pulmonary Sepsis                                |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| 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                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Respiratory Syncytial Virus Infection           |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Pyelonephritis                                  |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Respiratory Tract Infection                     |                 |                |  |
| subjects affected / exposed                     | 3 / 109 (2.75%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 2 / 3           | 0 / 1          |  |
| deaths causally related to treatment / all      | 1 / 1           | 1 / 1          |  |
| Septic Shock                                    |                 |                |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 1 / 1          |  |
| Sepsis  |                 |                |  |
| subjects affected / exposed                     | 3 / 109 (2.75%) | 2 / 55 (3.64%) |  |
| occurrences causally related to treatment / all | 1 / 3           | 1 / 3          |  |
| deaths causally related to treatment / all      | 2 / 2           | 0 / 0          |  |
| Sinusitis                                       |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Tracheobronchitis                               |                 |                |  |
| subjects affected / exposed                     | 2 / 109 (1.83%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Upper Respiratory Tract Infection               |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 1 / 55 (1.82%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Urinary Tract Infection                         |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Varicella                                       |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Varicella Zoster Virus Infection                |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Metabolism and nutrition disorders              |                 |                |  |
| Decreased Appetite                              |                 |                |  |



|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Dehydration                                     |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Electrolyte Imbalance                           |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hypercalcaemia                                  |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Tumour Lysis Syndrome                           |                 |                |  |
| subjects affected / exposed                     | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Hyperuricaemia                                  |                 |                |  |
| subjects affected / exposed                     | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

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

| Non-serious adverse events  | Phase 1: Isatuximab<br>≤1mg/kg Q2W | Phase 1: Isatuximab<br>3mg/kg Q2W | Phase 1: Isatuximab<br>5mg/kg Q2W |
|---|------------------------------------|-----------------------------------|-----------------------------------|
| Total subjects affected by non-serious adverse events               |                                    |                                   |                                   |
| subjects affected / exposed   | 16 / 16 (100.00%)                  | 6 / 6 (100.00%)                   | 3 / 3 (100.00%)                   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                    |                                   |                                   |
| Basal Cell Carcinoma  |                                    |                                   |                                   |
| subjects affected / exposed   | 0 / 16 (0.00%)                     | 0 / 6 (0.00%)                     | 0 / 3 (0.00%)                     |
| occurrences (all)   | 0                                  | 0                                 | 0                                 |
| Tumour Pain   |                                    |                                   |                                   |

|   |                     |                    |                     |
|---|---------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)        | 0 / 16 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 1 / 3 (33.33%)<br>1 |
| Vascular disorders                                      |                     |                    |                     |
| Hypertension  |                     |                    |                     |
| subjects affected / exposed                             | 1 / 16 (6.25%)      | 0 / 6 (0.00%)      | 0 / 3 (0.00%)       |
| occurrences (all)                                       | 1                   | 0                  | 0                   |
| Hot Flush   |                     |                    |                     |
| subjects affected / exposed                             | 0 / 16 (0.00%)      | 0 / 6 (0.00%)      | 0 / 3 (0.00%)       |
| occurrences (all)                                       | 0                   | 0                  | 0                   |
| Flushing  |                     |                    |                     |
| subjects affected / exposed                             | 0 / 16 (0.00%)      | 0 / 6 (0.00%)      | 1 / 3 (33.33%)      |
| occurrences (all)                                       | 0                   | 0                  | 1                   |
| Hypotension   |                     |                    |                     |
| subjects affected / exposed                             | 0 / 16 (0.00%)      | 0 / 6 (0.00%)      | 0 / 3 (0.00%)       |
| occurrences (all)                                       | 0                   | 0                  | 0                   |
| Pallor  |                     |                    |                     |
| subjects affected / exposed                             | 0 / 16 (0.00%)      | 0 / 6 (0.00%)      | 0 / 3 (0.00%)       |
| occurrences (all)                                       | 0                   | 0                  | 0                   |
| Peripheral Coldness                                     |                     |                    |                     |
| subjects affected / exposed                             | 0 / 16 (0.00%)      | 0 / 6 (0.00%)      | 0 / 3 (0.00%)       |
| occurrences (all)                                       | 0                   | 0                  | 0                   |
| General disorders and administration<br>site conditions |                     |                    |                     |
| Asthenia  |                     |                    |                     |
| subjects affected / exposed                             | 0 / 16 (0.00%)      | 0 / 6 (0.00%)      | 0 / 3 (0.00%)       |
| occurrences (all)                                       | 0                   | 0                  | 0                   |
| Chest Discomfort  |                     |                    |                     |
| subjects affected / exposed                             | 0 / 16 (0.00%)      | 0 / 6 (0.00%)      | 0 / 3 (0.00%)       |
| occurrences (all)                                       | 0                   | 0                  | 0                   |
| Chills  |                     |                    |                     |
| subjects affected / exposed                             | 4 / 16 (25.00%)     | 1 / 6 (16.67%)     | 0 / 3 (0.00%)       |
| occurrences (all)                                       | 6                   | 1                  | 0                   |
| Face Oedema   |                     |                    |                     |
| subjects affected / exposed                             | 0 / 16 (0.00%)      | 0 / 6 (0.00%)      | 1 / 3 (33.33%)      |
| occurrences (all)                                       | 0                   | 0                  | 2                   |
| Fatigue   |                     |                    |                     |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 8 / 16 (50.00%) | 2 / 6 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all)           | 10              | 2              | 1              |
| Implant Site Pain           |                 |                |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Feeling Hot                 |                 |                |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Influenza Like Illness      |                 |                |                |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Malaise                     |                 |                |                |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Injection Site Pain         |                 |                |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Non-Cardiac Chest Pain      |                 |                |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)           | 0               | 0              | 1              |
| Oedema Peripheral           |                 |                |                |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 2               | 0              | 0              |
| Pain                        |                 |                |                |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Peripheral Swelling         |                 |                |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Pyrexia                     |                 |                |                |
| subjects affected / exposed | 4 / 16 (25.00%) | 0 / 6 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)           | 4               | 0              | 1              |
| Immune system disorders     |                 |                |                |
| Cytokine Release Syndrome   |                 |                |                |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| Reproductive system and breast disorders        |                 |                |                |
| Nipple Pain                                     |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Vulvovaginal Pain                               |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Respiratory, thoracic and mediastinal disorders |                 |                |                |
| Bronchospasm                                    |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Epistaxis                                       |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Dyspnoea Exertional                             |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Dyspnoea  |                 |                |                |
| subjects affected / exposed                     | 2 / 16 (12.50%) | 1 / 6 (16.67%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 4               | 1              | 0              |
| Cough   |                 |                |                |
| subjects affected / exposed                     | 3 / 16 (18.75%) | 2 / 6 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all)                               | 5               | 2              | 1              |
| Hypoxia   |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                               | 0               | 0              | 1              |
| Laryngeal Discomfort                            |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 1 / 6 (16.67%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 1              | 0              |
| Laryngospasm                                    |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Nasal Congestion                                |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                               | 0               | 0              | 1              |
| Oropharyngeal Pain                              |                 |                |                |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Productive Cough            |                |                |               |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Rhinitis Allergic           |                |                |               |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Rhinorrhoea                 |                |                |               |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Throat Lesion               |                |                |               |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Throat Tightness            |                |                |               |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Sinus Congestion            |                |                |               |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Sneezing                    |                |                |               |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Throat Irritation           |                |                |               |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Upper-Airway Cough Syndrome |                |                |               |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 6 (16.67%) | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 1              | 0             |
| Tracheal Stenosis           |                |                |               |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Wheezing                    |                |                |               |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Psychiatric disorders       |                |                |               |

|  |                |                |               |
|--|----------------|----------------|---------------|
| Abnormal Dreams                              |                |                |               |
| subjects affected / exposed                  | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                            | 1              | 0              | 0             |
| Agitation                                    |                |                |               |
| subjects affected / exposed                  | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                            | 1              | 0              | 0             |
| Confusional State                            |                |                |               |
| subjects affected / exposed                  | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                            | 0              | 0              | 0             |
| Bradyphrenia                                 |                |                |               |
| subjects affected / exposed                  | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                            | 1              | 0              | 0             |
| Anxiety                                      |                |                |               |
| subjects affected / exposed                  | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                            | 0              | 0              | 0             |
| Depression                                   |                |                |               |
| subjects affected / exposed                  | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                            | 1              | 0              | 0             |
| Insomnia                                     |                |                |               |
| subjects affected / exposed                  | 1 / 16 (6.25%) | 1 / 6 (16.67%) | 0 / 3 (0.00%) |
| occurrences (all)                            | 1              | 1              | 0             |
| Restlessness                                 |                |                |               |
| subjects affected / exposed                  | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                            | 0              | 0              | 0             |
| Nightmare                                    |                |                |               |
| subjects affected / exposed                  | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                            | 0              | 0              | 0             |
| Irritability                                 |                |                |               |
| subjects affected / exposed                  | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                            | 1              | 0              | 0             |
| Investigations                               |                |                |               |
| Carbon Monoxide Diffusing Capacity Decreased |                |                |               |
| subjects affected / exposed                  | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                            | 0              | 0              | 0             |
| Blood Creatinine Increased                   |                |                |               |

|  |                 |                |                |
|--|-----------------|----------------|----------------|
| subjects affected / exposed                    | 2 / 16 (12.50%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 2               | 0              | 0              |
| Electrocardiogram T Wave Abnormal              |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| Lymphocyte Count Decreased                     |                 |                |                |
| subjects affected / exposed                    | 2 / 16 (12.50%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 2               | 0              | 0              |
| Platelet Count Decreased                       |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| Neutrophil Count Decreased                     |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| Qrs Axis Abnormal                              |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| Weight Decreased                               |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| Injury, poisoning and procedural complications |                 |                |                |
| Accidental Overdose                            |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| Contusion                                      |                 |                |                |
| subjects affected / exposed                    | 2 / 16 (12.50%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 3               | 0              | 0              |
| Infusion Related Reaction                      |                 |                |                |
| subjects affected / exposed                    | 5 / 16 (31.25%) | 3 / 6 (50.00%) | 2 / 3 (66.67%) |
| occurrences (all)                              | 7               | 4              | 2              |
| Fall   |                 |                |                |
| subjects affected / exposed                    | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                              | 0               | 0              | 0              |
| Joint Injury                                   |                 |                |                |

|  |                     |                    |                     |
|--|---------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 16 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 1 / 3 (33.33%)<br>1 |
| Procedural Pain<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 16 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| Sports Injury<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 16 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| Scapula Fracture<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 16 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| Cardiac disorders<br>Bundle Branch Block Right<br>subjects affected / exposed<br>occurrences (all) | 0 / 16 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 16 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| Bradycardia<br>subjects affected / exposed<br>occurrences (all)                                    | 1 / 16 (6.25%)<br>1 | 0 / 6 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| Right Ventricular Hypertrophy<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 16 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| Angina Pectoris<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 16 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 16 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| Sinus Tachycardia<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 16 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  |
| Nervous system disorders<br>Balance Disorder   |                     |                    |                     |



|                               |                 |                |                |
|-------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed   | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)             | 2               | 0              | 0              |
| Amnesia                       |                 |                |                |
| subjects affected / exposed   | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)             | 0               | 0              | 0              |
| Dizziness                     |                 |                |                |
| subjects affected / exposed   | 1 / 16 (6.25%)  | 1 / 6 (16.67%) | 0 / 3 (0.00%)  |
| occurrences (all)             | 1               | 1              | 0              |
| Cranial Nerve Paralysis       |                 |                |                |
| subjects affected / exposed   | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)             | 0               | 0              | 0              |
| Cognitive Disorder            |                 |                |                |
| subjects affected / exposed   | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)             | 0               | 0              | 0              |
| Dysgeusia                     |                 |                |                |
| subjects affected / exposed   | 2 / 16 (12.50%) | 1 / 6 (16.67%) | 1 / 3 (33.33%) |
| occurrences (all)             | 2               | 1              | 1              |
| Head Discomfort               |                 |                |                |
| subjects affected / exposed   | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)             | 1               | 0              | 0              |
| Headache                      |                 |                |                |
| subjects affected / exposed   | 5 / 16 (31.25%) | 0 / 6 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)             | 8               | 0              | 1              |
| Paraesthesia                  |                 |                |                |
| subjects affected / exposed   | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)             | 0               | 0              | 0              |
| Mental Impairment             |                 |                |                |
| subjects affected / exposed   | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)             | 0               | 0              | 0              |
| Hypoaesthesia                 |                 |                |                |
| subjects affected / exposed   | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)             | 0               | 0              | 0              |
| Peripheral Sensory Neuropathy |                 |                |                |
| subjects affected / exposed   | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)             | 1               | 0              | 0              |
| Vith Nerve Paralysis          |                 |                |                |

|                                      |                 |                |                |
|--------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed          | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Toxic Encephalopathy                 |                 |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Restless Legs Syndrome               |                 |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Blood and lymphatic system disorders |                 |                |                |
| Anaemia                              |                 |                |                |
| subjects affected / exposed          | 6 / 16 (37.50%) | 2 / 6 (33.33%) | 0 / 3 (0.00%)  |
| occurrences (all)                    | 6               | 2              | 0              |
| Thrombocytopenia                     |                 |                |                |
| subjects affected / exposed          | 2 / 16 (12.50%) | 1 / 6 (16.67%) | 0 / 3 (0.00%)  |
| occurrences (all)                    | 2               | 1              | 0              |
| Neutropenia                          |                 |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Eye disorders                        |                 |                |                |
| Conjunctival Haemorrhage             |                 |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Scleral Discolouration               |                 |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Diplopia                             |                 |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                    | 0               | 0              | 1              |
| Dry Eye                              |                 |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Lacrimation Increased                |                 |                |                |
| subjects affected / exposed          | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Vision Blurred                       |                 |                |                |

|                             |                 |               |                |
|-----------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 2               | 0             | 0              |
| Visual Impairment           |                 |               |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0             | 0              |
| Gastrointestinal disorders  |                 |               |                |
| Abdominal Discomfort        |                 |               |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0             | 0              |
| Abdominal Distension        |                 |               |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0             | 0              |
| Abdominal Pain              |                 |               |                |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0             | 0              |
| Abdominal Pain Upper        |                 |               |                |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0             | 0              |
| Abdominal Tenderness        |                 |               |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0             | 0              |
| Dry Mouth                   |                 |               |                |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0             | 0              |
| Diarrhoea                   |                 |               |                |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 6 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all)           | 4               | 0             | 1              |
| Constipation                |                 |               |                |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 6 (0.00%) | 2 / 3 (66.67%) |
| occurrences (all)           | 1               | 0             | 2              |
| Dyspepsia                   |                 |               |                |
| subjects affected / exposed | 0 / 16 (0.00%)  | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0               | 0             | 0              |
| Gastrointestinal Pain       |                 |               |                |
| subjects affected / exposed | 1 / 16 (6.25%)  | 0 / 6 (0.00%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 1               | 0             | 0              |

|  |                 |                |                |
|--|-----------------|----------------|----------------|
| Dysphagia                              |                 |                |                |
| subjects affected / exposed            | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Gastroesophageal Reflux Disease        |                 |                |                |
| subjects affected / exposed            | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 1               | 0              | 0              |
| Glossitis                              |                 |                |                |
| subjects affected / exposed            | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Glossodynia                            |                 |                |                |
| subjects affected / exposed            | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 1               | 0              | 0              |
| Haemorrhoids                           |                 |                |                |
| subjects affected / exposed            | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Nausea                                 |                 |                |                |
| subjects affected / exposed            | 4 / 16 (25.00%) | 2 / 6 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all)                      | 6               | 2              | 1              |
| Mouth Ulceration                       |                 |                |                |
| subjects affected / exposed            | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Rectal Haemorrhage                     |                 |                |                |
| subjects affected / exposed            | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Vomiting                               |                 |                |                |
| subjects affected / exposed            | 2 / 16 (12.50%) | 1 / 6 (16.67%) | 1 / 3 (33.33%) |
| occurrences (all)                      | 2               | 1              | 1              |
| Toothache                              |                 |                |                |
| subjects affected / exposed            | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Stomatitis                             |                 |                |                |
| subjects affected / exposed            | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                      | 1               | 0              | 0              |
| Skin and subcutaneous tissue disorders |                 |                |                |
| Actinic Keratosis                      |                 |                |                |

