



## Clinical trial results:

### A Phase 1/2 Multicenter Study Evaluating the Safety and Efficacy of KTE-C19 in Adults with Refractory Aggressive Non-Hodgkin Lymphoma Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-005007-86 |
| Trial protocol           | NL DE FR       |
| Global end of trial date | 27 July 2023   |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 23 June 2024 |
| First version publication date | 23 June 2024 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | KTE-C19-101 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02348216 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Gilead Sciences   |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404                                     |
| Public contact               | Gilead Clinical Study Information Center, Gilead Sciences,<br>GileadClinicalTrials@gilead.com |
| Scientific contact           | Gilead Clinical Study Information Center, Gilead Sciences,<br>GileadClinicalTrials@gilead.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                       | 27 July 2023 |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 27 July 2023 |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 27 July 2023 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

This study was separated into 3 distinct phases designated as the Phase 1 study, Phase 2 pivotal study (Cohort 1 and Cohort 2), and Phase 2 safety management study (Cohort 3 and Cohort 4, Cohort 5 and Cohort 6).

The primary objectives of this study were:

- Phase 1 Study: Evaluate the safety of axicabtagene ciloleucel regimens
- Phase 2 Pivotal Study; Evaluate the efficacy of axicabtagene ciloleucel
- Phase 2 Safety Management Study: Assess the impact of prophylactic regimens or earlier interventions on the rate and severity of cytokine release syndrome (CRS) and neurologic toxicities

Subjects who received an infusion of KTE-C19 completed the remainder of the 15 year follow-up assessments in a separate long-term follow-up study, KT-US-982-5968.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements. This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 21 April 2015 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | Yes           |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Canada: 25         |
| Country: Number of subjects enrolled | France: 32         |
| Country: Number of subjects enrolled | Germany: 24        |
| Country: Number of subjects enrolled | Israel: 6          |
| Country: Number of subjects enrolled | Netherlands: 42    |
| Country: Number of subjects enrolled | United States: 178 |
| Worldwide total number of subjects   | 307                |
| EEA total number of subjects         | 98                 |

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)                      | 215 |
| From 65 to 84 years                       | 91  |
| 85 years and over                         | 1   |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled at study sites in Canada, France, Germany, Israel, Netherlands, and the United States.

### Pre-assignment

Screening details:

390 participants were screened. Participants who initially responded and subsequently relapsed, became eligible for second course of conditioning chemotherapy and axicabtagene ciloleucel. Participants received the same axicabtagene ciloleucel regimen as the original target dose.

### Period 1

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

### Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes  |
| <b>Arm title</b>             | Phase 1 Study: Axicabtagene Ciloleucel and Conditioning Chemot |

Arm description:

Participants with diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL), or transformed follicular lymphoma (TFL) received conditioning chemotherapy (fludarabine 30 mg/m<sup>2</sup> intravenously [IV] over 30 minutes and cyclophosphamide 500 mg/m<sup>2</sup> IV over 60 minutes) on Days - 5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel chimeric antigen receptor (CAR) transduced autologous T cells administered IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of body weight (BW) on Day 0.

|  |                         |
|--|-------------------------|
| Arm type                               | Experimental            |
| Investigational medicinal product name | Axicabtagene Ciloleucel |
| Investigational medicinal product code |                         |
| Other name                             | Yescarta®               |
| Pharmaceutical forms                   | Solution for infusion   |
| Routes of administration               | Intravenous use         |

Dosage and administration details:

A single infusion of chimeric antigen receptor (CAR)-transduced autologous T cells administered intravenously at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg.

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

Dosage and administration details:

Administered according to package insert

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

Dosage and administration details:

Administered according to package insert

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | Phase 2 (Pivotal Study): Cohort 1 |
|------------------|-----------------------------------|

Arm description:

Participants with refractory DLBCL received conditioning chemotherapy (fludarabine 30 mg/m<sup>2</sup> IV over 30 minutes and cyclophosphamide 500 mg/m<sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0.

|  |                         |
|--|-------------------------|
| Arm type                               | Experimental            |
| Investigational medicinal product name | Axicabtagene Ciloleucel |
| Investigational medicinal product code |                         |
| Other name                             | Yescarta®               |
| Pharmaceutical forms                   | Solution for infusion   |
| Routes of administration               | Intravenous use         |

Dosage and administration details:

A single infusion of chimeric antigen receptor (CAR)-transduced autologous T cells administered intravenously at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg.

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

Dosage and administration details:

Administered according to package insert

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

Dosage and administration details:

Administered according to package insert

|                  |                                   |
|------------------|-----------------------------------|
| <b>Arm title</b> | Phase 2 (Pivotal Study): Cohort 2 |
|------------------|-----------------------------------|

Arm description:

Participants with refractory PMBCL or TFL received conditioning chemotherapy (fludarabine 30 mg/m<sup>2</sup> IV over 30 minutes and cyclophosphamide 500 mg/m<sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0.

|  |                         |
|--|-------------------------|
| Arm type                               | Experimental            |
| Investigational medicinal product name | Axicabtagene Ciloleucel |
| Investigational medicinal product code |                         |
| Other name                             | Yescarta®               |
| Pharmaceutical forms                   | Solution for infusion   |
| Routes of administration               | Intravenous use         |

Dosage and administration details:

A single infusion of chimeric antigen receptor (CAR)-transduced autologous T cells administered intravenously at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg.

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

Dosage and administration details:

Administered according to package insert

|  |                       |
|--|-----------------------|
| Investigational medicinal product name | Cyclophosphamide      |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |

|                          |                 |
|--------------------------|-----------------|
| Routes of administration | Intravenous use |
|--------------------------|-----------------|

Dosage and administration details:

Administered according to package insert

|                  |   |
|------------------|---|
| <b>Arm title</b> | Phase 2 (Safety Management Study): Cohort 3 |
|------------------|---|

Arm description:

Participants with relapsed or refractory transplant ineligible DLBCL, PMBCL, or TFL received conditioning chemotherapy (fludarabine 30 mg/m<sup>2</sup> IV over 30 minutes and cyclophosphamide 500 mg/m<sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0. Participants also received a prophylactic regimen of levetiracetam (750 mg orally or IV twice daily (BID) starting on Day 0) and tocilizumab (8 mg/kg IV over 1 hour (not to exceed 800 mg)) on Day 2).

|  |                         |
|--|-------------------------|
| Arm type                               | Experimental            |
| Investigational medicinal product name | Axicabtagene Ciloleucel |
| Investigational medicinal product code |                         |
| Other name                             | Yescarta®               |
| Pharmaceutical forms                   | Solution for infusion   |
| Routes of administration               | Intravenous use         |

Dosage and administration details:

A single infusion of chimeric antigen receptor (CAR)-transduced autologous T cells administered intravenously at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg.

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

Dosage and administration details:

Administered according to package insert

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

Dosage and administration details:

Administered according to package insert

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

Dosage and administration details:

Administered according to package insert

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

Dosage and administration details:

Administered according to package insert

|                  |   |
|------------------|---|
| <b>Arm title</b> | Phase 2 (Safety Management Study): Cohort 4 |
|------------------|---|

#### Arm description:

Participants with r/r DLBCL,PMBCL,TFL,or high-grade B-cell lymphoma(HGBCL)after 2 systemic lines of therapy will receive optional bridging therapy(dexamethasone 20mg to 40mg,eitherorally or IV daily for 1 to 4 days or 1g/m<sup>2</sup> of high-dose methylprednisolone(HDMP)for 3 days with rituximab at 375mg/m<sup>2</sup> weekly for 3 weeks or bendamustine 90 mg/m<sup>2</sup> on Days 1 and 2 and rituximab 375mg/m<sup>2</sup> on Day 1),conditioning chemotherapy(fludarabine 30mg/m<sup>2</sup> IV and cyclophosphamide 500mg/m<sup>2</sup> IV)on Days -5,-4, and -3;followed by single infusion of axicabtagene ciloleucel CAR transduced autologous T cells IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW. Participants will receive a prophylactic regimen of levetiracetam(750 mg orally or IV twice daily(BID)starting on Day 0).Participants received tocilizumab(initiated on persistent Grade 1 cytokine release syndrome(CRS)for over 24 hours)and dexamethasone(persistent Grade 1 CRS for over 72 hours and at onset of Grade 1 neurologic toxicity).

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

#### Dosage and administration details:

Administered according to package insert

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

#### Dosage and administration details:

Administered according to package insert

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

#### Dosage and administration details:

Administered according to package insert

|  |                         |
|--|-------------------------|
| Investigational medicinal product name | Axicabtagene Ciloleucel |
| Investigational medicinal product code |                         |
| Other name                             | Yescarta®               |
| Pharmaceutical forms                   | Solution for infusion   |
| Routes of administration               | Intravenous use         |

#### Dosage and administration details:

A single infusion of chimeric antigen receptor (CAR)-transduced autologous T cells administered intravenously at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg.

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

#### Dosage and administration details:

Administered according to package insert

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

|  |   |
|--|---|
| Dosage and administration details:   |   |
| Administered according to package insert   |   |
| Investigational medicinal product name   | High-dose methylprednisolone                |
| Investigational medicinal product code   |   |
| Other name   |   |
| Pharmaceutical forms   | Solution for infusion                       |
| Routes of administration   | Intravenous use                             |
| Dosage and administration details:   |   |
| Administered according to package insert   |   |
| Investigational medicinal product name   | Dexamethasone                               |
| Investigational medicinal product code   |   |
| Other name   |   |
| Pharmaceutical forms   | Solution for infusion                       |
| Routes of administration   | Intravenous use                             |
| Dosage and administration details:   |   |
| Administered according to package insert   |   |
| Investigational medicinal product name   | Tocilizumab                                 |
| Investigational medicinal product code   |   |
| Other name   |   |
| Pharmaceutical forms   | Solution for infusion                       |
| Routes of administration   | Intravenous use                             |
| Dosage and administration details:   |   |
| Administered according to package insert   |   |
| <b>Arm title</b>   | Phase 2 (Safety Management Study): Cohort 5 |
| Arm description:   |   |
| Participants with r/r DLBCL, PMBCL ,TFL, or HGBCL after 2 systemic lines of therapy received debulking therapy (R-CHOP:rituximab 375mg/m <sup>2</sup> D1,doxorubicin 50mg/m <sup>2</sup> D1,prednisone 100mg D1 to D5,cyclophosphamide 750mg/m <sup>2</sup> D1,vincristine 1.4 mg/m <sup>2</sup> D1 or R-ICE:rituximab 375mg/ m <sup>2</sup> D1,ifosfamide 5g/m <sup>2</sup> 24h-CI D2,carboplatin AUC5 D2 maximum dose 800mg,etoposide 100 mg/m <sup>2</sup> /day D1 to D3 or R-GEMOX:rituximab 375mg/m <sup>2</sup> D1,gemcitabine 1000mg/m <sup>2</sup> D2,oxaliplatin 100mg/m <sup>2</sup> D2 or R-GDP:rituximab 375mg/m <sup>2</sup> D1 or D8,gemcitabine 1g/m <sup>2</sup> D1 & D8,dexamethasone 40mg D1 to D4,cisplatin 75mg/m <sup>2</sup> D1(or carboplatin AUC5 D1) or radiotherapy:20 to 30 Gy), conditioning chemotherapy (fludarabine 30mg/m <sup>2</sup> IV and cyclophosphamide 500mg/m <sup>2</sup> IV)on Days -5,-4, and -3; followed by single infusion of axicabtagene ciloleucel at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0. Participants also received a prophylactic regimen of levetiracetam (750 mg orally or IV BID starting on D0).D=Day. |   |
| Arm type   | Experimental                                |
| Investigational medicinal product name   | Axicabtagene Ciloleucel                     |
| Investigational medicinal product code   |   |
| Other name   | Yescarta®                                   |
| Pharmaceutical forms   | Solution for infusion                       |
| Routes of administration   | Intravenous use                             |
| Dosage and administration details:   |   |
| A single infusion of chimeric antigen receptor (CAR)-transduced autologous T cells administered intravenously at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg.  |   |
| Investigational medicinal product name   | Fludarabine                                 |
| Investigational medicinal product code   |   |
| Other name   |   |
| Pharmaceutical forms   | Solution for infusion                       |
| Routes of administration   | Intravenous use                             |
| Dosage and administration details:   |   |
| Administered according to package insert   |   |



|  |                       |
|--|-----------------------|
| Investigational medicinal product name   | Cyclophosphamide      |
| Investigational medicinal product code   |                       |
| Other name                               |                       |
| Pharmaceutical forms                     | Solution for infusion |
| Routes of administration                 | Intravenous use       |
| Dosage and administration details:       |                       |
| Administered according to package insert |                       |
| Investigational medicinal product name   | Levetiracetam         |
| Investigational medicinal product code   |                       |
| Other name                               |                       |
| Pharmaceutical forms                     | Solution for infusion |
| Routes of administration                 | Intravenous use       |
| Dosage and administration details:       |                       |
| Administered according to package insert |                       |
| Investigational medicinal product name   | Rituximab             |
| Investigational medicinal product code   |                       |
| Other name                               |                       |
| Pharmaceutical forms                     | Solution for infusion |
| Routes of administration                 | Intravenous use       |
| Dosage and administration details:       |                       |
| Administered according to package insert |                       |
| Investigational medicinal product name   | Doxorubicin           |
| Investigational medicinal product code   |                       |
| Other name                               |                       |
| Pharmaceutical forms                     | Solution for infusion |
| Routes of administration                 | Intravenous use       |
| Dosage and administration details:       |                       |
| Administered according to package insert |                       |
| Investigational medicinal product name   | Prednisone            |
| Investigational medicinal product code   |                       |
| Other name                               |                       |
| Pharmaceutical forms                     | Tablet                |
| Routes of administration                 | Oral use              |
| Dosage and administration details:       |                       |
| Administered according to package insert |                       |
| Investigational medicinal product name   | Vincristine           |
| Investigational medicinal product code   |                       |
| Other name                               |                       |
| Pharmaceutical forms                     | Solution for infusion |
| Routes of administration                 | Intravenous use       |
| Dosage and administration details:       |                       |
| Administered according to package insert |                       |
| Investigational medicinal product name   | Ifosfamide            |
| Investigational medicinal product code   |                       |
| Other name                               |                       |
| Pharmaceutical forms                     | Solution for infusion |
| Routes of administration                 | Intravenous use       |
| Dosage and administration details:       |                       |
| Administered according to package insert |                       |
| Investigational medicinal product name   | Carboplatin           |
| Investigational medicinal product code   |                       |
| Other name                               |                       |

|   |   |
|---|---|
| Pharmaceutical forms  | Solution for infusion                       |
| Routes of administration  | Intravenous use                             |
| Dosage and administration details:  |   |
| Administered according to package insert  |   |
| Investigational medicinal product name  | Etoposide                                   |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Solution for infusion                       |
| Routes of administration  | Intravenous use                             |
| Dosage and administration details:  |   |
| Administered according to package insert  |   |
| Investigational medicinal product name  | Gemcitabine                                 |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Solution for infusion                       |
| Routes of administration  | Intravenous use                             |
| Dosage and administration details:  |   |
| Administered according to package insert  |   |
| Investigational medicinal product name  | Oxaliplatin                                 |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Solution for infusion                       |
| Routes of administration  | Intravenous use                             |
| Dosage and administration details:  |   |
| Administered according to package insert  |   |
| Investigational medicinal product name  | Cisplatin                                   |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Solution for infusion                       |
| Routes of administration  | Intravenous use                             |
| Dosage and administration details:  |   |
| Administered according to package insert  |   |
| <b>Arm title</b>  | Phase 2 (Safety Management Study): Cohort 6 |
| Arm description:  |   |
| <p>Participants with r/r DLBCL,PMBCL,TFL orHGBCL after 2 systemic lines of therapy may receive bridging therapy(dexamethasone 20mg to 40mg,orally or IV daily for 1 to 4 days or 1g/m<sup>2</sup> HDMP for 3 days with rituximab at 375mg/m<sup>2</sup> weekly for 3 weeks or bendamustine 90 mg/m<sup>2</sup> on Days 1 and 2 and rituximab 375mg/m<sup>2</sup> on Day 1),conditioning chemotherapy(fludarabine 30mg/m<sup>2</sup> IV and cyclophosphamide 500mg/m<sup>2</sup> IV)on Days -5,-4, and -3; followed by single infusion of axicabtagene ciloleucel CAR transduced autologous T cells IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0.Participants will also receive a prophylactic regimen of levetiracetam 750 mg orally or IV twice daily(BID)starting on Day 0)and corticosteroids(dexamethasone, 10 mg once daily on Days 0, 1, and 2).Participants received tocilizumab(initiated on persistent Grade 1 CRS for over 24 hours)and dexamethasone(persistent Grade 1 CRS for over 72 hours and at onset of Grade 1 neurologic toxicity).</p> |   |
| Arm type  | Experimental                                |
| Investigational medicinal product name  | Levetiracetam                               |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Solution for infusion                       |
| Routes of administration  | Intravenous use                             |
| Dosage and administration details:  |   |
| Administered according to package insert  |   |

|  |                         |
|--|-------------------------|
| Investigational medicinal product name | Axicabtagene Ciloleucel |
| Investigational medicinal product code |                         |
| Other name                             | Yescarta®               |
| Pharmaceutical forms                   | Solution for infusion   |
| Routes of administration               | Intravenous use         |

Dosage and administration details:

A single infusion of chimeric antigen receptor (CAR)-transduced autologous T cells administered intravenously at a target dose of  $2 \times 10^6$  anti-CD19 CAR T cells/kg.

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

Dosage and administration details:

Administered according to package insert

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

Dosage and administration details:

Administered according to package insert

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

Dosage and administration details:

Administered according to package insert

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

Dosage and administration details:

Administered according to package insert

|  |                              |
|--|------------------------------|
| Investigational medicinal product name | High-dose methylprednisolone |
| Investigational medicinal product code |                              |
| Other name                             |                              |
| Pharmaceutical forms                   | Solution for infusion        |
| Routes of administration               | Intravenous use              |

Dosage and administration details:

Administered according to package insert

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

Dosage and administration details:

Administered according to package insert

|  |                       |
|--|-----------------------|
| Investigational medicinal product name   | Rituximab             |
| Investigational medicinal product code   |                       |
| Other name                               |                       |
| Pharmaceutical forms                     | Solution for infusion |
| Routes of administration                 | Intravenous use       |
| Dosage and administration details:       |                       |
| Administered according to package insert |                       |
| Investigational medicinal product name   | Tocilizumab           |
| Investigational medicinal product code   |                       |
| Other name                               |                       |
| Pharmaceutical forms                     | Solution for infusion |
| Routes of administration                 | Intravenous use       |
| Dosage and administration details:       |                       |
| Administered according to package insert |                       |

| Number of subjects in period 1                       | Phase 1 Study:<br>Axicabtagene<br>Ciloleucel and<br>Conditioning Chemot | Phase 2 (Pivotal<br>Study): Cohort 1 | Phase 2 (Pivotal<br>Study): Cohort 2 |
|--|---|--------------------------------------|--------------------------------------|
|  |   |                                      |                                      |
| Started  | 8   | 81                                   | 30                                   |
| Completed  | 0   | 0                                    | 0                                    |
| Not completed  | 8   | 81                                   | 30                                   |
| Enrolled but did not take<br>axicabtagene ciloleucel | 1   | 4                                    | 6                                    |
| Death  | 5   | 53                                   | 11                                   |
| Full consent withdrawal                              | -   | -                                    | -                                    |
| Reason not specified                                 | 2   | 19                                   | 11                                   |
| Lost to follow-up                                    | -   | 5                                    | 2                                    |

| Number of subjects in period 1                       | Phase 2 (Safety<br>Management<br>Study): Cohort 3 | Phase 2 (Safety<br>Management<br>Study): Cohort 4 | Phase 2 (Safety<br>Management<br>Study): Cohort 5 |
|--|---|---|---|
| Started  | 42  | 46  | 58  |
| Completed  | 0   | 0   | 0   |
| Not completed  | 42  | 46  | 58  |
| Enrolled but did not take<br>axicabtagene ciloleucel | 4   | 5   | 8   |
| Death  | 20  | 16  | 32  |
| Full consent withdrawal                              | 1   | 3   | -   |
| Reason not specified                                 | 17  | 21  | 17  |
| Lost to follow-up                                    | -   | 1   | 1   |

| Number of subjects in period 1 | Phase 2 (Safety<br>Management<br>Study): Cohort 6 |
|--------------------------------|---|
| Started                        | 42  |
| Completed                      | 0   |
| Not completed                  | 42  |

|   |    |
|---|----|
| Enrolled but did not take axicabtagene ciloleucel | 2  |
| Death   | 17 |
| Full consent withdrawal                           | 3  |
| Reason not specified                              | 19 |
| Lost to follow-up                                 | 1  |

## Baseline characteristics

### Reporting groups

|  |  |
|--|--|
| Reporting group title  | Phase 1 Study: Axicabtagene Ciloleucel and Conditioning Chemot |
| Reporting group description:<br>Participants with diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL), or transformed follicular lymphoma (TFL) received conditioning chemotherapy (fludarabine 30 mg/m <sup>2</sup> intravenously [IV] over 30 minutes and cyclophosphamide 500 mg/m <sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel chimeric antigen receptor (CAR) transduced autologous T cells administered IV at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of body weight (BW) on Day 0.  |  |
| Reporting group title  | Phase 2 (Pivotal Study): Cohort 1                              |
| Reporting group description:<br>Participants with refractory DLBCL received conditioning chemotherapy (fludarabine 30 mg/m <sup>2</sup> IV over 30 minutes and cyclophosphamide 500 mg/m <sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0.  |  |
| Reporting group title  | Phase 2 (Pivotal Study): Cohort 2                              |
| Reporting group description:<br>Participants with refractory PMBCL or TFL received conditioning chemotherapy (fludarabine 30 mg/m <sup>2</sup> IV over 30 minutes and cyclophosphamide 500 mg/m <sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0.   |  |
| Reporting group title  | Phase 2 (Safety Management Study): Cohort 3                    |
| Reporting group description:<br>Participants with relapsed or refractory transplant ineligible DLBCL, PMBCL, or TFL received conditioning chemotherapy (fludarabine 30 mg/m <sup>2</sup> IV over 30 minutes and cyclophosphamide 500 mg/m <sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0. Participants also received a prophylactic regimen of levetiracetam (750 mg orally or IV twice daily (BID) starting on Day 0) and tocilizumab (8 mg/kg IV over 1 hour (not to exceed 800 mg)) on Day 2).   |  |
| Reporting group title  | Phase 2 (Safety Management Study): Cohort 4                    |
| Reporting group description:<br>Participants with r/r DLBCL, PMBCL, TFL, or high-grade B-cell lymphoma (HGBCL) after 2 systemic lines of therapy will receive optional bridging therapy (dexamethasone 20mg to 40mg, either orally or IV daily for 1 to 4 days or 1g/m <sup>2</sup> of high-dose methylprednisolone (HDMP) for 3 days with rituximab at 375mg/m <sup>2</sup> weekly for 3 weeks or bendamustine 90 mg/m <sup>2</sup> on Days 1 and 2 and rituximab 375mg/m <sup>2</sup> on Day 1), conditioning chemotherapy (fludarabine 30mg/m <sup>2</sup> IV and cyclophosphamide 500mg/m <sup>2</sup> IV) on Days -5, -4, and -3; followed by single infusion of axicabtagene ciloleucel CAR transduced autologous T cells IV at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of BW. Participants will receive a prophylactic regimen of levetiracetam (750 mg orally or IV twice daily (BID) starting on Day 0). Participants received tocilizumab (initiated on persistent Grade 1 cytokine release syndrome (CRS) for over 24 hours) and dexamethasone (persistent Grade 1 CRS for over 72 hours and at onset of Grade 1 neurologic toxicity).  |  |
| Reporting group title  | Phase 2 (Safety Management Study): Cohort 5                    |
| Reporting group description:<br>Participants with r/r DLBCL, PMBCL, TFL, or HGBCL after 2 systemic lines of therapy received debulking therapy (R-CHOP: rituximab 375mg/m <sup>2</sup> D1, doxorubicin 50mg/m <sup>2</sup> D1, prednisone 100mg D1 to D5, cyclophosphamide 750mg/m <sup>2</sup> D1, vincristine 1.4 mg/m <sup>2</sup> D1 or R-ICE: rituximab 375mg/m <sup>2</sup> D1, ifosfamide 5g/m <sup>2</sup> 24h-CI D2, carboplatin AUC5 D2 maximum dose 800mg, etoposide 100 mg/m <sup>2</sup> /day D1 to D3 or R-GEMOX: rituximab 375mg/m <sup>2</sup> D1, gemcitabine 1000mg/m <sup>2</sup> D2, oxaliplatin 100mg/m <sup>2</sup> D2 or R-GDP: rituximab 375mg/m <sup>2</sup> D1 or D8, gemcitabine 1g/m <sup>2</sup> D1 & D8, dexamethasone 40mg D1 to D4, cisplatin 75mg/m <sup>2</sup> D1 (or carboplatin AUC5 D1) or radiotherapy: 20 to 30 Gy), conditioning chemotherapy (fludarabine 30mg/m <sup>2</sup> IV and cyclophosphamide 500mg/m <sup>2</sup> IV) on Days -5, -4, and -3; followed by single infusion of axicabtagene ciloleucel at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0. Participants also received a prophylactic regimen of levetiracetam (750 mg orally or IV BID starting on D0). D=Day. |  |
| Reporting group title  | Phase 2 (Safety Management Study): Cohort 6                    |

# Reporting group description:

Participants with r/r DLBCL,PMBCL,TFL orHGBCL after 2 systemic lines of therapy may receive bridging therapy(dexamethasone 20mg to 40mg,orally or IV daily for 1 to 4 days or 1g/m<sup>2</sup> HDMP for 3 days with rituximab at 375mg/m<sup>2</sup> weekly for 3 weeks or bendamustine 90 mg/m<sup>2</sup> on Days 1 and 2 and rituximab 375mg/m<sup>2</sup> on Day 1),conditioning chemotherapy(fludarabine 30mg/m<sup>2</sup> IV and cyclophosphamide 500mg/m<sup>2</sup> IV)on Days -5,-4, and -3; followed by single infusion of axicabtagene ciloleucel CAR transduced autologous T cells IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0.Participants will also receive a prophylactic regimen of levetiracetam 750 mg orally or IV twice daily(BID)starting on Day 0)and corticosteroids(dexamethasone, 10 mg once daily on Days 0, 1, and 2).Participants received tocilizumab(initiated on persistent Grade 1 CRS for over 24 hours)and dexamethasone(persistent Grade 1 CRS for over 72 hours and at onset of Grade 1 neurologic toxicity).