|                              |                |                |               |
|------------------------------|----------------|----------------|---------------|
| subjects affected / exposed  | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)            | 0              | 0              | 0             |
| <b>Dermatitis Contact</b>    |                |                |               |
| subjects affected / exposed  | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)            | 1              | 0              | 0             |
| <b>Dermatitis Acneiform</b>  |                |                |               |
| subjects affected / exposed  | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)            | 0              | 0              | 0             |
| <b>Alopecia</b>              |                |                |               |
| subjects affected / exposed  | 0 / 16 (0.00%) | 1 / 6 (16.67%) | 0 / 3 (0.00%) |
| occurrences (all)            | 0              | 1              | 0             |
| <b>Erythema</b>              |                |                |               |
| subjects affected / exposed  | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)            | 0              | 0              | 0             |
| <b>Hair Texture Abnormal</b> |                |                |               |
| subjects affected / exposed  | 0 / 16 (0.00%) | 1 / 6 (16.67%) | 0 / 3 (0.00%) |
| occurrences (all)            | 0              | 1              | 0             |
| <b>Hyperhidrosis</b>         |                |                |               |
| subjects affected / exposed  | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)            | 0              | 0              | 0             |
| <b>Pruritus</b>              |                |                |               |
| subjects affected / exposed  | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)            | 0              | 0              | 0             |
| <b>Pain Of Skin</b>          |                |                |               |
| subjects affected / exposed  | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)            | 0              | 0              | 0             |
| <b>Onychoclasia</b>          |                |                |               |
| subjects affected / exposed  | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)            | 1              | 0              | 0             |
| <b>Rash</b>                  |                |                |               |
| subjects affected / exposed  | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)            | 0              | 0              | 0             |
| <b>Rash Maculo-Papular</b>   |                |                |               |
| subjects affected / exposed  | 0 / 16 (0.00%) | 1 / 6 (16.67%) | 0 / 3 (0.00%) |
| occurrences (all)            | 0              | 1              | 0             |
| <b>Rash Macular</b>          |                |                |               |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 1 / 6 (16.67%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 1              | 0              |
| Rash Erythematous                               |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Rash Pruritic                                   |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Skin Disorder                                   |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Skin Ulcer                                      |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 1 / 6 (16.67%) | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 1              | 0              |
| Renal and urinary disorders                     |                 |                |                |
| Acute Kidney Injury                             |                 |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 1               | 0              | 0              |
| Urinary Incontinence                            |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Pollakiuria                                     |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                 |                |                |
| Arthralgia                                      |                 |                |                |
| subjects affected / exposed                     | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Back Pain                                       |                 |                |                |
| subjects affected / exposed                     | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                               | 1               | 0              | 1              |
| Bone Pain                                       |                 |                |                |
| subjects affected / exposed                     | 2 / 16 (12.50%) | 0 / 6 (0.00%)  | 2 / 3 (66.67%) |
| occurrences (all)                               | 2               | 0              | 2              |
| Bursitis  |                 |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Flank Pain                  |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 6 (16.67%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Groin Pain                  |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 6 (16.67%) | 0 / 3 (0.00%)  |
| occurrences (all)           | 1              | 1              | 0              |
| Joint Swelling              |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Limb Discomfort             |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Muscle Fatigue              |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Muscle Spasms               |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Musculoskeletal Pain        |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)           | 0              | 0              | 1              |
| Musculoskeletal Chest Pain  |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)           | 1              | 0              | 1              |
| Muscular Weakness           |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Myalgia                     |                |                |                |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Neck Pain                   |                |                |                |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Pain In Extremity           |                |                |                |

|                                   |                 |                |               |
|-----------------------------------|-----------------|----------------|---------------|
| subjects affected / exposed       | 2 / 16 (12.50%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                 | 2               | 0              | 0             |
| Pathological Fracture             |                 |                |               |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0             |
| Spinal Osteoarthritis             |                 |                |               |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0             |
| Spinal Pain                       |                 |                |               |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0             |
| Infections and infestations       |                 |                |               |
| Gastroenteritis Viral             |                 |                |               |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 1 / 6 (16.67%) | 0 / 3 (0.00%) |
| occurrences (all)                 | 0               | 1              | 0             |
| Bronchitis                        |                 |                |               |
| subjects affected / exposed       | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                 | 1               | 0              | 0             |
| Angular Cheilitis                 |                 |                |               |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0             |
| Gingivitis                        |                 |                |               |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0             |
| Herpes Simplex                    |                 |                |               |
| subjects affected / exposed       | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                 | 1               | 0              | 0             |
| Lower Respiratory Tract Infection |                 |                |               |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0             |
| Influenza                         |                 |                |               |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0             |
| Hordeolum                         |                 |                |               |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0             |



|                                   |                 |                |                |
|-----------------------------------|-----------------|----------------|----------------|
| Nasopharyngitis                   |                 |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0              |
| Otitis Media                      |                 |                |                |
| subjects affected / exposed       | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 1               | 0              | 0              |
| Oral Candidiasis                  |                 |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0              |
| Sinusitis                         |                 |                |                |
| subjects affected / exposed       | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                 | 1               | 0              | 1              |
| Rhinitis                          |                 |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0              |
| Respiratory Tract Infection       |                 |                |                |
| subjects affected / exposed       | 1 / 16 (6.25%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 1               | 0              | 0              |
| Pyuria                            |                 |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0              |
| Pneumonia                         |                 |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 1 / 6 (16.67%) | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0               | 1              | 0              |
| Tooth Abscess                     |                 |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0              |
| Tooth Infection                   |                 |                |                |
| subjects affected / exposed       | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 0               | 0              | 0              |
| Urinary Tract Infection           |                 |                |                |
| subjects affected / exposed       | 2 / 16 (12.50%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                 | 2               | 0              | 0              |
| Upper Respiratory Tract Infection |                 |                |                |
| subjects affected / exposed       | 1 / 16 (6.25%)  | 1 / 6 (16.67%) | 1 / 3 (33.33%) |
| occurrences (all)                 | 4               | 1              | 1              |

|                                    |                 |                |                |
|------------------------------------|-----------------|----------------|----------------|
| Metabolism and nutrition disorders |                 |                |                |
| Decreased Appetite                 |                 |                |                |
| subjects affected / exposed        | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 1 / 3 (33.33%) |
| occurrences (all)                  | 0               | 0              | 1              |
| Dehydration                        |                 |                |                |
| subjects affected / exposed        | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0              |
| Hypercalcaemia                     |                 |                |                |
| subjects affected / exposed        | 2 / 16 (12.50%) | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 2               | 0              | 0              |
| Hyperglycaemia                     |                 |                |                |
| subjects affected / exposed        | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0              |
| Hypophosphataemia                  |                 |                |                |
| subjects affected / exposed        | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0              |
| Hypomagnesaemia                    |                 |                |                |
| subjects affected / exposed        | 0 / 16 (0.00%)  | 1 / 6 (16.67%) | 1 / 3 (33.33%) |
| occurrences (all)                  | 0               | 1              | 1              |
| Hypokalaemia                       |                 |                |                |
| subjects affected / exposed        | 0 / 16 (0.00%)  | 2 / 6 (33.33%) | 1 / 3 (33.33%) |
| occurrences (all)                  | 0               | 2              | 3              |
| Hypocalcaemia                      |                 |                |                |
| subjects affected / exposed        | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0              |
| Hyperuricaemia                     |                 |                |                |
| subjects affected / exposed        | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0              |
| Hyperkalaemia                      |                 |                |                |
| subjects affected / exposed        | 0 / 16 (0.00%)  | 0 / 6 (0.00%)  | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0              |
| Pseudohyponatraemia                |                 |                |                |
| subjects affected / exposed        | 0 / 16 (0.00%)  | 1 / 6 (16.67%) | 0 / 3 (0.00%)  |
| occurrences (all)                  | 0               | 1              | 0              |

|                                   |  |   |                                   |
|-----------------------------------|--|---|-----------------------------------|
| <b>Non-serious adverse events</b> | Phase1:Isatuximab<br>(CD38+HM and<br>Standard Risk | Phase 1: Isatuximab<br>(CD38 + HM and<br>High Risk Multiple | Phase 1: Isatuximab<br>10mg/kg QW |
|-----------------------------------|--|---|-----------------------------------|

|   | Multiple Myeloma) | Myeloma)          |                 |
|---|-------------------|-------------------|-----------------|
| Total subjects affected by non-serious adverse events               |                   |                   |                 |
| subjects affected / exposed   | 26 / 26 (100.00%) | 18 / 18 (100.00%) | 6 / 6 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |                   |                 |
| Basal Cell Carcinoma  |                   |                   |                 |
| subjects affected / exposed   | 0 / 26 (0.00%)    | 1 / 18 (5.56%)    | 0 / 6 (0.00%)   |
| occurrences (all)   | 0                 | 2                 | 0               |
| Tumour Pain   |                   |                   |                 |
| subjects affected / exposed   | 0 / 26 (0.00%)    | 0 / 18 (0.00%)    | 0 / 6 (0.00%)   |
| occurrences (all)   | 0                 | 0                 | 0               |
| Vascular disorders  |                   |                   |                 |
| Hypertension  |                   |                   |                 |
| subjects affected / exposed   | 1 / 26 (3.85%)    | 2 / 18 (11.11%)   | 1 / 6 (16.67%)  |
| occurrences (all)   | 1                 | 2                 | 2               |
| Hot Flush   |                   |                   |                 |
| subjects affected / exposed   | 0 / 26 (0.00%)    | 0 / 18 (0.00%)    | 1 / 6 (16.67%)  |
| occurrences (all)   | 0                 | 0                 | 1               |
| Flushing  |                   |                   |                 |
| subjects affected / exposed   | 0 / 26 (0.00%)    | 0 / 18 (0.00%)    | 1 / 6 (16.67%)  |
| occurrences (all)   | 0                 | 0                 | 1               |
| Hypotension   |                   |                   |                 |
| subjects affected / exposed   | 0 / 26 (0.00%)    | 0 / 18 (0.00%)    | 0 / 6 (0.00%)   |
| occurrences (all)   | 0                 | 0                 | 0               |
| Pallor  |                   |                   |                 |
| subjects affected / exposed   | 0 / 26 (0.00%)    | 1 / 18 (5.56%)    | 0 / 6 (0.00%)   |
| occurrences (all)   | 0                 | 1                 | 0               |
| Peripheral Coldness   |                   |                   |                 |
| subjects affected / exposed   | 0 / 26 (0.00%)    | 1 / 18 (5.56%)    | 0 / 6 (0.00%)   |
| occurrences (all)   | 0                 | 1                 | 0               |
| General disorders and administration site conditions                |                   |                   |                 |
| Asthenia  |                   |                   |                 |
| subjects affected / exposed   | 4 / 26 (15.38%)   | 2 / 18 (11.11%)   | 0 / 6 (0.00%)   |
| occurrences (all)   | 4                 | 2                 | 0               |
| Chest Discomfort  |                   |                   |                 |
| subjects affected / exposed   | 1 / 26 (3.85%)    | 1 / 18 (5.56%)    | 2 / 6 (33.33%)  |
| occurrences (all)   | 1                 | 1                 | 3               |

|                             |                 |                 |                |
|-----------------------------|-----------------|-----------------|----------------|
| Chills                      |                 |                 |                |
| subjects affected / exposed | 3 / 26 (11.54%) | 1 / 18 (5.56%)  | 2 / 6 (33.33%) |
| occurrences (all)           | 3               | 1               | 3              |
| Face Oedema                 |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Fatigue                     |                 |                 |                |
| subjects affected / exposed | 8 / 26 (30.77%) | 5 / 18 (27.78%) | 4 / 6 (66.67%) |
| occurrences (all)           | 10              | 6               | 7              |
| Implant Site Pain           |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0               | 0               | 1              |
| Feeling Hot                 |                 |                 |                |
| subjects affected / exposed | 1 / 26 (3.85%)  | 2 / 18 (11.11%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 1               | 2               | 0              |
| Influenza Like Illness      |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Malaise                     |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0               | 0               | 1              |
| Injection Site Pain         |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0               | 0               | 1              |
| Non-Cardiac Chest Pain      |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Oedema Peripheral           |                 |                 |                |
| subjects affected / exposed | 2 / 26 (7.69%)  | 3 / 18 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all)           | 3               | 3               | 1              |
| Pain                        |                 |                 |                |
| subjects affected / exposed | 1 / 26 (3.85%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0              |
| Peripheral Swelling         |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |

|   |  |   |   |
|---|--|---|---|
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 5 / 26 (19.23%)<br>6   | 3 / 18 (16.67%)<br>4  | 1 / 6 (16.67%)<br>1   |
| Immune system disorders<br>Cytokine Release Syndrome<br>subjects affected / exposed<br>occurrences (all)  | 0 / 26 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Nipple Pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Vulvovaginal Pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 26 (0.00%)<br>0<br><br>0 / 26 (0.00%)<br>0   | 0 / 18 (0.00%)<br>0<br><br>0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0<br><br>0 / 6 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders<br>Bronchospasm<br>subjects affected / exposed<br>occurrences (all)<br><br>Epistaxis<br>subjects affected / exposed<br>occurrences (all)<br><br>Dyspnoea Exertional<br>subjects affected / exposed<br>occurrences (all)<br><br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Hypoxia<br>subjects affected / exposed<br>occurrences (all)<br><br>Laryngeal Discomfort<br>subjects affected / exposed<br>occurrences (all) | 2 / 26 (7.69%)<br>2<br><br>3 / 26 (11.54%)<br>3<br><br>0 / 26 (0.00%)<br>0<br><br>4 / 26 (15.38%)<br>5<br><br>6 / 26 (23.08%)<br>6<br><br>1 / 26 (3.85%)<br>1<br><br>0 / 26 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1<br><br>0 / 18 (0.00%)<br>0<br><br>0 / 18 (0.00%)<br>0<br><br>5 / 18 (27.78%)<br>7<br><br>2 / 18 (11.11%)<br>3<br><br>0 / 18 (0.00%)<br>0<br><br>0 / 18 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0<br><br>0 / 6 (0.00%)<br>0<br><br>0 / 6 (0.00%)<br>0<br><br>1 / 6 (16.67%)<br>2<br><br>3 / 6 (50.00%)<br>4<br><br>1 / 6 (16.67%)<br>1<br><br>0 / 6 (0.00%)<br>0 |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| Laryngospasm                |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Nasal Congestion            |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Oropharyngeal Pain          |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Productive Cough            |                |                 |                |
| subjects affected / exposed | 1 / 26 (3.85%) | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 1              | 0               | 4              |
| Rhinitis Allergic           |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 1 / 18 (5.56%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0              | 1               | 1              |
| Rhinorrhoea                 |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 3 / 18 (16.67%) | 1 / 6 (16.67%) |
| occurrences (all)           | 0              | 3               | 1              |
| Throat Lesion               |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Throat Tightness            |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Sinus Congestion            |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 2 / 18 (11.11%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 2               | 0              |
| Sneezing                    |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Throat Irritation           |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Upper-Airway Cough Syndrome |                |                 |                |
| subjects affected / exposed | 1 / 26 (3.85%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0              |

|   |                      |                      |                     |
|---|----------------------|----------------------|---------------------|
| Tracheal Stenosis<br>subjects affected / exposed<br>occurrences (all) | 0 / 26 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Wheezing<br>subjects affected / exposed<br>occurrences (all)          | 1 / 26 (3.85%)<br>1  | 2 / 18 (11.11%)<br>2 | 0 / 6 (0.00%)<br>0  |
| Psychiatric disorders   |                      |                      |                     |
| Abnormal Dreams<br>subjects affected / exposed<br>occurrences (all)   | 0 / 26 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Agitation<br>subjects affected / exposed<br>occurrences (all)         | 1 / 26 (3.85%)<br>1  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Confusional State<br>subjects affected / exposed<br>occurrences (all) | 2 / 26 (7.69%)<br>2  | 1 / 18 (5.56%)<br>1  | 1 / 6 (16.67%)<br>1 |
| Bradyphrenia<br>subjects affected / exposed<br>occurrences (all)      | 0 / 26 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)           | 0 / 26 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  | 1 / 6 (16.67%)<br>1 |
| Depression<br>subjects affected / exposed<br>occurrences (all)        | 1 / 26 (3.85%)<br>1  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)          | 3 / 26 (11.54%)<br>3 | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Restlessness<br>subjects affected / exposed<br>occurrences (all)      | 1 / 26 (3.85%)<br>1  | 0 / 18 (0.00%)<br>0  | 1 / 6 (16.67%)<br>3 |
| Nightmare<br>subjects affected / exposed<br>occurrences (all)         | 0 / 26 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Irritability  |                      |                      |                     |

|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 26 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Investigations                                   |                     |                     |                    |
| Carbon Monoxide Diffusing Capacity Decreased     |                     |                     |                    |
| subjects affected / exposed                      | 1 / 26 (3.85%)      | 1 / 18 (5.56%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 1                   | 1                   | 0                  |
| Blood Creatinine Increased                       |                     |                     |                    |
| subjects affected / exposed                      | 1 / 26 (3.85%)      | 0 / 18 (0.00%)      | 1 / 6 (16.67%)     |
| occurrences (all)                                | 1                   | 0                   | 1                  |
| Electrocardiogram T Wave Abnormal                |                     |                     |                    |
| subjects affected / exposed                      | 0 / 26 (0.00%)      | 0 / 18 (0.00%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Lymphocyte Count Decreased                       |                     |                     |                    |
| subjects affected / exposed                      | 1 / 26 (3.85%)      | 0 / 18 (0.00%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                  |
| Platelet Count Decreased                         |                     |                     |                    |
| subjects affected / exposed                      | 0 / 26 (0.00%)      | 0 / 18 (0.00%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Neutrophil Count Decreased                       |                     |                     |                    |
| subjects affected / exposed                      | 0 / 26 (0.00%)      | 0 / 18 (0.00%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Qrs Axis Abnormal                                |                     |                     |                    |
| subjects affected / exposed                      | 0 / 26 (0.00%)      | 0 / 18 (0.00%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Weight Decreased                                 |                     |                     |                    |
| subjects affected / exposed                      | 3 / 26 (11.54%)     | 0 / 18 (0.00%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 3                   | 0                   | 0                  |
| Injury, poisoning and procedural complications   |                     |                     |                    |
| Accidental Overdose                              |                     |                     |                    |
| subjects affected / exposed                      | 0 / 26 (0.00%)      | 1 / 18 (5.56%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                  |
| Contusion  |                     |                     |                    |
| subjects affected / exposed                      | 0 / 26 (0.00%)      | 0 / 18 (0.00%)      | 0 / 6 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                  |
| Infusion Related Reaction                        |                     |                     |                    |