| Reporting group values                | Phase 1 Study:<br>Axicabtagene<br>Ciloleucel and<br>Conditioning Chemot | Phase 2 (Pivotal<br>Study): Cohort 1 | Phase 2 (Pivotal<br>Study): Cohort 2 |
|---------------------------------------|---|--------------------------------------|--------------------------------------|
| Number of subjects                    | 8   | 81                                   | 30                                   |
| Age categorical<br>Units: Subjects    |   |                                      |                                      |
| 18 – 64 Years                         | 5   | 64                                   | 21                                   |
| 65 – 84 Years                         | 3   | 17                                   | 9                                    |
| 85 Years and Over                     | 0   | 0                                    | 0                                    |
| Gender categorical<br>Units: Subjects |   |                                      |                                      |
| Female                                | 2   | 27                                   | 7                                    |
| Male                                  | 6   | 54                                   | 23                                   |
| Race<br>Units: Subjects               |   |                                      |                                      |
| White                                 | 6   | 71                                   | 23                                   |
| Other or More Than One Race           | 1   | 6                                    | 3                                    |
| Black or African American             | 1   | 3                                    | 1                                    |
| Asian                                 | 0   | 1                                    | 3                                    |
| Ethnicity<br>Units: Subjects          |   |                                      |                                      |
| Hispanic or Latino                    | 1   | 18                                   | 2                                    |
| Not Hispanic or Latino                | 7   | 63                                   | 28                                   |
| Unknown or Not Reported               | 0   | 0                                    | 0                                    |

| Reporting group values                | Phase 2 (Safety<br>Management<br>Study): Cohort 3 | Phase 2 (Safety<br>Management<br>Study): Cohort 4 | Phase 2 (Safety<br>Management<br>Study): Cohort 5 |
|---------------------------------------|---|---|---|
| Number of subjects                    | 42  | 46  | 58  |
| Age categorical<br>Units: Subjects    |   |   |   |
| 18 – 64 Years                         | 33  | 32  | 39  |
| 65 – 84 Years                         | 9   | 14  | 19  |
| 85 Years and Over                     | 0   | 0   | 0   |
| Gender categorical<br>Units: Subjects |   |   |   |
| Female                                | 18  | 13  | 15  |
| Male                                  | 24  | 33  | 43  |
| Race<br>Units: Subjects               |   |   |   |
| White                                 | 34  | 37  | 39  |

|                              |    |    |    |
|------------------------------|----|----|----|
| Other or More Than One Race  | 3  | 9  | 12 |
| Black or African American    | 4  | 0  | 2  |
| Asian                        | 1  | 0  | 5  |
| Ethnicity<br>Units: Subjects |    |    |    |
| Hispanic or Latino           | 6  | 0  | 1  |
| Not Hispanic or Latino       | 36 | 45 | 57 |
| Unknown or Not Reported      | 0  | 1  | 0  |

| <b>Reporting group values</b>         | Phase 2 (Safety Management Study): Cohort 6 | Total |  |
|---------------------------------------|---|-------|--|
| Number of subjects                    | 42  | 307   |  |
| Age categorical<br>Units: Subjects    |   |       |  |
| 18 – 64 Years                         | 21  | 215   |  |
| 65 – 84 Years                         | 20  | 91    |  |
| 85 Years and Over                     | 1   | 1     |  |
| Gender categorical<br>Units: Subjects |   |       |  |
| Female                                | 18  | 100   |  |
| Male                                  | 24  | 207   |  |
| Race<br>Units: Subjects               |   |       |  |
| White                                 | 36  | 246   |  |
| Other or More Than One Race           | 5   | 39    |  |
| Black or African American             | 1   | 12    |  |
| Asian                                 | 0   | 10    |  |
| Ethnicity<br>Units: Subjects          |   |       |  |
| Hispanic or Latino                    | 3   | 31    |  |
| Not Hispanic or Latino                | 39  | 275   |  |
| Unknown or Not Reported               | 0   | 1     |  |



## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | Phase 1 Study: Axicabtagene Ciloleucel and Conditioning Chemot |
| Reporting group description:<br>Participants with diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL), or transformed follicular lymphoma (TFL) received conditioning chemotherapy (fludarabine 30 mg/m <sup>2</sup> intravenously [IV] over 30 minutes and cyclophosphamide 500 mg/m <sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel chimeric antigen receptor (CAR) transduced autologous T cells administered IV at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of body weight (BW) on Day 0.  |  |
| Reporting group title  | Phase 2 (Pivotal Study): Cohort 1                              |
| Reporting group description:<br>Participants with refractory DLBCL received conditioning chemotherapy (fludarabine 30 mg/m <sup>2</sup> IV over 30 minutes and cyclophosphamide 500 mg/m <sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0.  |  |
| Reporting group title  | Phase 2 (Pivotal Study): Cohort 2                              |
| Reporting group description:<br>Participants with refractory PMBCL or TFL received conditioning chemotherapy (fludarabine 30 mg/m <sup>2</sup> IV over 30 minutes and cyclophosphamide 500 mg/m <sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0.   |  |
| Reporting group title  | Phase 2 (Safety Management Study): Cohort 3                    |
| Reporting group description:<br>Participants with relapsed or refractory transplant ineligible DLBCL, PMBCL, or TFL received conditioning chemotherapy (fludarabine 30 mg/m <sup>2</sup> IV over 30 minutes and cyclophosphamide 500 mg/m <sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0. Participants also received a prophylactic regimen of levetiracetam (750 mg orally or IV twice daily (BID) starting on Day 0) and tocilizumab (8 mg/kg IV over 1 hour (not to exceed 800 mg)) on Day 2).   |  |
| Reporting group title  | Phase 2 (Safety Management Study): Cohort 4                    |
| Reporting group description:<br>Participants with r/r DLBCL, PMBCL, TFL, or high-grade B-cell lymphoma (HGBCL) after 2 systemic lines of therapy will receive optional bridging therapy (dexamethasone 20mg to 40mg, either orally or IV daily for 1 to 4 days or 1g/m <sup>2</sup> of high-dose methylprednisolone (HDMP) for 3 days with rituximab at 375mg/m <sup>2</sup> weekly for 3 weeks or bendamustine 90 mg/m <sup>2</sup> on Days 1 and 2 and rituximab 375mg/m <sup>2</sup> on Day 1), conditioning chemotherapy (fludarabine 30mg/m <sup>2</sup> IV and cyclophosphamide 500mg/m <sup>2</sup> IV) on Days -5, -4, and -3; followed by single infusion of axicabtagene ciloleucel CAR transduced autologous T cells IV at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of BW. Participants will receive a prophylactic regimen of levetiracetam (750 mg orally or IV twice daily (BID) starting on Day 0). Participants received tocilizumab (initiated on persistent Grade 1 cytokine release syndrome (CRS) for over 24 hours) and dexamethasone (persistent Grade 1 CRS for over 72 hours and at onset of Grade 1 neurologic toxicity).  |  |
| Reporting group title  | Phase 2 (Safety Management Study): Cohort 5                    |
| Reporting group description:<br>Participants with r/r DLBCL, PMBCL, TFL, or HGBCL after 2 systemic lines of therapy received debulking therapy (R-CHOP: rituximab 375mg/m <sup>2</sup> D1, doxorubicin 50mg/m <sup>2</sup> D1, prednisone 100mg D1 to D5, cyclophosphamide 750mg/m <sup>2</sup> D1, vincristine 1.4 mg/m <sup>2</sup> D1 or R-ICE: rituximab 375mg/m <sup>2</sup> D1, ifosfamide 5g/m <sup>2</sup> 24h-CI D2, carboplatin AUC5 D2 maximum dose 800mg, etoposide 100 mg/m <sup>2</sup> /day D1 to D3 or R-GEMOX: rituximab 375mg/m <sup>2</sup> D1, gemcitabine 1000mg/m <sup>2</sup> D2, oxaliplatin 100mg/m <sup>2</sup> D2 or R-GDP: rituximab 375mg/m <sup>2</sup> D1 or D8, gemcitabine 1g/m <sup>2</sup> D1 & D8, dexamethasone 40mg D1 to D4, cisplatin 75mg/m <sup>2</sup> D1 (or carboplatin AUC5 D1) or radiotherapy: 20 to 30 Gy), conditioning chemotherapy (fludarabine 30mg/m <sup>2</sup> IV and cyclophosphamide 500mg/m <sup>2</sup> IV) on Days -5, -4, and -3; followed by single infusion of axicabtagene ciloleucel at a target dose of 2 x 10 <sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0. Participants also received a prophylactic regimen of levetiracetam (750 mg orally or IV BID starting on D0). D=Day. |  |
| Reporting group title  | Phase 2 (Safety Management Study): Cohort 6                    |

#### Reporting group description:

Participants with r/r DLBCL,PMBCL,TFL orHGBCL after 2 systemic lines of therapy may receive bridging therapy(dexamethasone 20mg to 40mg,orally or IV daily for 1 to 4 days or 1g/m<sup>2</sup> HDMP for 3 days with rituximab at 375mg/m<sup>2</sup> weekly for 3 weeks or bendamustine 90 mg/m<sup>2</sup> on Days 1 and 2 and rituximab 375mg/m<sup>2</sup> on Day 1),conditioning chemotherapy(fludarabine 30mg/m<sup>2</sup> IV and cyclophosphamide 500mg/m<sup>2</sup> IV)on Days -5,-4, and -3; followed by single infusion of axicabtagene ciloleucel CAR transduced autologous T cells IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0.Participants will also receive a prophylactic regimen of levetiracetam 750 mg orally or IV twice daily(BID)starting on Day 0)and corticosteroids(dexamethasone, 10 mg once daily on Days 0, 1, and 2).Participants received tocilizumab(initiated on persistent Grade 1 CRS for over 24 hours)and dexamethasone(persistent Grade 1 CRS for over 72 hours and at onset of Grade 1 neurologic toxicity).

### Primary: Phase 2 Pivotal Study (Cohorts 1 and 2): Overall Response Rate (ORR) as Assessed by Investigator per Revised International Working Group (IWG) Response Criteria for Malignant Lymphoma

|                 |   |
|-----------------|---|
| End point title | Phase 2 Pivotal Study (Cohorts 1 and 2): Overall Response Rate (ORR) as Assessed by Investigator per Revised International Working Group (IWG) Response Criteria for Malignant Lymphoma <sup>[1][2]</sup> |
|-----------------|---|

#### End point description:

ORR was defined either a complete response (CR) or partial response (PR),assessed by the study investigators by revised IWG Response Criteria for Malignant Lymphoma (Cheson et al, 2007).CR: complete disappearance of all detectable clinical evidence of disease and symptoms; all lymph nodes and nodal masses must have regressed to normal size; spleen and/or liver must be normal size,not be palpable,and no nodules;bone marrow aspirate and biopsy must show no evidence of disease.PR: a ≥ 50% decrease in sum of product of diameters (SPD) of up to 6 of the largest dominant nodes or nodal masses;no increase in size of nodes, liver or spleen and no new sites; multiple splenic and hepatic nodules regress by ≥ 50% in the SPD; > 50% decrease in the greatest transverse diameter for single nodules. 95% confidence interval (CI) was calculated by Clopper-Pearson method. The Modified Intent-to-Treat (mITT) analysis set included all participants treated with at least 1.0 x 10<sup>6</sup> anti-CD19 CAR T cells/kg.

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

#### End point timeframe:

First infusion date of axicabtagene ciloleucel up to last follow-up visit (maximum duration: 7.7 years)

#### 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: No statistical comparison was planned or performed.

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

Justification: As the endpoint was focused on only the arms under Phase 2 (Cohorts 1 and 2) of the study, all the arms in the baseline period were not included.

| End point values                  | Phase 2 (Pivotal Study): Cohort 1 | Phase 2 (Pivotal Study): Cohort 2 |  |  |
|-----------------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type                | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed       | 77                                | 24                                |  |  |
| Units: percentage of participants |                                   |                                   |  |  |
| number (confidence interval 95%)  | 83 (73 to 91)                     | 83 (63 to 95)                     |  |  |

### Statistical analyses

No statistical analyses for this end point

**Primary: Phase 1 Study: Number of Participants Experiencing Adverse Events (AEs) defined as Dose Limiting Toxicities (DLTs)**

|                 |  |
|-----------------|--|
| End point title | Phase 1 Study: Number of Participants Experiencing Adverse Events (AEs) defined as Dose Limiting Toxicities (DLTs) <sup>[3][4]</sup> |
|-----------------|--|

## End point description:

DLT was defined as axicabtagene ciloleucel-related events with onset within first 30 days following infusion: Grade (GR) 4 neutropenia lasting > 21 days and GR 4 thrombocytopenia lasting > 35 days from day of cell transfer; Any axicabtagene ciloleucel-related AE requiring intubation; All other GR 3 toxicities lasting > 3 days and all GR 4 toxicities, exception conditions: aphasia/dysphasia or confusion/cognitive disturbance which resolved to GR ≤ 1 ; fever GR 3; myelosuppression, decreased hemoglobin, neutropenia and thrombocytopenia ; immediate hypersensitivity reactions occurring within 2 hours of cell infusion that were reversible to a ≤ GR 2 within 24 hours of cell administration; hypogammaglobulinemia GR 3 or 4. DLT-Evaluable Analysis Set included participants treated in Phase 1 dosing cohort who received the target dose and were followed for at least 30 days after the axicabtagene ciloleucel infusion.

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

## End point timeframe:

First infusion date of axicabtagene ciloleucel up to 30 days

## 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: No statistical comparison was planned or performed.

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

Justification: As the endpoint was focused on only the arms under Phase 1 of the study, all the arms in the baseline period were not included.

|                             |  |  |  |  |
|-----------------------------|--|--|--|--|
| <b>End point values</b>     | Phase 1 Study: Axicabtagene Ciloleucel and Conditioning Chemot |  |  |  |
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 6  |  |  |  |
| Units: participants         | 1  |  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Phase 2 Safety Management Study (Cohort 3): Percentage of Participants With Treatment-Emergent Cytokine Release Syndrome (CRS) and Neurologic Toxicities by Severity Grades**

|                 |   |
|-----------------|---|
| End point title | Phase 2 Safety Management Study (Cohort 3): Percentage of Participants With Treatment-Emergent Cytokine Release Syndrome (CRS) and Neurologic Toxicities by Severity Grades <sup>[5][6]</sup> |
|-----------------|---|

## End point description:

TEAE was defined as any AE with onset on or after the start of treatment. CRS events were graded by Lee et al 2014. Grade 1: No life threatening symptoms and require symptomatic treatment only; Grade 2: Symptoms require and respond to moderate intervention; Grade 3: Symptoms require and respond to aggressive intervention; Grade 4: Life-threatening symptoms, requirements for ventilator support or continuous venovenous hemodialysis (CVVHD), and Grade 5: Death. Neurologic toxicities were graded by Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. Grade 1: Mild, asymptomatic or mild symptoms; Grade 2: Moderate and minimal, local or noninvasive intervention; Grade 3: Severe or medically significant but not life-threatening, hospitalization; Grade 4: Life-threatening and urgent intervention indicated; Grade 5: Death related to AE. The Safety Analysis Set included all participants treated with any dose of axicabtagene ciloleucel.

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

End point timeframe:

First infusion date of axicabtagene ciloleucel up to last follow-up visit (maximum duration: 6.8 years)

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: No statistical comparison was planned or performed.

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

Justification: As the endpoint was focused on only the arms under Phase 2 (Cohort 3) of the study, all the arms in the baseline period were not included.

|  |   |  |  |  |
|--|---|--|--|--|
| <b>End point values</b>                    | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>3 |  |  |  |
| Subject group type                         | Reporting group   |  |  |  |
| Number of subjects analysed                | 38  |  |  |  |
| Units: percentage of participants          |   |  |  |  |
| number (not applicable)                    |   |  |  |  |
| Worst Grade 1 CRS                          | 34  |  |  |  |
| Worst Grade 2 CRS                          | 55  |  |  |  |
| Worst Grade 3 CRS                          | 0   |  |  |  |
| Worst Grade 4 CRS                          | 3   |  |  |  |
| Worst Grade 5 CRS                          | 0   |  |  |  |
| Worst Grade $\geq$ 3 CRS                   | 3   |  |  |  |
| Worst Grade 1 Neurologic Toxicities        | 24  |  |  |  |
| Worst Grade 2 Neurologic Toxicities        | 21  |  |  |  |
| Worst Grade 3 Neurologic Toxicities        | 37  |  |  |  |
| Worst Grade 4 Neurologic Toxicities        | 3   |  |  |  |
| Worst Grade 5 Neurologic Toxicities        | 3   |  |  |  |
| Worst Grade $\geq$ 3 Neurologic Toxicities | 42  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Phase 2 Safety Management Study (Cohort 4): Percentage of Participants With Treatment-Emergent CRS and Neurologic Toxicities by Severity Grades

|                 |   |
|-----------------|---|
| End point title | Phase 2 Safety Management Study (Cohort 4): Percentage of Participants With Treatment-Emergent CRS and Neurologic Toxicities by Severity Grades <sup>[7][8]</sup> |
|-----------------|---|

End point description:

TEAE was defined as any AE with onset on or after the start of treatment. CRS events were graded by Lee et al 2014. Grade 1 : No life threatening symptoms and require symptomatic treatment only; Grade 2: Symptoms require and respond to moderate intervention; Grade 3: Symptoms require and respond to aggressive intervention; Grade 4: Life-threatening symptoms and requirements for ventilator support or CVVHD, and Grade 5: Death. Neurologic toxicities were graded by CTCAE version 4.03. Grade 1: Mild, asymptomatic or mild symptoms and intervention not indicated; Grade 2: Moderate and minimal, local or noninvasive intervention indicated; Grade 3: Severe or medically significant but not immediately life-threatening, hospitalization or prolongation of hospitalization indicated; Grade 4: Life-threatening and urgent intervention indicated; Grade 5: Death related to AE. The Safety Analysis Set included all participants treated with any dose of axicabtagene ciloleucel.

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

End point timeframe:

First infusion date of axicabtagene ciloleucel up to last follow-up visit (maximum duration: 5.4 years)

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: No statistical comparison was planned or performed.

[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: No statistical comparison was planned or performed.

| End point values                           | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>4 |  |  |  |
|--|---|--|--|--|
| Subject group type                         | Reporting group   |  |  |  |
| Number of subjects analysed                | 41  |  |  |  |
| Units: percentage of participants          |   |  |  |  |
| number (not applicable)                    |   |  |  |  |
| Worst Grade 1 CRS                          | 32  |  |  |  |
| Worst Grade 2 CRS                          | 59  |  |  |  |
| Worst Grade 3 CRS                          | 2   |  |  |  |
| Worst Grade 4 CRS                          | 0   |  |  |  |
| Worst Grade 5 CRS                          | 0   |  |  |  |
| Worst Grade $\geq$ 3 CRS                   | 2   |  |  |  |
| Worst Grade 1 Neurologic Toxicities        | 34  |  |  |  |
| Worst Grade 2 Neurologic Toxicities        | 10  |  |  |  |
| Worst Grade 3 Neurologic Toxicities        | 17  |  |  |  |
| Worst Grade 4 Neurologic Toxicities        | 0   |  |  |  |
| Worst Grade 5 Neurologic Toxicities        | 0   |  |  |  |
| Worst Grade $\geq$ 3 Neurologic Toxicities | 17  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Phase 2 Safety Management Study (Cohort 5): Percentage of Participants With Treatment-Emergent CRS and Neurologic Toxicities by Severity Grades

|                 |  |
|-----------------|--|
| End point title | Phase 2 Safety Management Study (Cohort 5): Percentage of Participants With Treatment-Emergent CRS and Neurologic Toxicities by Severity Grades <sup>[9][10]</sup> |
|-----------------|--|

End point description:

TEAE was defined as any AE with onset on or after the start of treatment. CRS events were graded by Lee et al 2014. Grade 1 : No life threatening symptoms and require symptomatic treatment only; Grade 2: Symptoms require and respond to moderate intervention; Grade 3: Symptoms require and respond to aggressive intervention; Grade 4: Life-threatening symptoms and requirements for ventilator support or CVVHD, and Grade 5: Death. Neurologic toxicities were graded by CTCAE version 4.03. Grade 1: Mild, asymptomatic or mild symptoms and intervention not indicated; Grade 2: Moderate and minimal, local or noninvasive intervention indicated; Grade 3: Severe or medically significant but not immediately life-threatening, hospitalization or prolongation of hospitalization indicated; Grade 4: Life-threatening and urgent intervention indicated; Grade 5: Death related to AE. The Safety Analysis Set included all participants treated with any dose of axicabtagene ciloleucel.

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

End point timeframe:

First infusion date of axicabtagene ciloleucel up to last follow-up visit (maximum duration: 4.4 years)

Notes:

[9] - 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: No statistical comparison was planned or performed.

[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: The data has been reported only for the specified arms for which participants were available and data was evaluable for the specified outcome measure.

| End point values                           | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>5 |  |  |  |
|--|---|--|--|--|
| Subject group type                         | Reporting group   |  |  |  |
| Number of subjects analysed                | 50  |  |  |  |
| Units: percentage of participants          |   |  |  |  |
| number (not applicable)                    |   |  |  |  |
| Worst Grade 1 CRS                          | 38  |  |  |  |
| Worst Grade 2 CRS                          | 46  |  |  |  |
| Worst Grade 3 CRS                          | 0   |  |  |  |
| Worst Grade 4 CRS                          | 2   |  |  |  |
| Worst Grade 5 CRS                          | 0   |  |  |  |
| Worst Grade $\geq$ 3 CRS                   | 2   |  |  |  |
| Worst Grade 1 Neurologic Toxicities        | 26  |  |  |  |
| Worst Grade 2 Neurologic Toxicities        | 18  |  |  |  |
| Worst Grade 3 Neurologic Toxicities        | 10  |  |  |  |
| Worst Grade 4 Neurologic Toxicities        | 2   |  |  |  |
| Worst Grade 5 Neurologic Toxicities        | 0   |  |  |  |
| Worst Grade $\geq$ 3 Neurologic Toxicities | 12  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Phase 2 Safety Management Study (Cohort 6): Percentage of Participants With Treatment-Emergent CRS and Neurologic Toxicities by Severity Grades

|                 |   |
|-----------------|---|
| End point title | Phase 2 Safety Management Study (Cohort 6): Percentage of Participants With Treatment-Emergent CRS and Neurologic Toxicities by Severity Grades <sup>[11][12]</sup> |
|-----------------|---|

End point description:

TEAE was defined as any AE with onset on or after the start of treatment. CRS events were graded by Lee et al 2014. Grade 1 : No life threatening symptoms and require symptomatic treatment only; Grade 2: Symptoms require and respond to moderate intervention; Grade 3: Symptoms require and respond to aggressive intervention; Grade 4: Life-threatening symptoms and requirements for ventilator support or CVVHD, and Grade 5: Death. Neurologic toxicities were graded by CTCAE version 4.03. Grade 1: Mild, asymptomatic or mild symptoms and intervention not indicated; Grade 2: Moderate and minimal, local or noninvasive intervention indicated; Grade 3: Severe or medically significant but not immediately life-threatening, hospitalization or prolongation of hospitalization indicated; Grade 4: Life-threatening and urgent intervention indicated; Grade 5: Death related to AE. The Safety Analysis Set included all participants treated with any dose of axicabtagene ciloleucel.

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

End point timeframe:

First infusion date of axicabtagene ciloleucel up to last follow-up visit (maximum duration: 4.1 years)

Notes:

[11] - 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: No statistical comparison was planned or performed.

[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: The data has been reported only for the specified arms for which participants were available and data was evaluable for the specified outcome measure.

| End point values                           | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>6 |  |  |  |
|--|---|--|--|--|
| Subject group type                         | Reporting group   |  |  |  |
| Number of subjects analysed                | 40  |  |  |  |
| Units: percentage of participants          |   |  |  |  |
| number (not applicable)                    |   |  |  |  |
| Worst Grade 1 CRS                          | 35  |  |  |  |
| Worst Grade 2 CRS                          | 45  |  |  |  |
| Worst Grade 3 CRS                          | 0   |  |  |  |
| Worst Grade 4 CRS                          | 0   |  |  |  |
| Worst Grade 5 CRS                          | 0   |  |  |  |
| Worst Grade $\geq$ 3 CRS                   | 0   |  |  |  |
| Worst Grade 1 Neurologic Toxicities        | 23  |  |  |  |
| Worst Grade 2 Neurologic Toxicities        | 18  |  |  |  |
| Worst Grade 3 Neurologic Toxicities        | 8   |  |  |  |
| Worst Grade 4 Neurologic Toxicities        | 5   |  |  |  |
| Worst Grade 5 Neurologic Toxicities        | 5   |  |  |  |
| Worst Grade $\geq$ 3 Neurologic Toxicities | 18  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2: Duration of Response (DOR) as Assessed by Investigator per Revised IWG Response Criteria for Malignant Lymphoma

|                 |  |
|-----------------|--|
| End point title | Phase 2: Duration of Response (DOR) as Assessed by Investigator per Revised IWG Response Criteria for Malignant Lymphoma <sup>[13]</sup> |
|-----------------|--|

End point description:

Among participants who experience an objective response (OR), DOR was defined as the date of their first objective response (CR or PR which was subsequently confirmed) to disease progression per the revised IWG Response Criteria for Malignant Lymphoma or death regardless of cause. CR and PR as defined in outcome measure 1. Participants in the mITT Analysis Set with objective response were analyzed. 99.99=median was not estimable because almost 50% of participants were censored; 99=lower limit of 95% CI was not estimable because almost 50% of participants were censored; 99999=upper limit of 95% CI was not estimable because almost 50% of participants were censored.