|  |                        |                        |                     |
|--|------------------------|------------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 12 / 26 (46.15%)<br>12 | 10 / 18 (55.56%)<br>13 | 4 / 6 (66.67%)<br>4 |
| Fall<br>subjects affected / exposed<br>occurrences (all)   | 1 / 26 (3.85%)<br>1    | 0 / 18 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Joint Injury<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 26 (0.00%)<br>0    | 0 / 18 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Procedural Pain<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 26 (0.00%)<br>0    | 0 / 18 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Sports Injury<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 26 (0.00%)<br>0    | 0 / 18 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Scapula Fracture<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 26 (0.00%)<br>0    | 0 / 18 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Cardiac disorders<br>Bundle Branch Block Right<br>subjects affected / exposed<br>occurrences (all) | 0 / 26 (0.00%)<br>0    | 0 / 18 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 26 (0.00%)<br>0    | 0 / 18 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Bradycardia<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 26 (0.00%)<br>0    | 0 / 18 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Right Ventricular Hypertrophy<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 26 (0.00%)<br>0    | 0 / 18 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Angina Pectoris<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 26 (0.00%)<br>0    | 1 / 18 (5.56%)<br>1    | 0 / 6 (0.00%)<br>0  |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 26 (0.00%)<br>0    | 0 / 18 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |

|   |                      |                      |                     |
|---|----------------------|----------------------|---------------------|
| Sinus Tachycardia<br>subjects affected / exposed<br>occurrences (all)       | 0 / 26 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Nervous system disorders  |                      |                      |                     |
| Balance Disorder<br>subjects affected / exposed<br>occurrences (all)        | 0 / 26 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Amnesia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 26 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)               | 2 / 26 (7.69%)<br>3  | 1 / 18 (5.56%)<br>1  | 1 / 6 (16.67%)<br>1 |
| Cranial Nerve Paralysis<br>subjects affected / exposed<br>occurrences (all) | 0 / 26 (0.00%)<br>0  | 1 / 18 (5.56%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Cognitive Disorder<br>subjects affected / exposed<br>occurrences (all)      | 0 / 26 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)               | 0 / 26 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Head Discomfort<br>subjects affected / exposed<br>occurrences (all)         | 0 / 26 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                | 5 / 26 (19.23%)<br>5 | 2 / 18 (11.11%)<br>2 | 0 / 6 (0.00%)<br>0  |
| Paraesthesia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 26 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Mental Impairment<br>subjects affected / exposed<br>occurrences (all)       | 0 / 26 (0.00%)<br>0  | 0 / 18 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Hypoaesthesia   |                      |                      |                     |

|                                      |                  |                 |                |
|--------------------------------------|------------------|-----------------|----------------|
| subjects affected / exposed          | 0 / 26 (0.00%)   | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0                | 1               | 0              |
| Peripheral Sensory Neuropathy        |                  |                 |                |
| subjects affected / exposed          | 0 / 26 (0.00%)   | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0                | 0               | 0              |
| Vith Nerve Paralysis                 |                  |                 |                |
| subjects affected / exposed          | 0 / 26 (0.00%)   | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0                | 1               | 0              |
| Toxic Encephalopathy                 |                  |                 |                |
| subjects affected / exposed          | 0 / 26 (0.00%)   | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0                | 1               | 0              |
| Restless Legs Syndrome               |                  |                 |                |
| subjects affected / exposed          | 1 / 26 (3.85%)   | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                    | 1                | 0               | 5              |
| Blood and lymphatic system disorders |                  |                 |                |
| Anaemia                              |                  |                 |                |
| subjects affected / exposed          | 10 / 26 (38.46%) | 4 / 18 (22.22%) | 1 / 6 (16.67%) |
| occurrences (all)                    | 13               | 7               | 2              |
| Thrombocytopenia                     |                  |                 |                |
| subjects affected / exposed          | 3 / 26 (11.54%)  | 1 / 18 (5.56%)  | 1 / 6 (16.67%) |
| occurrences (all)                    | 4                | 2               | 2              |
| Neutropenia                          |                  |                 |                |
| subjects affected / exposed          | 1 / 26 (3.85%)   | 1 / 18 (5.56%)  | 1 / 6 (16.67%) |
| occurrences (all)                    | 2                | 2               | 2              |
| Eye disorders                        |                  |                 |                |
| Conjunctival Haemorrhage             |                  |                 |                |
| subjects affected / exposed          | 0 / 26 (0.00%)   | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                    | 0                | 0               | 1              |
| Scleral Discolouration               |                  |                 |                |
| subjects affected / exposed          | 0 / 26 (0.00%)   | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                    | 0                | 0               | 1              |
| Diplopia                             |                  |                 |                |
| subjects affected / exposed          | 0 / 26 (0.00%)   | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0                | 0               | 0              |
| Dry Eye                              |                  |                 |                |

|                             |                 |                 |                |
|-----------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Lacrimation Increased       |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0               | 0               | 1              |
| Vision Blurred              |                 |                 |                |
| subjects affected / exposed | 1 / 26 (3.85%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1               | 1               | 0              |
| Visual Impairment           |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0               | 0               | 1              |
| Gastrointestinal disorders  |                 |                 |                |
| Abdominal Discomfort        |                 |                 |                |
| subjects affected / exposed | 1 / 26 (3.85%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1               | 1               | 0              |
| Abdominal Distension        |                 |                 |                |
| subjects affected / exposed | 1 / 26 (3.85%)  | 1 / 18 (5.56%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 1               | 1               | 1              |
| Abdominal Pain              |                 |                 |                |
| subjects affected / exposed | 4 / 26 (15.38%) | 1 / 18 (5.56%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 4               | 1               | 1              |
| Abdominal Pain Upper        |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Abdominal Tenderness        |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Dry Mouth                   |                 |                 |                |
| subjects affected / exposed | 1 / 26 (3.85%)  | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 1               | 0               | 1              |
| Diarrhoea                   |                 |                 |                |
| subjects affected / exposed | 6 / 26 (23.08%) | 4 / 18 (22.22%) | 1 / 6 (16.67%) |
| occurrences (all)           | 9               | 6               | 1              |
| Constipation                |                 |                 |                |
| subjects affected / exposed | 2 / 26 (7.69%)  | 1 / 18 (5.56%)  | 2 / 6 (33.33%) |
| occurrences (all)           | 2               | 1               | 2              |

|                                  |                  |                 |                |
|----------------------------------|------------------|-----------------|----------------|
| Dyspepsia                        |                  |                 |                |
| subjects affected / exposed      | 1 / 26 (3.85%)   | 2 / 18 (11.11%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 1                | 2               | 0              |
| Gastrointestinal Pain            |                  |                 |                |
| subjects affected / exposed      | 0 / 26 (0.00%)   | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                | 0                | 0               | 0              |
| Dysphagia                        |                  |                 |                |
| subjects affected / exposed      | 1 / 26 (3.85%)   | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                | 1                | 0               | 0              |
| Gastrooesophageal Reflux Disease |                  |                 |                |
| subjects affected / exposed      | 0 / 26 (0.00%)   | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                | 0                | 0               | 0              |
| Glossitis                        |                  |                 |                |
| subjects affected / exposed      | 0 / 26 (0.00%)   | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                | 0                | 0               | 1              |
| Glossodynia                      |                  |                 |                |
| subjects affected / exposed      | 0 / 26 (0.00%)   | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                | 0                | 0               | 0              |
| Haemorrhoids                     |                  |                 |                |
| subjects affected / exposed      | 0 / 26 (0.00%)   | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                | 0                | 0               | 0              |
| Nausea                           |                  |                 |                |
| subjects affected / exposed      | 10 / 26 (38.46%) | 6 / 18 (33.33%) | 4 / 6 (66.67%) |
| occurrences (all)                | 13               | 8               | 6              |
| Mouth Ulceration                 |                  |                 |                |
| subjects affected / exposed      | 0 / 26 (0.00%)   | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                | 0                | 1               | 0              |
| Rectal Haemorrhage               |                  |                 |                |
| subjects affected / exposed      | 0 / 26 (0.00%)   | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                | 0                | 1               | 0              |
| Vomiting                         |                  |                 |                |
| subjects affected / exposed      | 6 / 26 (23.08%)  | 4 / 18 (22.22%) | 1 / 6 (16.67%) |
| occurrences (all)                | 7                | 5               | 2              |
| Toothache                        |                  |                 |                |
| subjects affected / exposed      | 1 / 26 (3.85%)   | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                | 1                | 1               | 0              |

|  |                |                 |                |
|--|----------------|-----------------|----------------|
| Stomatitis                             |                |                 |                |
| subjects affected / exposed            | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Skin and subcutaneous tissue disorders |                |                 |                |
| Actinic Keratosis                      |                |                 |                |
| subjects affected / exposed            | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                      | 0              | 0               | 1              |
| Dermatitis Contact                     |                |                 |                |
| subjects affected / exposed            | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Dermatitis Acneiform                   |                |                 |                |
| subjects affected / exposed            | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Alopecia                               |                |                 |                |
| subjects affected / exposed            | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Erythema                               |                |                 |                |
| subjects affected / exposed            | 1 / 26 (3.85%) | 2 / 18 (11.11%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 1              | 2               | 0              |
| Hair Texture Abnormal                  |                |                 |                |
| subjects affected / exposed            | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Hyperhidrosis                          |                |                 |                |
| subjects affected / exposed            | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                      | 0              | 0               | 1              |
| Pruritus                               |                |                 |                |
| subjects affected / exposed            | 2 / 26 (7.69%) | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 2              | 1               | 0              |
| Pain Of Skin                           |                |                 |                |
| subjects affected / exposed            | 1 / 26 (3.85%) | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                      | 1              | 0               | 1              |
| Onychoclasia                           |                |                 |                |
| subjects affected / exposed            | 1 / 26 (3.85%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 1              | 0               | 0              |
| Rash                                   |                |                 |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0               | 1              |
| Rash Maculo-Papular                             |                |                 |                |
| subjects affected / exposed                     | 1 / 26 (3.85%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 2              | 0               | 0              |
| Rash Macular                                    |                |                 |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0               | 1              |
| Rash Erythematous                               |                |                 |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0               | 1              |
| Rash Pruritic                                   |                |                 |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0               | 1              |
| Skin Disorder                                   |                |                 |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Skin Ulcer                                      |                |                 |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Renal and urinary disorders                     |                |                 |                |
| Acute Kidney Injury                             |                |                 |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Urinary Incontinence                            |                |                 |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0               | 1              |
| Pollakiuria                                     |                |                 |                |
| subjects affected / exposed                     | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Musculoskeletal and connective tissue disorders |                |                 |                |
| Arthralgia                                      |                |                 |                |
| subjects affected / exposed                     | 1 / 26 (3.85%) | 2 / 18 (11.11%) | 1 / 6 (16.67%) |
| occurrences (all)                               | 1              | 2               | 1              |
| Back Pain                                       |                |                 |                |

|                             |                 |                 |                |
|-----------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 6 / 26 (23.08%) | 7 / 18 (38.89%) | 1 / 6 (16.67%) |
| occurrences (all)           | 6               | 7               | 2              |
| Bone Pain                   |                 |                 |                |
| subjects affected / exposed | 4 / 26 (15.38%) | 3 / 18 (16.67%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 5               | 4               | 0              |
| Bursitis                    |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Flank Pain                  |                 |                 |                |
| subjects affected / exposed | 2 / 26 (7.69%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 2               | 0               | 0              |
| Groin Pain                  |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Joint Swelling              |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0               | 0               | 1              |
| Limb Discomfort             |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Muscle Fatigue              |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0               | 0               | 1              |
| Muscle Spasms               |                 |                 |                |
| subjects affected / exposed | 3 / 26 (11.54%) | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 3               | 0               | 3              |
| Musculoskeletal Pain        |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Musculoskeletal Chest Pain  |                 |                 |                |
| subjects affected / exposed | 1 / 26 (3.85%)  | 2 / 18 (11.11%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 1               | 2               | 0              |
| Muscular Weakness           |                 |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0               | 0               | 1              |
| Myalgia                     |                 |                 |                |



|                                   |                 |                 |                |
|-----------------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed       | 1 / 26 (3.85%)  | 0 / 18 (0.00%)  | 2 / 6 (33.33%) |
| occurrences (all)                 | 1               | 0               | 3              |
| Neck Pain                         |                 |                 |                |
| subjects affected / exposed       | 0 / 26 (0.00%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 1               | 0              |
| Pain In Extremity                 |                 |                 |                |
| subjects affected / exposed       | 3 / 26 (11.54%) | 0 / 18 (0.00%)  | 2 / 6 (33.33%) |
| occurrences (all)                 | 3               | 0               | 3              |
| Pathological Fracture             |                 |                 |                |
| subjects affected / exposed       | 2 / 26 (7.69%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 2               | 1               | 0              |
| Spinal Osteoarthritis             |                 |                 |                |
| subjects affected / exposed       | 0 / 26 (0.00%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 1               | 0              |
| Spinal Pain                       |                 |                 |                |
| subjects affected / exposed       | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 0               | 0              |
| Infections and infestations       |                 |                 |                |
| Gastroenteritis Viral             |                 |                 |                |
| subjects affected / exposed       | 0 / 26 (0.00%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 0               | 0              |
| Bronchitis                        |                 |                 |                |
| subjects affected / exposed       | 1 / 26 (3.85%)  | 3 / 18 (16.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                 | 1               | 5               | 0              |
| Angular Cheilitis                 |                 |                 |                |
| subjects affected / exposed       | 0 / 26 (0.00%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 1               | 0              |
| Gingivitis                        |                 |                 |                |
| subjects affected / exposed       | 0 / 26 (0.00%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 1               | 0              |
| Herpes Simplex                    |                 |                 |                |
| subjects affected / exposed       | 1 / 26 (3.85%)  | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 1               | 0               | 0              |
| Lower Respiratory Tract Infection |                 |                 |                |
| subjects affected / exposed       | 0 / 26 (0.00%)  | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)                 | 0               | 1               | 0              |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| Influenza                   |                |                 |                |
| subjects affected / exposed | 1 / 26 (3.85%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0              |
| Hordeolum                   |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0              | 0               | 1              |
| Nasopharyngitis             |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Otitis Media                |                |                 |                |
| subjects affected / exposed | 1 / 26 (3.85%) | 2 / 18 (11.11%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 1              | 2               | 0              |
| Oral Candidiasis            |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Sinusitis                   |                |                 |                |
| subjects affected / exposed | 2 / 26 (7.69%) | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 2              | 1               | 0              |
| Rhinitis                    |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Respiratory Tract Infection |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Pyuria                      |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Pneumonia                   |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Tooth Abscess               |                |                 |                |
| subjects affected / exposed | 0 / 26 (0.00%) | 1 / 18 (5.56%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Tooth Infection             |                |                 |                |
| subjects affected / exposed | 2 / 26 (7.69%) | 0 / 18 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 2              | 0               | 0              |

|   |                       |                      |                     |
|---|-----------------------|----------------------|---------------------|
| Urinary Tract Infection<br>subjects affected / exposed<br>occurrences (all)           | 1 / 26 (3.85%)<br>1   | 0 / 18 (0.00%)<br>0  | 1 / 6 (16.67%)<br>2 |
| Upper Respiratory Tract Infection<br>subjects affected / exposed<br>occurrences (all) | 7 / 26 (26.92%)<br>11 | 3 / 18 (16.67%)<br>3 | 3 / 6 (50.00%)<br>4 |
| Metabolism and nutrition disorders  |                       |                      |                     |
| Decreased Appetite<br>subjects affected / exposed<br>occurrences (all)                | 5 / 26 (19.23%)<br>5  | 3 / 18 (16.67%)<br>4 | 1 / 6 (16.67%)<br>1 |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 26 (0.00%)<br>0   | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 26 (0.00%)<br>0   | 1 / 18 (5.56%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 26 (3.85%)<br>1   | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 26 (0.00%)<br>0   | 1 / 18 (5.56%)<br>1  | 1 / 6 (16.67%)<br>1 |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 26 (0.00%)<br>0   | 2 / 18 (11.11%)<br>2 | 0 / 6 (0.00%)<br>0  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 26 (3.85%)<br>1   | 1 / 18 (5.56%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Hypocalcaemia<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 26 (0.00%)<br>0   | 0 / 18 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Hyperuricaemia<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 26 (3.85%)<br>1   | 0 / 18 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Hyperkalaemia   |                       |                      |                     |

|                             |                 |                |               |
|-----------------------------|-----------------|----------------|---------------|
| subjects affected / exposed | 3 / 26 (11.54%) | 1 / 18 (5.56%) | 0 / 6 (0.00%) |
| occurrences (all)           | 3               | 1              | 0             |
| Pseudohyponatraemia         |                 |                |               |
| subjects affected / exposed | 0 / 26 (0.00%)  | 0 / 18 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |