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

End point timeframe:

First OR to last follow-up visit (maximum duration: 7.7, 6.8, 5.4, 4.4, 4.1 years for Cohorts 1, 2, 3, 4, 5, and 6 respectively)

Notes:

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

Justification: As the endpoint was focused on only the arms under Phase 2 of the study, all the arms in the baseline period were not included.

| End point values                 | Phase 2<br>(Pivotal<br>Study): Cohort<br>1 | Phase 2<br>(Pivotal<br>Study): Cohort<br>2 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>3 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>4 |
|----------------------------------|--|--|---|---|
| Subject group type               | Reporting group                            | Reporting group                            | Reporting group   | Reporting group   |
| Number of subjects analysed      | 64   | 20   | 24  | 31  |
| Units: months                    |  |  |   |   |
| median (confidence interval 95%) | 5.0 (2.1 to<br>34.7)                       | 75.4 (11.1 to<br>9999)                     | 99.99 (5.0 to<br>99999)                                 | 99.99 (99 to<br>99999)                                  |

| End point values                 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>5 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>6 |  |  |
|----------------------------------|---|---|--|--|
| Subject group type               | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed      | 36  | 38  |  |  |
| Units: months                    |   |   |  |  |
| median (confidence interval 95%) | 27.5 (2.2 to<br>99999)                                  | 99.99 (7.8 to<br>99999)                                 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1 Study: ORR as Assessed by Investigator per Revised IWG Response Criteria for Malignant Lymphoma

|                 |   |
|-----------------|---|
| End point title | Phase 1 Study: ORR as Assessed by Investigator per Revised IWG Response Criteria for Malignant Lymphoma <sup>[14]</sup> |
|-----------------|---|

End point description:

ORR was defined as the percentage of participants achieving either a CR or a PR, as assessed by the study investigators using revised IWG Response Criteria for Malignant Lymphoma (Cheson et al, 2007). CR: complete disappearance of all detectable clinical evidence of disease and disease-related symptoms; all lymph nodes and nodal masses must have regressed to normal size; spleen and/or liver must be normal size, not be palpable, and no nodules; bone marrow aspirate and biopsy must show no evidence of disease. PR: a  $\geq 50\%$  decrease in SPD of up to 6 of the largest dominant nodes or nodal masses; no increase in size of nodes, liver or spleen and no new sites of disease; multiple splenic and hepatic nodules (if present) must regress by  $\geq 50\%$  in the SPD;  $> 50\%$  decrease in the greatest transverse diameter for single nodules. Participants in the Safety Analysis Set were analyzed.

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

End point timeframe:

First infusion date of axicabtagene ciloleucel to the data cutoff date of 27 January 2017 (maximum: 20 months)



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: As the endpoint was focused on only the arms under Phase 1 of the study, all the arms in the baseline period were not included.

| End point values                  | Phase 1 Study:<br>Axicabtagene<br>Ciloleucel and<br>Conditioning<br>Chemot |  |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Reporting group  |  |  |  |
| Number of subjects analysed       | 7  |  |  |  |
| Units: percentage of participants |  |  |  |  |
| number (not applicable)           | 71   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Pivotal Study (Cohorts 1 and 2): ORR per Independent Radiological Review Committee (IRRC)

|                 |   |
|-----------------|---|
| End point title | Phase 2 Pivotal Study (Cohorts 1 and 2): ORR per Independent Radiological Review Committee (IRRC) <sup>[15]</sup> |
|-----------------|---|

End point description:

ORR was defined as the percentage of participants achieving either a CR or a PR, as assessed by the IRRC using revised IWG Response Criteria for Malignant Lymphoma. CR: complete disappearance of all detectable clinical evidence of disease and disease-related symptoms; all lymph nodes and nodal masses must have regressed to normal size; spleen and/or liver must be normal size, not be palpable, and no nodules; bone marrow aspirate and biopsy must show no evidence of disease. PR: a  $\geq 50\%$  decrease in SPD of up to 6 of the largest dominant nodes or nodal masses; no increase in size of nodes, liver or spleen and no new sites of disease; multiple splenic and hepatic nodules (if present) must regress by  $\geq 50\%$  in the SPD;  $> 50\%$  decrease in the greatest transverse diameter for single nodules. 95% CI was calculated by Clopper-Pearson method. Participants in the mITT Analysis Set were analyzed.

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

End point timeframe:

First infusion date of axicabtagene ciloleucel to the data cutoff date of 11 August 2018 (maximum: 2.7 years)

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: As the endpoint was focused on the arms under Phase 2 (Cohorts 1 and 2) of the study, all the arms in the baseline period were not included.

| End point values                  | Phase 2<br>(Pivotal<br>Study): Cohort<br>1 | Phase 2<br>(Pivotal<br>Study): Cohort<br>2 |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed       | 77   | 24   |  |  |
| Units: percentage of participants |  |  |  |  |
| number (confidence interval 95%)  | 70 (59 to 80)                              | 88 (68 to 97)                              |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2 Safety Management Study (Cohorts 3, 4, 5, and 6): ORR as Assessed by Investigator per the Revised IWG Response Criteria for Malignant Lymphoma

|                 |  |
|-----------------|--|
| End point title | Phase 2 Safety Management Study (Cohorts 3, 4, 5, and 6): ORR as Assessed by Investigator per the Revised IWG Response Criteria for Malignant Lymphoma <sup>[16]</sup> |
|-----------------|--|

#### End point description:

ORR was defined as the percentage of participants achieving either a CR or a PR, as assessed by the study investigators using revised IWG Response Criteria for Malignant Lymphoma (Cheson et al, 2007). CR: complete disappearance of all detectable clinical evidence of disease and disease-related symptoms; all lymph nodes and nodal masses must have regressed to normal size; spleen and/or liver must be normal size, not be palpable, and no nodules; bone marrow aspirate and biopsy must show no evidence of disease. PR: a  $\geq 50\%$  decrease in SPD of up to 6 of the largest dominant nodes or nodal masses; no increase in size of nodes, liver or spleen and no new sites of disease; multiple splenic and hepatic nodules (if present) must regress by  $\geq 50\%$  in the SPD;  $> 50\%$  decrease in the greatest transverse diameter for single nodules. 95% CI was calculated by Clopper-Pearson method. Participants in the mITT Analysis Set were analyzed.

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

#### End point timeframe:

First infusion date of axicabtagene ciloleucel to last follow-up visit (maximum duration: 6.8, 5.4, 4.4, 4.1 years for Cohorts 3, 4, 5, and 6 respectively)

#### 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: As the endpoint was focused on only the arms under the Phase 2 safety Management Study (Cohorts 3, 4, 5, and 6) of the study, all the arms in the baseline period were not included.

| End point values                  | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>3 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>4 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>5 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>6 |
|-----------------------------------|---|---|---|---|
| Subject group type                | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed       | 38  | 41  | 50  | 40  |
| Units: percentage of participants |   |   |   |   |
| number (confidence interval 95%)  | 63 (46 to 78)   | 76 (60 to 88)   | 72 (58 to 84)   | 95 (83 to 99)   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2: Progression-Free Survival (PFS) as Assessed by Investigator per Revised IWG Response Criteria for Malignant Lymphoma

|                 |   |
|-----------------|---|
| End point title | Phase 2: Progression-Free Survival (PFS) as Assessed by |
|-----------------|---|

## End point description:

PFS was defined as the time from the axicabtagene ciloleucel infusion date to the date of disease progression per the revised IWG Response Criteria for Malignant Lymphoma (Cheson et al, 2007) or death from any cause. Participants not meeting the criteria for progression by the analysis data cutoff date were censored. Disease progression was defined by at least one of  $\geq 50\%$  increase from nadir in the sum of the products of at least 2 lymph nodes, a 50% increase in the product of the diameters of a single lymph node; appearance of a new lesion  $> 1.5$  cm in any axis;  $\geq 50\%$  increase in size of splenic or hepatic nodules;  $\geq 50\%$  increase in the longest diameter node  $> 1$  cm in its short axis. KM estimates was used for analyses. Participants in the mITT Analysis Set were analyzed. 99.99=median was not estimable because almost 50% of participants were censored;99999= upper limit of 95% 99.99=median was not estimable because almost 50% of participants were censored.

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

## End point timeframe:

First infusion date of axicabtagene ciloleucel to disease progression or death regardless of cause (maximum duration: 7.7, 6.8, 5.4, 4.4, 4.1 years for Cohorts 1, 2, 3, 4, 5, and 6 respectively)

## 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: As the endpoint was focused on only the arms under Phase 2 of the study, all the arms in the baseline period were not included.

| End point values                 | Phase 2 (Pivotal Study): Cohort 1 | Phase 2 (Pivotal Study): Cohort 2 | Phase 2 (Safety Management Study): Cohort 3 | Phase 2 (Safety Management Study): Cohort 4 |
|----------------------------------|-----------------------------------|-----------------------------------|---|---|
| Subject group type               | Reporting group                   | Reporting group                   | Reporting group                             | Reporting group                             |
| Number of subjects analysed      | 77                                | 24                                | 38  | 41  |
| Units: months                    |                                   |                                   |   |   |
| median (confidence interval 95%) | 5.1 (3.0 to 8.8)                  | 49.1 (3.7 to 99999)               | 6.2 (2.4 to 99999)                          | 99.99 (3.0 to 99999)                        |

| End point values                 | Phase 2 (Safety Management Study): Cohort 5 | Phase 2 (Safety Management Study): Cohort 6 |  |  |
|----------------------------------|---|---|--|--|
| Subject group type               | Reporting group                             | Reporting group                             |  |  |
| Number of subjects analysed      | 50  | 40  |  |  |
| Units: months                    |   |   |  |  |
| median (confidence interval 95%) | 3.1 (2.9 to 29.1)                           | 99.99 (8.7 to 99999)                        |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 2 Pivotal Study (Cohorts 1 and 2): Duration of Response (DOR) Using IRRC per Cheson 2007

|                 |  |
|-----------------|--|
| End point title | Phase 2 Pivotal Study (Cohorts 1 and 2): Duration of Response (DOR) Using IRRC per Cheson 2007 <sup>[18]</sup> |
|-----------------|--|

---

**End point description:**

Among participants who experience an objective response, DOR was defined as the date of their first objective response (CR or PR which was subsequently confirmed) to PD, as assessed by the IRRC using revised IWG Response Criteria for Malignant Lymphoma (Cheson et al, 2007) or death regardless of cause. CR and PR as defined in outcome measure 1. PD was defined by at least one:  $\geq 50\%$  increase from nadir in the sum of the products of at least 2 lymph nodes, or at least a 50% increase in the product of the diameters of a single node; appearance of a new lesion  $> 1.5$  cm in any axis;  $\geq 50\%$  increase in size of nodules;  $\geq 50\%$  increase in the longest diameter of a node  $> 1$  cm in its short axis. Kaplan-Meier (KM) estimates. Participants in the mITT Analysis Set with objective response were analyzed. 99.99=median was not estimable because almost 50% of participants were censored; 99999=upper limit of CI was not estimable because almost 50% of participants were censored.

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

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**End point timeframe:**

First objective response up to the data cutoff date of 11 August 2018 (maximum: 2.7 years)

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**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: As the endpoint was focused on the arms under Phase 2 (Cohorts 1 and 2) of the study, all the arms in the baseline period were not included.

| End point values                 | Phase 2<br>(Pivotal<br>Study): Cohort<br>1 | Phase 2<br>(Pivotal<br>Study): Cohort<br>2 |  |  |
|----------------------------------|--|--|--|--|
| Subject group type               | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed      | 54   | 21   |  |  |
| Units: months                    |  |  |  |  |
| median (confidence interval 95%) | 99.99 (5.4 to 99999)                       | 99.99 (11.1 to 99999)                      |  |  |

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Phase 2: Overall Survival (OS)**

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|                 |  |
|-----------------|--|
| End point title | Phase 2: Overall Survival (OS) <sup>[19]</sup> |
|-----------------|--|

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**End point description:**

OS was defined as the time from axicabtagene ciloleucel infusion to the date of death. Participants who did not die by the analysis data cutoff date were censored at their last contact date. KM estimates was used for analyses. Participants in the mITT Analysis Set were analyzed. 99.99=median was not estimable because almost 50% of participants were censored; 99999= upper limit of 95% 99.99=median was not estimable because almost 50% of participants were censored.

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

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**End point timeframe:**

First infusion date of axicabtagene ciloleucel to the date of death regardless of cause (maximum duration: 7.7, 6.8, 5.4, 4.4, 4.1 years for Cohorts 1, 2, 3, 4, 5, and 6 respectively)

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**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: As the endpoint was focused on only the arms under Phase 2 of the study, all the arms in the baseline period were not included.

| End point values                 | Phase 2 (Pivotal Study): Cohort 1 | Phase 2 (Pivotal Study): Cohort 2 | Phase 2 (Safety Management Study): Cohort 3 | Phase 2 (Safety Management Study): Cohort 4 |
|----------------------------------|-----------------------------------|-----------------------------------|---|---|
| Subject group type               | Reporting group                   | Reporting group                   | Reporting group                             | Reporting group                             |
| Number of subjects analysed      | 77                                | 24                                | 38  | 41  |
| Units: months                    |                                   |                                   |   |   |
| median (confidence interval 95%) | 15.4 (10.4 to 45.7)               | 99.99 (15.0 to 99999)             | 34.8 (5.4 to 99999)                         | 99.99 (14.6 to 99999)                       |

| End point values                 | Phase 2 (Safety Management Study): Cohort 5 | Phase 2 (Safety Management Study): Cohort 6 |  |  |
|----------------------------------|---|---|--|--|
| Subject group type               | Reporting group                             | Reporting group                             |  |  |
| Number of subjects analysed      | 50  | 40  |  |  |
| Units: months                    |   |   |  |  |
| median (confidence interval 95%) | 20.6 (12.6 to 43.1)                         | 99.99 (18.9 to 99999)                       |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Pivotal Study (Cohorts 1 and 2): Best Overall Response Using IRRC per Cheson 2007

|                 |   |
|-----------------|---|
| End point title | Phase 2 Pivotal Study (Cohorts 1 and 2): Best Overall Response Using IRRC per Cheson 2007 <sup>[20]</sup> |
|-----------------|---|

End point description:

The best overall response for each participant was based on the assessments of response (CR, PR, stable disease [SD], PD, and not done [ND]) made by the the IRRC using IWG 2007 criteria (Cheson et al, 2007). CR and PR as defined in outcome measure 1. PD defined by at least one of the following: ≥ 50% increase from nadir in the sum of the products of at least 2 lymph nodes, or at least a 50% increase in the product of the diameters of a single lymph node; appearance of a new lesion > 1.5 cm in any axis; ≥ 50% increase in size of splenic or hepatic nodules; ≥ 50% increase in the longest diameter of any single previously identified node > 1 cm in its short axis. SD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. Percentage of participants with best overall response of CR, PR, SD, PD, and ND was reported. Participants in the mITT Analysis Set were analyzed.

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

End point timeframe:

First infusion date of axicabtagene ciloleucel to the data cutoff date of 11 August 2018 (maximum: 2.7 years)

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: As the endpoint was focused on the arms under Phase 2 (Cohorts 1 and 2) of the study, all the arms in the baseline period were not included.

| End point values                  | Phase 2<br>(Pivotal<br>Study): Cohort<br>1 | Phase 2<br>(Pivotal<br>Study): Cohort<br>2 |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed       | 77   | 24   |  |  |
| Units: percentage of participants |  |  |  |  |
| number (not applicable)           |  |  |  |  |
| CR                                | 51   | 67   |  |  |
| PR                                | 19   | 21   |  |  |
| SD                                | 21   | 4  |  |  |
| PD                                | 8  | 4  |  |  |
| ND                                | 1  | 4  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Pivotal Study (Cohorts 1 and 2): PFS Using IRRC per Cheson 2007

|                 |   |
|-----------------|---|
| End point title | Phase 2 Pivotal Study (Cohorts 1 and 2): PFS Using IRRC per Cheson 2007 <sup>[21]</sup> |
|-----------------|---|

End point description:

PFS was defined as the time from the axicabtagene ciloleucel infusion date to the date of disease progression as assessed by the IRRC using revised IWG Response Criteria for Malignant Lymphoma (Cheson et al, 2007) or death from any cause. Participants not meeting the criteria for progression by the analysis data cutoff date were censored at their last evaluable disease assessment date. PD defined by at least:  $\geq 50\%$  increase from nadir in the sum of the products of at least 2 lymph nodes, or at least a 50% increase in the product of the diameters of a single node; appearance of a new lesion  $> 1.5$  cm;  $\geq 50\%$  increase in size of nodules;  $\geq 50\%$  increase in the longest diameter of any node  $> 1$  cm in its short axis. KM estimates were used for analyses. Participants in the mITT Analysis Set were analyzed. 99.99=median was not estimable because almost 50% of participants were censored; 99999= upper limit of 95% of CI was not estimable because almost 50% of participants were censored.

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

End point timeframe:

First infusion date of axicabtagene ciloleucel to the data cutoff date of 11 August 2018 (maximum: 2.7 years)

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: As the endpoint was focused on only the arms under Phase 2 (Cohorts 1 and 2) of the study, all the arms in the baseline period were not included.

| End point values                 | Phase 2<br>(Pivotal<br>Study): Cohort<br>1 | Phase 2<br>(Pivotal<br>Study): Cohort<br>2 |  |  |
|----------------------------------|--|--|--|--|
| Subject group type               | Reporting group                            | Reporting group                            |  |  |
| Number of subjects analysed      | 77   | 24   |  |  |
| Units: months                    |  |  |  |  |
| median (confidence interval 95%) | 6.9 (4.5 to 15.0)                          | 99.99 (9.0 to 99999)                       |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Experiencing Treatment-Emergent Adverse Events (TEAEs)

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants Experiencing Treatment-Emergent Adverse Events (TEAEs) |
|-----------------|---|

End point description:

An adverse event was defined as any untoward medical occurrence in a clinical trial participants. The event did not necessarily have a relationship with study treatment. Adverse events included worsening of a pre-existing medical condition. Worsening indicated that the pre-existing medical condition had increased in severity, frequency, and/or duration or had an association with a worse outcome. A pre-existing condition that had not worsened during the study or involved an intervention such as elective cosmetic surgery or a medical procedure while on study, was not considered an adverse event. TEAE was defined as any AE with onset on or after the start of treatment. Participants in the Safety Analysis Set were analyzed.

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

End point timeframe:

First infusion date of axicabtagene ciloleucel up to last follow up visit (maximum duration: 7.7 years)

| End point values                  | Phase 1 Study: Axicabtagene Ciloleucel and Conditioning Chemot | Phase 2 (Pivotal Study): Cohort 1 | Phase 2 (Pivotal Study): Cohort 2 | Phase 2 (Safety Management Study): Cohort 3 |
|-----------------------------------|--|-----------------------------------|-----------------------------------|---|
| Subject group type                | Reporting group  | Reporting group                   | Reporting group                   | Reporting group                             |
| Number of subjects analysed       | 7  | 77                                | 24                                | 38  |
| Units: percentage of participants |  |                                   |                                   |   |
| number (not applicable)           | 100  | 100                               | 100                               | 100   |

| End point values                  | Phase 2 (Safety Management Study): Cohort 4 | Phase 2 (Safety Management Study): Cohort 5 | Phase 2 (Safety Management Study): Cohort 6 |  |
|-----------------------------------|---|---|---|--|
| Subject group type                | Reporting group                             | Reporting group                             | Reporting group                             |  |
| Number of subjects analysed       | 41  | 50  | 40  |  |
| Units: percentage of participants |   |   |   |  |
| number (not applicable)           | 100   | 100   | 100   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Clinically Significant Changes in Laboratory Values Reported as Grade 3 or Higher TEAEs

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants With Clinically Significant Changes in Laboratory Values Reported as Grade 3 or Higher TEAEs |
|-----------------|---|

End point description:

Grading categories were determined by Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. Grade 1: mild, Grade 2: moderate, Grade 3: severe or medically significant, Grade 4: life-threatening. Participants in the Safety Analysis Set were analyzed.

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

End point timeframe:

First infusion date of axicabtagene ciloleucel up to last follow up visit (maximum duration: 7.7 years)

| End point values                  | Phase 1 Study: Axicabtagene Ciloleucel and Conditioning Chemot | Phase 2 (Pivotal Study): Cohort 1 | Phase 2 (Pivotal Study): Cohort 2 | Phase 2 (Safety Management Study): Cohort 3 |
|-----------------------------------|--|-----------------------------------|-----------------------------------|---|
| Subject group type                | Reporting group  | Reporting group                   | Reporting group                   | Reporting group                             |
| Number of subjects analysed       | 7  | 77                                | 24                                | 38  |
| Units: percentage of participants |  |                                   |                                   |   |
| number (not applicable)           | 100  | 96                                | 96                                | 97  |

| End point values                  | Phase 2 (Safety Management Study): Cohort 4 | Phase 2 (Safety Management Study): Cohort 5 | Phase 2 (Safety Management Study): Cohort 6 |  |
|-----------------------------------|---|---|---|--|
| Subject group type                | Reporting group                             | Reporting group                             | Reporting group                             |  |
| Number of subjects analysed       | 41  | 50  | 40  |  |
| Units: percentage of participants |   |   |   |  |
| number (not applicable)           | 98  | 100   | 100   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants with Anti-Axicabtagene Ciloleucel Antibodies

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with Anti-Axicabtagene Ciloleucel Antibodies |
|-----------------|---|

End point description:

Participants in the Safety Analysis Set were analyzed.

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



End point timeframe:

First infusion date of axicabtagene ciloleucel up to last follow-up visit (maximum duration: 7.7, 6.8, 5.4, 4.4, 4.1 years for Phase 1 and Phase 2 Cohorts 1, 2, 3, 4, 5, and 6 respectively)

| End point values                  | Phase 1 Study:<br>Axicabtagene<br>Ciloleucel and<br>Conditioning<br>Chemot | Phase 2<br>(Pivotal<br>Study): Cohort<br>1 | Phase 2<br>(Pivotal<br>Study): Cohort<br>2 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>3 |
|-----------------------------------|--|--|--|---|
| Subject group type                | Reporting group  | Reporting group                            | Reporting group                            | Reporting group   |
| Number of subjects analysed       | 7  | 77   | 24   | 38  |
| Units: percentage of participants |  |  |  |   |
| number (not applicable)           | 29   | 5  | 8  | 11  |

| End point values                  | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>4 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>5 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>6 |  |
|-----------------------------------|---|---|---|--|
| Subject group type                | Reporting group   | Reporting group   | Reporting group   |  |
| Number of subjects analysed       | 41  | 50  | 40  |  |
| Units: percentage of participants |   |   |   |  |
| number (not applicable)           | 0   | 8   | 8   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacokinetics: Peak Level of Anti-CD19 CAR T Cells in Blood

|                 |  |
|-----------------|--|
| End point title | Pharmacokinetics: Peak Level of Anti-CD19 CAR T Cells in Blood |
|-----------------|--|

End point description:

Peak was defined as the maximum number of CAR T cells measured post-infusion. Participants in the Safety Analysis Set with available data were analyzed.

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

End point timeframe:

Baseline up to Month 60 (for Phase 1 and Phase 2 Cohorts 1, 2, and 3); Baseline up to Month 24 (for Phase 2 Cohorts 4, 5, and 6)

| End point values                      | Phase 1 Study: Axicabtagene Ciloleucel and Conditioning Chemot | Phase 2 (Pivotal Study): Cohort 1 | Phase 2 (Pivotal Study): Cohort 2 | Phase 2 (Safety Management Study): Cohort 3 |
|---------------------------------------|--|-----------------------------------|-----------------------------------|---|
| Subject group type                    | Reporting group  | Reporting group                   | Reporting group                   | Reporting group                             |
| Number of subjects analysed           | 6  | 76                                | 22                                | 36  |
| Units: cells/μL                       |  |                                   |                                   |   |
| median (inter-quartile range (Q1-Q3)) | 58.512 (18.028 to 147.732)                                     | 31.512 (12.445 to 74.746)         | 58.633 (27.884 to 103.190)        | 53.670 (22.813 to 146.075)                  |

| End point values                      | Phase 2 (Safety Management Study): Cohort 4 | Phase 2 (Safety Management Study): Cohort 5 | Phase 2 (Safety Management Study): Cohort 6 |  |
|---------------------------------------|---|---|---|--|
| Subject group type                    | Reporting group                             | Reporting group                             | Reporting group                             |  |
| Number of subjects analysed           | 39  | 49  | 40  |  |
| Units: cells/μL                       |   |   |   |  |
| median (inter-quartile range (Q1-Q3)) | 52.91 (27.25 to 92.78)                      | 26.63 (12.52 to 117.53)                     | 64.38 (6.27 to 131.24)                      |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacodynamics: Peak Level of Cytokines in Serum (Phase 1 and Phase 2 Cohorts 1, 2, and 3)

|                 |  |
|-----------------|--|
| End point title | Pharmacodynamics: Peak Level of Cytokines in Serum (Phase 1 and Phase 2 Cohorts 1, 2, and 3) <sup>[22]</sup> |
|-----------------|--|

End point description:

Peak was defined as the maximum post-baseline level of the cytokine. Following key cytokines were measured: interferon-gamma induced protein 10 (IP-10), ferritin, granzyme B, intercellular adhesion molecule (ICAM-1), interferon-gamma (IFN-gamma), interleukin-1 receptor antagonist (IL-1RA), IL-2, interleukin-2 receptor alpha (IL-2 R alpha), IL-6, IL-7, IL-8, IL-10, IL-15, perforin, tumor necrosis factor alpha (TNF alpha), and vascular cell adhesion molecule- 1 (VCAM-1). Participants in the Safety Analysis Set were analyzed.

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

End point timeframe:

Baseline up to Month 3

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: The data has been reported only for the specified arms for which participants were available and data was evaluable for the specified outcome measure.

| End point values              | Phase 1 Study:<br>Axicabtagene<br>Ciloleucel and<br>Conditioning<br>Chemot | Phase 2<br>(Pivotal<br>Study): Cohort<br>1 | Phase 2<br>(Pivotal<br>Study): Cohort<br>2 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>3 |
|-------------------------------|--|--|--|---|
| Subject group type            | Reporting group  | Reporting group                            | Reporting group                            | Reporting group   |
| Number of subjects analysed   | 7  | 77   | 24   | 38  |
| Units: pg/mL                  |  |  |  |   |
| median (full range (min-max)) |  |  |  |   |
| IP-10                         | 2000.0 (147.0 to 2000.0)   | 2000.0 (628.1 to 2000.0)                   | 2000.0 (434.2 to 2000.0)                   | 2000.0 (541.0 to 2000.0)                                |
| Granzyme B                    | 33.1 (0.6 to 463.8)  | 31.1 (1.0 to 3306.0)                       | 17.3 (1.0 to 406.8)                        | 44.1 (1.0 to 534.6)                                     |
| ICAM-1                        | 792754.3 (537796.8 to 2424877.7)   | 1322829.3 (557025.0 to 7495123.2)          | 989188.4 (544589.3 to 4588974.8)           | 1009966.4 (256768.6 to 4879749.7)                       |
| IFN-gamma                     | 792.0 (81.1 to 1876.0)   | 493.8 (32.4 to 1876.0)                     | 364.9 (7.5 to 1876.0)                      | 1857.2 (65.0 to 1876.0)                                 |
| IL-1 RA                       | 2173.3 (544.3 to 4000.0)   | 2371.2 (510.8 to 4000.0)                   | 1999.9 (649.9 to 4000.0)                   | 2160.5 (653.7 to 4000.0)                                |
| IL-2                          | 18.4 (3.1 to 91.0)   | 25.0 (0.9 to 123.1)                        | 13.4 (0.9 to 63.7)                         | 20.0 (0.9 to 189.4)                                     |
| IL-2 R alpha                  | 16872.7 (2189.0 to 34044.5)  | 14383.7 (78.0 to 100000.0)                 | 7817.3 (78.0 to 66024.6)                   | 12386.4 (3002.6 to 100000.0)                            |
| IL-6                          | 305.3 (2.4 to 976.0)   | 89.4 (3.5 to 976.0)                        | 44.6 (3.6 to 976.0)                        | 921.8 (13.3 to 976.0)                                   |
| IL-7                          | 51.5 (31.2 to 71.5)  | 38.9 (13.8 to 153.5)                       | 44.1 (27.9 to 98.8)                        | 38.8 (19.1 to 83.8)                                     |
| IL-8                          | 86.4 (17.1 to 750.0)   | 118.4 (14.2 to 750.0)                      | 77.2 (9.8 to 750.0)                        | 120.9 (10.3 to 750.0)                                   |
| IL-10                         | 52.5 (3.8 to 614.0)  | 43.9 (0.7 to 466.0)                        | 18.8 (0.7 to 263.6)                        | 48.2 (1.8 to 466.0)                                     |
| IL-15                         | 57.1 (18.7 to 271.3)   | 56.5 (13.1 to 226.6)                       | 47.6 (11.3 to 195.2)                       | 50.3 (21.9 to 537.3)                                    |
| Perforin                      | 5389.0 (2582.7 to 20724.3)   | 11309.5 (2282.3 to 39818.9)                | 8278.7 (2332.6 to 31857.7)                 | 15411.9 (4327.4 to 30575.9)                             |
| TNF alpha                     | 10.5 (1.8 to 443.1)  | 8.6 (2.6 to 166.9)                         | 6.8 (2.2 to 44.9)                          | 10.9 (3.3 to 52.1)                                      |
| VCAM-1                        | 1387033.6 (609223.2 to 8424222.9)  | 1478356.8 (642372.6 to 3859375.8)          | 1058453.9 (634769.7 to 2864040.2)          | 1367940.7 (721050.0 to 5184238.4)                       |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacodynamics: Peak Level of Cytokines (IP-10, Granzyme B, IFN-gamma, IL-1 RA, IL-10, IL-15, IL-2, IL-6, IL-7, IL-8, TNF alpha, and GM-CSF) in Serum (Phase 2 Cohorts 4, 5, and 6)

|                 |   |
|-----------------|---|
| End point title | Pharmacodynamics: Peak Level of Cytokines (IP-10, Granzyme B, IFN-gamma, IL-1 RA, IL-10, IL-15, IL-2, IL-6, IL-7, IL-8, TNF alpha, and GM-CSF) in Serum (Phase 2 Cohorts 4, 5, and 6) <sup>[23]</sup> |
|-----------------|---|

End point description:

Peak was defined as the maximum post-baseline level of the cytokine. Following key cytokines were measured: IP-10, granzyme B, IFN-gamma, IL-1 RA, IL-2, IL-6, IL-7, IL-8, IL-10, IL-15, TNF alpha, and

granulocyte-macrophage colony-stimulating factor (GM-CSF). Participants in the Safety Analysis Set with available data were analyzed.

|                        |           |
|------------------------|-----------|
| End point type         | Secondary |
| End point timeframe:   |           |
| Baseline up to Month 3 |           |

Notes:

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

Justification: The data has been reported only for the specified arms for which participants were available and data was evaluable for the specified outcome measure.

| End point values              | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>4 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>5 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>6 |  |
|-------------------------------|---|---|---|--|
| Subject group type            | Reporting group   | Reporting group   | Reporting group   |  |
| Number of subjects analysed   | 41  | 50  | 40  |  |
| Units: pg/mL                  |   |   |   |  |
| median (full range (min-max)) |   |   |   |  |
| IP-10                         | 1549.70<br>(469.20 to<br>2000.00)                       | 1746.15<br>(349.80 to<br>2000.00)                       | 1560.03<br>(347.00 to<br>2000.00)                       |  |
| Granzyme B                    | 23.10 (1.00 to<br>322.60)                               | 27.90 (1.00 to<br>375.76)                               | 18.40 (1.00 to<br>162.30)                               |  |
| IFN-gamma                     | 334.50 (24.90<br>to 1876.00)                            | 314.90 (7.50<br>to 1876.00)                             | 207.95 (18.80<br>to 1876.00)                            |  |
| IL-1 RA (N=31, 50, 40)        | 1093.70<br>(193.30 to<br>4493.10)                       | 908.00 (229.00<br>to 9000.00)                           | 1279.50<br>(227.00 to<br>9000.00)                       |  |
| IL-2                          | 11.20 (0.90 to<br>79.40)                                | 11.85 (0.90 to<br>142.70)                               | 8.40 (0.90 to<br>277.60)                                |  |
| IL-6                          | 136.70 (1.60<br>to 976.00)                              | 97.95 (1.60 to<br>976.00)                               | 47.25 (1.60 to<br>976.00)                               |  |
| IL-7                          | 33.10 (18.00<br>to 67.50)                               | 29.80 (1.40 to<br>65.20)                                | 28.25 (13.20<br>to 74.30)                               |  |
| IL-8                          | 67.40 (8.50 to<br>750.00)                               | 75.10 (5.80 to<br>750.00)                               | 52.55 (10.00<br>to 750.00)                              |  |
| IL-10                         | 19.60 (1.40 to<br>466.00)                               | 14.45 (0.70 to<br>300.90)                               | 13.30 (0.70 to<br>171.20)                               |  |
| IL-15                         | 45.80 (22.30<br>to 272.70)                              | 34.15 (1.40 to<br>140.00)                               | 37.20 (9.50 to<br>86.30)                                |  |
| TNF alpha                     | 5.70 (2.00 to<br>54.60)                                 | 5.25 (1.40 to<br>33.30)                                 | 4.80 (2.10 to<br>20.20)                                 |  |
| GM-CSF                        | 4.40 (1.90 to<br>47.00)                                 | 2.90 (1.90 to<br>35.60)                                 | 1.90 (1.90 to<br>47.40)                                 |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacodynamics: Peak Level of Cytokines (Ferritin, ICAM-1, IL-2 R, Perforin, and VCAM-1) in Serum (Phase 2 Cohorts 4, 5, and 6)

|                 |   |
|-----------------|---|
| End point title | Pharmacodynamics: Peak Level of Cytokines (Ferritin, ICAM-1, IL-2 R, Perforin, and VCAM-1) in Serum (Phase 2 Cohorts 4, 5, and 6) <sup>[24]</sup> |
|-----------------|---|

End point description:

Peak was defined as the maximum post-baseline level of the cytokine. Following key cytokines were measured: Ferritin, ICAM-1, IL-2 R, Perforin, and VCAM-1. Participants in the Safety Analysis Set were analyzed.

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

End point timeframe:

Baseline up to Month 3

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: The data has been reported only for the specified arms for which participants were available and data was evaluable for the specified outcome measure.

| End point values              | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>4 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>5 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>6 |  |
|-------------------------------|---|---|---|--|
| Subject group type            | Reporting group   | Reporting group   | Reporting group   |  |
| Number of subjects analysed   | 41  | 50  | 40  |  |
| Units: ng/mL                  |   |   |   |  |
| median (full range (min-max)) |   |   |   |  |
| Ferritin                      | 1086.36 (95.55 to 23900)                                | 1516.11 (89.29 to 31600)                                | 903.50 (171.61 to 6555.10)                              |  |
| ICAM-1                        | 907.97 (359.51 to 5141.64)                              | 636.74 (361.38 to 4835.93)                              | 654.81 (355.15 to 4419.09)                              |  |
| IL-2 R                        | 10.78 (2.81 to 94.59)                                   | 7.82 (1.36 to 83.60)                                    | 6.43 (1.70 to 33.31)                                    |  |
| Perforin                      | 17.22 (3.88 to 44.42)                                   | 10.85 (2.53 to 100.00)                                  | 10.12 (1.97 to 39.62)                                   |  |
| VCAM-1                        | 1255.32 (594.51 to 3932.61)                             | 854.63 (476.60 to 6501.14)                              | 836.04 (411.93 to 5079.25)                              |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacodynamics: Peak Level of Cytokine (CRP) in Serum

|                 |   |
|-----------------|---|
| End point title | Pharmacodynamics: Peak Level of Cytokine (CRP) in Serum |
|-----------------|---|

End point description:

Peak was defined as the maximum post-baseline level of the cytokine. Participants in the Safety Analysis Set were analyzed.

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

End point timeframe:

Baseline up to Month 3

| End point values              | Phase 1 Study: Axicabtagene Ciloleucel and Conditioning Chemot | Phase 2 (Pivotal Study): Cohort 1 | Phase 2 (Pivotal Study): Cohort 2 | Phase 2 (Safety Management Study): Cohort 3 |
|-------------------------------|--|-----------------------------------|-----------------------------------|---|
| Subject group type            | Reporting group  | Reporting group                   | Reporting group                   | Reporting group                             |
| Number of subjects analysed   | 7  | 77                                | 24                                | 38  |
| Units: mg/mL                  |  |                                   |                                   |   |
| median (full range (min-max)) | 112.6 (14.6 to 655.0)  | 215.7 (31.0 to 496.0)             | 186.6 (18.5 to 496.0)             | 137.8 (2.1 to 496.0)                        |

| End point values              | Phase 2 (Safety Management Study): Cohort 4 | Phase 2 (Safety Management Study): Cohort 5 | Phase 2 (Safety Management Study): Cohort 6 |  |
|-------------------------------|---|---|---|--|
| Subject group type            | Reporting group                             | Reporting group                             | Reporting group                             |  |
| Number of subjects analysed   | 41  | 50  | 40  |  |
| Units: mg/mL                  |   |   |   |  |
| median (full range (min-max)) | 126.53 (18.19 to 496.00)                    | 74.84 (1.81 to 496.00)                      | 76.11 (7.31 to 496.00)                      |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Pharmacodynamics: Peak Level of Cytokine (Ferritin) in Serum (Phase 1 and Phase 2 Cohorts 1 and 2)

|                 |  |
|-----------------|--|
| End point title | Pharmacodynamics: Peak Level of Cytokine (Ferritin) in Serum (Phase 1 and Phase 2 Cohorts 1 and 2) <sup>[25]</sup> |
|-----------------|--|

End point description:

Peak was defined as the maximum post-baseline level of the cytokine. Participants in the Safety Analysis Set were analyzed.

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

End point timeframe:

Baseline up to Month 3

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: The data has been reported only for the specified arms for which participants were available and data was evaluable for the specified outcome measure.

| End point values              | Phase 1 Study: Axicabtagene Ciloleucel and Conditioning Chemot | Phase 2 (Pivotal Study): Cohort 1 | Phase 2 (Pivotal Study): Cohort 2 |  |
|-------------------------------|--|-----------------------------------|-----------------------------------|--|
| Subject group type            | Reporting group  | Reporting group                   | Reporting group                   |  |
| Number of subjects analysed   | 7  | 77                                | 24                                |  |
| Units: pg/mL                  |  |                                   |                                   |  |
| median (full range (min-max)) | 1973400.0 (1201900.0 to  | 3681400.0 (780.0 to               | 1979360.0 (780.0 to               |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacodynamics: Peak Level of Cytokine (Ferritin) in Serum (Phase 2 Cohort 3)

|                 |   |
|-----------------|---|
| End point title | Pharmacodynamics: Peak Level of Cytokine (Ferritin) in Serum (Phase 2 Cohort 3) <sup>[26]</sup> |
|-----------------|---|

End point description:

Peak was defined as the maximum post-baseline level of the cytokine. Participants in the Safety Analysis Set were analyzed.

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

End point timeframe:

Baseline up to Month 3

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: The data has been reported only for the specified arms for which participants were available and data was evaluable for the specified outcome measure.

|                               |   |  |  |  |
|-------------------------------|---|--|--|--|
| <b>End point values</b>       | Phase 2 (Safety Management Study): Cohort 3 |  |  |  |
| Subject group type            | Reporting group                             |  |  |  |
| Number of subjects analysed   | 38  |  |  |  |
| Units: ng/mL                  |   |  |  |  |
| median (full range (min-max)) | 2440.2 (0.8 to 25000.0)                     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Positive Replication Competent Retrovirus (RCR)

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants With Positive Replication Competent Retrovirus (RCR) |
|-----------------|---|

End point description:

RCR was analyzed in blood samples by central laboratory. Because axicabtagene ciloleucel comprised retroviral vector transduced T cells, the presence of RCR in the blood of treated participants was reported. Participants in the Safety Analysis Set were analyzed.

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

End point timeframe:

Day 0 (pre-infusion) up to last follow-up visit (maximum duration: 7.7, 6.8, 5.4, 4.4, 4.1 years for

| End point values                  | Phase 1 Study:<br>Axicabtagene<br>Ciloleucel and<br>Conditioning<br>Chemot | Phase 2<br>(Pivotal<br>Study): Cohort<br>1 | Phase 2<br>(Pivotal<br>Study): Cohort<br>2 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>3 |
|-----------------------------------|--|--|--|---|
| Subject group type                | Reporting group  | Reporting group                            | Reporting group                            | Reporting group   |
| Number of subjects analysed       | 7  | 77   | 24   | 38  |
| Units: percentage of participants |  |  |  |   |
| number (not applicable)           | 0  | 0  | 0  | 0   |

| End point values                  | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>4 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>5 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>6 |  |
|-----------------------------------|---|---|---|--|
| Subject group type                | Reporting group   | Reporting group   | Reporting group   |  |
| Number of subjects analysed       | 41  | 50  | 40  |  |
| Units: percentage of participants |   |   |   |  |
| number (not applicable)           | 0   | 0   | 0   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Safety Management Study: Number of Participants With the European Quality of Life Five Dimension Five Level Scale (EQ-5D) Score

|                 |   |
|-----------------|---|
| End point title | Phase 2 Safety Management Study: Number of Participants With the European Quality of Life Five Dimension Five Level Scale (EQ-5D) Score <sup>[27]</sup> |
|-----------------|---|

End point description:

EQ-5D is a self-reported questionnaire used for assessing the overall health status of a participant scoring 5 dimensions of health: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension was divided into 5 levels of severity: "No problem", "Slight problems", "Moderate problems", "Severe problems", and "Extreme problems (unable to perform)". EQ-5D health states, defined by the EQ-5D descriptive system, are converted into a single summary index by applying a formula that attaches values (also called QOL weights or QOL utilities) to each of the levels in each dimension. EQ-5D Summary Index values range from -0.11 (worst health state) to 1.00 (perfect health state). Participants in Safety Analysis Set with available data were analyzed.

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

End point timeframe:

Baseline, Week 4, Month 3, and Month 6

Notes:

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

Justification: The data has been reported only for the specified arms for which participants were available and data was evaluable for the specified outcome measure.



| End point values                                      | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>3 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>4 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>5 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>6 |
|---|---|---|---|---|
| Subject group type                                    | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed                           | 38  | 39  | 47  | 34  |
| Units: participants                                   |   |   |   |   |
| Baseline: Mobility : No problem                       | 30  | 25  | 33  | 26  |
| Baseline: Mobility : Slight problem                   | 7   | 9   | 5   | 4   |
| Baseline: Mobility : Moderate problem                 | 1   | 5   | 7   | 3   |
| Baseline: Mobility : Severe problem                   | 0   | 0   | 1   | 1   |
| Baseline: Mobility : Unable to perform                | 0   | 0   | 1   | 0   |
| Wk 4: Mobility : No problem<br>N=32,37,38,29          | 16  | 21  | 23  | 20  |
| Wk 4: Mobility : Slight problem<br>N=32,37,38,29      | 11  | 7   | 9   | 5   |
| Wk 4: Mobility : Moderate problem<br>N=32,37,38,29    | 4   | 5   | 4   | 4   |
| Wk 4: Mobility : Severe problem<br>N=32,37,38,29      | 0   | 3   | 1   | 0   |
| Wk 4: Mobility : Unable to perform<br>N=32,37,38,29   | 1   | 1   | 1   | 0   |
| Month 3: Mobility : No problem<br>N=23,31,33,29       | 14  | 20  | 21  | 22  |
| Month 3: Mobility : Slight problem<br>N=23,31,33,29   | 6   | 8   | 6   | 3   |
| Month 3: Mobility : Moderate problem<br>N=23,31,33,29 | 2   | 2   | 6   | 3   |
| Month 3: Mobility : Severe problem<br>N=23,31,33,29   | 1   | 1   | 0   | 1   |
| Mon 3: Mobility : Unable to perform<br>N=23,31,33,29  | 0   | 0   | 0   | 0   |
| Month 6: Mobility : No problem<br>N=18,25,17,27       | 10  | 19  | 11  | 15  |
| Month 6: Mobility : Slight problem<br>N=18,25,17,27   | 6   | 4   | 2   | 8   |
| Month 6: Mobility : Moderate problem<br>N=18,25,17,27 | 2   | 2   | 4   | 3   |
| Month 6: Mobility : Severe problem<br>N=18,25,17,27   | 0   | 0   | 0   | 1   |
| Mon 6: Mobility : Unable to perform<br>N=18,25,17,27  | 0   | 0   | 0   | 0   |
| Baseline: Self-care : No problem                      | 37  | 38  | 44  | 32  |
| Baseline: Self-care : Slight problem                  | 1   | 1   | 3   | 1   |
| Baseline: Self-care : Moderate problem                | 0   | 0   | 0   | 1   |
| Baseline: Self-care : Severe problem                  | 0   | 0   | 0   | 0   |
| Baseline: Self-care : Unable to perform               | 0   | 0   | 0   | 0   |
| Wk 4: Self-care : No problem<br>N=32,37,38,29         | 25  | 33  | 31  | 24  |
| Wk 4: Self-care : Slight problem<br>N=32,37,38,29     | 5   | 3   | 6   | 3   |
| Wk 4: Self-care : Moderate problem<br>N=32,37,38,29   | 1   | 0   | 1   | 1   |
| Wk 4: Self-care : Severe problem<br>N=32,37,38,29     | 0   | 1   | 0   | 1   |
| Wk 4: Self-care : Unable to perform<br>N=32,37,38,29  | 1   | 0   | 0   | 0   |
| Month 3: Self-care : No problem<br>N=23,31,33,29      | 19  | 29  | 32  | 25  |

|   |    |    |    |    |
|---|----|----|----|----|
| Month 3: Self-care : Slight problem<br>N=23,31,33,29  | 4  | 2  | 1  | 4  |
| Mon 3: Self-care : Moderate problem<br>N=23,31,33,29  | 0  | 0  | 0  | 0  |
| Month 3: Self-care : Severe problem<br>N=23,31,33,29  | 0  | 0  | 0  | 0  |
| Mon 3: Self-care : Unable to perform<br>N=23,31,33,29 | 0  | 0  | 0  | 0  |
| Month 6: Self-care : No problem<br>N=18,25,17,27      | 17 | 25 | 16 | 20 |
| Month 6: Self-care : Slight problem<br>N=18,25,17,27  | 1  | 0  | 1  | 7  |
| Mon 6: Self-care : Moderate problem<br>N=18,25,17,27  | 0  | 0  | 0  | 0  |
| Month 6: Self-care : Severe problem<br>N=18,25,17,27  | 0  | 0  | 0  | 0  |
| Mon 6: Self-care : Unable to perform<br>N=18,25,17,27 | 0  | 0  | 0  | 0  |
| Baseline: Usual activities : No problem               | 22 | 22 | 24 | 16 |
| Baseline: Usual activities : Slight<br>problem        | 10 | 6  | 13 | 14 |
| Baseline: Usual activities : Moderate<br>problem      | 4  | 8  | 8  | 2  |
| Baseline: Usual activities : Severe<br>problem        | 2  | 1  | 1  | 2  |
| Baseline: Usual activities : Unable to<br>perform     | 0  | 2  | 1  | 0  |
| Wk 4: Usual activities : No problem<br>N=32,37,37,29  | 6  | 12 | 12 | 12 |
| Wk 4: Usu act : Slight problem<br>N=32,37,37,29       | 13 | 11 | 13 | 11 |
| Wk 4: Usu act : Moderate problem<br>N=32,37,37,29     | 11 | 8  | 8  | 4  |
| Wk 4: Usu act : Severe problem<br>N=32,37,37,29       | 0  | 3  | 2  | 1  |
| Wk 4: Usu act : Unable to perform<br>N=32,37,37,29    | 2  | 3  | 2  | 1  |
| Mon 3: Usual activities : No problem<br>N=23,31,33,29 | 8  | 16 | 19 | 12 |
| Mon 3: Usu act : Slight problem<br>N=23,31,33,29      | 9  | 9  | 10 | 14 |
| Mon 3: Usu act : Moderate problem<br>N=23,31,33,29    | 5  | 5  | 2  | 2  |
| Mon 3: Usu act : Severe problem<br>N=23,31,33,29      | 1  | 1  | 1  | 1  |
| Mon 3: Usu act : Unable to perform<br>N=23,31,33,29   | 0  | 0  | 1  | 0  |
| Mon 6: Usual activities : No problem<br>N=18,25,17,27 | 9  | 15 | 10 | 11 |
| Mon 6: Usu act : Slight problem<br>N=18,25,17,27      | 5  | 7  | 4  | 12 |
| Mon 6: Usu act : Moderate problem<br>N=18,25,17,27    | 3  | 3  | 2  | 3  |
| Mon 6: Usu act : Severe problem<br>N=18,25,17,27      | 1  | 0  | 1  | 0  |
| Mon 6: Usu act : Unable to perform<br>N=18,25,17,27   | 0  | 0  | 0  | 1  |
| Baseline: Pain/Discomfort : No problem                | 18 | 17 | 16 | 15 |
| Baseline: Pain/Discomfort : Slight<br>problem         | 9  | 17 | 18 | 14 |
| Baseline: Pain/Discomfort : Moderate<br>problem       | 8  | 5  | 7  | 4  |

|  |    |    |    |    |
|--|----|----|----|----|
| Baseline: Pain/Discomfort : Severe problem           | 1  | 0  | 5  | 1  |
| Baseline: Pain/Discomfort : Unable to perform        | 2  | 0  | 1  | 0  |
| Wk 4: Pain/Discomfort : No problem<br>N=32,37,37,29  | 12 | 19 | 20 | 17 |
| Wk 4: Pai : Slight problem<br>N=32,37,37,29          | 12 | 13 | 10 | 9  |
| Wk 4: Pai : Moderate problem<br>N=32,37,37,29        | 7  | 2  | 5  | 3  |
| Wk 4: Pai : Severe problem<br>N=32,37,37,29          | 1  | 3  | 2  | 0  |
| Wk 4: Pai : Unable to perform<br>N=32,37,37,29       | 0  | 0  | 0  | 0  |
| Mon 3: Pain/Discomfort : No problem<br>N=23,31,33,29 | 9  | 10 | 18 | 16 |
| Mon 3: Pai : Slight problem<br>N=23,31,33,29         | 5  | 14 | 9  | 5  |
| Mon 3: Pai : Moderate problem<br>N=23,31,33,29       | 9  | 6  | 6  | 5  |
| Mon 3: Pai : Severe problem<br>N=23,31,33,29         | 0  | 1  | 0  | 3  |
| Mon 3: Pai : Unable to perform<br>N=23,31,33,29      | 0  | 0  | 0  | 0  |
| Mon 6: Pain/Discomfort : No problem<br>N=17,25,17,27 | 8  | 9  | 6  | 12 |
| Mon 6: Pai : Slight problem<br>N=17,25,17,27         | 4  | 14 | 8  | 8  |
| Mon 6: Pai : Moderate problem<br>N=17,25,17,27       | 5  | 1  | 3  | 4  |
| Mon 6: Pai : Severe problem<br>N=17,25,17,27         | 0  | 1  | 0  | 3  |
| Mon 6: Pai : Unable to perform<br>N=17,25,17,27      | 0  | 0  | 0  | 0  |
| Baseline: Anxiety/Depression : No problem            | 16 | 23 | 18 | 21 |
| Baseline: Anxiety/Depression : Slight problem        | 16 | 13 | 17 | 9  |
| Baseline: Anxiety/Depression : Moderate problem      | 3  | 3  | 10 | 3  |
| Baseline: Anxiety/Depression : Severe problem        | 1  | 0  | 1  | 1  |
| Baseline: Anxiety/Depression : Unable to perform     | 2  | 0  | 1  | 0  |
| Wk 4: Anx : No problem N=32,37,38,29                 | 9  | 25 | 21 | 23 |
| Wk 4: Anx : Slight problem<br>N=32,37,38,29          | 15 | 8  | 12 | 3  |
| Wk 4: Anx : Moderate problem<br>N=32,37,38,29        | 7  | 3  | 5  | 3  |
| Wk 4: Anx : Severe problem<br>N=32,37,38,29          | 1  | 1  | 0  | 0  |
| Wk 4: Anx : Unable to perform<br>N=32,37,38,29       | 0  | 0  | 0  | 0  |
| Mon 3: Anx : No problem<br>N=23,31,33,29             | 11 | 19 | 16 | 19 |
| Mon 3: Anx : Slight problem<br>N=23,31,33,29         | 5  | 8  | 12 | 7  |
| Mon 3: Anx : Moderate problem<br>N=23,31,33,29       | 6  | 4  | 4  | 2  |
| Mon 3: Anx : Severe problem<br>N=23,31,33,29         | 1  | 0  | 1  | 1  |

|   |   |    |   |    |
|---|---|----|---|----|
| Mon 3: Anx : Unable to perform<br>N=23,31,33,29 | 0 | 0  | 0 | 0  |
| Mon 6: Anx : No problem<br>N=18,25,17,26        | 9 | 14 | 7 | 18 |
| Mon 6: Anx : Slight problem<br>N=18,25,17,26    | 5 | 10 | 8 | 5  |
| Mon 6: Anx : Moderate problem<br>N=18,25,17,26  | 3 | 0  | 1 | 3  |
| Mon 6: Anx : Severe problem<br>N=18,25,17,26    | 0 | 1  | 1 | 0  |
| Mon 6: Anx : Unable to perform<br>N=18,25,17,26 | 1 | 0  | 0 | 0  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 2 Safety Management Study: EQ-5D Visual Analogue Scale (VAS) Score

|                 |  |
|-----------------|--|
| End point title | Phase 2 Safety Management Study: EQ-5D Visual Analogue Scale (VAS) Score <sup>[28]</sup> |
|-----------------|--|

End point description:

EQ-5D is a self-reported questionnaire used for assessing the overall health status of a participant. The EQ-5D-VAS records the participant's self-rated health on a vertical visual analogue scale and is asked to make a global assessment of their current state of health with 0 indicating the worst health they can imagine and 100 indicating the best health they can imagine. Participants in Safety Analysis Set with available data were analyzed.