| <b>Non-serious adverse events</b>                                   | Phase 1: Isatuximab<br>20mg/kg Q2W | Phase 1: Isatuximab<br>20mg/kg QW | Phase 2 Stage 1a:<br>Isatuximab 3mg/kg<br>Q2W |
|---|------------------------------------|-----------------------------------|---|
| Total subjects affected by non-serious adverse events               |                                    |                                   |   |
| subjects affected / exposed   | 6 / 7 (85.71%)                     | 6 / 7 (85.71%)                    | 22 / 23 (95.65%)                              |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                    |                                   |   |
| Basal Cell Carcinoma  |                                    |                                   |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                      | 0 / 7 (0.00%)                     | 0 / 23 (0.00%)                                |
| occurrences (all)   | 0                                  | 0                                 | 0   |
| Tumour Pain   |                                    |                                   |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                      | 0 / 7 (0.00%)                     | 0 / 23 (0.00%)                                |
| occurrences (all)   | 0                                  | 0                                 | 0   |
| Vascular disorders  |                                    |                                   |   |
| Hypertension  |                                    |                                   |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                      | 0 / 7 (0.00%)                     | 3 / 23 (13.04%)                               |
| occurrences (all)   | 0                                  | 0                                 | 3   |
| Hot Flush   |                                    |                                   |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                      | 0 / 7 (0.00%)                     | 0 / 23 (0.00%)                                |
| occurrences (all)   | 0                                  | 0                                 | 0   |
| Flushing  |                                    |                                   |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                      | 2 / 7 (28.57%)                    | 4 / 23 (17.39%)                               |
| occurrences (all)   | 0                                  | 39                                | 4   |
| Hypotension   |                                    |                                   |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                      | 0 / 7 (0.00%)                     | 3 / 23 (13.04%)                               |
| occurrences (all)   | 0                                  | 0                                 | 3   |
| Pallor  |                                    |                                   |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                      | 0 / 7 (0.00%)                     | 1 / 23 (4.35%)                                |
| occurrences (all)   | 0                                  | 0                                 | 1   |
| Peripheral Coldness   |                                    |                                   |   |
| subjects affected / exposed   | 0 / 7 (0.00%)                      | 0 / 7 (0.00%)                     | 0 / 23 (0.00%)                                |
| occurrences (all)   | 0                                  | 0                                 | 0   |
| General disorders and administration                                |                                    |                                   |   |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| site conditions             |                |                |                 |
| Asthenia                    |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Chest Discomfort            |                |                |                 |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 7 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 2              | 0              | 1               |
| Chills                      |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 3 / 23 (13.04%) |
| occurrences (all)           | 0              | 0              | 5               |
| Face Oedema                 |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Fatigue                     |                |                |                 |
| subjects affected / exposed | 4 / 7 (57.14%) | 1 / 7 (14.29%) | 5 / 23 (21.74%) |
| occurrences (all)           | 6              | 1              | 5               |
| Implant Site Pain           |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Feeling Hot                 |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Influenza Like Illness      |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Malaise                     |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 2 / 23 (8.70%)  |
| occurrences (all)           | 0              | 0              | 2               |
| Injection Site Pain         |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Non-Cardiac Chest Pain      |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Oedema Peripheral           |                |                |                 |

|   |                     |                    |                      |
|---|---------------------|--------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 | 2 / 23 (8.70%)<br>3  |
| Pain<br>subjects affected / exposed<br>occurrences (all)  | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0 | 1 / 23 (4.35%)<br>1  |
| Peripheral Swelling<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0 | 3 / 23 (13.04%)<br>3 |
| Immune system disorders<br>Cytokine Release Syndrome<br>subjects affected / exposed<br>occurrences (all)            | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Nipple Pain<br>subjects affected / exposed<br>occurrences (all)         | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Vulvovaginal Pain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders<br>Bronchospasm<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 | 0 / 23 (0.00%)<br>0  |
| Dyspnoea Exertional<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0 | 1 / 23 (4.35%)<br>1  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)  | 3 / 7 (42.86%)<br>3 | 0 / 7 (0.00%)<br>0 | 5 / 23 (21.74%)<br>6 |
| Cough   |                     |                    |                      |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 7 (28.57%) | 2 / 23 (8.70%) |
| occurrences (all)           | 1              | 2              | 3              |
| Hypoxia                     |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Laryngeal Discomfort        |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Laryngospasm                |                |                |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Nasal Congestion            |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Oropharyngeal Pain          |                |                |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Productive Cough            |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Rhinitis Allergic           |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 1 / 23 (4.35%) |
| occurrences (all)           | 0              | 1              | 1              |
| Rhinorrhoea                 |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)           | 0              | 0              | 1              |
| Throat Lesion               |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Throat Tightness            |                |                |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Sinus Congestion            |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)           | 0              | 0              | 1              |
| Sneezing                    |                |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Throat Irritation           |                |                |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Upper-Airway Cough Syndrome |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Tracheal Stenosis           |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Wheezing                    |                |                |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 7 (14.29%) | 1 / 23 (4.35%) |
| occurrences (all)           | 1              | 1              | 1              |
| Psychiatric disorders       |                |                |                |
| Abnormal Dreams             |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Agitation                   |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Confusional State           |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Bradyphrenia                |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Anxiety                     |                |                |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)           | 1              | 0              | 1              |
| Depression                  |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Insomnia                    |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 1 / 23 (4.35%) |
| occurrences (all)           | 0              | 1              | 1              |



|  |                |               |                 |
|--|----------------|---------------|-----------------|
| Restlessness                                   |                |               |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0               |
| Nightmare                                      |                |               |                 |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)                              | 1              | 0             | 0               |
| Irritability                                   |                |               |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0               |
| Investigations                                 |                |               |                 |
| Carbon Monoxide Diffusing Capacity Decreased   |                |               |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0               |
| Blood Creatinine Increased                     |                |               |                 |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 7 (0.00%) | 2 / 23 (8.70%)  |
| occurrences (all)                              | 1              | 0             | 2               |
| Electrocardiogram T Wave Abnormal              |                |               |                 |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)                              | 1              | 0             | 0               |
| Lymphocyte Count Decreased                     |                |               |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 1 / 23 (4.35%)  |
| occurrences (all)                              | 0              | 0             | 1               |
| Platelet Count Decreased                       |                |               |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 5 / 23 (21.74%) |
| occurrences (all)                              | 0              | 0             | 9               |
| Neutrophil Count Decreased                     |                |               |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 2 / 23 (8.70%)  |
| occurrences (all)                              | 0              | 0             | 2               |
| Qrs Axis Abnormal                              |                |               |                 |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)                              | 1              | 0             | 0               |
| Weight Decreased                               |                |               |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 1 / 23 (4.35%)  |
| occurrences (all)                              | 0              | 0             | 1               |
| Injury, poisoning and procedural complications |                |               |                 |

|                               |                |                |                 |
|-------------------------------|----------------|----------------|-----------------|
| Accidental Overdose           |                |                |                 |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Contusion                     |                |                |                 |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 1 / 23 (4.35%)  |
| occurrences (all)             | 0              | 1              | 1               |
| Infusion Related Reaction     |                |                |                 |
| subjects affected / exposed   | 4 / 7 (57.14%) | 3 / 7 (42.86%) | 9 / 23 (39.13%) |
| occurrences (all)             | 4              | 74             | 11              |
| Fall                          |                |                |                 |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Joint Injury                  |                |                |                 |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Procedural Pain               |                |                |                 |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (0.00%)  |
| occurrences (all)             | 0              | 1              | 0               |
| Sports Injury                 |                |                |                 |
| subjects affected / exposed   | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)             | 1              | 0              | 0               |
| Scapula Fracture              |                |                |                 |
| subjects affected / exposed   | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)             | 1              | 0              | 0               |
| Cardiac disorders             |                |                |                 |
| Bundle Branch Block Right     |                |                |                 |
| subjects affected / exposed   | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)             | 1              | 0              | 0               |
| Palpitations                  |                |                |                 |
| subjects affected / exposed   | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)             | 1              | 0              | 0               |
| Bradycardia                   |                |                |                 |
| subjects affected / exposed   | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Right Ventricular Hypertrophy |                |                |                 |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Angina Pectoris             |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Tachycardia                 |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Sinus Tachycardia           |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Nervous system disorders    |                |                |                 |
| Balance Disorder            |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Amnesia                     |                |                |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Dizziness                   |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 1 / 23 (4.35%)  |
| occurrences (all)           | 0              | 1              | 1               |
| Cranial Nerve Paralysis     |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Cognitive Disorder          |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 2              | 0               |
| Dysgeusia                   |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Head Discomfort             |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Headache                    |                |                |                 |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 7 (14.29%) | 4 / 23 (17.39%) |
| occurrences (all)           | 4              | 33             | 4               |

|                                      |                |                |                 |
|--------------------------------------|----------------|----------------|-----------------|
| Paraesthesia                         |                |                |                 |
| subjects affected / exposed          | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0               |
| Mental Impairment                    |                |                |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Hypoaesthesia                        |                |                |                 |
| subjects affected / exposed          | 2 / 7 (28.57%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                    | 2              | 0              | 0               |
| Peripheral Sensory Neuropathy        |                |                |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 2 / 23 (8.70%)  |
| occurrences (all)                    | 0              | 0              | 2               |
| Vith Nerve Paralysis                 |                |                |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Toxic Encephalopathy                 |                |                |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Restless Legs Syndrome               |                |                |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 1 / 23 (4.35%)  |
| occurrences (all)                    | 0              | 2              | 1               |
| Blood and lymphatic system disorders |                |                |                 |
| Anaemia                              |                |                |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 9 / 23 (39.13%) |
| occurrences (all)                    | 0              | 0              | 14              |
| Thrombocytopenia                     |                |                |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 2 / 23 (8.70%)  |
| occurrences (all)                    | 0              | 0              | 2               |
| Neutropenia                          |                |                |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)                    | 0              | 0              | 1               |
| Eye disorders                        |                |                |                 |
| Conjunctival Haemorrhage             |                |                |                 |
| subjects affected / exposed          | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Scleral Discolouration               |                |                |                 |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Diplopia                    |                |               |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Dry Eye                     |                |               |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 1              | 0             | 0              |
| Lacrimation Increased       |                |               |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Vision Blurred              |                |               |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Visual Impairment           |                |               |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Gastrointestinal disorders  |                |               |                |
| Abdominal Discomfort        |                |               |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Abdominal Distension        |                |               |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all)           | 0              | 0             | 1              |
| Abdominal Pain              |                |               |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all)           | 1              | 0             | 1              |
| Abdominal Pain Upper        |                |               |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Abdominal Tenderness        |                |               |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0              | 0             | 0              |
| Dry Mouth                   |                |               |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%) | 1 / 23 (4.35%) |
| occurrences (all)           | 1              | 0             | 1              |

|                                  |                |                |                 |
|----------------------------------|----------------|----------------|-----------------|
| Diarrhoea                        |                |                |                 |
| subjects affected / exposed      | 1 / 7 (14.29%) | 2 / 7 (28.57%) | 5 / 23 (21.74%) |
| occurrences (all)                | 1              | 2              | 7               |
| Constipation                     |                |                |                 |
| subjects affected / exposed      | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 6 / 23 (26.09%) |
| occurrences (all)                | 0              | 0              | 6               |
| Dyspepsia                        |                |                |                 |
| subjects affected / exposed      | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Gastrointestinal Pain            |                |                |                 |
| subjects affected / exposed      | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Dysphagia                        |                |                |                 |
| subjects affected / exposed      | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Gastrooesophageal Reflux Disease |                |                |                 |
| subjects affected / exposed      | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Glossitis                        |                |                |                 |
| subjects affected / exposed      | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Glossodynia                      |                |                |                 |
| subjects affected / exposed      | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Haemorrhoids                     |                |                |                 |
| subjects affected / exposed      | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Nausea                           |                |                |                 |
| subjects affected / exposed      | 1 / 7 (14.29%) | 1 / 7 (14.29%) | 6 / 23 (26.09%) |
| occurrences (all)                | 4              | 1              | 6               |
| Mouth Ulceration                 |                |                |                 |
| subjects affected / exposed      | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Rectal Haemorrhage               |                |                |                 |
| subjects affected / exposed      | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |

|  |                |                |                |
|--|----------------|----------------|----------------|
| Vomiting                               |                |                |                |
| subjects affected / exposed            | 1 / 7 (14.29%) | 1 / 7 (14.29%) | 1 / 23 (4.35%) |
| occurrences (all)                      | 2              | 1              | 1              |
| Toothache                              |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Stomatitis                             |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 1              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Actinic Keratosis                      |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Dermatitis Contact                     |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Dermatitis Acneiform                   |                |                |                |
| subjects affected / exposed            | 2 / 7 (28.57%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                      | 2              | 0              | 0              |
| Alopecia                               |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Erythema                               |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Hair Texture Abnormal                  |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Hyperhidrosis                          |                |                |                |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Pruritus                               |                |                |                |
| subjects affected / exposed            | 1 / 7 (14.29%) | 1 / 7 (14.29%) | 0 / 23 (0.00%) |
| occurrences (all)                      | 2              | 1              | 0              |
| Pain Of Skin                           |                |                |                |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Onychoclasia                |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Rash                        |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 7 (14.29%) | 1 / 23 (4.35%) |
| occurrences (all)           | 0             | 1              | 1              |
| Rash Maculo-Papular         |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Rash Macular                |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Rash Erythematous           |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Rash Pruritic               |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)           | 0             | 0              | 1              |
| Skin Disorder               |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 7 (14.29%) | 0 / 23 (0.00%) |
| occurrences (all)           | 0             | 1              | 0              |
| Skin Ulcer                  |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Renal and urinary disorders |               |                |                |
| Acute Kidney Injury         |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)           | 0             | 0              | 2              |
| Urinary Incontinence        |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Pollakiuria                 |               |                |                |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |



|   |                |                |                 |
|---|----------------|----------------|-----------------|
| Musculoskeletal and connective tissue disorders |                |                |                 |
| Arthralgia                                      |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 3 / 23 (13.04%) |
| occurrences (all)                               | 0              | 0              | 3               |
| Back Pain                                       |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 2 / 23 (8.70%)  |
| occurrences (all)                               | 0              | 5              | 2               |
| Bone Pain                                       |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)                               | 0              | 0              | 1               |
| Bursitis  |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Flank Pain                                      |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Groin Pain                                      |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)                               | 0              | 0              | 1               |
| Joint Swelling                                  |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Limb Discomfort                                 |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Muscle Fatigue                                  |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Muscle Spasms                                   |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Musculoskeletal Pain                            |                |                |                 |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0               |
| Musculoskeletal Chest Pain                      |                |                |                 |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 3 / 23 (13.04%) |
| occurrences (all)           | 0              | 3              | 3               |
| Muscular Weakness           |                |                |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Myalgia                     |                |                |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Neck Pain                   |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%)  |
| occurrences (all)           | 0              | 0              | 1               |
| Pain In Extremity           |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 2 / 23 (8.70%)  |
| occurrences (all)           | 0              | 0              | 2               |
| Pathological Fracture       |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Spinal Osteoarthritis       |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Spinal Pain                 |                |                |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0               |
| Infections and infestations |                |                |                 |
| Gastroenteritis Viral       |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Bronchitis                  |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Angular Cheilitis           |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Gingivitis                  |                |                |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |

|                                   |                |                |                |
|-----------------------------------|----------------|----------------|----------------|
| Herpes Simplex                    |                |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Lower Respiratory Tract Infection |                |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Influenza                         |                |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Hordeolum                         |                |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Nasopharyngitis                   |                |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 1 / 23 (4.35%) |
| occurrences (all)                 | 0              | 8              | 1              |
| Otitis Media                      |                |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |
| Oral Candidiasis                  |                |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 2 / 23 (8.70%) |
| occurrences (all)                 | 0              | 0              | 2              |
| Sinusitis                         |                |                |                |
| subjects affected / exposed       | 1 / 7 (14.29%) | 0 / 7 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                 | 1              | 0              | 1              |
| Rhinitis                          |                |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Respiratory Tract Infection       |                |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 0 / 23 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Pyuria                            |                |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 1 / 7 (14.29%) | 0 / 23 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |
| Pneumonia                         |                |                |                |
| subjects affected / exposed       | 0 / 7 (0.00%)  | 0 / 7 (0.00%)  | 1 / 23 (4.35%) |
| occurrences (all)                 | 0              | 0              | 1              |

|   |                     |                     |                      |
|---|---------------------|---------------------|----------------------|
| Tooth Abscess<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Tooth Infection<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Urinary Tract Infection<br>subjects affected / exposed<br>occurrences (all)           | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0  | 1 / 23 (4.35%)<br>1  |
| Upper Respiratory Tract Infection<br>subjects affected / exposed<br>occurrences (all) | 3 / 7 (42.86%)<br>4 | 1 / 7 (14.29%)<br>1 | 4 / 23 (17.39%)<br>5 |
| Metabolism and nutrition disorders  |                     |                     |                      |
| Decreased Appetite<br>subjects affected / exposed<br>occurrences (all)                | 1 / 7 (14.29%)<br>1 | 1 / 7 (14.29%)<br>1 | 4 / 23 (17.39%)<br>4 |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 3 / 23 (13.04%)<br>5 |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 1 / 23 (4.35%)<br>1  |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 0 / 23 (0.00%)<br>0  |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 7 (0.00%)<br>0  | 0 / 7 (0.00%)<br>0  | 1 / 23 (4.35%)<br>1  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 7 (14.29%)<br>1 | 0 / 7 (0.00%)<br>0  | 1 / 23 (4.35%)<br>1  |
| Hypocalcaemia   |                     |                     |                      |

|                             |               |               |                 |
|-----------------------------|---------------|---------------|-----------------|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0               |
| Hyperuricaemia              |               |               |                 |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 3 / 23 (13.04%) |
| occurrences (all)           | 0             | 0             | 3               |
| Hyperkalaemia               |               |               |                 |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0               |
| Pseudohyponatraemia         |               |               |                 |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 7 (0.00%) | 0 / 23 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0               |