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

End point timeframe:

Baseline, Week 4, Month 3, and Month 6

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: As the endpoint was focused on only the arms under Phase 2 of the study, all the arms in the baseline period were not included.

| End point values                     | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>3 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>4 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>5 | Phase 2<br>(Safety<br>Management<br>Study): Cohort<br>6 |
|--------------------------------------|---|---|---|---|
| Subject group type                   | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed          | 38  | 38  | 47  | 34  |
| Units: units on a scale              |   |   |   |   |
| arithmetic mean (standard deviation) |   |   |   |   |
| Baseline                             | 71.2 (± 21.3)   | 69.5 (± 18.8)   | 66.7 (± 20.7)   | 70.9 (± 17.0)   |
| Wk 4 N=32,36,38,29                   | 67.8 (± 15.6)   | 67.2 (± 20.9)   | 70.8 (± 14.8)   | 76.1 (± 13.2)   |
| Month 3 N=23,31,33,29                | 74.9 (± 16.6)   | 78.8 (± 14.7)   | 73.3 (± 19.9)   | 76.5 (± 15.0)   |
| Month 6 N=18,25,17,27                | 77.1 (± 21.4)   | 85.1 (± 12.1)   | 77.1 (± 14.7)   | 79.8 (± 14.0)   |

## Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse event: Up to 7.7 years; All-cause Death: Enrollment up to last followup visit (maximum: 7.7 years); Death for Participant Flow of Phase 2 Cohort 1 (53) is more than deaths (49) reported here because deaths are separately given for main and retreatment arms.

Adverse event reporting additional description:

Adverse events: The Safety Analysis Set included participants treated with any dose of axicabtagene ciloleucel; Retreatment groups: The Safety-Retreatment Analysis Set included participants re-treated of axicabtagene ciloleucel. All-cause mortality: All Enrolled Analysis Set included enrolled participants, Retreatment group: Safety-Retreatment Analysis Set.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 26.0 |
|--------------------|------|

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 1 Study: Axicabtagene Ciloleucel and Conditioning Chemot |
|-----------------------|--|

Reporting group description:

Participants with diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma (PMBCL), or transformed follicular lymphoma (TFL) received conditioning chemotherapy (fludarabine 30 mg/m<sup>2</sup> intravenously [IV] over 30 minutes and cyclophosphamide 500 mg/m<sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel chimeric antigen receptor (CAR) transduced autologous T cells administered IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of body weight (BW) on Day 0.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Phase 2 (Pivotal Study): Cohort 1 |
|-----------------------|-----------------------------------|

Reporting group description:

Participants with refractory DLBCL received conditioning chemotherapy (fludarabine 30 mg/m<sup>2</sup> IV over 30 minutes and cyclophosphamide 500 mg/m<sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Phase 2 (Pivotal Study): Cohort 2 |
|-----------------------|-----------------------------------|

Reporting group description:

Participants with refractory PMBCL or TFL received conditioning chemotherapy (fludarabine 30 mg/m<sup>2</sup> IV over 30 minutes and cyclophosphamide 500 mg/m<sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase 2 (Safety Management Study): Cohort 3 |
|-----------------------|---|

Reporting group description:

Participants with relapsed or refractory transplant ineligible DLBCL, PMBCL, or TFL received conditioning chemotherapy (fludarabine 30 mg/m<sup>2</sup> IV over 30 minutes and cyclophosphamide 500 mg/m<sup>2</sup> IV over 60 minutes) on Days -5, -4, and -3; followed by a single infusion of axicabtagene ciloleucel CAR transduced autologous T cells administered IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0. Participants also received a prophylactic regimen of levetiracetam (750 mg orally or IV twice daily (BID) starting on Day 0) and tocilizumab (8 mg/kg IV over 1 hour (not to exceed 800 mg)) on Day 2).

|                       |   |
|-----------------------|---|
| Reporting group title | Phase 2 (Safety Management Study): Cohort 4 |
|-----------------------|---|

Reporting group description:

Participants with r/r DLBCL, PMBCL, TFL, or high-grade B-cell lymphoma (HGBCL) after 2 systemic lines of therapy will receive optional bridging therapy (dexamethasone 20 mg to 40 mg, either orally or IV daily for 1 to 4 days or 1 g/m<sup>2</sup> of high-dose methylprednisolone (HDMP) for 3 days with rituximab at 375 mg/m<sup>2</sup> weekly for 3 weeks or bendamustine 90 mg/m<sup>2</sup> on Days 1 and 2 and rituximab 375 mg/m<sup>2</sup> on Day 1), conditioning chemotherapy (fludarabine 30 mg/m<sup>2</sup> IV and cyclophosphamide 500 mg/m<sup>2</sup> IV) on Days -5, -4, and -3; followed by single infusion of axicabtagene ciloleucel CAR transduced autologous T cells IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW. Participants will receive a prophylactic regimen of levetiracetam (750 mg orally or IV twice daily (BID) starting on Day 0). Participants received tocilizumab (initiated on persistent Grade 1 cytokine release syndrome (CRS) for over 24 hours) and dexamethasone (persistent Grade 1 CRS for over 72 hours and at

onset of Grade 1 neurologic toxicity).

|                       |   |
|-----------------------|---|
| Reporting group title | Phase 2 (Safety Management Study): Cohort 5 |
|-----------------------|---|

Reporting group description:

Participants with r/r DLBCL, PMBCL, TFL, or HGBCL after 2 systemic lines of therapy received debulking therapy (R-CHOP: rituximab 375mg/m<sup>2</sup> D1, doxorubicin 50mg/m<sup>2</sup> D1, prednisone 100mg D1 to D5, cyclophosphamide 750mg/m<sup>2</sup> D1, vincristine 1.4 mg/m<sup>2</sup> D1 or R-ICE: rituximab 375mg/m<sup>2</sup> D1, ifosfamide 5g/m<sup>2</sup> 24h-CI D2, carboplatin AUC5 D2 maximum dose 800mg, etoposide 100 mg/m<sup>2</sup>/day D1 to D3 or R-GEMOX: rituximab 375mg/m<sup>2</sup> D1, gemcitabine 1000mg/m<sup>2</sup> D2, oxaliplatin 100mg/m<sup>2</sup> D2 or R-GDP: rituximab 375mg/m<sup>2</sup> D1 or D8, gemcitabine 1g/m<sup>2</sup> D1 & D8, dexamethasone 40mg D1 to D4, cisplatin 75mg/m<sup>2</sup> D1 (or carboplatin AUC5 D1) or radiotherapy: 20 to 30 Gy), conditioning chemotherapy (fludarabine 30mg/m<sup>2</sup> IV and cyclophosphamide 500mg/m<sup>2</sup> IV) on Days -5, -4, and -3; followed by single infusion of axicabtagene ciloleucel at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0. Participants also received a prophylactic regimen of levetiracetam (750 mg orally or IV BID starting on D0). D=Day.

|                       |   |
|-----------------------|---|
| Reporting group title | Retreatment Axicabtagene Ciloleucel: Phase 2 Cohort 5 |
|-----------------------|---|

Reporting group description:

Participants who initially responded and subsequently relapsed, became eligible for second course of conditioning chemotherapy and axicabtagene ciloleucel. Participants received the same axicabtagene ciloleucel regimen as the original target dose.

|                       |  |
|-----------------------|--|
| Reporting group title | Retreatment Axicabtagene Ciloleucel: Phase 1 |
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Reporting group description:

Participants who initially responded and subsequently relapsed, became eligible for second course of conditioning chemotherapy and axicabtagene ciloleucel. Participants received the axicabtagene ciloleucel regimen selected for Phase 2.

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| Reporting group title | Retreatment Axicabtagene Ciloleucel: Phase 2 Cohort 1 |
|-----------------------|---|

Reporting group description:

Participants who initially responded and subsequently relapsed, became eligible for second course of conditioning chemotherapy and axicabtagene ciloleucel. Participants received the same axicabtagene ciloleucel regimen as the original target dose.

|                       |   |
|-----------------------|---|
| Reporting group title | Retreatment Axicabtagene Ciloleucel: Phase 2 Cohort 2 |
|-----------------------|---|

Reporting group description:

Participants who initially responded and subsequently relapsed, became eligible for second course of conditioning chemotherapy and axicabtagene ciloleucel. Participants received the same axicabtagene ciloleucel regimen as the original target dose.

|                       |   |
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| Reporting group title | Retreatment Axicabtagene Ciloleucel: Phase 2 Cohort 3 |
|-----------------------|---|

Reporting group description:

Participants who initially responded and subsequently relapsed, became eligible for second course of conditioning chemotherapy and axicabtagene ciloleucel. Participants received the same axicabtagene ciloleucel regimen as the original target dose.

|                       |   |
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| Reporting group title | Retreatment Axicabtagene Ciloleucel: Phase 2 Cohort 4 |
|-----------------------|---|

Reporting group description:

Participants who initially responded and subsequently relapsed, became eligible for second course of conditioning chemotherapy and axicabtagene ciloleucel. Participants received the same axicabtagene ciloleucel regimen as the original target dose.

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| Reporting group title | Phase 2 (Safety Management Study): Cohort 6 |
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Reporting group description:

Participants with r/r DLBCL, PMBCL, TFL or HGBCL after 2 systemic lines of therapy may receive bridging therapy (dexamethasone 20mg to 40mg, orally or IV daily for 1 to 4 days or 1g/m<sup>2</sup> HDMP for 3 days with rituximab at 375mg/m<sup>2</sup> weekly for 3 weeks or bendamustine 90 mg/m<sup>2</sup> on Days 1 and 2 and rituximab 375mg/m<sup>2</sup> on Day 1), conditioning chemotherapy (fludarabine 30mg/m<sup>2</sup> IV and cyclophosphamide 500mg/m<sup>2</sup> IV) on Days -5, -4, and -3; followed by single infusion of axicabtagene ciloleucel CAR transduced autologous T cells IV at a target dose of 2 x 10<sup>6</sup> anti-CD19 CAR T cells/kg of BW on Day 0. Participants will also receive a prophylactic regimen of levetiracetam 750 mg orally or IV twice daily (BID) starting on Day 0) and corticosteroids (dexamethasone, 10 mg once daily on Days 0, 1, and 2). Participants received tocilizumab (initiated on persistent Grade 1 CRS for over 24 hours) and dexamethasone (persistent Grade 1 CRS for over 72 hours and at onset of Grade 1 neurologic toxicity).

| Serious adverse events  | Phase 1 Study:<br>Axicabtagene<br>Ciloleucel and<br>Conditioning Chemot | Phase 2 (Pivotal<br>Study): Cohort 1 | Phase 2 (Pivotal<br>Study): Cohort 2 |
|---|---|--------------------------------------|--------------------------------------|
| Total subjects affected by serious adverse events                   |   |                                      |                                      |
| subjects affected / exposed   | 5 / 7 (71.43%)  | 40 / 77 (51.95%)                     | 14 / 24 (58.33%)                     |
| number of deaths (all causes)                                       | 5   | 49                                   | 13                                   |
| number of deaths resulting from adverse events                      |   |                                      |                                      |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |                                      |                                      |
| B-cell lymphoma   |   |                                      |                                      |
| subjects affected / exposed   | 1 / 7 (14.29%)  | 4 / 77 (5.19%)                       | 0 / 24 (0.00%)                       |
| occurrences causally related to treatment / all                     | 0 / 1   | 0 / 4                                | 0 / 0                                |
| deaths causally related to treatment / all                          | 0 / 1   | 0 / 4                                | 0 / 0                                |
| Myelodysplastic syndrome  |   |                                      |                                      |
| subjects affected / exposed   | 0 / 7 (0.00%)   | 1 / 77 (1.30%)                       | 2 / 24 (8.33%)                       |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 1                                | 0 / 2                                |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0                                | 0 / 1                                |
| Squamous cell carcinoma   |   |                                      |                                      |
| subjects affected / exposed   | 0 / 7 (0.00%)   | 2 / 77 (2.60%)                       | 0 / 24 (0.00%)                       |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 3                                | 0 / 0                                |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0                                | 0 / 0                                |
| Acute myeloid leukaemia   |   |                                      |                                      |
| subjects affected / exposed   | 0 / 7 (0.00%)   | 0 / 77 (0.00%)                       | 0 / 24 (0.00%)                       |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0                                | 0 / 0                                |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0                                | 0 / 0                                |
| Diffuse large B-cell lymphoma                                       |   |                                      |                                      |
| subjects affected / exposed   | 0 / 7 (0.00%)   | 0 / 77 (0.00%)                       | 0 / 24 (0.00%)                       |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0                                | 0 / 0                                |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0                                | 0 / 0                                |
| Carcinoma in situ   |   |                                      |                                      |
| subjects affected / exposed   | 0 / 7 (0.00%)   | 1 / 77 (1.30%)                       | 0 / 24 (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                                |
| Cancer pain   |   |                                      |                                      |



|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Basal cell carcinoma                            |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Central nervous system lymphoma                 |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 neoplasm malignant                         |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Vascular disorders                              |               |                |                |
| Hypotension                                     |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 2 / 77 (2.60%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 2          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hypertension                                    |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Embolism  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Shock   |               |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                |                |                |
| Gait disturbance                                     |                |                |                |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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                          | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (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          |
| Asthenia   |                |                |                |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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%)  | 5 / 77 (6.49%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all      | 0 / 0          | 1 / 5          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| General physical health ~ deterioration              |                |                |                |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Oedema peripheral                                    |                |                |                |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0          |
| Pain   |                |                |                |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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                              |                |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Haemophagocytic lymphohistiocytosis             |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 1 / 1          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |               |                |                |
| Hypoxia   |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 4 / 77 (5.19%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 4 / 4          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Respiratory failure                             |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 respiratory failure                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Aspiration                                      |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pulmonary embolism                              |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 1          |
| Pneumonitis                                     |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Chronic obstructive pulmonary ~ disease         |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 oedema                                |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Reexpansion pulmonary oedema                    |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Respiratory distress                            |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Psychiatric disorders                           |               |                |                |
| Confusional state                               |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 3 / 77 (3.90%) | 2 / 24 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 3 / 3          | 3 / 3          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Agitation                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 2 / 24 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 1          | 1 / 2          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Disorientation                                  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Depression                                      |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Anxiety   |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Delirium  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Mental status changes                           |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hallucination                                   |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Restlessness                                    |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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                                  |               |                |                |
| Alanine aminotransferase increased              |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Ejection fraction decreased                     |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 3 / 77 (3.90%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 3 / 3          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Gamma-glutamyltransferase                       |               |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| increased                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Platelet count decreased                        |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Neutrophil count decreased                      |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Troponin T increased                            |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |               |                |                |
| Hip fracture                                    |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Brain herniation                                |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Radius fracture                                 |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Seroma  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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                               |               |                |                |
| Cardiac arrest                                  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 2 / 77 (2.60%) | 2 / 24 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 2          | 1 / 2          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Atrial fibrillation                             |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 3 / 77 (3.90%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0         | 2 / 3          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Atrial flutter                                  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 2 / 77 (2.60%) | 0 / 24 (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          |
| Cardiac failure                                 |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Arrhythmia                                      |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 left ventricular failure                  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Cardiomyopathy                                  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pericarditis                                    |               |                |                |

|  |                |                  |                 |
|--|----------------|------------------|-----------------|
| subjects affected / exposed                              | 0 / 7 (0.00%)  | 0 / 77 (0.00%)   | 0 / 24 (0.00%)  |
| occurrences causally related to treatment / all          | 0 / 0          | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all               | 0 / 0          | 0 / 0            | 0 / 0           |
| Sinus tachycardia  |                |                  |                 |
| subjects affected / exposed                              | 0 / 7 (0.00%)  | 0 / 77 (0.00%)   | 0 / 24 (0.00%)  |
| 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                                 |                |                  |                 |
| Somnolence   |                |                  |                 |
| subjects affected / exposed                              | 0 / 7 (0.00%)  | 3 / 77 (3.90%)   | 0 / 24 (0.00%)  |
| occurrences causally related to treatment / all          | 0 / 0          | 3 / 3            | 0 / 0           |
| deaths causally related to treatment / all               | 0 / 0          | 0 / 0            | 0 / 0           |
| Encephalopathy   |                |                  |                 |
| subjects affected / exposed                              | 1 / 7 (14.29%) | 16 / 77 (20.78%) | 3 / 24 (12.50%) |
| occurrences causally related to treatment / all          | 1 / 1          | 17 / 17          | 5 / 5           |
| deaths causally related to treatment / all               | 0 / 0          | 0 / 0            | 0 / 0           |
| Aphasia  |                |                  |                 |
| subjects affected / exposed                              | 0 / 7 (0.00%)  | 3 / 77 (3.90%)   | 1 / 24 (4.17%)  |
| occurrences causally related to treatment / all          | 0 / 0          | 3 / 3            | 1 / 1           |
| deaths causally related to treatment / all               | 0 / 0          | 0 / 0            | 0 / 0           |
| Seizure  |                |                  |                 |
| subjects affected / exposed                              | 0 / 7 (0.00%)  | 1 / 77 (1.30%)   | 0 / 24 (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           |
| Tremor   |                |                  |                 |
| subjects affected / exposed                              | 0 / 7 (0.00%)  | 0 / 77 (0.00%)   | 0 / 24 (0.00%)  |
| 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 effector cell-associated ~ neurotoxicity syndrome |                |                  |                 |
| subjects affected / exposed                              | 0 / 7 (0.00%)  | 0 / 77 (0.00%)   | 0 / 24 (0.00%)  |
| occurrences causally related to treatment / all          | 0 / 0          | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all               | 0 / 0          | 0 / 0            | 0 / 0           |
| Dysgraphia   |                |                  |                 |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Syncope   |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Depressed level of consciousness                |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (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          |
| Dysarthria                                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Haemorrhage intracranial                        |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (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          |
| Leukoencephalopathy                             |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (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          |
| Presyncope                                      |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Apraxia   |                |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Ataxia  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Brain injury                                    |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 1 / 1          |
| Cerebral venous sinus thrombosis                |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cerebellar infarction                           |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Brain oedema                                    |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cognitive disorder                              |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Disturbance in attention                        |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Dyspraxia                                       |               |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hemiparesis                                     |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Lethargy  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Memory impairment                               |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Migraine with aura                              |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Toxic encephalopathy                            |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 like phenomena                          |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Quadriplegia                                    |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |               |                |                |
| Febrile neutropenia                             |               |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 7 (14.29%) | 4 / 77 (5.19%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 5          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neutropenia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (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          |
| Anaemia   |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 marrow failure                             |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (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          |
| Pancytopenia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (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          |
| Febrile bone marrow aplasia                     |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Leukopenia                                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| 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 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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                                   |                |                |                |
| Visual impairment                               |                |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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                      |               |                |                |
| Vomiting  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Abdominal pain                                  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Dysphagia                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Ascites   |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pancreatitis                                    |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Diarrhoea                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Enteritis                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Tongue ulceration                               |               |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Rectal haemorrhage                              |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Gastritis                                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hepatobiliary disorders                         |               |                |                |
| Cholecystitis                                   |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |               |                |                |
| Toxic skin eruption                             |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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%) | 3 / 77 (3.90%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 2 / 3          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Renal failure                                   |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Anuria  |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cystitis haemorrhagic                           |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Haematuria                                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 |                |                |                |
| Back pain                                       |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (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          |
| Muscular weakness                               |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (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          |
| Pain in extremity                               |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (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          |
| Amyotrophy                                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Arthralgia                                      |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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%)  | 1 / 77 (1.30%) | 0 / 24 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Musculoskeletal pain                            |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%)  |
| 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                     |                |                |                 |
| Pneumonia                                       |                |                |                 |
| subjects affected / exposed                     | 2 / 7 (28.57%) | 7 / 77 (9.09%) | 3 / 24 (12.50%) |
| occurrences causally related to treatment / all | 1 / 2          | 1 / 9          | 1 / 3           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Sepsis  |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 1 / 24 (4.17%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Covid-19  |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%)  |
| 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 / 7 (0.00%)  | 3 / 77 (3.90%) | 1 / 24 (4.17%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 3          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Herpes zoster                                   |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 2 / 77 (2.60%) | 0 / 24 (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           |
| Septic shock                                    |                |                |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Bacteraemia                                     |                |                |                 |



|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cellulitis                                      |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 bacteraemia                         |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 2 / 77 (2.60%) | 0 / 24 (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          |
| Clostridium difficile infection                 |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Clostridium difficile colitis                   |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Rhinovirus infection                            |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cytomegalovirus colitis                         |               |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Adenovirus infection                            |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Anal abscess                                    |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cytomegalovirus enteritis                       |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Device related sepsis                           |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Encephalitis                                    |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Human herpesvirus 6 encephalitis                |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Klebsiella infection                            |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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                                      |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Myelitis  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Oral herpes                                     |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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          |
| Parainfluenzae virus infection                  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 sepsis                             |               |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Peritonitis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 infection                |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 necrotising                           |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 influenzal                            |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 staphylococcal                        |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (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          |
| Pseudomonal sepsis                              |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (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 tract infection                     |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rhinitis  |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rotavirus infection                             |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (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 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Soft tissue infection                           |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urosepsis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Viral upper respiratory tract ~ infection       |                |                |                |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Dehydration                                     |                |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%) | 2 / 77 (2.60%) | 0 / 24 (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          |
| Acidosis  |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Decreased appetite                              |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| 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 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hypoglycaemia                                   |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hyponatraemia                                   |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Lactic acidosis                                 |               |                |                |
| subjects affected / exposed                     | 0 / 7 (0.00%) | 1 / 77 (1.30%) | 0 / 24 (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          |

| Serious adverse events                            | Phase 2 (Safety Management Study): Cohort 3 | Phase 2 (Safety Management Study): Cohort 4 | Phase 2 (Safety Management Study): Cohort 5 |
|---|---|---|---|
| Total subjects affected by serious adverse events |   |   |   |
| subjects affected / exposed                       | 26 / 38 (68.42%)                            | 24 / 41 (58.54%)                            | 27 / 50 (54.00%)                            |
| number of deaths (all causes)                     | 23  | 20  | 37  |
| number of deaths resulting from adverse events    |   |   |   |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |                |
| B-cell lymphoma   |                |                |                |
| subjects affected / exposed   | 3 / 38 (7.89%) | 3 / 41 (7.32%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 3          | 0 / 3          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 3          | 0 / 3          | 0 / 0          |
| Myelodysplastic syndrome  |                |                |                |
| subjects affected / exposed   | 2 / 38 (5.26%) | 0 / 41 (0.00%) | 2 / 50 (4.00%) |
| occurrences causally related to treatment / all                     | 1 / 2          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all                          | 0 / 1          | 0 / 0          | 0 / 2          |
| Squamous cell carcinoma   |                |                |                |
| subjects affected / exposed   | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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 myeloid leukaemia   |                |                |                |
| subjects affected / exposed   | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 1          | 0 / 1          |
| Diffuse large B-cell lymphoma                                       |                |                |                |
| subjects affected / exposed   | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                          | 0 / 1          | 0 / 0          | 0 / 1          |
| Carcinoma in situ   |                |                |                |
| subjects affected / exposed   | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Cancer pain   |                |                |                |
| subjects affected / exposed   | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Basal cell carcinoma  |                |                |                |
| subjects affected / exposed   | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |

|  |                 |                |                |
|--|-----------------|----------------|----------------|
| Central nervous system lymphoma                      |                 |                |                |
| subjects affected / exposed                          | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Lung neoplasm malignant                              |                 |                |                |
| subjects affected / exposed                          | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 / 38 (0.00%)  | 1 / 41 (2.44%) | 0 / 50 (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                                   |                 |                |                |
| Hypotension  |                 |                |                |
| subjects affected / exposed                          | 4 / 38 (10.53%) | 2 / 41 (4.88%) | 3 / 50 (6.00%) |
| occurrences causally related to treatment / all      | 3 / 4           | 2 / 2          | 3 / 3          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Hypertension   |                 |                |                |
| subjects affected / exposed                          | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Embolism   |                 |                |                |
| subjects affected / exposed                          | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Shock  |                 |                |                |
| subjects affected / exposed                          | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 |                 |                |                |
| Gait disturbance                                     |                 |                |                |
| subjects affected / exposed                          | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |



|   |                |                |                 |
|---|----------------|----------------|-----------------|
| Fatigue   |                |                |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| 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 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| 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                     | 3 / 38 (7.89%) | 2 / 41 (4.88%) | 5 / 50 (10.00%) |
| occurrences causally related to treatment / all | 1 / 4          | 2 / 2          | 3 / 5           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| General physical health ~ deterioration         |                |                |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Oedema peripheral                               |                |                |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| 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 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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           |
| Immune system disorders                         |                |                |                 |
| Haemophagocytic lymphohistiocytosis             |                |                |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                |                |                 |
| Hypoxia   |                |                |                 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 2 / 38 (5.26%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory failure                             |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 2 / 41 (4.88%) | 0 / 50 (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          |
| Acute respiratory failure                       |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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  |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Aspiration                                      |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonitis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Pleural effusion                                |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Chronic obstructive pulmonary ~ disease         |                |                |                |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| 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 oedema                                |                |                |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Reexpansion pulmonary oedema                    |                |                |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| 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 distress                            |                |                |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Psychiatric disorders                           |                |                |                 |
| Confusional state                               |                |                |                 |
| subjects affected / exposed                     | 3 / 38 (7.89%) | 1 / 41 (2.44%) | 5 / 50 (10.00%) |
| occurrences causally related to treatment / all | 3 / 3          | 1 / 1          | 4 / 5           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Agitation                                       |                |                |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Disorientation                                  |                |                |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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           |
| Depression                                      |                |                |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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           |
| Anxiety   |                |                |                 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Delirium  |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Mental status changes                           |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hallucination                                   |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Restlessness                                    |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| Alanine aminotransferase increased              |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ejection fraction decreased                     |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Gamma-glutamyltransferase increased             |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Platelet count decreased                        |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Neutrophil count decreased                      |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Troponin T increased                            |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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  |                |                |                |
| Hip fracture                                    |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Brain herniation                                |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Radius fracture                                 |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Seroma  |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Cardiac arrest                                  |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Atrial fibrillation                             |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 flutter                                  |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tachycardia                                     |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Arrhythmia                                      |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Acute left ventricular failure                  |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiomyopathy                                  |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Pericarditis                                    |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Sinus tachycardia                               |                |                |                |

|  |                 |                |                |
|--|-----------------|----------------|----------------|
| subjects affected / exposed                              | 1 / 38 (2.63%)  | 0 / 41 (0.00%) | 0 / 50 (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          |
| Nervous system disorders                                 |                 |                |                |
| Somnolence   |                 |                |                |
| subjects affected / exposed                              | 2 / 38 (5.26%)  | 3 / 41 (7.32%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all          | 2 / 2           | 3 / 3          | 1 / 1          |
| deaths causally related to treatment / all               | 0 / 0           | 0 / 0          | 0 / 0          |
| Encephalopathy   |                 |                |                |
| subjects affected / exposed                              | 9 / 38 (23.68%) | 1 / 41 (2.44%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all          | 10 / 10         | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all               | 0 / 0           | 0 / 0          | 0 / 0          |
| Aphasia  |                 |                |                |
| subjects affected / exposed                              | 1 / 38 (2.63%)  | 0 / 41 (0.00%) | 3 / 50 (6.00%) |
| occurrences causally related to treatment / all          | 2 / 2           | 0 / 0          | 3 / 3          |
| deaths causally related to treatment / all               | 0 / 0           | 0 / 0          | 0 / 0          |
| Seizure  |                 |                |                |
| subjects affected / exposed                              | 1 / 38 (2.63%)  | 0 / 41 (0.00%) | 0 / 50 (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          |
| Tremor   |                 |                |                |
| subjects affected / exposed                              | 0 / 38 (0.00%)  | 1 / 41 (2.44%) | 4 / 50 (8.00%) |
| occurrences causally related to treatment / all          | 0 / 0           | 1 / 1          | 4 / 4          |
| deaths causally related to treatment / all               | 0 / 0           | 0 / 0          | 0 / 0          |
| Immune effector cell-associated ~ neurotoxicity syndrome |                 |                |                |
| subjects affected / exposed                              | 1 / 38 (2.63%)  | 2 / 41 (4.88%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all          | 1 / 1           | 2 / 2          | 1 / 1          |
| deaths causally related to treatment / all               | 0 / 0           | 0 / 0          | 0 / 0          |
| Dysgraphia   |                 |                |                |
| subjects affected / exposed                              | 0 / 38 (0.00%)  | 1 / 41 (2.44%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all          | 0 / 0           | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all               | 0 / 0           | 0 / 0          | 0 / 0          |
| Headache   |                 |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Depressed level of consciousness                |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dysarthria                                      |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Haemorrhage intracranial                        |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Leukoencephalopathy                             |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Presyncope                                      |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Apraxia   |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ataxia  |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Brain injury                                    |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cerebral venous sinus thrombosis                |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Cerebellar infarction                           |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Brain oedema                                    |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0          |
| Cognitive disorder                              |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Disturbance in attention                        |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Dyspraxia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hemiparesis                                     |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lethargy  |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Memory impairment                               |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Migraine with aura                              |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Toxic encephalopathy                            |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 like phenomena                          |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Quadriplegia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |                |                |                |
| Febrile neutropenia                             |                |                |                |
| subjects affected / exposed                     | 2 / 38 (5.26%) | 1 / 41 (2.44%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 1 / 1          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neutropenia                                     |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 38 (2.63%) | 2 / 41 (4.88%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 2 / 2          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Anaemia   |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bone marrow failure                             |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Pancytopenia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 2 / 50 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 3          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Febrile bone marrow aplasia                     |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Leukopenia                                      |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Eye disorders                                   |                |                |                |
| Visual impairment                               |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                |                |                |

|   |                |                |                |  |
|---|----------------|----------------|----------------|--|
| Vomiting  |                |                |                |  |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 1 / 41 (2.44%) | 0 / 50 (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          |  |
| Abdominal pain                                  |                |                |                |  |
| subjects affected / exposed                     | 2 / 38 (5.26%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 4          | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |  |
| Dysphagia                                       |                |                |                |  |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |  |
| Ascites   |                |                |                |  |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |  |
| Pancreatitis                                    |                |                |                |  |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 1 / 41 (2.44%) | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |  |
| Diarrhoea                                       |                |                |                |  |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |  |
| Enteritis                                       |                |                |                |  |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |  |
| Tongue ulceration                               |                |                |                |  |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |  |
| Rectal haemorrhage                              |                |                |                |  |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Gastritis                                       |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Hepatobiliary disorders                         |                |                |                |
| Cholecystitis                                   |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                |                |                |
| Toxic skin eruption                             |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal failure                                   |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 1 / 41 (2.44%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| Anuria  |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Cystitis haemorrhagic                           |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Haematuria                                      |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Back pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Muscular weakness                               |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 2 / 50 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pain in extremity                               |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Amyotrophy                                      |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Arthralgia                                      |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 3 / 41 (7.32%) | 3 / 50 (6.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 2 / 3          | 1 / 3          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| Sepsis  |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 2 / 50 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 1 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Covid-19  |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary tract infection                         |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Septic shock                                    |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 3 / 50 (6.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 3 / 3          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 3 / 3          |
| Bacteraemia                                     |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 1 / 41 (2.44%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| Cellulitis                                      |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 2 / 50 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumocystis jirovecii pneumonia                |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Escherichia bacteraemia                         |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Clostridium difficile infection                 |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Clostridium difficile colitis                   |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rhinovirus infection                            |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Covid-19 pneumonia                              |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cytomegalovirus colitis                         |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Bronchitis                                      |                |                |                |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Adenovirus infection                            |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Anal abscess                                    |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Atypical pneumonia                              |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Cytomegalovirus enteritis                       |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 sepsis                           |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Encephalitis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Escherichia sepsis                              |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Human herpesvirus 6 encephalitis                |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Klebsiella infection                            |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Meningitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Myelitis  |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Oral herpes                                     |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Pneumococcal sepsis                             |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Peritonitis                                     |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumocystis jirovecii infection                |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia necrotising                           |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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          |
| Pneumonia influenzal                            |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| Pneumonia respiratory syncytial ~ viral         |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (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 staphylococcal                        |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pseudomonal sepsis                              |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Rhinitis  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Rotavirus infection                             |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Soft tissue infection                           |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urosepsis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Viral upper respiratory tract ~ infection       |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Dehydration                                     |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Acidosis  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Decreased appetite                              |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 1 / 41 (2.44%) | 0 / 50 (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          |
| Hypercalcaemia                                  |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypoglycaemia                                   |                |                |                |
| subjects affected / exposed                     | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hyponatraemia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lactic acidosis                                 |                |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| 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>                                       | Retreatment<br>Axicabtagene<br>Ciloleucel: Phase 2<br>Cohort 5 | Retreatment<br>Axicabtagene<br>Ciloleucel: Phase 1 | Retreatment<br>Axicabtagene<br>Ciloleucel: Phase 2<br>Cohort 1 |
|---|--|--|--|
| Total subjects affected by serious adverse events                   |  |  |  |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 1 / 1 (100.00%)                                    | 5 / 9 (55.56%)   |
| number of deaths (all causes)                                       | 2  | 1  | 8  |
| number of deaths resulting from adverse events                      |  |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |
| B-cell lymphoma   |  |  |  |

|   |               |                 |                |
|---|---------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%)   | 2 / 9 (22.22%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 2          |
| Myelodysplastic syndrome                        |               |                 |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 1 (100.00%) | 0 / 9 (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                         |               |                 |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| 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 myeloid leukaemia                         |               |                 |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Diffuse large B-cell lymphoma                   |               |                 |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Carcinoma in situ                               |               |                 |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Cancer pain                                     |               |                 |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Basal cell carcinoma                            |               |                 |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Central nervous system lymphoma                 |               |                 |                |

|  |               |               |               |
|--|---------------|---------------|---------------|
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 neoplasm malignant                              |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Vascular disorders                                   |               |               |               |
| Hypotension  |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypertension   |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Embolism   |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Shock  |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 |               |               |               |
| Gait disturbance                                     |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Fatigue   |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pyrexia   |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| General physical health ~ deterioration         |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Oedema peripheral                               |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pain  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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                         |               |               |                |
| Haemophagocytic lymphohistiocytosis             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 |               |               |                |
| Hypoxia   |               |               |                |



|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 failure                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 respiratory failure                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Dyspnoea  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Aspiration                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumonitis                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pleural effusion                                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Chronic obstructive pulmonary ~ disease         |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 oedema                                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Reexpansion pulmonary oedema                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 distress                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Psychiatric disorders                           |               |               |               |
| Confusional state                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Agitation                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Disorientation                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Depression                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Anxiety   |               |               |               |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Delirium  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Mental status changes                           |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hallucination                                   |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Restlessness                                    |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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                                  |               |               |                |
| Alanine aminotransferase increased              |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Ejection fraction decreased                     |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Gamma-glutamyltransferase increased             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Platelet count decreased                        |               |               |                |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Neutrophil count decreased                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Troponin T increased                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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  |               |               |               |
| Hip fracture                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Brain herniation                                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Radius fracture                                 |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Seroma  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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                               |               |               |               |
| Cardiac arrest                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Atrial fibrillation                             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 flutter                                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Tachycardia                                     |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Arrhythmia                                      |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 left ventricular failure                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Cardiomyopathy                                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pericarditis                                    |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Sinus tachycardia                               |               |               |                |

|  |               |               |               |
|--|---------------|---------------|---------------|
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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                                 |               |               |               |
| Somnolence   |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Encephalopathy   |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Aphasia  |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Seizure  |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Tremor   |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 effector cell-associated ~ neurotoxicity syndrome |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Dysgraphia   |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Headache   |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Syncope   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Depressed level of consciousness                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Dysarthria                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Haemorrhage intracranial                        |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Leukoencephalopathy                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Presyncope                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Apraxia   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Ataxia  |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Brain injury                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cerebral venous sinus thrombosis                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cerebellar infarction                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Brain oedema                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cognitive disorder                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Disturbance in attention                        |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Dyspraxia                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hemiparesis                                     |               |               |               |



|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Lethargy  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Memory impairment                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Migraine with aura                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Toxic encephalopathy                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 like phenomena                          |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Quadriplegia                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Blood and lymphatic system disorders            |               |               |               |
| Febrile neutropenia                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Neutropenia                                     |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Anaemia   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 marrow failure                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pancytopenia                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 bone marrow aplasia                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Leukopenia                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Thrombocytopenia                                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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                                   |               |               |               |
| Visual impairment                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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                      |               |               |               |

|   |               |               |               |  |
|---|---------------|---------------|---------------|--|
| Vomiting  |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Abdominal pain                                  |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Dysphagia                                       |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Ascites   |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Pancreatitis                                    |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Diarrhoea                                       |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Enteritis                                       |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Tongue ulceration                               |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Rectal haemorrhage                              |               |               |               |  |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Nausea  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Gastritis                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hepatobiliary disorders                         |               |               |                |
| Cholecystitis                                   |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Skin and subcutaneous tissue disorders          |               |               |                |
| Toxic skin eruption                             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Renal and urinary disorders                     |               |               |                |
| Acute kidney injury                             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Anuria  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Cystitis haemorrhagic                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Haematuria                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 |               |               |               |
| Back pain                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Muscular weakness                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pain in extremity                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Amyotrophy                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Arthralgia                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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                     |               |               |                |
| Pneumonia                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Sepsis  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Covid-19  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Urinary tract infection                         |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Septic shock                                    |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Bacteraemia                                     |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 bacteraemia                         |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Clostridium difficile infection                 |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Clostridium difficile colitis                   |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Rhinovirus infection                            |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Cytomegalovirus colitis                         |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Bronchitis                                      |               |               |                |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Adenovirus infection                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Anal abscess                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cytomegalovirus enteritis                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 sepsis                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Encephalitis                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Human herpesvirus 6 encephalitis                |               |               |               |



|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Influenza                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Klebsiella infection                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Meningitis                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Myelitis  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Oral herpes                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 sepsis                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Peritonitis                                     |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 infection                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 necrotising                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 influenzal                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 staphylococcal                        |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pseudomonal sepsis                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Rhinitis  |               |               |               |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Rotavirus infection                             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Soft tissue infection                           |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Urosepsis                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Viral upper respiratory tract ~ infection       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Metabolism and nutrition disorders              |               |               |                |
| Dehydration                                     |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Acidosis  |               |               |                |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Decreased appetite                              |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hypercalcaemia                                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hypoglycaemia                                   |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hyponatraemia                                   |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Lactic acidosis                                 |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| 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>                                       | Retreatment<br>Axicabtagene<br>Ciloleucel: Phase 2<br>Cohort 2 | Retreatment<br>Axicabtagene<br>Ciloleucel: Phase 2<br>Cohort 3 | Retreatment<br>Axicabtagene<br>Ciloleucel: Phase 2<br>Cohort 4 |
|---|--|--|--|
| Total subjects affected by serious adverse events                   |  |  |  |
| subjects affected / exposed   | 1 / 2 (50.00%)   | 2 / 2 (100.00%)  | 0 / 2 (0.00%)  |
| number of deaths (all causes)                                       | 2  | 1  | 2  |
| number of deaths resulting from adverse events                      |  |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |
| B-cell lymphoma   |  |  |  |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 1          | 0 / 0         |
| Myelodysplastic syndrome                        |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Squamous cell carcinoma                         |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Acute myeloid leukaemia                         |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Diffuse large B-cell lymphoma                   |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Carcinoma in situ                               |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Cancer pain                                     |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Basal cell carcinoma                            |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Central nervous system lymphoma                 |               |                |               |

|  |               |               |               |
|--|---------------|---------------|---------------|
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Lung neoplasm malignant                              |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Prostate cancer                                      |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Vascular disorders                                   |               |               |               |
| Hypotension  |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypertension   |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Embolism   |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| Shock  |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |
| General disorders and administration site conditions |               |               |               |
| Gait disturbance                                     |               |               |               |
| subjects affected / exposed                          | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0         | 0 / 0         | 0 / 0         |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Fatigue   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Asthenia  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pyrexia   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| General physical health ~ deterioration         |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Oedema peripheral                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pain  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Immune system disorders                         |               |               |               |
| Haemophagocytic lymphohistiocytosis             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders |               |               |               |
| Hypoxia   |               |               |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Respiratory failure                             |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Acute respiratory failure                       |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Dyspnoea  |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Aspiration                                      |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pulmonary embolism                              |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pneumonitis                                     |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pleural effusion                                |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Chronic obstructive pulmonary ~ disease         |               |                |               |



|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary oedema                                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Reexpansion pulmonary oedema                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Respiratory distress                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Psychiatric disorders                           |               |               |               |
| Confusional state                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Agitation                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Disorientation                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Depression                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Anxiety   |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Delirium  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Mental status changes                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hallucination                                   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Restlessness                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Investigations                                  |               |               |               |
| Alanine aminotransferase increased              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Ejection fraction decreased                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Gamma-glutamyltransferase increased             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Platelet count decreased                        |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Neutrophil count decreased                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Troponin T increased                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Injury, poisoning and procedural complications  |               |               |               |
| Hip fracture                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Brain herniation                                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Radius fracture                                 |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Seroma  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiac disorders                               |               |               |               |
| Cardiac arrest                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Atrial fibrillation                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Atrial flutter                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiac failure                                 |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Tachycardia                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Arrhythmia                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Acute left ventricular failure                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiomyopathy                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pericarditis                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Sinus tachycardia                               |               |               |               |

|  |               |               |               |
|--|---------------|---------------|---------------|
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Nervous system disorders                                 |               |               |               |
| Somnolence   |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Encephalopathy   |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Aphasia  |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Seizure  |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Tremor   |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Immune effector cell-associated ~ neurotoxicity syndrome |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Dysgraphia   |               |               |               |
| subjects affected / exposed                              | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all          | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all               | 0 / 0         | 0 / 0         | 0 / 0         |
| Headache   |               |               |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Syncope   |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Depressed level of consciousness                |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Dysarthria                                      |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Haemorrhage intracranial                        |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Leukoencephalopathy                             |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Presyncope                                      |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Apraxia   |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Ataxia  |               |                |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Brain injury                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cerebral venous sinus thrombosis                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cerebellar infarction                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Brain oedema                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cognitive disorder                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Disturbance in attention                        |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Dyspraxia                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hemiparesis                                     |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Lethargy  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Memory impairment                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Migraine with aura                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Toxic encephalopathy                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Seizure like phenomena                          |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Quadriplegia                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Blood and lymphatic system disorders            |               |               |               |
| Febrile neutropenia                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Neutropenia                                     |               |               |               |



|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Anaemia   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Bone marrow failure                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pancytopenia                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Febrile bone marrow aplasia                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Leukopenia                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Thrombocytopenia                                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Eye disorders                                   |               |               |               |
| Visual impairment                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Gastrointestinal disorders                      |               |               |               |

|   |               |               |               |  |
|---|---------------|---------------|---------------|--|
| Vomiting  |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Abdominal pain                                  |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Dysphagia                                       |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Ascites   |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Pancreatitis                                    |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Diarrhoea                                       |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Enteritis                                       |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Tongue ulceration                               |               |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |  |
| Rectal haemorrhage                              |               |               |               |  |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Nausea  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Gastritis                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hepatobiliary disorders                         |               |               |               |
| Cholecystitis                                   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Skin and subcutaneous tissue disorders          |               |               |               |
| Toxic skin eruption                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Renal and urinary disorders                     |               |               |               |
| Acute kidney injury                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Renal failure                                   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Anuria  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Cystitis haemorrhagic                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Haematuria                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Musculoskeletal and connective tissue disorders |               |               |               |
| Back pain                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Muscular weakness                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pain in extremity                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Amyotrophy                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Arthralgia                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Bone pain                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |                |               |               |
|---|----------------|---------------|---------------|
| Musculoskeletal pain                            |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Infections and infestations                     |                |               |               |
| Pneumonia                                       |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Sepsis  |                |               |               |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 0         |
| Covid-19  |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Urinary tract infection                         |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Herpes zoster                                   |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Septic shock                                    |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Bacteraemia                                     |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Cellulitis                                      |                |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumocystis jirovecii pneumonia                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Escherichia bacteraemia                         |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Clostridium difficile infection                 |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Clostridium difficile colitis                   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Rhinovirus infection                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Covid-19 pneumonia                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cytomegalovirus colitis                         |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Bronchitis                                      |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Adenovirus infection                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Anal abscess                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Atypical pneumonia                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cytomegalovirus enteritis                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Device related sepsis                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Encephalitis                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Escherichia sepsis                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Human herpesvirus 6 encephalitis                |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Influenza                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Klebsiella infection                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Meningitis                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Myelitis  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Oral herpes                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Parainfluenzae virus infection                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumococcal sepsis                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Peritonitis                                     |               |               |               |



|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumocystis jirovecii infection                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumonia necrotising                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumonia influenzal                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumonia respiratory syncytial ~ viral         |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumonia staphylococcal                        |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pseudomonal sepsis                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Respiratory tract infection                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Rhinitis  |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Rotavirus infection                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Sinusitis                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Soft tissue infection                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Urosepsis                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Upper respiratory tract infection               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Viral upper respiratory tract ~ infection       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Metabolism and nutrition disorders              |               |               |               |
| Dehydration                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Acidosis  |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Decreased appetite                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypercalcaemia                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypoglycaemia                                   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hyponatraemia                                   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Lactic acidosis                                 |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |   |  |  |
|---|---|--|--|
| <b>Serious adverse events</b>                                       | Phase 2 (Safety Management Study): Cohort 6 |  |  |
| Total subjects affected by serious adverse events                   |   |  |  |
| subjects affected / exposed   | 25 / 40 (62.50%)                            |  |  |
| number of deaths (all causes)                                       | 20  |  |  |
| number of deaths resulting from adverse events                      |   |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |  |  |
| B-cell lymphoma   |   |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| subjects affected / exposed                     | 2 / 40 (5.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |  |
| deaths causally related to treatment / all      | 0 / 2          |  |  |  |
| Myelodysplastic syndrome                        |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Squamous cell carcinoma                         |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Acute myeloid leukaemia                         |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Diffuse large B-cell lymphoma                   |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Carcinoma in situ                               |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Cancer pain                                     |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Basal cell carcinoma                            |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Central nervous system lymphoma                 |                |  |  |  |

|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed                          | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Lung neoplasm malignant                              |                |  |  |
| subjects affected / exposed                          | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Prostate cancer                                      |                |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Vascular disorders                                   |                |  |  |
| Hypotension  |                |  |  |
| subjects affected / exposed                          | 2 / 40 (5.00%) |  |  |
| occurrences causally related to treatment / all      | 2 / 2          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Hypertension   |                |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Embolism   |                |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Shock  |                |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General disorders and administration site conditions |                |  |  |
| Gait disturbance                                     |                |  |  |
| subjects affected / exposed                          | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all      | 0 / 0          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| Fatigue   |                 |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Asthenia  |                 |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%)  |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Pyrexia   |                 |  |  |  |
| subjects affected / exposed                     | 4 / 40 (10.00%) |  |  |  |
| occurrences causally related to treatment / all | 2 / 4           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| General physical health ~ deterioration         |                 |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Oedema peripheral                               |                 |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Pain  |                 |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Immune system disorders                         |                 |  |  |  |
| Haemophagocytic lymphohistiocytosis             |                 |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |  |
| Hypoxia   |                 |  |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Respiratory failure                             |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 1 / 1          |  |  |  |
| Acute respiratory failure                       |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Dyspnoea  |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Aspiration                                      |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pulmonary embolism                              |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumonitis                                     |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pleural effusion                                |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Chronic obstructive pulmonary ~ disease         |                |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 40 (2.50%)  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pulmonary oedema                                |                 |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Reexpansion pulmonary oedema                    |                 |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory distress                            |                 |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychiatric disorders                           |                 |  |  |
| Confusional state                               |                 |  |  |
| subjects affected / exposed                     | 5 / 40 (12.50%) |  |  |
| occurrences causally related to treatment / all | 5 / 5           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Agitation                                       |                 |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Disorientation                                  |                 |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Depression                                      |                 |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Anxiety   |                 |  |  |



|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Delirium  |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Mental status changes                           |                |  |  |
| subjects affected / exposed                     | 2 / 40 (5.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hallucination                                   |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Restlessness                                    |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Investigations                                  |                |  |  |
| Alanine aminotransferase increased              |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Ejection fraction decreased                     |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gamma-glutamyltransferase increased             |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Platelet count decreased                        |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Neutrophil count decreased                      |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Troponin T increased                            |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Injury, poisoning and procedural complications  |                |  |  |
| Hip fracture                                    |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Brain herniation                                |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Radius fracture                                 |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Seroma  |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac disorders                               |                |  |  |
| Cardiac arrest                                  |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| Atrial fibrillation                             |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Atrial flutter                                  |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Cardiac failure                                 |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Tachycardia                                     |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Arrhythmia                                      |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Acute left ventricular failure                  |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Cardiomyopathy                                  |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pericarditis                                    |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Sinus tachycardia                               |                |  |  |  |