| <b>Non-serious adverse events</b>                                   | Phase 2 Stage 1a:<br>Isatuximab 10mg/kg<br>Q2W | Phase 2 Stage 1a:<br>Isatuximab 10mg/kg<br>Q2W; Then Q4W | Phase 2 Stage 1b:<br>Isatuximab 20mg/kg<br>QW and Then Q2W |
|---|--|--|--|
| Total subjects affected by non-serious adverse events               |  |  |  |
| subjects affected / exposed   | 23 / 24 (95.83%)                               | 25 / 25 (100.00%)  | 24 / 25 (96.00%)   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |
| Basal Cell Carcinoma  |  |  |  |
| subjects affected / exposed   | 0 / 24 (0.00%)                                 | 1 / 25 (4.00%)   | 0 / 25 (0.00%)   |
| occurrences (all)   | 0  | 1  | 0  |
| Tumour Pain   |  |  |  |
| subjects affected / exposed   | 0 / 24 (0.00%)                                 | 0 / 25 (0.00%)   | 0 / 25 (0.00%)   |
| occurrences (all)   | 0  | 0  | 0  |
| Vascular disorders  |  |  |  |
| Hypertension  |  |  |  |
| subjects affected / exposed   | 2 / 24 (8.33%)                                 | 1 / 25 (4.00%)   | 0 / 25 (0.00%)   |
| occurrences (all)   | 8  | 1  | 0  |
| Hot Flush   |  |  |  |
| subjects affected / exposed   | 0 / 24 (0.00%)                                 | 2 / 25 (8.00%)   | 1 / 25 (4.00%)   |
| occurrences (all)   | 0  | 2  | 1  |
| Flushing  |  |  |  |
| subjects affected / exposed   | 1 / 24 (4.17%)                                 | 3 / 25 (12.00%)  | 4 / 25 (16.00%)  |
| occurrences (all)   | 1  | 4  | 5  |
| Hypotension   |  |  |  |
| subjects affected / exposed   | 2 / 24 (8.33%)                                 | 1 / 25 (4.00%)   | 1 / 25 (4.00%)   |
| occurrences (all)   | 2  | 1  | 1  |
| Pallor  |  |  |  |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 0 / 25 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                                    | 0               | 0                | 0               |
| Peripheral Coldness                                  |                 |                  |                 |
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 1 / 25 (4.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                                    | 0               | 1                | 0               |
| General disorders and administration site conditions |                 |                  |                 |
| Asthenia   |                 |                  |                 |
| subjects affected / exposed                          | 2 / 24 (8.33%)  | 0 / 25 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                                    | 2               | 0                | 0               |
| Chest Discomfort                                     |                 |                  |                 |
| subjects affected / exposed                          | 4 / 24 (16.67%) | 3 / 25 (12.00%)  | 6 / 25 (24.00%) |
| occurrences (all)                                    | 4               | 3                | 6               |
| Chills   |                 |                  |                 |
| subjects affected / exposed                          | 5 / 24 (20.83%) | 8 / 25 (32.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)                                    | 6               | 12               | 2               |
| Face Oedema  |                 |                  |                 |
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 0 / 25 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                                    | 0               | 0                | 0               |
| Fatigue  |                 |                  |                 |
| subjects affected / exposed                          | 7 / 24 (29.17%) | 11 / 25 (44.00%) | 9 / 25 (36.00%) |
| occurrences (all)                                    | 7               | 12               | 9               |
| Implant Site Pain                                    |                 |                  |                 |
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 0 / 25 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                                    | 0               | 0                | 0               |
| Feeling Hot  |                 |                  |                 |
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 0 / 25 (0.00%)   | 1 / 25 (4.00%)  |
| occurrences (all)                                    | 0               | 0                | 1               |
| Influenza Like Illness                               |                 |                  |                 |
| subjects affected / exposed                          | 2 / 24 (8.33%)  | 1 / 25 (4.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                                    | 2               | 2                | 0               |
| Malaise  |                 |                  |                 |
| subjects affected / exposed                          | 2 / 24 (8.33%)  | 0 / 25 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                                    | 2               | 0                | 0               |
| Injection Site Pain                                  |                 |                  |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Non-Cardiac Chest Pain                          |                 |                 |                 |
| subjects affected / exposed                     | 3 / 24 (12.50%) | 0 / 25 (0.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)                               | 4               | 0               | 2               |
| Oedema Peripheral                               |                 |                 |                 |
| subjects affected / exposed                     | 5 / 24 (20.83%) | 1 / 25 (4.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)                               | 6               | 1               | 3               |
| Pain  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 2 / 25 (8.00%)  | 4 / 25 (16.00%) |
| occurrences (all)                               | 2               | 2               | 5               |
| Peripheral Swelling                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                               | 1               | 0               | 0               |
| Pyrexia   |                 |                 |                 |
| subjects affected / exposed                     | 5 / 24 (20.83%) | 4 / 25 (16.00%) | 3 / 25 (12.00%) |
| occurrences (all)                               | 6               | 4               | 3               |
| Immune system disorders                         |                 |                 |                 |
| Cytokine Release Syndrome                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Reproductive system and breast disorders        |                 |                 |                 |
| Nipple Pain                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Vulvovaginal Pain                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Bronchospasm                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)                               | 0               | 0               | 1               |
| Epistaxis                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 4 / 25 (16.00%) | 3 / 25 (12.00%) |
| occurrences (all)                               | 1               | 4               | 3               |
| Dyspnoea Exertional                             |                 |                 |                 |

|                             |                  |                 |                 |
|-----------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 24 (8.33%)   | 3 / 25 (12.00%) | 1 / 25 (4.00%)  |
| occurrences (all)           | 2                | 3               | 1               |
| Dyspnoea                    |                  |                 |                 |
| subjects affected / exposed | 5 / 24 (20.83%)  | 8 / 25 (32.00%) | 4 / 25 (16.00%) |
| occurrences (all)           | 6                | 8               | 4               |
| Cough                       |                  |                 |                 |
| subjects affected / exposed | 10 / 24 (41.67%) | 7 / 25 (28.00%) | 8 / 25 (32.00%) |
| occurrences (all)           | 14               | 10              | 11              |
| Hypoxia                     |                  |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)   | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0               |
| Laryngeal Discomfort        |                  |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)   | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0               |
| Laryngospasm                |                  |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)   | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0               |
| Nasal Congestion            |                  |                 |                 |
| subjects affected / exposed | 3 / 24 (12.50%)  | 4 / 25 (16.00%) | 3 / 25 (12.00%) |
| occurrences (all)           | 5                | 5               | 3               |
| Oropharyngeal Pain          |                  |                 |                 |
| subjects affected / exposed | 4 / 24 (16.67%)  | 4 / 25 (16.00%) | 0 / 25 (0.00%)  |
| occurrences (all)           | 5                | 5               | 0               |
| Productive Cough            |                  |                 |                 |
| subjects affected / exposed | 3 / 24 (12.50%)  | 3 / 25 (12.00%) | 1 / 25 (4.00%)  |
| occurrences (all)           | 3                | 3               | 2               |
| Rhinitis Allergic           |                  |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)   | 1 / 25 (4.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0                | 1               | 0               |
| Rhinorrhoea                 |                  |                 |                 |
| subjects affected / exposed | 1 / 24 (4.17%)   | 1 / 25 (4.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 1                | 1               | 1               |
| Throat Lesion               |                  |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)   | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0               |
| Throat Tightness            |                  |                 |                 |



|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 25 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 1              | 0               | 1               |
| Sinus Congestion            |                |                 |                 |
| subjects affected / exposed | 2 / 24 (8.33%) | 2 / 25 (8.00%)  | 3 / 25 (12.00%) |
| occurrences (all)           | 2              | 3               | 3               |
| Sneezing                    |                |                 |                 |
| subjects affected / exposed | 1 / 24 (4.17%) | 2 / 25 (8.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 1              | 2               | 0               |
| Throat Irritation           |                |                 |                 |
| subjects affected / exposed | 1 / 24 (4.17%) | 1 / 25 (4.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)           | 2              | 1               | 2               |
| Upper-Airway Cough Syndrome |                |                 |                 |
| subjects affected / exposed | 2 / 24 (8.33%) | 1 / 25 (4.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 3              | 1               | 0               |
| Tracheal Stenosis           |                |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Wheezing                    |                |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%) | 5 / 25 (20.00%) | 3 / 25 (12.00%) |
| occurrences (all)           | 0              | 5               | 3               |
| Psychiatric disorders       |                |                 |                 |
| Abnormal Dreams             |                |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Agitation                   |                |                 |                 |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0               |
| Confusional State           |                |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 25 (0.00%)  | 3 / 25 (12.00%) |
| occurrences (all)           | 0              | 0               | 3               |
| Bradyphrenia                |                |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Anxiety                     |                |                 |                 |
| subjects affected / exposed | 1 / 24 (4.17%) | 1 / 25 (4.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 1              | 1               | 1               |

|  |                 |                |                 |
|--|-----------------|----------------|-----------------|
| Depression                                   |                 |                |                 |
| subjects affected / exposed                  | 1 / 24 (4.17%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                            | 1               | 0              | 0               |
| Insomnia                                     |                 |                |                 |
| subjects affected / exposed                  | 6 / 24 (25.00%) | 2 / 25 (8.00%) | 3 / 25 (12.00%) |
| occurrences (all)                            | 7               | 2              | 3               |
| Restlessness                                 |                 |                |                 |
| subjects affected / exposed                  | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                            | 0               | 0              | 0               |
| Nightmare                                    |                 |                |                 |
| subjects affected / exposed                  | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                            | 0               | 0              | 0               |
| Irritability                                 |                 |                |                 |
| subjects affected / exposed                  | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                            | 0               | 0              | 0               |
| Investigations                               |                 |                |                 |
| Carbon Monoxide Diffusing Capacity Decreased |                 |                |                 |
| subjects affected / exposed                  | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                            | 0               | 0              | 0               |
| Blood Creatinine Increased                   |                 |                |                 |
| subjects affected / exposed                  | 2 / 24 (8.33%)  | 1 / 25 (4.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                            | 2               | 2              | 0               |
| Electrocardiogram T Wave Abnormal            |                 |                |                 |
| subjects affected / exposed                  | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                            | 0               | 0              | 0               |
| Lymphocyte Count Decreased                   |                 |                |                 |
| subjects affected / exposed                  | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                            | 0               | 0              | 0               |
| Platelet Count Decreased                     |                 |                |                 |
| subjects affected / exposed                  | 0 / 24 (0.00%)  | 2 / 25 (8.00%) | 1 / 25 (4.00%)  |
| occurrences (all)                            | 0               | 2              | 1               |
| Neutrophil Count Decreased                   |                 |                |                 |
| subjects affected / exposed                  | 1 / 24 (4.17%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                            | 2               | 0              | 0               |
| Qrs Axis Abnormal                            |                 |                |                 |

|   |                        |                        |                        |
|---|------------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                              | 0 / 24 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    |
| Weight Decreased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 24 (0.00%)<br>0    | 2 / 25 (8.00%)<br>2    | 2 / 25 (8.00%)<br>2    |
| Injury, poisoning and procedural complications                                |                        |                        |                        |
| Accidental Overdose<br>subjects affected / exposed<br>occurrences (all)       | 0 / 24 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 24 (0.00%)<br>0    | 1 / 25 (4.00%)<br>1    | 1 / 25 (4.00%)<br>1    |
| Infusion Related Reaction<br>subjects affected / exposed<br>occurrences (all) | 13 / 24 (54.17%)<br>17 | 14 / 25 (56.00%)<br>14 | 15 / 25 (60.00%)<br>16 |
| Fall<br>subjects affected / exposed<br>occurrences (all)                      | 2 / 24 (8.33%)<br>2    | 0 / 25 (0.00%)<br>0    | 3 / 25 (12.00%)<br>5   |
| Joint Injury<br>subjects affected / exposed<br>occurrences (all)              | 0 / 24 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    |
| Procedural Pain<br>subjects affected / exposed<br>occurrences (all)           | 1 / 24 (4.17%)<br>1    | 0 / 25 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    |
| Sports Injury<br>subjects affected / exposed<br>occurrences (all)             | 0 / 24 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    |
| Scapula Fracture<br>subjects affected / exposed<br>occurrences (all)          | 0 / 24 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    |
| Cardiac disorders   |                        |                        |                        |
| Bundle Branch Block Right<br>subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    | 0 / 25 (0.00%)<br>0    |
| Palpitations  |                        |                        |                        |

|                               |                |                |                 |
|-------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed   | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%)  |
| occurrences (all)             | 0              | 1              | 0               |
| Bradycardia                   |                |                |                 |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Right Ventricular Hypertrophy |                |                |                 |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Angina Pectoris               |                |                |                 |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 1 / 25 (4.00%)  |
| occurrences (all)             | 0              | 0              | 1               |
| Tachycardia                   |                |                |                 |
| subjects affected / exposed   | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 1 / 25 (4.00%)  |
| occurrences (all)             | 0              | 2              | 1               |
| Sinus Tachycardia             |                |                |                 |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Nervous system disorders      |                |                |                 |
| Balance Disorder              |                |                |                 |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Amnesia                       |                |                |                 |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Dizziness                     |                |                |                 |
| subjects affected / exposed   | 1 / 24 (4.17%) | 1 / 25 (4.00%) | 3 / 25 (12.00%) |
| occurrences (all)             | 1              | 1              | 3               |
| Cranial Nerve Paralysis       |                |                |                 |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Cognitive Disorder            |                |                |                 |
| subjects affected / exposed   | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Dysgeusia                     |                |                |                 |
| subjects affected / exposed   | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 1 / 25 (4.00%)  |
| occurrences (all)             | 1              | 0              | 1               |

|                                      |                 |                 |                 |
|--------------------------------------|-----------------|-----------------|-----------------|
| Head Discomfort                      |                 |                 |                 |
| subjects affected / exposed          | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Headache                             |                 |                 |                 |
| subjects affected / exposed          | 5 / 24 (20.83%) | 7 / 25 (28.00%) | 7 / 25 (28.00%) |
| occurrences (all)                    | 6               | 8               | 8               |
| Paraesthesia                         |                 |                 |                 |
| subjects affected / exposed          | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)                    | 0               | 0               | 2               |
| Mental Impairment                    |                 |                 |                 |
| subjects affected / exposed          | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Hypoaesthesia                        |                 |                 |                 |
| subjects affected / exposed          | 1 / 24 (4.17%)  | 0 / 25 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)                    | 1               | 0               | 1               |
| Peripheral Sensory Neuropathy        |                 |                 |                 |
| subjects affected / exposed          | 2 / 24 (8.33%)  | 0 / 25 (0.00%)  | 4 / 25 (16.00%) |
| occurrences (all)                    | 2               | 0               | 4               |
| Vith Nerve Paralysis                 |                 |                 |                 |
| subjects affected / exposed          | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Toxic Encephalopathy                 |                 |                 |                 |
| subjects affected / exposed          | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Restless Legs Syndrome               |                 |                 |                 |
| subjects affected / exposed          | 2 / 24 (8.33%)  | 1 / 25 (4.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 2               | 1               | 0               |
| Blood and lymphatic system disorders |                 |                 |                 |
| Anaemia                              |                 |                 |                 |
| subjects affected / exposed          | 3 / 24 (12.50%) | 8 / 25 (32.00%) | 8 / 25 (32.00%) |
| occurrences (all)                    | 3               | 11              | 12              |
| Thrombocytopenia                     |                 |                 |                 |
| subjects affected / exposed          | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 6 / 25 (24.00%) |
| occurrences (all)                    | 0               | 0               | 9               |
| Neutropenia                          |                 |                 |                 |

|  |                     |                      |                      |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                             | 1 / 24 (4.17%)<br>1 | 0 / 25 (0.00%)<br>0  | 3 / 25 (12.00%)<br>4 |
| Eye disorders  |                     |                      |                      |
| Conjunctival Haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0  | 0 / 25 (0.00%)<br>0  |
| Scleral Discolouration<br>subjects affected / exposed<br>occurrences (all)   | 0 / 24 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0  | 0 / 25 (0.00%)<br>0  |
| Diplopia<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 24 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0  | 0 / 25 (0.00%)<br>0  |
| Dry Eye<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 24 (4.17%)<br>1 | 0 / 25 (0.00%)<br>0  | 0 / 25 (0.00%)<br>0  |
| Lacrimation Increased<br>subjects affected / exposed<br>occurrences (all)    | 1 / 24 (4.17%)<br>1 | 0 / 25 (0.00%)<br>0  | 1 / 25 (4.00%)<br>2  |
| Vision Blurred<br>subjects affected / exposed<br>occurrences (all)           | 0 / 24 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0  | 0 / 25 (0.00%)<br>0  |
| Visual Impairment<br>subjects affected / exposed<br>occurrences (all)        | 0 / 24 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0  | 0 / 25 (0.00%)<br>0  |
| Gastrointestinal disorders   |                     |                      |                      |
| Abdominal Discomfort<br>subjects affected / exposed<br>occurrences (all)     | 0 / 24 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0  | 0 / 25 (0.00%)<br>0  |
| Abdominal Distension<br>subjects affected / exposed<br>occurrences (all)     | 0 / 24 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0  | 1 / 25 (4.00%)<br>1  |
| Abdominal Pain<br>subjects affected / exposed<br>occurrences (all)           | 0 / 24 (0.00%)<br>0 | 3 / 25 (12.00%)<br>3 | 2 / 25 (8.00%)<br>2  |
| Abdominal Pain Upper   |                     |                      |                      |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed      | 2 / 24 (8.33%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                | 2               | 0               | 0               |
| Abdominal Tenderness             |                 |                 |                 |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Dry Mouth                        |                 |                 |                 |
| subjects affected / exposed      | 1 / 24 (4.17%)  | 0 / 25 (0.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)                | 1               | 0               | 2               |
| Diarrhoea                        |                 |                 |                 |
| subjects affected / exposed      | 7 / 24 (29.17%) | 9 / 25 (36.00%) | 5 / 25 (20.00%) |
| occurrences (all)                | 13              | 11              | 9               |
| Constipation                     |                 |                 |                 |
| subjects affected / exposed      | 4 / 24 (16.67%) | 2 / 25 (8.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)                | 4               | 3               | 2               |
| Dyspepsia                        |                 |                 |                 |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Gastrointestinal Pain            |                 |                 |                 |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Dysphagia                        |                 |                 |                 |
| subjects affected / exposed      | 2 / 24 (8.33%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                | 2               | 0               | 0               |
| Gastrooesophageal Reflux Disease |                 |                 |                 |
| subjects affected / exposed      | 1 / 24 (4.17%)  | 1 / 25 (4.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                | 1               | 1               | 0               |
| Glossitis                        |                 |                 |                 |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Glossodynia                      |                 |                 |                 |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Haemorrhoids                     |                 |                 |                 |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 2 / 25 (8.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)                | 0               | 3               | 2               |
| Nausea                           |                 |                 |                 |