|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed                              | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all          | 0 / 0          |  |  |
| deaths causally related to treatment / all               | 0 / 0          |  |  |
| Nervous system disorders                                 |                |  |  |
| Somnolence   |                |  |  |
| subjects affected / exposed                              | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all          | 1 / 1          |  |  |
| deaths causally related to treatment / all               | 0 / 0          |  |  |
| Encephalopathy   |                |  |  |
| subjects affected / exposed                              | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all          | 0 / 0          |  |  |
| deaths causally related to treatment / all               | 0 / 0          |  |  |
| Aphasia  |                |  |  |
| subjects affected / exposed                              | 3 / 40 (7.50%) |  |  |
| occurrences causally related to treatment / all          | 2 / 3          |  |  |
| deaths causally related to treatment / all               | 0 / 0          |  |  |
| Seizure  |                |  |  |
| subjects affected / exposed                              | 3 / 40 (7.50%) |  |  |
| occurrences causally related to treatment / all          | 2 / 3          |  |  |
| deaths causally related to treatment / all               | 0 / 0          |  |  |
| Tremor   |                |  |  |
| subjects affected / exposed                              | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all          | 0 / 0          |  |  |
| deaths causally related to treatment / all               | 0 / 0          |  |  |
| Immune effector cell-associated ~ neurotoxicity syndrome |                |  |  |
| subjects affected / exposed                              | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all          | 0 / 0          |  |  |
| deaths causally related to treatment / all               | 0 / 0          |  |  |
| Dysgraphia   |                |  |  |
| subjects affected / exposed                              | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all          | 1 / 1          |  |  |
| deaths causally related to treatment / all               | 0 / 0          |  |  |
| Headache   |                |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Syncope   |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Depressed level of consciousness                |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Dysarthria                                      |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Haemorrhage intracranial                        |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Leukoencephalopathy                             |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 1 / 1          |  |  |  |
| Presyncope                                      |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Apraxia   |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Ataxia  |                |  |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Brain injury                                    |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Cerebral venous sinus thrombosis                |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Cerebellar infarction                           |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Brain oedema                                    |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Cognitive disorder                              |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Disturbance in attention                        |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Dyspraxia                                       |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Hemiparesis                                     |                |  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Lethargy  |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Memory impairment                               |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Migraine with aura                              |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Toxic encephalopathy                            |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 1 / 1          |  |  |
| Seizure like phenomena                          |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Quadriplegia                                    |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Blood and lymphatic system disorders            |                |  |  |
| Febrile neutropenia                             |                |  |  |
| subjects affected / exposed                     | 2 / 40 (5.00%) |  |  |
| occurrences causally related to treatment / all | 2 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Neutropenia                                     |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Anaemia   |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Bone marrow failure                             |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pancytopenia                                    |                |  |  |
| subjects affected / exposed                     | 2 / 40 (5.00%) |  |  |
| occurrences causally related to treatment / all | 2 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Febrile bone marrow aplasia                     |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Leukopenia                                      |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Thrombocytopenia                                |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Eye disorders                                   |                |  |  |
| Visual impairment                               |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal disorders                      |                |  |  |



|   |                |  |  |  |
|---|----------------|--|--|--|
| Vomiting  |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Abdominal pain                                  |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Dysphagia                                       |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Ascites   |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pancreatitis                                    |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Diarrhoea                                       |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Enteritis                                       |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Tongue ulceration                               |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Rectal haemorrhage                              |                |  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nausea  |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastritis                                       |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hepatobiliary disorders                         |                |  |  |
| Cholecystitis                                   |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Skin and subcutaneous tissue disorders          |                |  |  |
| Toxic skin eruption                             |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal and urinary disorders                     |                |  |  |
| Acute kidney injury                             |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal failure                                   |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Anuria  |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Cystitis haemorrhagic                           |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Haematuria                                      |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Back pain                                       |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Muscular weakness                               |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pain in extremity                               |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Amyotrophy                                      |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Arthralgia                                      |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Bone pain                                       |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Musculoskeletal pain                            |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Pneumonia                                       |                |  |  |
| subjects affected / exposed                     | 3 / 40 (7.50%) |  |  |
| occurrences causally related to treatment / all | 3 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Sepsis  |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Covid-19  |                |  |  |
| subjects affected / exposed                     | 3 / 40 (7.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 4          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| Urinary tract infection                         |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Herpes zoster                                   |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Septic shock                                    |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Bacteraemia                                     |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cellulitis                                      |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pneumocystis jirovecii pneumonia                |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Escherichia bacteraemia                         |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Clostridium difficile infection                 |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Clostridium difficile colitis                   |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Rhinovirus infection                            |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Covid-19 pneumonia                              |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cytomegalovirus colitis                         |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Bronchitis                                      |                |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Adenovirus infection                            |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Anal abscess                                    |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Atypical pneumonia                              |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Cytomegalovirus enteritis                       |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Device related sepsis                           |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Encephalitis                                    |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Escherichia sepsis                              |                |  |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Human herpesvirus 6 encephalitis                |                |  |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Influenza                                       |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Klebsiella infection                            |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Meningitis                                      |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Myelitis  |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Oral herpes                                     |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Parainfluenzae virus infection                  |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumococcal sepsis                             |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Peritonitis                                     |                |  |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumocystis jirovecii infection                |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumonia necrotising                           |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumonia influenzal                            |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumonia respiratory syncytial ~ viral         |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumonia staphylococcal                        |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pseudomonal sepsis                              |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Respiratory tract infection                     |                |  |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Rhinitis  |                |  |  |  |



|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Rotavirus infection                             |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Sinusitis                                       |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Soft tissue infection                           |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Urosepsis                                       |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| Upper respiratory tract infection               |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Viral upper respiratory tract ~ infection       |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |
| Dehydration                                     |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Acidosis  |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Decreased appetite                              |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hypercalcaemia                                  |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hypoglycaemia                                   |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hyponatraemia                                   |                |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Lactic acidosis                                 |                |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                                   | Phase 1 Study:<br>Axicabtagene<br>Ciloleucel and<br>Conditioning Chemot | Phase 2 (Pivotal<br>Study): Cohort 1 | Phase 2 (Pivotal<br>Study): Cohort 2 |
|---|---|--------------------------------------|--------------------------------------|
| Total subjects affected by non-serious adverse events               |   |                                      |                                      |
| subjects affected / exposed   | 7 / 7 (100.00%)   | 77 / 77 (100.00%)                    | 23 / 24 (95.83%)                     |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |                                      |                                      |
| Squamous cell carcinoma   |   |                                      |                                      |

|  |                |                  |                  |
|--|----------------|------------------|------------------|
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 77 (0.00%)   | 0 / 24 (0.00%)   |
| occurrences (all)                                    | 0              | 0                | 0                |
| Myelodysplastic syndrome                             |                |                  |                  |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 1 / 77 (1.30%)   | 0 / 24 (0.00%)   |
| occurrences (all)                                    | 0              | 1                | 0                |
| Cancer pain  |                |                  |                  |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 77 (0.00%)   | 0 / 24 (0.00%)   |
| occurrences (all)                                    | 0              | 0                | 0                |
| Vascular disorders                                   |                |                  |                  |
| Hypotension  |                |                  |                  |
| subjects affected / exposed                          | 3 / 7 (42.86%) | 44 / 77 (57.14%) | 14 / 24 (58.33%) |
| occurrences (all)                                    | 3              | 49               | 22               |
| Hypertension   |                |                  |                  |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 9 / 77 (11.69%)  | 4 / 24 (16.67%)  |
| occurrences (all)                                    | 1              | 14               | 8                |
| Capillary leak syndrome                              |                |                  |                  |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 2 / 77 (2.60%)   | 0 / 24 (0.00%)   |
| occurrences (all)                                    | 1              | 2                | 0                |
| Deep vein thrombosis                                 |                |                  |                  |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 2 / 77 (2.60%)   | 0 / 24 (0.00%)   |
| occurrences (all)                                    | 0              | 2                | 0                |
| Hot flush  |                |                  |                  |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 77 (0.00%)   | 0 / 24 (0.00%)   |
| occurrences (all)                                    | 0              | 0                | 0                |
| Embolism   |                |                  |                  |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 77 (0.00%)   | 0 / 24 (0.00%)   |
| occurrences (all)                                    | 0              | 0                | 0                |
| Subclavian vein thrombosis                           |                |                  |                  |
| subjects affected / exposed                          | 0 / 7 (0.00%)  | 0 / 77 (0.00%)   | 0 / 24 (0.00%)   |
| occurrences (all)                                    | 0              | 0                | 0                |
| General disorders and administration site conditions |                |                  |                  |
| Chills   |                |                  |                  |
| subjects affected / exposed                          | 1 / 7 (14.29%) | 32 / 77 (41.56%) | 7 / 24 (29.17%)  |
| occurrences (all)                                    | 1              | 34               | 7                |
| Fatigue  |                |                  |                  |

|                             |                 |                  |                  |
|-----------------------------|-----------------|------------------|------------------|
| subjects affected / exposed | 2 / 7 (28.57%)  | 34 / 77 (44.16%) | 12 / 24 (50.00%) |
| occurrences (all)           | 3               | 41               | 15               |
| Pyrexia                     |                 |                  |                  |
| subjects affected / exposed | 7 / 7 (100.00%) | 66 / 77 (85.71%) | 21 / 24 (87.50%) |
| occurrences (all)           | 9               | 81               | 32               |
| Asthenia                    |                 |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)   | 5 / 77 (6.49%)   | 2 / 24 (8.33%)   |
| occurrences (all)           | 0               | 5                | 2                |
| Pain                        |                 |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)   | 5 / 77 (6.49%)   | 1 / 24 (4.17%)   |
| occurrences (all)           | 0               | 5                | 1                |
| Malaise                     |                 |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)   | 4 / 77 (5.19%)   | 0 / 24 (0.00%)   |
| occurrences (all)           | 0               | 4                | 0                |
| Non-cardiac chest pain      |                 |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)   | 5 / 77 (6.49%)   | 2 / 24 (8.33%)   |
| occurrences (all)           | 0               | 5                | 2                |
| Gait disturbance            |                 |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)   | 2 / 77 (2.60%)   | 0 / 24 (0.00%)   |
| occurrences (all)           | 0               | 2                | 0                |
| Influenza like illness      |                 |                  |                  |
| subjects affected / exposed | 1 / 7 (14.29%)  | 0 / 77 (0.00%)   | 0 / 24 (0.00%)   |
| occurrences (all)           | 1               | 0                | 0                |
| Oedema                      |                 |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)   | 1 / 77 (1.30%)   | 0 / 24 (0.00%)   |
| occurrences (all)           | 0               | 1                | 0                |
| Oedema peripheral           |                 |                  |                  |
| subjects affected / exposed | 1 / 7 (14.29%)  | 12 / 77 (15.58%) | 2 / 24 (8.33%)   |
| occurrences (all)           | 1               | 14               | 2                |
| Chest pain                  |                 |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)   | 0 / 77 (0.00%)   | 0 / 24 (0.00%)   |
| occurrences (all)           | 0               | 0                | 0                |
| Peripheral swelling         |                 |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)   | 2 / 77 (2.60%)   | 0 / 24 (0.00%)   |
| occurrences (all)           | 0               | 2                | 0                |
| Swelling                    |                 |                  |                  |

|  |                     |                        |                       |
|--|---------------------|------------------------|-----------------------|
| subjects affected / exposed<br>occurrences (all)   | 1 / 7 (14.29%)<br>1 | 1 / 77 (1.30%)<br>1    | 1 / 24 (4.17%)<br>1   |
| Puncture site pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0    | 0 / 24 (0.00%)<br>0   |
| Catheter site pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0    | 1 / 24 (4.17%)<br>1   |
| Hernia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 7 (14.29%)<br>1 | 0 / 77 (0.00%)<br>0    | 0 / 24 (0.00%)<br>0   |
| Immune system disorders<br>Hypogammaglobulinaemia<br>subjects affected / exposed<br>occurrences (all)          | 3 / 7 (42.86%)<br>3 | 10 / 77 (12.99%)<br>10 | 3 / 24 (12.50%)<br>3  |
| Graft versus host disease<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0    | 0 / 24 (0.00%)<br>0   |
| Reproductive system and breast disorders<br>Scrotal oedema<br>subjects affected / exposed<br>occurrences (all) | 0 / 7 (0.00%)<br>0  | 1 / 77 (1.30%)<br>1    | 0 / 24 (0.00%)<br>0   |
| Perineal pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0    | 0 / 24 (0.00%)<br>0   |
| Respiratory, thoracic and mediastinal disorders<br>Hypoxia<br>subjects affected / exposed<br>occurrences (all) | 4 / 7 (57.14%)<br>5 | 24 / 77 (31.17%)<br>27 | 5 / 24 (20.83%)<br>5  |
| Cough<br>subjects affected / exposed<br>occurrences (all)  | 2 / 7 (28.57%)<br>4 | 18 / 77 (23.38%)<br>20 | 6 / 24 (25.00%)<br>12 |
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)   | 1 / 7 (14.29%)<br>2 | 4 / 77 (5.19%)<br>4    | 1 / 24 (4.17%)<br>1   |
| Oropharyngeal pain   |                     |                        |                       |

|                             |                |                  |                 |
|-----------------------------|----------------|------------------|-----------------|
| subjects affected / exposed | 1 / 7 (14.29%) | 4 / 77 (5.19%)   | 2 / 24 (8.33%)  |
| occurrences (all)           | 1              | 5                | 2               |
| Pleural effusion            |                |                  |                 |
| subjects affected / exposed | 3 / 7 (42.86%) | 9 / 77 (11.69%)  | 1 / 24 (4.17%)  |
| occurrences (all)           | 3              | 9                | 1               |
| Dyspnoea                    |                |                  |                 |
| subjects affected / exposed | 3 / 7 (42.86%) | 11 / 77 (14.29%) | 4 / 24 (16.67%) |
| occurrences (all)           | 4              | 11               | 5               |
| Wheezing                    |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 4 / 77 (5.19%)   | 0 / 24 (0.00%)  |
| occurrences (all)           | 0              | 4                | 0               |
| Pulmonary oedema            |                |                  |                 |
| subjects affected / exposed | 2 / 7 (28.57%) | 5 / 77 (6.49%)   | 0 / 24 (0.00%)  |
| occurrences (all)           | 2              | 6                | 0               |
| Upper-airway cough syndrome |                |                  |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 4 / 77 (5.19%)   | 1 / 24 (4.17%)  |
| occurrences (all)           | 1              | 4                | 1               |
| Tachypnoea                  |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 2 / 77 (2.60%)   | 1 / 24 (4.17%)  |
| occurrences (all)           | 0              | 2                | 1               |
| Hiccups                     |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 3 / 77 (3.90%)   | 1 / 24 (4.17%)  |
| occurrences (all)           | 0              | 3                | 1               |
| Laryngeal haemorrhage       |                |                  |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 77 (0.00%)   | 0 / 24 (0.00%)  |
| occurrences (all)           | 1              | 0                | 0               |
| Rhinitis allergic           |                |                  |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 77 (0.00%)   | 1 / 24 (4.17%)  |
| occurrences (all)           | 1              | 0                | 1               |
| Rhinorrhoea                 |                |                  |                 |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 77 (1.30%)   | 0 / 24 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Atelectasis                 |                |                  |                 |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 77 (2.60%)   | 0 / 24 (0.00%)  |
| occurrences (all)           | 1              | 2                | 0               |
| Paranasal cyst              |                |                  |                 |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 7 (14.29%)<br>1 | 0 / 77 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0 |
| Psychiatric disorders                            |                     |                     |                     |
| Anxiety  |                     |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 9 / 77 (11.69%)     | 3 / 24 (12.50%)     |
| occurrences (all)                                | 0                   | 9                   | 3                   |
| Insomnia   |                     |                     |                     |
| subjects affected / exposed                      | 1 / 7 (14.29%)      | 7 / 77 (9.09%)      | 2 / 24 (8.33%)      |
| occurrences (all)                                | 1                   | 7                   | 4                   |
| Confusional state                                |                     |                     |                     |
| subjects affected / exposed                      | 1 / 7 (14.29%)      | 19 / 77 (24.68%)    | 8 / 24 (33.33%)     |
| occurrences (all)                                | 1                   | 20                  | 10                  |
| Agitation  |                     |                     |                     |
| subjects affected / exposed                      | 1 / 7 (14.29%)      | 5 / 77 (6.49%)      | 3 / 24 (12.50%)     |
| occurrences (all)                                | 1                   | 6                   | 3                   |
| Hallucination                                    |                     |                     |                     |
| subjects affected / exposed                      | 1 / 7 (14.29%)      | 4 / 77 (5.19%)      | 0 / 24 (0.00%)      |
| occurrences (all)                                | 1                   | 4                   | 0                   |
| Mental status changes                            |                     |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 4 / 77 (5.19%)      | 1 / 24 (4.17%)      |
| occurrences (all)                                | 0                   | 4                   | 1                   |
| Delirium   |                     |                     |                     |
| subjects affected / exposed                      | 1 / 7 (14.29%)      | 1 / 77 (1.30%)      | 0 / 24 (0.00%)      |
| occurrences (all)                                | 1                   | 2                   | 0                   |
| Bradyphrenia                                     |                     |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 1 / 77 (1.30%)      | 0 / 24 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Disorientation                                   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 1 / 77 (1.30%)      | 1 / 24 (4.17%)      |
| occurrences (all)                                | 0                   | 1                   | 1                   |
| Depression                                       |                     |                     |                     |
| subjects affected / exposed                      | 0 / 7 (0.00%)       | 1 / 77 (1.30%)      | 1 / 24 (4.17%)      |
| occurrences (all)                                | 0                   | 1                   | 1                   |
| Restlessness                                     |                     |                     |                     |
| subjects affected / exposed                      | 1 / 7 (14.29%)      | 2 / 77 (2.60%)      | 1 / 24 (4.17%)      |
| occurrences (all)                                | 1                   | 2                   | 1                   |

|  |                     |                        |                       |
|--|---------------------|------------------------|-----------------------|
| Mood altered<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0    | 1 / 24 (4.17%)<br>1   |
| Investigations   |                     |                        |                       |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all)     | 2 / 7 (28.57%)<br>7 | 23 / 77 (29.87%)<br>63 | 8 / 24 (33.33%)<br>15 |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)             | 2 / 7 (28.57%)<br>6 | 25 / 77 (32.47%)<br>46 | 5 / 24 (20.83%)<br>10 |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)           | 2 / 7 (28.57%)<br>9 | 27 / 77 (35.06%)<br>63 | 7 / 24 (29.17%)<br>16 |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)           | 2 / 7 (28.57%)<br>2 | 12 / 77 (15.58%)<br>24 | 6 / 24 (25.00%)<br>9  |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)         | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0    | 0 / 24 (0.00%)<br>0   |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                     | 2 / 7 (28.57%)<br>3 | 11 / 77 (14.29%)<br>18 | 4 / 24 (16.67%)<br>9  |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 2 / 7 (28.57%)<br>2 | 11 / 77 (14.29%)<br>14 | 5 / 24 (20.83%)<br>7  |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)   | 3 / 7 (42.86%)<br>3 | 13 / 77 (16.88%)<br>14 | 5 / 24 (20.83%)<br>8  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)           | 0 / 7 (0.00%)<br>0  | 4 / 77 (5.19%)<br>5    | 2 / 24 (8.33%)<br>2   |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 7 (14.29%)<br>1 | 3 / 77 (3.90%)<br>3    | 1 / 24 (4.17%)<br>3   |
| Serum ferritin increased   |                     |                        |                       |



|                                     |                |                |                |
|-------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed         | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 1 / 24 (4.17%) |
| occurrences (all)                   | 0              | 1              | 1              |
| Weight increased                    |                |                |                |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 4 / 77 (5.19%) | 0 / 24 (0.00%) |
| occurrences (all)                   | 0              | 6              | 0              |
| Blood bilirubin increased           |                |                |                |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 3 / 77 (3.90%) | 1 / 24 (4.17%) |
| occurrences (all)                   | 0              | 4              | 1              |
| Gamma-glutamyltransferase increased |                |                |                |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Blood immunoglobulin G decreased    |                |                |                |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences (all)                   | 0              | 3              | 0              |
| Blood potassium decreased           |                |                |                |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Urine output decreased              |                |                |                |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Immunoglobulins decreased           |                |                |                |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Blood fibrinogen decreased          |                |                |                |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Oxygen saturation decreased         |                |                |                |
| subjects affected / exposed         | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences (all)                   | 0              | 1              | 0              |
| Blood albumin decreased             |                |                |                |
| subjects affected / exposed         | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                   | 1              | 0              | 0              |
| Blood magnesium decreased           |                |                |                |
| subjects affected / exposed         | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                   | 1              | 0              | 0              |

|  |                |                  |                 |
|--|----------------|------------------|-----------------|
| Injury, poisoning and procedural complications |                |                  |                 |
| Skin abrasion                                  |                |                  |                 |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 1 / 77 (1.30%)   | 0 / 24 (0.00%)  |
| occurrences (all)                              | 1              | 1                | 0               |
| Infusion related reaction                      |                |                  |                 |
| subjects affected / exposed                    | 2 / 7 (28.57%) | 1 / 77 (1.30%)   | 1 / 24 (4.17%)  |
| occurrences (all)                              | 2              | 1                | 1               |
| Fall   |                |                  |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 5 / 77 (6.49%)   | 2 / 24 (8.33%)  |
| occurrences (all)                              | 0              | 5                | 2               |
| Head injury                                    |                |                  |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 0 / 77 (0.00%)   | 0 / 24 (0.00%)  |
| occurrences (all)                              | 0              | 0                | 0               |
| Procedural pain                                |                |                  |                 |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 1 / 77 (1.30%)   | 0 / 24 (0.00%)  |
| occurrences (all)                              | 1              | 1                | 0               |
| Cardiac disorders                              |                |                  |                 |
| Atrial fibrillation                            |                |                  |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 5 / 77 (6.49%)   | 1 / 24 (4.17%)  |
| occurrences (all)                              | 0              | 5                | 1               |
| Sinus bradycardia                              |                |                  |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 5 / 77 (6.49%)   | 2 / 24 (8.33%)  |
| occurrences (all)                              | 0              | 5                | 8               |
| Ventricular arrhythmia                         |                |                  |                 |
| subjects affected / exposed                    | 1 / 7 (14.29%) | 3 / 77 (3.90%)   | 2 / 24 (8.33%)  |
| occurrences (all)                              | 1              | 3                | 2               |
| Sinus tachycardia                              |                |                  |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 19 / 77 (24.68%) | 2 / 24 (8.33%)  |
| occurrences (all)                              | 0              | 25               | 11              |
| Tachycardia                                    |                |                  |                 |
| subjects affected / exposed                    | 3 / 7 (42.86%) | 29 / 77 (37.66%) | 8 / 24 (33.33%) |
| occurrences (all)                              | 3              | 35               | 9               |
| Bradycardia                                    |                |                  |                 |
| subjects affected / exposed                    | 0 / 7 (0.00%)  | 1 / 77 (1.30%)   | 0 / 24 (0.00%)  |
| occurrences (all)                              | 0              | 4                | 0               |
| Acute left ventricular failure                 |                |                  |                 |

|                             |                |                  |                  |
|-----------------------------|----------------|------------------|------------------|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 77 (0.00%)   | 0 / 24 (0.00%)   |
| occurrences (all)           | 1              | 0                | 0                |
| Ventricular tachycardia     |                |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 3 / 77 (3.90%)   | 0 / 24 (0.00%)   |
| occurrences (all)           | 0              | 4                | 0                |
| Nervous system disorders    |                |                  |                  |
| Tremor                      |                |                  |                  |
| subjects affected / exposed | 4 / 7 (57.14%) | 23 / 77 (29.87%) | 6 / 24 (25.00%)  |
| occurrences (all)           | 4              | 23               | 7                |
| Headache                    |                |                  |                  |
| subjects affected / exposed | 3 / 7 (42.86%) | 34 / 77 (44.16%) | 12 / 24 (50.00%) |
| occurrences (all)           | 4              | 39               | 14               |
| Encephalopathy              |                |                  |                  |
| subjects affected / exposed | 4 / 7 (57.14%) | 20 / 77 (25.97%) | 6 / 24 (25.00%)  |
| occurrences (all)           | 5              | 22               | 7                |
| Dysarthria                  |                |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 3 / 77 (3.90%)   | 1 / 24 (4.17%)   |
| occurrences (all)           | 0              | 3                | 1                |
| Somnolence                  |                |                  |                  |
| subjects affected / exposed | 3 / 7 (42.86%) | 10 / 77 (12.99%) | 4 / 24 (16.67%)  |
| occurrences (all)           | 3              | 12               | 5                |
| Aphasia                     |                |                  |                  |
| subjects affected / exposed | 1 / 7 (14.29%) | 13 / 77 (16.88%) | 4 / 24 (16.67%)  |
| occurrences (all)           | 1              | 14               | 5                |
| Dizziness                   |                |                  |                  |
| subjects affected / exposed | 1 / 7 (14.29%) | 12 / 77 (15.58%) | 9 / 24 (37.50%)  |
| occurrences (all)           | 1              | 13               | 10               |
| Memory impairment           |                |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 6 / 77 (7.79%)   | 2 / 24 (8.33%)   |
| occurrences (all)           | 0              | 6                | 2                |
| Paraesthesia                |                |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 77 (1.30%)   | 0 / 24 (0.00%)   |
| occurrences (all)           | 0              | 1                | 0                |
| Dysgeusia                   |                |                  |                  |
| subjects affected / exposed | 0 / 7 (0.00%)  | 5 / 77 (6.49%)   | 2 / 24 (8.33%)   |
| occurrences (all)           | 0              | 5                | 2                |

|                                 |                |                |                |
|---------------------------------|----------------|----------------|----------------|
| Dyskinesia                      |                |                |                |
| subjects affected / exposed     | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)               | 1              | 0              | 0              |
| Dysgraphia                      |                |                |                |
| subjects affected / exposed     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Seizure                         |                |                |                |
| subjects affected / exposed     | 0 / 7 (0.00%)  | 3 / 77 (3.90%) | 0 / 24 (0.00%) |
| occurrences (all)               | 0              | 6              | 0              |
| Disturbance in attention        |                |                |                |
| subjects affected / exposed     | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 2 / 24 (8.33%) |
| occurrences (all)               | 0              | 1              | 3              |
| Post herpetic neuralgia         |                |                |                |
| subjects affected / exposed     | 1 / 7 (14.29%) | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences (all)               | 1              | 1              | 0              |
| Head discomfort                 |                |                |                |
| subjects affected / exposed     | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences (all)               | 0              | 1              | 0              |
| Dementia                        |                |                |                |
| subjects affected / exposed     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Peripheral sensory neuropathy   |                |                |                |
| subjects affected / exposed     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences (all)               | 0              | 0              | 1              |
| Apraxia                         |                |                |                |
| subjects affected / exposed     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Muscle contractions involuntary |                |                |                |
| subjects affected / exposed     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Poor sucking reflex             |                |                |                |
| subjects affected / exposed     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |
| Peripheral motor neuropathy     |                |                |                |
| subjects affected / exposed     | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)               | 0              | 0              | 0              |