|  |                 |                  |                 |
|--|-----------------|------------------|-----------------|
| subjects affected / exposed            | 9 / 24 (37.50%) | 11 / 25 (44.00%) | 7 / 25 (28.00%) |
| occurrences (all)                      | 14              | 16               | 8               |
| Mouth Ulceration                       |                 |                  |                 |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 25 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                      | 0               | 0                | 0               |
| Rectal Haemorrhage                     |                 |                  |                 |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 25 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                      | 0               | 0                | 0               |
| Vomiting                               |                 |                  |                 |
| subjects affected / exposed            | 4 / 24 (16.67%) | 7 / 25 (28.00%)  | 6 / 25 (24.00%) |
| occurrences (all)                      | 7               | 9                | 10              |
| Toothache                              |                 |                  |                 |
| subjects affected / exposed            | 1 / 24 (4.17%)  | 0 / 25 (0.00%)   | 1 / 25 (4.00%)  |
| occurrences (all)                      | 1               | 0                | 1               |
| Stomatitis                             |                 |                  |                 |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 1 / 25 (4.00%)   | 1 / 25 (4.00%)  |
| occurrences (all)                      | 0               | 2                | 1               |
| Skin and subcutaneous tissue disorders |                 |                  |                 |
| Actinic Keratosis                      |                 |                  |                 |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 1 / 25 (4.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                      | 0               | 1                | 0               |
| Dermatitis Contact                     |                 |                  |                 |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 1 / 25 (4.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                      | 0               | 1                | 0               |
| Dermatitis Acneiform                   |                 |                  |                 |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 25 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                      | 0               | 0                | 0               |
| Alopecia                               |                 |                  |                 |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 25 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                      | 0               | 0                | 0               |
| Erythema                               |                 |                  |                 |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 25 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                      | 0               | 0                | 0               |
| Hair Texture Abnormal                  |                 |                  |                 |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 25 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                      | 0               | 0                | 0               |



|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Hyperhidrosis               |                |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all)           | 1              | 0              | 1              |
| Pruritus                    |                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Pain Of Skin                |                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Onychoclasia                |                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash                        |                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Rash Maculo-Papular         |                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Rash Macular                |                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash Erythematous           |                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Rash Pruritic               |                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Skin Disorder               |                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Skin Ulcer                  |                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Renal and urinary disorders |                |                |                |
| Acute Kidney Injury         |                |                |                |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 25 (0.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)                               | 1               | 0               | 2               |
| Urinary Incontinence                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 1 / 25 (4.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)                               | 0               | 1               | 2               |
| Pollakiuria                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 2 / 25 (8.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0               | 2               | 0               |
| Musculoskeletal and connective tissue disorders |                 |                 |                 |
| Arthralgia                                      |                 |                 |                 |
| subjects affected / exposed                     | 5 / 24 (20.83%) | 3 / 25 (12.00%) | 5 / 25 (20.00%) |
| occurrences (all)                               | 7               | 5               | 5               |
| Back Pain                                       |                 |                 |                 |
| subjects affected / exposed                     | 7 / 24 (29.17%) | 3 / 25 (12.00%) | 3 / 25 (12.00%) |
| occurrences (all)                               | 8               | 3               | 3               |
| Bone Pain                                       |                 |                 |                 |
| subjects affected / exposed                     | 3 / 24 (12.50%) | 1 / 25 (4.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)                               | 3               | 1               | 2               |
| Bursitis  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Flank Pain                                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 25 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)                               | 1               | 0               | 1               |
| Groin Pain                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Joint Swelling                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Limb Discomfort                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Muscle Fatigue                                  |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Muscle Spasms               |                 |                 |                 |
| subjects affected / exposed | 2 / 24 (8.33%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 2               | 0               | 0               |
| Musculoskeletal Pain        |                 |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 25 (4.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 0               | 1               | 1               |
| Musculoskeletal Chest Pain  |                 |                 |                 |
| subjects affected / exposed | 1 / 24 (4.17%)  | 2 / 25 (8.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 1               | 2               | 1               |
| Muscular Weakness           |                 |                 |                 |
| subjects affected / exposed | 1 / 24 (4.17%)  | 0 / 25 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 1               | 0               | 1               |
| Myalgia                     |                 |                 |                 |
| subjects affected / exposed | 4 / 24 (16.67%) | 1 / 25 (4.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 7               | 1               | 1               |
| Neck Pain                   |                 |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 25 (4.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 0               | 1               | 1               |
| Pain In Extremity           |                 |                 |                 |
| subjects affected / exposed | 2 / 24 (8.33%)  | 4 / 25 (16.00%) | 4 / 25 (16.00%) |
| occurrences (all)           | 2               | 5               | 4               |
| Pathological Fracture       |                 |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Spinal Osteoarthritis       |                 |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Spinal Pain                 |                 |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Infections and infestations |                 |                 |                 |
| Gastroenteritis Viral       |                 |                 |                 |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 25 (4.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |

|                                   |                 |                |                |
|-----------------------------------|-----------------|----------------|----------------|
| Bronchitis                        |                 |                |                |
| subjects affected / exposed       | 2 / 24 (8.33%)  | 1 / 25 (4.00%) | 1 / 25 (4.00%) |
| occurrences (all)                 | 2               | 1              | 1              |
| Angular Cheilitis                 |                 |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0              |
| Gingivitis                        |                 |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0              |
| Herpes Simplex                    |                 |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0              |
| Lower Respiratory Tract Infection |                 |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0              |
| Influenza                         |                 |                |                |
| subjects affected / exposed       | 1 / 24 (4.17%)  | 2 / 25 (8.00%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 1               | 2              | 0              |
| Hordeolum                         |                 |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0              |
| Nasopharyngitis                   |                 |                |                |
| subjects affected / exposed       | 2 / 24 (8.33%)  | 2 / 25 (8.00%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 3               | 2              | 0              |
| Otitis Media                      |                 |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 0               | 0              | 0              |
| Oral Candidiasis                  |                 |                |                |
| subjects affected / exposed       | 3 / 24 (12.50%) | 2 / 25 (8.00%) | 1 / 25 (4.00%) |
| occurrences (all)                 | 3               | 3              | 1              |
| Sinusitis                         |                 |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all)                 | 0               | 0              | 1              |
| Rhinitis                          |                 |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 0               | 1              | 0              |

|                                    |                 |                 |                 |
|------------------------------------|-----------------|-----------------|-----------------|
| Respiratory Tract Infection        |                 |                 |                 |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0               | 0               | 0               |
| Pyuria                             |                 |                 |                 |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0               | 0               | 0               |
| Pneumonia                          |                 |                 |                 |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0               | 0               | 0               |
| Tooth Abscess                      |                 |                 |                 |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0               | 0               | 0               |
| Tooth Infection                    |                 |                 |                 |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 1 / 25 (4.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0               | 1               | 0               |
| Urinary Tract Infection            |                 |                 |                 |
| subjects affected / exposed        | 1 / 24 (4.17%)  | 0 / 25 (0.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)                  | 1               | 0               | 2               |
| Upper Respiratory Tract Infection  |                 |                 |                 |
| subjects affected / exposed        | 7 / 24 (29.17%) | 9 / 25 (36.00%) | 6 / 25 (24.00%) |
| occurrences (all)                  | 17              | 20              | 9               |
| Metabolism and nutrition disorders |                 |                 |                 |
| Decreased Appetite                 |                 |                 |                 |
| subjects affected / exposed        | 3 / 24 (12.50%) | 3 / 25 (12.00%) | 5 / 25 (20.00%) |
| occurrences (all)                  | 4               | 3               | 5               |
| Dehydration                        |                 |                 |                 |
| subjects affected / exposed        | 4 / 24 (16.67%) | 0 / 25 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)                  | 4               | 0               | 1               |
| Hypercalcaemia                     |                 |                 |                 |
| subjects affected / exposed        | 3 / 24 (12.50%) | 0 / 25 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)                  | 3               | 0               | 2               |
| Hyperglycaemia                     |                 |                 |                 |
| subjects affected / exposed        | 0 / 24 (0.00%)  | 0 / 25 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0               | 0               | 0               |
| Hypophosphataemia                  |                 |                 |                 |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 25 (4.00%) | 1 / 25 (4.00%) |
| occurrences (all)           | 0               | 1              | 1              |
| Hypomagnesaemia             |                 |                |                |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0               | 2              | 0              |
| Hypokalaemia                |                 |                |                |
| subjects affected / exposed | 3 / 24 (12.50%) | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 3               | 1              | 0              |
| Hypocalcaemia               |                 |                |                |
| subjects affected / exposed | 1 / 24 (4.17%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 1               | 0              | 0              |
| Hyperuricaemia              |                 |                |                |
| subjects affected / exposed | 0 / 24 (0.00%)  | 1 / 25 (4.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0               | 1              | 0              |
| Hyperkalaemia               |                 |                |                |
| subjects affected / exposed | 1 / 24 (4.17%)  | 1 / 25 (4.00%) | 1 / 25 (4.00%) |
| occurrences (all)           | 2               | 1              | 1              |
| Pseudohyponatraemia         |                 |                |                |
| subjects affected / exposed | 0 / 24 (0.00%)  | 0 / 25 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0               | 0              | 0              |

| <b>Non-serious adverse events</b>                                   | Phase 2 Stage 2:<br>Isatuximab Alone | Phase 2 Stage 2:<br>Isatuximab +<br>Dexamethasone |  |
|---|--------------------------------------|---|--|
| Total subjects affected by non-serious adverse events               |                                      |   |  |
| subjects affected / exposed   | 92 / 109 (84.40%)                    | 47 / 55 (85.45%)                                  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                      |   |  |
| Basal Cell Carcinoma  |                                      |   |  |
| subjects affected / exposed   | 0 / 109 (0.00%)                      | 0 / 55 (0.00%)                                    |  |
| occurrences (all)   | 0                                    | 0   |  |
| Tumour Pain   |                                      |   |  |
| subjects affected / exposed   | 0 / 109 (0.00%)                      | 0 / 55 (0.00%)                                    |  |
| occurrences (all)   | 0                                    | 0   |  |
| Vascular disorders  |                                      |   |  |
| Hypertension  |                                      |   |  |
| subjects affected / exposed   | 1 / 109 (0.92%)                      | 4 / 55 (7.27%)                                    |  |
| occurrences (all)   | 1                                    | 4   |  |
| Hot Flush   |                                      |   |  |

|  |                   |                  |  |
|--|-------------------|------------------|--|
| subjects affected / exposed                          | 3 / 109 (2.75%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)                                    | 3                 | 1                |  |
| Flushing   |                   |                  |  |
| subjects affected / exposed                          | 5 / 109 (4.59%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)                                    | 5                 | 1                |  |
| Hypotension  |                   |                  |  |
| subjects affected / exposed                          | 5 / 109 (4.59%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)                                    | 5                 | 1                |  |
| Pallor   |                   |                  |  |
| subjects affected / exposed                          | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                                    | 0                 | 0                |  |
| Peripheral Coldness                                  |                   |                  |  |
| subjects affected / exposed                          | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                                    | 0                 | 0                |  |
| General disorders and administration site conditions |                   |                  |  |
| Asthenia   |                   |                  |  |
| subjects affected / exposed                          | 8 / 109 (7.34%)   | 7 / 55 (12.73%)  |  |
| occurrences (all)                                    | 9                 | 7                |  |
| Chest Discomfort                                     |                   |                  |  |
| subjects affected / exposed                          | 1 / 109 (0.92%)   | 2 / 55 (3.64%)   |  |
| occurrences (all)                                    | 1                 | 2                |  |
| Chills   |                   |                  |  |
| subjects affected / exposed                          | 9 / 109 (8.26%)   | 4 / 55 (7.27%)   |  |
| occurrences (all)                                    | 10                | 5                |  |
| Face Oedema  |                   |                  |  |
| subjects affected / exposed                          | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                                    | 0                 | 0                |  |
| Fatigue  |                   |                  |  |
| subjects affected / exposed                          | 18 / 109 (16.51%) | 11 / 55 (20.00%) |  |
| occurrences (all)                                    | 106               | 17               |  |
| Implant Site Pain                                    |                   |                  |  |
| subjects affected / exposed                          | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                                    | 0                 | 0                |  |
| Feeling Hot  |                   |                  |  |

|   |                      |                      |  |
|---|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 0 / 109 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0  |  |
| Influenza Like Illness<br>subjects affected / exposed<br>occurrences (all)                                  | 2 / 109 (1.83%)<br>2 | 2 / 55 (3.64%)<br>2  |  |
| Malaise<br>subjects affected / exposed<br>occurrences (all)   | 0 / 109 (0.00%)<br>0 | 2 / 55 (3.64%)<br>2  |  |
| Injection Site Pain<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 109 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0  |  |
| Non-Cardiac Chest Pain<br>subjects affected / exposed<br>occurrences (all)                                  | 3 / 109 (2.75%)<br>3 | 0 / 55 (0.00%)<br>0  |  |
| Oedema Peripheral<br>subjects affected / exposed<br>occurrences (all)                                       | 5 / 109 (4.59%)<br>5 | 5 / 55 (9.09%)<br>5  |  |
| Pain<br>subjects affected / exposed<br>occurrences (all)  | 5 / 109 (4.59%)<br>5 | 3 / 55 (5.45%)<br>3  |  |
| Peripheral Swelling<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 109 (0.92%)<br>1 | 1 / 55 (1.82%)<br>1  |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 4 / 109 (3.67%)<br>4 | 7 / 55 (12.73%)<br>7 |  |
| Immune system disorders<br>Cytokine Release Syndrome<br>subjects affected / exposed<br>occurrences (all)    | 0 / 109 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0  |  |
| Reproductive system and breast disorders<br>Nipple Pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 109 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0  |  |
| Vulvovaginal Pain   |                      |                      |  |



|   |                   |                  |  |
|---|-------------------|------------------|--|
| subjects affected / exposed                     | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                               | 0                 | 0                |  |
| Respiratory, thoracic and mediastinal disorders |                   |                  |  |
| Bronchospasm                                    |                   |                  |  |
| subjects affected / exposed                     | 5 / 109 (4.59%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)                               | 5                 | 1                |  |
| Epistaxis                                       |                   |                  |  |
| subjects affected / exposed                     | 6 / 109 (5.50%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)                               | 6                 | 1                |  |
| Dyspnoea Exertional                             |                   |                  |  |
| subjects affected / exposed                     | 3 / 109 (2.75%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                               | 3                 | 0                |  |
| Dyspnoea  |                   |                  |  |
| subjects affected / exposed                     | 17 / 109 (15.60%) | 7 / 55 (12.73%)  |  |
| occurrences (all)                               | 19                | 7                |  |
| Cough   |                   |                  |  |
| subjects affected / exposed                     | 19 / 109 (17.43%) | 12 / 55 (21.82%) |  |
| occurrences (all)                               | 22                | 16               |  |
| Hypoxia   |                   |                  |  |
| subjects affected / exposed                     | 1 / 109 (0.92%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                               | 1                 | 0                |  |
| Laryngeal Discomfort                            |                   |                  |  |
| subjects affected / exposed                     | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                               | 0                 | 0                |  |
| Laryngospasm                                    |                   |                  |  |
| subjects affected / exposed                     | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                               | 0                 | 0                |  |
| Nasal Congestion                                |                   |                  |  |
| subjects affected / exposed                     | 9 / 109 (8.26%)   | 2 / 55 (3.64%)   |  |
| occurrences (all)                               | 10                | 2                |  |
| Oropharyngeal Pain                              |                   |                  |  |
| subjects affected / exposed                     | 3 / 109 (2.75%)   | 4 / 55 (7.27%)   |  |
| occurrences (all)                               | 3                 | 4                |  |
| Productive Cough                                |                   |                  |  |

|                             |                 |                |  |
|-----------------------------|-----------------|----------------|--|
| subjects affected / exposed | 5 / 109 (4.59%) | 0 / 55 (0.00%) |  |
| occurrences (all)           | 5               | 0              |  |
| Rhinitis Allergic           |                 |                |  |
| subjects affected / exposed | 3 / 109 (2.75%) | 1 / 55 (1.82%) |  |
| occurrences (all)           | 3               | 1              |  |
| Rhinorrhoea                 |                 |                |  |
| subjects affected / exposed | 3 / 109 (2.75%) | 1 / 55 (1.82%) |  |
| occurrences (all)           | 3               | 1              |  |
| Throat Lesion               |                 |                |  |
| subjects affected / exposed | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |
| Throat Tightness            |                 |                |  |
| subjects affected / exposed | 1 / 109 (0.92%) | 1 / 55 (1.82%) |  |
| occurrences (all)           | 1               | 1              |  |
| Sinus Congestion            |                 |                |  |
| subjects affected / exposed | 1 / 109 (0.92%) | 3 / 55 (5.45%) |  |
| occurrences (all)           | 1               | 4              |  |
| Sneezing                    |                 |                |  |
| subjects affected / exposed | 2 / 109 (1.83%) | 1 / 55 (1.82%) |  |
| occurrences (all)           | 2               | 1              |  |
| Throat Irritation           |                 |                |  |
| subjects affected / exposed | 5 / 109 (4.59%) | 3 / 55 (5.45%) |  |
| occurrences (all)           | 5               | 3              |  |
| Upper-Airway Cough Syndrome |                 |                |  |
| subjects affected / exposed | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences (all)           | 1               | 0              |  |
| Tracheal Stenosis           |                 |                |  |
| subjects affected / exposed | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |
| Wheezing                    |                 |                |  |
| subjects affected / exposed | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)           | 0               | 1              |  |
| Psychiatric disorders       |                 |                |  |
| Abnormal Dreams             |                 |                |  |
| subjects affected / exposed | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)           | 0               | 0              |  |

|  |                 |                  |  |
|--|-----------------|------------------|--|
| Agitation                                    |                 |                  |  |
| subjects affected / exposed                  | 1 / 109 (0.92%) | 2 / 55 (3.64%)   |  |
| occurrences (all)                            | 1               | 2                |  |
| Confusional State                            |                 |                  |  |
| subjects affected / exposed                  | 2 / 109 (1.83%) | 0 / 55 (0.00%)   |  |
| occurrences (all)                            | 2               | 0                |  |
| Bradyphrenia                                 |                 |                  |  |
| subjects affected / exposed                  | 0 / 109 (0.00%) | 0 / 55 (0.00%)   |  |
| occurrences (all)                            | 0               | 0                |  |
| Anxiety                                      |                 |                  |  |
| subjects affected / exposed                  | 4 / 109 (3.67%) | 1 / 55 (1.82%)   |  |
| occurrences (all)                            | 4               | 1                |  |
| Depression                                   |                 |                  |  |
| subjects affected / exposed                  | 3 / 109 (2.75%) | 1 / 55 (1.82%)   |  |
| occurrences (all)                            | 3               | 1                |  |
| Insomnia                                     |                 |                  |  |
| subjects affected / exposed                  | 2 / 109 (1.83%) | 14 / 55 (25.45%) |  |
| occurrences (all)                            | 4               | 19               |  |
| Restlessness                                 |                 |                  |  |
| subjects affected / exposed                  | 0 / 109 (0.00%) | 1 / 55 (1.82%)   |  |
| occurrences (all)                            | 0               | 1                |  |
| Nightmare                                    |                 |                  |  |
| subjects affected / exposed                  | 0 / 109 (0.00%) | 0 / 55 (0.00%)   |  |
| occurrences (all)                            | 0               | 0                |  |
| Irritability                                 |                 |                  |  |
| subjects affected / exposed                  | 1 / 109 (0.92%) | 1 / 55 (1.82%)   |  |
| occurrences (all)                            | 1               | 1                |  |
| Investigations                               |                 |                  |  |
| Carbon Monoxide Diffusing Capacity Decreased |                 |                  |  |
| subjects affected / exposed                  | 0 / 109 (0.00%) | 0 / 55 (0.00%)   |  |
| occurrences (all)                            | 0               | 0                |  |
| Blood Creatinine Increased                   |                 |                  |  |
| subjects affected / exposed                  | 1 / 109 (0.92%) | 1 / 55 (1.82%)   |  |
| occurrences (all)                            | 2               | 1                |  |
| Electrocardiogram T Wave Abnormal            |                 |                  |  |

|  |                   |                  |  |
|--|-------------------|------------------|--|
| subjects affected / exposed                    | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                              | 0                 | 0                |  |
| Lymphocyte Count Decreased                     |                   |                  |  |
| subjects affected / exposed                    | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                              | 0                 | 0                |  |
| Platelet Count Decreased                       |                   |                  |  |
| subjects affected / exposed                    | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                              | 0                 | 0                |  |
| Neutrophil Count Decreased                     |                   |                  |  |
| subjects affected / exposed                    | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                              | 0                 | 0                |  |
| Qrs Axis Abnormal                              |                   |                  |  |
| subjects affected / exposed                    | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                              | 0                 | 0                |  |
| Weight Decreased                               |                   |                  |  |
| subjects affected / exposed                    | 2 / 109 (1.83%)   | 2 / 55 (3.64%)   |  |
| occurrences (all)                              | 2                 | 2                |  |
| Injury, poisoning and procedural complications |                   |                  |  |
| Accidental Overdose                            |                   |                  |  |
| subjects affected / exposed                    | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                              | 0                 | 0                |  |
| Contusion                                      |                   |                  |  |
| subjects affected / exposed                    | 2 / 109 (1.83%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)                              | 3                 | 1                |  |
| Infusion Related Reaction                      |                   |                  |  |
| subjects affected / exposed                    | 38 / 109 (34.86%) | 20 / 55 (36.36%) |  |
| occurrences (all)                              | 41                | 21               |  |
| Fall   |                   |                  |  |
| subjects affected / exposed                    | 2 / 109 (1.83%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                              | 2                 | 0                |  |
| Joint Injury                                   |                   |                  |  |
| subjects affected / exposed                    | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)                              | 0                 | 0                |  |
| Procedural Pain                                |                   |                  |  |

|  |                      |                     |  |
|--|----------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 1 / 109 (0.92%)<br>1 | 0 / 55 (0.00%)<br>0 |  |
| Sports Injury<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 109 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Scapula Fracture<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 109 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Cardiac disorders<br>Bundle Branch Block Right<br>subjects affected / exposed<br>occurrences (all) | 0 / 109 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 109 (0.00%)<br>0 | 2 / 55 (3.64%)<br>3 |  |
| Bradycardia<br>subjects affected / exposed<br>occurrences (all)                                    | 1 / 109 (0.92%)<br>1 | 0 / 55 (0.00%)<br>0 |  |
| Right Ventricular Hypertrophy<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 109 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Angina Pectoris<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 109 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                                    | 3 / 109 (2.75%)<br>3 | 3 / 55 (5.45%)<br>3 |  |
| Sinus Tachycardia<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 109 (0.00%)<br>0 | 1 / 55 (1.82%)<br>1 |  |
| Nervous system disorders<br>Balance Disorder<br>subjects affected / exposed<br>occurrences (all)   | 0 / 109 (0.00%)<br>0 | 0 / 55 (0.00%)<br>0 |  |
| Amnesia  |                      |                     |  |

|                               |                   |                 |
|-------------------------------|-------------------|-----------------|
| subjects affected / exposed   | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |
| occurrences (all)             | 0                 | 0               |
| Dizziness                     |                   |                 |
| subjects affected / exposed   | 3 / 109 (2.75%)   | 4 / 55 (7.27%)  |
| occurrences (all)             | 3                 | 5               |
| Cranial Nerve Paralysis       |                   |                 |
| subjects affected / exposed   | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |
| occurrences (all)             | 0                 | 0               |
| Cognitive Disorder            |                   |                 |
| subjects affected / exposed   | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |
| occurrences (all)             | 0                 | 0               |
| Dysgeusia                     |                   |                 |
| subjects affected / exposed   | 0 / 109 (0.00%)   | 1 / 55 (1.82%)  |
| occurrences (all)             | 0                 | 1               |
| Head Discomfort               |                   |                 |
| subjects affected / exposed   | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |
| occurrences (all)             | 0                 | 0               |
| Headache                      |                   |                 |
| subjects affected / exposed   | 15 / 109 (13.76%) | 8 / 55 (14.55%) |
| occurrences (all)             | 22                | 9               |
| Paraesthesia                  |                   |                 |
| subjects affected / exposed   | 2 / 109 (1.83%)   | 1 / 55 (1.82%)  |
| occurrences (all)             | 3                 | 1               |
| Mental Impairment             |                   |                 |
| subjects affected / exposed   | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |
| occurrences (all)             | 0                 | 0               |
| Hypoaesthesia                 |                   |                 |
| subjects affected / exposed   | 4 / 109 (3.67%)   | 0 / 55 (0.00%)  |
| occurrences (all)             | 5                 | 0               |
| Peripheral Sensory Neuropathy |                   |                 |
| subjects affected / exposed   | 2 / 109 (1.83%)   | 5 / 55 (9.09%)  |
| occurrences (all)             | 2                 | 5               |
| Vith Nerve Paralysis          |                   |                 |
| subjects affected / exposed   | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |
| occurrences (all)             | 0                 | 0               |
| Toxic Encephalopathy          |                   |                 |

|                                      |                 |                |  |
|--------------------------------------|-----------------|----------------|--|
| subjects affected / exposed          | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 0               | 0              |  |
| Restless Legs Syndrome               |                 |                |  |
| subjects affected / exposed          | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 0               | 0              |  |
| Blood and lymphatic system disorders |                 |                |  |
| Anaemia                              |                 |                |  |
| subjects affected / exposed          | 4 / 109 (3.67%) | 1 / 55 (1.82%) |  |
| occurrences (all)                    | 4               | 1              |  |
| Thrombocytopenia                     |                 |                |  |
| subjects affected / exposed          | 3 / 109 (2.75%) | 1 / 55 (1.82%) |  |
| occurrences (all)                    | 3               | 2              |  |
| Neutropenia                          |                 |                |  |
| subjects affected / exposed          | 5 / 109 (4.59%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 5               | 0              |  |
| Eye disorders                        |                 |                |  |
| Conjunctival Haemorrhage             |                 |                |  |
| subjects affected / exposed          | 0 / 109 (0.00%) | 1 / 55 (1.82%) |  |
| occurrences (all)                    | 0               | 1              |  |
| Scleral Discolouration               |                 |                |  |
| subjects affected / exposed          | 0 / 109 (0.00%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 0               | 0              |  |
| Diplopia                             |                 |                |  |
| subjects affected / exposed          | 1 / 109 (0.92%) | 1 / 55 (1.82%) |  |
| occurrences (all)                    | 1               | 1              |  |
| Dry Eye                              |                 |                |  |
| subjects affected / exposed          | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 1               | 0              |  |
| Lacrimation Increased                |                 |                |  |
| subjects affected / exposed          | 2 / 109 (1.83%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 2               | 0              |  |
| Vision Blurred                       |                 |                |  |
| subjects affected / exposed          | 1 / 109 (0.92%) | 0 / 55 (0.00%) |  |
| occurrences (all)                    | 2               | 0              |  |
| Visual Impairment                    |                 |                |  |

|                             |                   |                  |  |
|-----------------------------|-------------------|------------------|--|
| subjects affected / exposed | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)           | 0                 | 0                |  |
| Gastrointestinal disorders  |                   |                  |  |
| Abdominal Discomfort        |                   |                  |  |
| subjects affected / exposed | 1 / 109 (0.92%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)           | 1                 | 0                |  |
| Abdominal Distension        |                   |                  |  |
| subjects affected / exposed | 1 / 109 (0.92%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)           | 1                 | 1                |  |
| Abdominal Pain              |                   |                  |  |
| subjects affected / exposed | 7 / 109 (6.42%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)           | 8                 | 2                |  |
| Abdominal Pain Upper        |                   |                  |  |
| subjects affected / exposed | 1 / 109 (0.92%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)           | 1                 | 1                |  |
| Abdominal Tenderness        |                   |                  |  |
| subjects affected / exposed | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)           | 0                 | 0                |  |
| Dry Mouth                   |                   |                  |  |
| subjects affected / exposed | 1 / 109 (0.92%)   | 1 / 55 (1.82%)   |  |
| occurrences (all)           | 1                 | 1                |  |
| Diarrhoea                   |                   |                  |  |
| subjects affected / exposed | 23 / 109 (21.10%) | 11 / 55 (20.00%) |  |
| occurrences (all)           | 37                | 17               |  |
| Constipation                |                   |                  |  |
| subjects affected / exposed | 11 / 109 (10.09%) | 4 / 55 (7.27%)   |  |
| occurrences (all)           | 13                | 4                |  |
| Dyspepsia                   |                   |                  |  |
| subjects affected / exposed | 2 / 109 (1.83%)   | 5 / 55 (9.09%)   |  |
| occurrences (all)           | 2                 | 7                |  |
| Gastrointestinal Pain       |                   |                  |  |
| subjects affected / exposed | 0 / 109 (0.00%)   | 0 / 55 (0.00%)   |  |
| occurrences (all)           | 0                 | 0                |  |
| Dysphagia                   |                   |                  |  |
| subjects affected / exposed | 0 / 109 (0.00%)   | 2 / 55 (3.64%)   |  |
| occurrences (all)           | 0                 | 2                |  |



|  |                   |                 |  |
|--|-------------------|-----------------|--|
| Gastrooesophageal Reflux Disease       |                   |                 |  |
| subjects affected / exposed            | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                      | 0                 | 0               |  |
| Glossitis                              |                   |                 |  |
| subjects affected / exposed            | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                      | 0                 | 0               |  |
| Glossodynia                            |                   |                 |  |
| subjects affected / exposed            | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                      | 0                 | 0               |  |
| Haemorrhoids                           |                   |                 |  |
| subjects affected / exposed            | 1 / 109 (0.92%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                      | 1                 | 0               |  |
| Nausea                                 |                   |                 |  |
| subjects affected / exposed            | 16 / 109 (14.68%) | 7 / 55 (12.73%) |  |
| occurrences (all)                      | 18                | 32              |  |
| Mouth Ulceration                       |                   |                 |  |
| subjects affected / exposed            | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                      | 0                 | 0               |  |
| Rectal Haemorrhage                     |                   |                 |  |
| subjects affected / exposed            | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                      | 0                 | 0               |  |
| Vomiting                               |                   |                 |  |
| subjects affected / exposed            | 13 / 109 (11.93%) | 3 / 55 (5.45%)  |  |
| occurrences (all)                      | 15                | 3               |  |
| Toothache                              |                   |                 |  |
| subjects affected / exposed            | 2 / 109 (1.83%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                      | 2                 | 0               |  |
| Stomatitis                             |                   |                 |  |
| subjects affected / exposed            | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                      | 0                 | 0               |  |
| Skin and subcutaneous tissue disorders |                   |                 |  |
| Actinic Keratosis                      |                   |                 |  |
| subjects affected / exposed            | 1 / 109 (0.92%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                      | 1                 | 0               |  |
| Dermatitis Contact                     |                   |                 |  |

|                             |                 |                |
|-----------------------------|-----------------|----------------|
| subjects affected / exposed | 0 / 109 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Dermatitis Acneiform        |                 |                |
| subjects affected / exposed | 0 / 109 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Alopecia                    |                 |                |
| subjects affected / exposed | 1 / 109 (0.92%) | 0 / 55 (0.00%) |
| occurrences (all)           | 1               | 0              |
| Erythema                    |                 |                |
| subjects affected / exposed | 0 / 109 (0.00%) | 1 / 55 (1.82%) |
| occurrences (all)           | 0               | 1              |
| Hair Texture Abnormal       |                 |                |
| subjects affected / exposed | 0 / 109 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Hyperhidrosis               |                 |                |
| subjects affected / exposed | 1 / 109 (0.92%) | 3 / 55 (5.45%) |
| occurrences (all)           | 1               | 3              |
| Pruritus                    |                 |                |
| subjects affected / exposed | 3 / 109 (2.75%) | 2 / 55 (3.64%) |
| occurrences (all)           | 4               | 2              |
| Pain Of Skin                |                 |                |
| subjects affected / exposed | 0 / 109 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Onychoclasia                |                 |                |
| subjects affected / exposed | 0 / 109 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Rash                        |                 |                |
| subjects affected / exposed | 5 / 109 (4.59%) | 1 / 55 (1.82%) |
| occurrences (all)           | 5               | 1              |
| Rash Maculo-Papular         |                 |                |
| subjects affected / exposed | 0 / 109 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Rash Macular                |                 |                |
| subjects affected / exposed | 0 / 109 (0.00%) | 0 / 55 (0.00%) |
| occurrences (all)           | 0               | 0              |
| Rash Erythematous           |                 |                |

|   |                         |                       |  |
|---|-------------------------|-----------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 0 / 109 (0.00%)<br>0    | 0 / 55 (0.00%)<br>0   |  |
| Rash Pruritic<br>subjects affected / exposed<br>occurrences (all)   | 0 / 109 (0.00%)<br>0    | 0 / 55 (0.00%)<br>0   |  |
| Skin Disorder<br>subjects affected / exposed<br>occurrences (all)   | 0 / 109 (0.00%)<br>0    | 0 / 55 (0.00%)<br>0   |  |
| Skin Ulcer<br>subjects affected / exposed<br>occurrences (all)  | 0 / 109 (0.00%)<br>0    | 0 / 55 (0.00%)<br>0   |  |
| Renal and urinary disorders<br>Acute Kidney Injury<br>subjects affected / exposed<br>occurrences (all)            | 0 / 109 (0.00%)<br>0    | 0 / 55 (0.00%)<br>0   |  |
| Urinary Incontinence<br>subjects affected / exposed<br>occurrences (all)  | 0 / 109 (0.00%)<br>0    | 0 / 55 (0.00%)<br>0   |  |
| Pollakiuria<br>subjects affected / exposed<br>occurrences (all)   | 0 / 109 (0.00%)<br>0    | 0 / 55 (0.00%)<br>0   |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 12 / 109 (11.01%)<br>15 | 5 / 55 (9.09%)<br>10  |  |
| Back Pain<br>subjects affected / exposed<br>occurrences (all)   | 20 / 109 (18.35%)<br>23 | 9 / 55 (16.36%)<br>10 |  |
| Bone Pain<br>subjects affected / exposed<br>occurrences (all)   | 10 / 109 (9.17%)<br>12  | 1 / 55 (1.82%)<br>1   |  |
| Bursitis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 109 (0.00%)<br>0    | 0 / 55 (0.00%)<br>0   |  |
| Flank Pain  |                         |                       |  |