|   |                     |                        |                        |
|---|---------------------|------------------------|------------------------|
| Presyncope<br>subjects affected / exposed<br>occurrences (all)          | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0    | 1 / 24 (4.17%)<br>1    |
| Sensory loss<br>subjects affected / exposed<br>occurrences (all)        | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0    | 0 / 24 (0.00%)<br>0    |
| Blood and lymphatic system disorders                                    |                     |                        |                        |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)             | 4 / 7 (57.14%)<br>7 | 47 / 77 (61.04%)<br>75 | 13 / 24 (54.17%)<br>20 |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)         | 3 / 7 (42.86%)<br>5 | 26 / 77 (33.77%)<br>41 | 12 / 24 (50.00%)<br>20 |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)    | 2 / 7 (28.57%)<br>2 | 24 / 77 (31.17%)<br>30 | 6 / 24 (25.00%)<br>7   |
| Febrile neutropenia<br>subjects affected / exposed<br>occurrences (all) | 4 / 7 (57.14%)<br>4 | 21 / 77 (27.27%)<br>22 | 8 / 24 (33.33%)<br>9   |
| Pancytopenia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 7 (0.00%)<br>0  | 1 / 77 (1.30%)<br>1    | 1 / 24 (4.17%)<br>1    |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)          | 0 / 7 (0.00%)<br>0  | 13 / 77 (16.88%)<br>19 | 3 / 24 (12.50%)<br>7   |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 7 (0.00%)<br>0  | 5 / 77 (6.49%)<br>6    | 0 / 24 (0.00%)<br>0    |
| Ear and labyrinth disorders   |                     |                        |                        |
| Tinnitus<br>subjects affected / exposed<br>occurrences (all)            | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0    | 0 / 24 (0.00%)<br>0    |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)            | 0 / 7 (0.00%)<br>0  | 1 / 77 (1.30%)<br>1    | 0 / 24 (0.00%)<br>0    |
| Hypoacusis  |                     |                        |                        |

|  |                     |                        |                        |
|--|---------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                                     | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0    | 0 / 24 (0.00%)<br>0    |
| Eye disorders  |                     |                        |                        |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 7 (14.29%)<br>1 | 2 / 77 (2.60%)<br>2    | 2 / 24 (8.33%)<br>2    |
| Vitreous floaters<br>subjects affected / exposed<br>occurrences (all)                | 0 / 7 (0.00%)<br>0  | 1 / 77 (1.30%)<br>1    | 0 / 24 (0.00%)<br>0    |
| Eyelid function disorder<br>subjects affected / exposed<br>occurrences (all)         | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0    | 0 / 24 (0.00%)<br>0    |
| Gastrointestinal disorders   |                     |                        |                        |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 7 (14.29%)<br>1 | 17 / 77 (22.08%)<br>18 | 11 / 24 (45.83%)<br>12 |
| Constipation<br>subjects affected / exposed<br>occurrences (all)                     | 2 / 7 (28.57%)<br>3 | 15 / 77 (19.48%)<br>17 | 5 / 24 (20.83%)<br>9   |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 7 (14.29%)<br>1 | 22 / 77 (28.57%)<br>27 | 12 / 24 (50.00%)<br>13 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                        | 5 / 7 (71.43%)<br>5 | 29 / 77 (37.66%)<br>32 | 8 / 24 (33.33%)<br>9   |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 7 (14.29%)<br>1 | 8 / 77 (10.39%)<br>8   | 3 / 24 (12.50%)<br>3   |
| Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all) | 1 / 7 (14.29%)<br>1 | 2 / 77 (2.60%)<br>2    | 0 / 24 (0.00%)<br>0    |
| Anal incontinence<br>subjects affected / exposed<br>occurrences (all)                | 0 / 7 (0.00%)<br>0  | 1 / 77 (1.30%)<br>1    | 1 / 24 (4.17%)<br>1    |
| Stomatitis   |                     |                        |                        |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed            | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (0.00%)  |
| occurrences (all)                      | 0              | 1              | 0               |
| Dry mouth                              |                |                |                 |
| subjects affected / exposed            | 2 / 7 (28.57%) | 7 / 77 (9.09%) | 3 / 24 (12.50%) |
| occurrences (all)                      | 2              | 7              | 3               |
| Dyspepsia                              |                |                |                 |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 2 / 77 (2.60%) | 1 / 24 (4.17%)  |
| occurrences (all)                      | 0              | 2              | 1               |
| Abdominal distension                   |                |                |                 |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 5 / 77 (6.49%) | 2 / 24 (8.33%)  |
| occurrences (all)                      | 0              | 6              | 2               |
| Abdominal pain upper                   |                |                |                 |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 2 / 77 (2.60%) | 1 / 24 (4.17%)  |
| occurrences (all)                      | 0              | 2              | 1               |
| Dysphagia                              |                |                |                 |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 4 / 77 (5.19%) | 0 / 24 (0.00%)  |
| occurrences (all)                      | 0              | 4              | 0               |
| Toothache                              |                |                |                 |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Rectal haemorrhage                     |                |                |                 |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 1 / 24 (4.17%)  |
| occurrences (all)                      | 0              | 1              | 1               |
| Flatulence                             |                |                |                 |
| subjects affected / exposed            | 1 / 7 (14.29%) | 3 / 77 (3.90%) | 1 / 24 (4.17%)  |
| occurrences (all)                      | 1              | 3              | 1               |
| Ascites                                |                |                |                 |
| subjects affected / exposed            | 1 / 7 (14.29%) | 2 / 77 (2.60%) | 0 / 24 (0.00%)  |
| occurrences (all)                      | 1              | 2              | 0               |
| Odynophagia                            |                |                |                 |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Skin and subcutaneous tissue disorders |                |                |                 |
| Dry skin                               |                |                |                 |
| subjects affected / exposed            | 0 / 7 (0.00%)  | 2 / 77 (2.60%) | 0 / 24 (0.00%)  |
| occurrences (all)                      | 0              | 2              | 0               |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Rash                        |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 2 / 77 (2.60%) | 1 / 24 (4.17%) |
| occurrences (all)           | 0              | 2              | 1              |
| Pruritus                    |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 6 / 77 (7.79%) | 2 / 24 (8.33%) |
| occurrences (all)           | 0              | 6              | 2              |
| Hyperhidrosis               |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences (all)           | 0              | 0              | 1              |
| Alopecia                    |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 2 / 77 (2.60%) | 0 / 24 (0.00%) |
| occurrences (all)           | 0              | 2              | 0              |
| Erythema                    |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Night sweats                |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences (all)           | 0              | 0              | 1              |
| Renal and urinary disorders |                |                |                |
| Dysuria                     |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 2 / 77 (2.60%) | 2 / 24 (8.33%) |
| occurrences (all)           | 0              | 2              | 2              |
| Pollakiuria                 |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 2 / 77 (2.60%) | 0 / 24 (0.00%) |
| occurrences (all)           | 0              | 2              | 0              |
| Acute kidney injury         |                |                |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 6 / 77 (7.79%) | 0 / 24 (0.00%) |
| occurrences (all)           | 1              | 7              | 0              |
| Urinary incontinence        |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 7 / 77 (9.09%) | 1 / 24 (4.17%) |
| occurrences (all)           | 0              | 7              | 1              |
| Urinary retention           |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 4 / 77 (5.19%) | 0 / 24 (0.00%) |
| occurrences (all)           | 0              | 4              | 0              |
| Haematuria                  |                |                |                |



|   |                |                  |                 |
|---|----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 4 / 77 (5.19%)   | 0 / 24 (0.00%)  |
| occurrences (all)                               | 0              | 4                | 0               |
| Urinary tract obstruction                       |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 1 / 77 (1.30%)   | 0 / 24 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0               |
| Bladder spasm                                   |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 0 / 77 (0.00%)   | 0 / 24 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0               |
| Musculoskeletal and connective tissue disorders |                |                  |                 |
| Myalgia   |                |                  |                 |
| subjects affected / exposed                     | 2 / 7 (28.57%) | 10 / 77 (12.99%) | 3 / 24 (12.50%) |
| occurrences (all)                               | 2              | 10               | 3               |
| Pain in extremity                               |                |                  |                 |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 7 / 77 (9.09%)   | 4 / 24 (16.67%) |
| occurrences (all)                               | 1              | 7                | 4               |
| Muscular weakness                               |                |                  |                 |
| subjects affected / exposed                     | 3 / 7 (42.86%) | 11 / 77 (14.29%) | 2 / 24 (8.33%)  |
| occurrences (all)                               | 4              | 11               | 2               |
| Arthralgia                                      |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 12 / 77 (15.58%) | 2 / 24 (8.33%)  |
| occurrences (all)                               | 0              | 13               | 2               |
| Back pain                                       |                |                  |                 |
| subjects affected / exposed                     | 1 / 7 (14.29%) | 13 / 77 (16.88%) | 2 / 24 (8.33%)  |
| occurrences (all)                               | 1              | 14               | 2               |
| Muscle spasms                                   |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 2 / 77 (2.60%)   | 0 / 24 (0.00%)  |
| occurrences (all)                               | 0              | 2                | 0               |
| Flank pain                                      |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 2 / 77 (2.60%)   | 0 / 24 (0.00%)  |
| occurrences (all)                               | 0              | 2                | 0               |
| Bone pain                                       |                |                  |                 |
| subjects affected / exposed                     | 0 / 7 (0.00%)  | 2 / 77 (2.60%)   | 0 / 24 (0.00%)  |
| occurrences (all)                               | 0              | 2                | 0               |
| Neck pain                                       |                |                  |                 |

|   |                     |                     |                      |
|---|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                      | 2 / 7 (28.57%)<br>2 | 3 / 77 (3.90%)<br>3 | 1 / 24 (4.17%)<br>1  |
| Tenosynovitis stenosans<br>subjects affected / exposed<br>occurrences (all)           | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0  |
| Groin pain<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 7 (0.00%)<br>0  | 1 / 77 (1.30%)<br>1 | 0 / 24 (0.00%)<br>0  |
| Infections and infestations   |                     |                     |                      |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 2 / 7 (28.57%)<br>3 | 5 / 77 (6.49%)<br>5 | 4 / 24 (16.67%)<br>4 |
| Herpes zoster<br>subjects affected / exposed<br>occurrences (all)                     | 2 / 7 (28.57%)<br>2 | 3 / 77 (3.90%)<br>3 | 3 / 24 (12.50%)<br>3 |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)                         | 2 / 7 (28.57%)<br>2 | 3 / 77 (3.90%)<br>3 | 2 / 24 (8.33%)<br>3  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)           | 1 / 7 (14.29%)<br>1 | 3 / 77 (3.90%)<br>3 | 1 / 24 (4.17%)<br>1  |
| Pneumonia<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 7 (14.29%)<br>1 | 4 / 77 (5.19%)<br>4 | 0 / 24 (0.00%)<br>0  |
| Candida infection<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 7 (0.00%)<br>0  | 1 / 77 (1.30%)<br>1 | 1 / 24 (4.17%)<br>1  |
| Oral candidiasis<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 7 (14.29%)<br>1 | 1 / 77 (1.30%)<br>1 | 0 / 24 (0.00%)<br>0  |
| Clostridium difficile infection<br>subjects affected / exposed<br>occurrences (all)   | 0 / 7 (0.00%)<br>0  | 5 / 77 (6.49%)<br>5 | 0 / 24 (0.00%)<br>0  |
| Covid-19<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 7 (0.00%)<br>0  | 0 / 77 (0.00%)<br>0 | 0 / 24 (0.00%)<br>0  |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Nasopharyngitis                         |                |                |                |
| subjects affected / exposed             | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 1 / 24 (4.17%) |
| occurrences (all)                       | 0              | 0              | 1              |
| Conjunctivitis                          |                |                |                |
| subjects affected / exposed             | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 2 / 24 (8.33%) |
| occurrences (all)                       | 0              | 0              | 3              |
| Clostridium difficile colitis           |                |                |                |
| subjects affected / exposed             | 0 / 7 (0.00%)  | 2 / 77 (2.60%) | 1 / 24 (4.17%) |
| occurrences (all)                       | 0              | 2              | 1              |
| Respiratory syncytial virus infection   |                |                |                |
| subjects affected / exposed             | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Tooth infection                         |                |                |                |
| subjects affected / exposed             | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |
| Oral herpes                             |                |                |                |
| subjects affected / exposed             | 1 / 7 (14.29%) | 1 / 77 (1.30%) | 0 / 24 (0.00%) |
| occurrences (all)                       | 1              | 1              | 0              |
| Folliculitis                            |                |                |                |
| subjects affected / exposed             | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |
| Rhinitis                                |                |                |                |
| subjects affected / exposed             | 0 / 7 (0.00%)  | 2 / 77 (2.60%) | 0 / 24 (0.00%) |
| occurrences (all)                       | 0              | 2              | 0              |
| Ear infection                           |                |                |                |
| subjects affected / exposed             | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |
| Tinea versicolour                       |                |                |                |
| subjects affected / exposed             | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |
| Viral upper respiratory tract infection |                |                |                |
| subjects affected / exposed             | 1 / 7 (14.29%) | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                       | 1              | 0              | 0              |
| Wound infection                         |                |                |                |
| subjects affected / exposed             | 0 / 7 (0.00%)  | 0 / 77 (0.00%) | 0 / 24 (0.00%) |
| occurrences (all)                       | 0              | 0              | 0              |

|                                    |                |                  |                  |
|------------------------------------|----------------|------------------|------------------|
| Metabolism and nutrition disorders |                |                  |                  |
| Hypokalaemia                       |                |                  |                  |
| subjects affected / exposed        | 2 / 7 (28.57%) | 23 / 77 (29.87%) | 8 / 24 (33.33%)  |
| occurrences (all)                  | 2              | 28               | 11               |
| Decreased appetite                 |                |                  |                  |
| subjects affected / exposed        | 3 / 7 (42.86%) | 31 / 77 (40.26%) | 12 / 24 (50.00%) |
| occurrences (all)                  | 3              | 33               | 14               |
| Hypophosphataemia                  |                |                  |                  |
| subjects affected / exposed        | 3 / 7 (42.86%) | 19 / 77 (24.68%) | 6 / 24 (25.00%)  |
| occurrences (all)                  | 5              | 29               | 10               |
| Hyponatraemia                      |                |                  |                  |
| subjects affected / exposed        | 4 / 7 (57.14%) | 20 / 77 (25.97%) | 10 / 24 (41.67%) |
| occurrences (all)                  | 4              | 26               | 11               |
| Hypoalbuminaemia                   |                |                  |                  |
| subjects affected / exposed        | 2 / 7 (28.57%) | 22 / 77 (28.57%) | 9 / 24 (37.50%)  |
| occurrences (all)                  | 2              | 24               | 16               |
| Hypocalcaemia                      |                |                  |                  |
| subjects affected / exposed        | 2 / 7 (28.57%) | 23 / 77 (29.87%) | 11 / 24 (45.83%) |
| occurrences (all)                  | 2              | 25               | 11               |
| Hypernatraemia                     |                |                  |                  |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 0 / 77 (0.00%)   | 1 / 24 (4.17%)   |
| occurrences (all)                  | 0              | 0                | 2                |
| Hyperglycaemia                     |                |                  |                  |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 12 / 77 (15.58%) | 6 / 24 (25.00%)  |
| occurrences (all)                  | 0              | 23               | 26               |
| Hypomagnesaemia                    |                |                  |                  |
| subjects affected / exposed        | 2 / 7 (28.57%) | 5 / 77 (6.49%)   | 4 / 24 (16.67%)  |
| occurrences (all)                  | 3              | 5                | 4                |
| Dehydration                        |                |                  |                  |
| subjects affected / exposed        | 2 / 7 (28.57%) | 5 / 77 (6.49%)   | 4 / 24 (16.67%)  |
| occurrences (all)                  | 2              | 6                | 4                |
| Hyperkalaemia                      |                |                  |                  |
| subjects affected / exposed        | 0 / 7 (0.00%)  | 6 / 77 (7.79%)   | 1 / 24 (4.17%)   |
| occurrences (all)                  | 0              | 10               | 3                |
| Hypermagnesaemia                   |                |                  |                  |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 7 (0.00%)  | 1 / 77 (1.30%) | 2 / 24 (8.33%) |
| occurrences (all)           | 0              | 1              | 2              |
| Malnutrition                |                |                |                |
| subjects affected / exposed | 0 / 7 (0.00%)  | 4 / 77 (5.19%) | 0 / 24 (0.00%) |
| occurrences (all)           | 0              | 4              | 0              |
| Metabolic acidosis          |                |                |                |
| subjects affected / exposed | 1 / 7 (14.29%) | 3 / 77 (3.90%) | 0 / 24 (0.00%) |
| occurrences (all)           | 1              | 3              | 0              |

| <b>Non-serious adverse events</b>                                   | Phase 2 (Safety Management Study): Cohort 3 | Phase 2 (Safety Management Study): Cohort 4 | Phase 2 (Safety Management Study): Cohort 5 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events               |   |   |   |
| subjects affected / exposed   | 38 / 38 (100.00%)                           | 41 / 41 (100.00%)                           | 50 / 50 (100.00%)                           |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |   |   |
| Squamous cell carcinoma   |   |   |   |
| subjects affected / exposed   | 0 / 38 (0.00%)                              | 0 / 41 (0.00%)                              | 0 / 50 (0.00%)                              |
| occurrences (all)   | 0   | 0   | 0   |
| Myelodysplastic syndrome  |   |   |   |
| subjects affected / exposed   | 0 / 38 (0.00%)                              | 1 / 41 (2.44%)                              | 2 / 50 (4.00%)                              |
| occurrences (all)   | 0   | 1   | 2   |
| Cancer pain   |   |   |   |
| subjects affected / exposed   | 0 / 38 (0.00%)                              | 1 / 41 (2.44%)                              | 0 / 50 (0.00%)                              |
| occurrences (all)   | 0   | 1   | 0   |
| Vascular disorders  |   |   |   |
| Hypotension   |   |   |   |
| subjects affected / exposed   | 22 / 38 (57.89%)                            | 24 / 41 (58.54%)                            | 25 / 50 (50.00%)                            |
| occurrences (all)   | 30  | 30  | 28  |
| Hypertension  |   |   |   |
| subjects affected / exposed   | 2 / 38 (5.26%)                              | 2 / 41 (4.88%)                              | 3 / 50 (6.00%)                              |
| occurrences (all)   | 2   | 2   | 3   |
| Capillary leak syndrome   |   |   |   |
| subjects affected / exposed   | 0 / 38 (0.00%)                              | 1 / 41 (2.44%)                              | 0 / 50 (0.00%)                              |
| occurrences (all)   | 0   | 1   | 0   |
| Deep vein thrombosis  |   |   |   |
| subjects affected / exposed   | 2 / 38 (5.26%)                              | 0 / 41 (0.00%)                              | 0 / 50 (0.00%)                              |
| occurrences (all)   | 2   | 0   | 0   |
| Hot flush   |   |   |   |

|  |                  |                  |                  |
|--|------------------|------------------|------------------|
| subjects affected / exposed                          | 0 / 38 (0.00%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                                    | 0                | 0                | 0                |
| Embolism   |                  |                  |                  |
| subjects affected / exposed                          | 0 / 38 (0.00%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                                    | 0                | 0                | 0                |
| Subclavian vein thrombosis                           |                  |                  |                  |
| subjects affected / exposed                          | 0 / 38 (0.00%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                                    | 0                | 0                | 0                |
| General disorders and administration site conditions |                  |                  |                  |
| Chills   |                  |                  |                  |
| subjects affected / exposed                          | 11 / 38 (28.95%) | 11 / 41 (26.83%) | 14 / 50 (28.00%) |
| occurrences (all)                                    | 16               | 13               | 15               |
| Fatigue  |                  |                  |                  |
| subjects affected / exposed                          | 18 / 38 (47.37%) | 19 / 41 (46.34%) | 12 / 50 (24.00%) |
| occurrences (all)                                    | 21               | 20               | 13               |
| Pyrexia  |                  |                  |                  |
| subjects affected / exposed                          | 35 / 38 (92.11%) | 39 / 41 (95.12%) | 40 / 50 (80.00%) |
| occurrences (all)                                    | 48               | 49               | 60               |
| Asthenia   |                  |                  |                  |
| subjects affected / exposed                          | 3 / 38 (7.89%)   | 2 / 41 (4.88%)   | 4 / 50 (8.00%)   |
| occurrences (all)                                    | 3                | 2                | 5                |
| Pain   |                  |                  |                  |
| subjects affected / exposed                          | 5 / 38 (13.16%)  | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                                    | 5                | 0                | 0                |
| Malaise  |                  |                  |                  |
| subjects affected / exposed                          | 1 / 38 (2.63%)   | 1 / 41 (2.44%)   | 2 / 50 (4.00%)   |
| occurrences (all)                                    | 1                | 1                | 2                |
| Non-cardiac chest pain                               |                  |                  |                  |
| subjects affected / exposed                          | 2 / 38 (5.26%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                                    | 2                | 0                | 0                |
| Gait disturbance                                     |                  |                  |                  |
| subjects affected / exposed                          | 4 / 38 (10.53%)  | 0 / 41 (0.00%)   | 2 / 50 (4.00%)   |
| occurrences (all)                                    | 4                | 0                | 2                |
| Influenza like illness                               |                  |                  |                  |

|  |                 |                 |                |
|--|-----------------|-----------------|----------------|
| subjects affected / exposed              | 2 / 38 (5.26%)  | 2 / 41 (4.88%)  | 0 / 50 (0.00%) |
| occurrences (all)                        | 3               | 2               | 0              |
| Oedema                                   |                 |                 |                |
| subjects affected / exposed              | 0 / 38 (0.00%)  | 1 / 41 (2.44%)  | 2 / 50 (4.00%) |
| occurrences (all)                        | 0               | 1               | 2              |
| Oedema peripheral                        |                 |                 |                |
| subjects affected / exposed              | 6 / 38 (15.79%) | 2 / 41 (4.88%)  | 3 / 50 (6.00%) |
| occurrences (all)                        | 7               | 2               | 3              |
| Chest pain                               |                 |                 |                |
| subjects affected / exposed              | 1 / 38 (2.63%)  | 3 / 41 (7.32%)  | 0 / 50 (0.00%) |
| occurrences (all)                        | 1               | 3               | 0              |
| Peripheral swelling                      |                 |                 |                |
| subjects affected / exposed              | 0 / 38 (0.00%)  | 1 / 41 (2.44%)  | 0 / 50 (0.00%) |
| occurrences (all)                        | 0               | 1               | 0              |
| Swelling                                 |                 |                 |                |
| subjects affected / exposed              | 1 / 38 (2.63%)  | 0 / 41 (0.00%)  | 0 / 50 (0.00%) |
| occurrences (all)                        | 1               | 0               | 0              |
| Puncture site pain                       |                 |                 |                |
| subjects affected / exposed              | 0 / 38 (0.00%)  | 3 / 41 (7.32%)  | 0 / 50 (0.00%) |
| occurrences (all)                        | 0               | 3               | 0              |
| Catheter site pain                       |                 |                 |                |
| subjects affected / exposed              | 0 / 38 (0.00%)  | 0 / 41 (0.00%)  | 0 / 50 (0.00%) |
| occurrences (all)                        | 0               | 0               | 0              |
| Hernia                                   |                 |                 |                |
| subjects affected / exposed              | 0 / 38 (0.00%)  | 0 / 41 (0.00%)  | 0 / 50 (0.00%) |
| occurrences (all)                        | 0               | 0               | 0              |
| Immune system disorders                  |                 |                 |                |
| Hypogammaglobulinaemia                   |                 |                 |                |
| subjects affected / exposed              | 2 / 38 (5.26%)  | 6 / 41 (14.63%) | 1 / 50 (2.00%) |
| occurrences (all)                        | 2               | 6               | 1              |
| Graft versus host disease                |                 |                 |                |
| subjects affected / exposed              | 0 / 38 (0.00%)  | 0 / 41 (0.00%)  | 1 / 50 (2.00%) |
| occurrences (all)                        | 0               | 0               | 1              |
| Reproductive system and breast disorders |                 |                 |                |

|   |                 |                  |                 |
|---|-----------------|------------------|-----------------|
| Scrotal oedema                                  |                 |                  |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%)  | 0 / 41 (0.00%)   | 0 / 50 (0.00%)  |
| occurrences (all)                               | 0               | 0                | 0               |
| Perineal pain                                   |                 |                  |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%)  | 0 / 41 (0.00%)   | 0 / 50 (0.00%)  |
| occurrences (all)                               | 0               | 0                | 0               |
| Respiratory, thoracic and mediastinal disorders |                 |                  |                 |
| Hypoxia   |                 |                  |                 |
| subjects affected / exposed                     | 9 / 38 (23.68%) | 6 / 41 (14.63%)  | 5 / 50 (10.00%) |
| occurrences (all)                               | 10              | 6                | 5               |
| Cough   |                 |                  |                 |
| subjects affected / exposed                     | 9 / 38 (23.68%) | 11 / 41 (26.83%) | 6 / 50 (12.00%) |
| occurrences (all)                               | 11              | 12               | 6               |
| Nasal congestion                                |                 |                  |                 |
| subjects affected / exposed                     | 2 / 38 (5.26%)  | 1 / 41 (2.44%)   | 0 / 50 (0.00%)  |
| occurrences (all)                               | 2               | 1                | 0               |
| Oropharyngeal pain                              |                 |                  |                 |
| subjects affected / exposed                     | 2 / 38 (5.26%)  | 1 / 41 (2.44%)   | 2 / 50 (4.00%)  |
| occurrences (all)                               | 2               | 1                | 2               |
| Pleural effusion                                |                 |                  |                 |
| subjects affected / exposed                     | 5 / 38 (13.16%) | 2 / 41 (4.88%)   | 0 / 50 (0.00%)  |
| occurrences (all)                               | 5               | 3                | 0               |