|                             |                 |                  |
|-----------------------------|-----------------|------------------|
| subjects affected / exposed | 1 / 109 (0.92%) | 1 / 55 (1.82%)   |
| occurrences (all)           | 1               | 1                |
| Groin Pain                  |                 |                  |
| subjects affected / exposed | 3 / 109 (2.75%) | 0 / 55 (0.00%)   |
| occurrences (all)           | 3               | 0                |
| Joint Swelling              |                 |                  |
| subjects affected / exposed | 1 / 109 (0.92%) | 0 / 55 (0.00%)   |
| occurrences (all)           | 1               | 0                |
| Limb Discomfort             |                 |                  |
| subjects affected / exposed | 0 / 109 (0.00%) | 0 / 55 (0.00%)   |
| occurrences (all)           | 0               | 0                |
| Muscle Fatigue              |                 |                  |
| subjects affected / exposed | 1 / 109 (0.92%) | 0 / 55 (0.00%)   |
| occurrences (all)           | 2               | 0                |
| Muscle Spasms               |                 |                  |
| subjects affected / exposed | 4 / 109 (3.67%) | 1 / 55 (1.82%)   |
| occurrences (all)           | 5               | 1                |
| Musculoskeletal Pain        |                 |                  |
| subjects affected / exposed | 3 / 109 (2.75%) | 2 / 55 (3.64%)   |
| occurrences (all)           | 5               | 2                |
| Musculoskeletal Chest Pain  |                 |                  |
| subjects affected / exposed | 9 / 109 (8.26%) | 5 / 55 (9.09%)   |
| occurrences (all)           | 9               | 5                |
| Muscular Weakness           |                 |                  |
| subjects affected / exposed | 2 / 109 (1.83%) | 1 / 55 (1.82%)   |
| occurrences (all)           | 2               | 2                |
| Myalgia                     |                 |                  |
| subjects affected / exposed | 8 / 109 (7.34%) | 3 / 55 (5.45%)   |
| occurrences (all)           | 10              | 3                |
| Neck Pain                   |                 |                  |
| subjects affected / exposed | 0 / 109 (0.00%) | 1 / 55 (1.82%)   |
| occurrences (all)           | 0               | 1                |
| Pain In Extremity           |                 |                  |
| subjects affected / exposed | 8 / 109 (7.34%) | 10 / 55 (18.18%) |
| occurrences (all)           | 8               | 13               |
| Pathological Fracture       |                 |                  |

|                                   |                 |                 |  |
|-----------------------------------|-----------------|-----------------|--|
| subjects affected / exposed       | 4 / 109 (3.67%) | 1 / 55 (1.82%)  |  |
| occurrences (all)                 | 4               | 1               |  |
| Spinal Osteoarthritis             |                 |                 |  |
| subjects affected / exposed       | 0 / 109 (0.00%) | 1 / 55 (1.82%)  |  |
| occurrences (all)                 | 0               | 1               |  |
| Spinal Pain                       |                 |                 |  |
| subjects affected / exposed       | 1 / 109 (0.92%) | 2 / 55 (3.64%)  |  |
| occurrences (all)                 | 1               | 3               |  |
| Infections and infestations       |                 |                 |  |
| Gastroenteritis Viral             |                 |                 |  |
| subjects affected / exposed       | 0 / 109 (0.00%) | 1 / 55 (1.82%)  |  |
| occurrences (all)                 | 0               | 2               |  |
| Bronchitis                        |                 |                 |  |
| subjects affected / exposed       | 6 / 109 (5.50%) | 2 / 55 (3.64%)  |  |
| occurrences (all)                 | 8               | 4               |  |
| Angular Cheilitis                 |                 |                 |  |
| subjects affected / exposed       | 0 / 109 (0.00%) | 0 / 55 (0.00%)  |  |
| occurrences (all)                 | 0               | 0               |  |
| Gingivitis                        |                 |                 |  |
| subjects affected / exposed       | 0 / 109 (0.00%) | 0 / 55 (0.00%)  |  |
| occurrences (all)                 | 0               | 0               |  |
| Herpes Simplex                    |                 |                 |  |
| subjects affected / exposed       | 0 / 109 (0.00%) | 0 / 55 (0.00%)  |  |
| occurrences (all)                 | 0               | 0               |  |
| Lower Respiratory Tract Infection |                 |                 |  |
| subjects affected / exposed       | 1 / 109 (0.92%) | 0 / 55 (0.00%)  |  |
| occurrences (all)                 | 1               | 0               |  |
| Influenza                         |                 |                 |  |
| subjects affected / exposed       | 4 / 109 (3.67%) | 4 / 55 (7.27%)  |  |
| occurrences (all)                 | 6               | 5               |  |
| Hordeolum                         |                 |                 |  |
| subjects affected / exposed       | 0 / 109 (0.00%) | 0 / 55 (0.00%)  |  |
| occurrences (all)                 | 0               | 0               |  |
| Nasopharyngitis                   |                 |                 |  |
| subjects affected / exposed       | 4 / 109 (3.67%) | 7 / 55 (12.73%) |  |
| occurrences (all)                 | 7               | 8               |  |

|                                    |                   |                 |  |
|------------------------------------|-------------------|-----------------|--|
| Otitis Media                       |                   |                 |  |
| subjects affected / exposed        | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                  | 0                 | 0               |  |
| Oral Candidiasis                   |                   |                 |  |
| subjects affected / exposed        | 0 / 109 (0.00%)   | 1 / 55 (1.82%)  |  |
| occurrences (all)                  | 0                 | 1               |  |
| Sinusitis                          |                   |                 |  |
| subjects affected / exposed        | 5 / 109 (4.59%)   | 3 / 55 (5.45%)  |  |
| occurrences (all)                  | 5                 | 5               |  |
| Rhinitis                           |                   |                 |  |
| subjects affected / exposed        | 5 / 109 (4.59%)   | 1 / 55 (1.82%)  |  |
| occurrences (all)                  | 5                 | 1               |  |
| Respiratory Tract Infection        |                   |                 |  |
| subjects affected / exposed        | 3 / 109 (2.75%)   | 3 / 55 (5.45%)  |  |
| occurrences (all)                  | 4                 | 3               |  |
| Pyuria                             |                   |                 |  |
| subjects affected / exposed        | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                  | 0                 | 0               |  |
| Pneumonia                          |                   |                 |  |
| subjects affected / exposed        | 5 / 109 (4.59%)   | 3 / 55 (5.45%)  |  |
| occurrences (all)                  | 5                 | 3               |  |
| Tooth Abscess                      |                   |                 |  |
| subjects affected / exposed        | 0 / 109 (0.00%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                  | 0                 | 0               |  |
| Tooth Infection                    |                   |                 |  |
| subjects affected / exposed        | 2 / 109 (1.83%)   | 0 / 55 (0.00%)  |  |
| occurrences (all)                  | 2                 | 0               |  |
| Urinary Tract Infection            |                   |                 |  |
| subjects affected / exposed        | 8 / 109 (7.34%)   | 2 / 55 (3.64%)  |  |
| occurrences (all)                  | 9                 | 2               |  |
| Upper Respiratory Tract Infection  |                   |                 |  |
| subjects affected / exposed        | 14 / 109 (12.84%) | 8 / 55 (14.55%) |  |
| occurrences (all)                  | 16                | 9               |  |
| Metabolism and nutrition disorders |                   |                 |  |
| Decreased Appetite                 |                   |                 |  |

|                             |                   |                |
|-----------------------------|-------------------|----------------|
| subjects affected / exposed | 11 / 109 (10.09%) | 4 / 55 (7.27%) |
| occurrences (all)           | 11                | 4              |
| Dehydration                 |                   |                |
| subjects affected / exposed | 3 / 109 (2.75%)   | 0 / 55 (0.00%) |
| occurrences (all)           | 3                 | 0              |
| Hypercalcaemia              |                   |                |
| subjects affected / exposed | 0 / 109 (0.00%)   | 0 / 55 (0.00%) |
| occurrences (all)           | 0                 | 0              |
| Hyperglycaemia              |                   |                |
| subjects affected / exposed | 3 / 109 (2.75%)   | 3 / 55 (5.45%) |
| occurrences (all)           | 8                 | 3              |
| Hypophosphataemia           |                   |                |
| subjects affected / exposed | 0 / 109 (0.00%)   | 0 / 55 (0.00%) |
| occurrences (all)           | 0                 | 0              |
| Hypomagnesaemia             |                   |                |
| subjects affected / exposed | 0 / 109 (0.00%)   | 0 / 55 (0.00%) |
| occurrences (all)           | 0                 | 0              |
| Hypokalaemia                |                   |                |
| subjects affected / exposed | 1 / 109 (0.92%)   | 0 / 55 (0.00%) |
| occurrences (all)           | 2                 | 0              |
| Hypocalcaemia               |                   |                |
| subjects affected / exposed | 0 / 109 (0.00%)   | 1 / 55 (1.82%) |
| occurrences (all)           | 0                 | 4              |
| Hyperuricaemia              |                   |                |
| subjects affected / exposed | 0 / 109 (0.00%)   | 0 / 55 (0.00%) |
| occurrences (all)           | 0                 | 0              |
| Hyperkalaemia               |                   |                |
| subjects affected / exposed | 0 / 109 (0.00%)   | 0 / 55 (0.00%) |
| occurrences (all)           | 0                 | 0              |
| Pseudohyponatraemia         |                   |                |
| subjects affected / exposed | 0 / 109 (0.00%)   | 0 / 55 (0.00%) |
| occurrences (all)           | 0                 | 0              |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 16 December 2009  | The definition of DLT was revised to include hematological toxicities. A procedure to notify investigators of DLTs and SAEs within 24 hours of occurrence was provided. Clarifications and revisions were incorporated to ensure the first 2 participants in a multiple-dose cohort would not receive study treatment on the same day. Updates were incorporated to remove participants from the study who had dose delays >2 weeks for an AE from study. The definition of participants who were considered unsuitable for standard first-line treatment but suitable for treatment with study treatment was clarified. An assessment of vital signs 6 hours following the first infusion of study treatment was added.  |
| 07 April 2010     | Information regarding the Clinical Study Director was updated. The clinical trial summary, assessment schedule, and disease response evaluation were corrected. The PK/PD flowcharts were revised and corrections/updates were made. Clarifications were provided regarding the secondary endpoint(s) for PK samples. Appendix C was revised to reflect central labs. Minor edits for consistency in formatting were incorporated.  |
| 11 October 2010   | The study design was revised to include intra-participant dose escalation. The main selection criteria were revised to exclude participants whose platelet counts were $<50 \times 10^9 /L$ for all indications. The study treatment infusion rate was clarified for all participants. The study flowcharts were revised. Minor edits for formatting consistency were incorporated.   |
| 05 January 2011   | The study design was revised to remove intra-participant dose escalation. The main selection criteria for multiple myeloma were clarified to include participants with free light-chain disease. The main selection criteria were revised to exclude participants with platelet counts $<50 \times 10^9/L$ for all indications. The IP dilution and rate of infusion for participants were clarified. The study flowcharts were revised. Minor edits for formatting consistency were incorporated.  |
| 10 September 2012 | The definition for DLT was modified to remove Grade 2 or higher allergic reaction/hypersensitivity attributed to SAR650984. The study flowchart for basic dose escalation was modified. The Guidelines for Management of Hypersensitivity Reactions were changed to include clarification for the management of hypersensitivity reactions in the setting of routine premedication with methylprednisolone, diphenhydramine, and acetaminophen. The dose of drug per administration was clarified to indicate that actual body weight was to be measured at each cycle and should be used for dose escalation. Routine premedication with dexamethasone and diphenhydramine for mild hypersensitivity reactions previously observed was instituted. It was clarified that the selection of disease assessment parameter was based on clinical indication and the judgment of the investigator. The timing of safety evaluations, including laboratory assessments and electrocardiograms, was clarified to be consistent with the study flowcharts. Minor edits for formatting and consistency were incorporated. |
| 05 April 2013     | Dose escalation and expansion cohorts were added. Updates were made to the eligibility criteria. New infusion rate information was added for the 20 mg/kg dose escalation cohort. Assessments schedules were added or updated. Other administrative changes and clarifications were incorporated.   |
| 13 August 2013    | Exclusion criterion was clarified/added to better define required contraception. Information for the Clinical Study Director was updated.   |



|                |  |
|----------------|--|
| 19 March 2014  | The dose modification guidance was changed to enable participants in the Phase 1 part of the study to be considered for intra-participant dose modifications if they had received treatment for at least 12 weeks on the current dose level and had no study treatment related AE >Grade 1. The frequency of chest X-ray, spirometry, and diffusion capacity was reduced to only being required during the first 2 cycles, and thereafter as clinically indicated. Minor edits for formatting and consistency were incorporated. Phase 2 was added to the study to allow seamless enrollment of participants after the standard risk expansion cohort had completed enrollment; a few changes related to Phase 2 were made.  |
| 08 April 2014  | Phase 1 exclusion criterion and Phase 2 exclusion criterion: Clarified wording related to excipients to match Investigator's Brochure (IB). A time window for the collection of PK samples was included. Minor edits for formatting and consistency were incorporated.   |
| 22 August 2014 | Cohort 13 was added to the Phase 1 part of the study to enable evaluation of the 20 mg/kg weekly dose level. MRD and tumor cell CD38 messenger ribonucleic acid were added to the exploratory endpoints. The collection of an optional pharmacogenetics sample was added. The definition of adverse events of special interest (AESI) and overdose was clarified and updated based on the ongoing safety review. The definition of the high risk cohort was clarified (prior therapy inclusion requirements were clarified). The follow-up for related AEs and all SAEs ongoing at the time of study treatment discontinuation was clarified. The required assessments at 60 days and post-60 days after the last study treatment administration were clarified and harmonized. The guidelines for managing potential hypersensitivity reactions and potential tumor lysis syndrome (TLS) were clarified and harmonized with updated AESI language. The PK software used and PK parameters to be assessed were clarified. Minor edits for formatting and consistency were incorporated. An additional cohort was added to the Phase 2 part of the study to evaluate the dose of 20 mg/kg QW for 4 weeks followed by Q2W in 24 patients. Hereafter, there were 3 parts to the Phase 2 study. Clarified that Phase 1 and Phase 2 data were to be analyzed separately. Changed dose modification guidance to allow participants receiving 3/mg kg who had disease progression to escalate their dose if safety criteria were met. Immunoglobulin (Ig) D and IgE analyses were added. Study flowcharts were added/updated. Definitions added/clarified for AESIs, overdose, refractory disease, AESI, pregnancy. |
| 22 April 2016  | Serum pregnancy tests were added to the beginning of each cycle. A new section of contraceptive measures was added. The assessment of the study treatment was updated with general guidelines to be implements for infusion associated reactions and TLS. Appendix K was added to provide Investigators with background information and guidance regarding anti-CD38 interference with serologic testing. Minor edits for formatting and consistency were incorporated. Added a Phase 2 Stage 2 part: isatuximab alone (105 participants) or in combination with dexamethasone (55 participants). A few changes were applied to Stage 2.   |
| 12 July 2017   | Estimated glomerular filtration rate exclusion criterion was changed. Permitted participants in Phase 2 Stage 1 to switch formulation after the study cutoff. Clarified data collection for participants continuing treatment after analysis cut off date. Clarified timing and assessments at follow-up visits. Modified schedule and /or analyses for PK, ADA, and urinalysis. Modified definition of infusion associated reaction and AESI. Clarified intervals for dose delays/modifications. Clarified instructions when eliminating premedications could be reconsidered. Clarified definition of treatment exposure. Appendices added/deleted/modified to support changes in the protocol. Clarified dose delay management during Cycle 1 QW dosing. Added exception to dose delay criteria resulting in permanent treatment discontinuation if a participant had objective clinical benefit and after Investigator and Sponsor discussion. Added assessment for blood type, phenotype, and antibody screen pretreatment.   |
| 11 June 2019   | Based on updated PK characterization of isatuximab, the plasma half-life was re-estimated to 28 days. As duration of contraceptive measures was required to last for 5 half-lives, a revised duration of contraceptive measures and pregnancy testing of 5 months after the last isatuximab dose was required.   |

|              |  |
|--------------|--|
| 22 July 2020 | A risk of hepatitis reactivation was identified in the SAR650984 IB edition 11 and the respective updates were made. Treatment supply option (oral dexamethasone provided to the participant via a Sponsor-approved courier company) for participants who were unable to come to the study site because of a regional or national emergency declared by a governmental agency. Clarification was added for only necessary copies of medical records (hospitalization and examination reports for SAEs were not to be systematically requested) to be shared with Sponsor. Since ADA were not tested beyond final analysis cutoff date, 30-day follow up sampling (30 days following last use of study drug) was considered sufficient. |
|--------------|--|

Notes:

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## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported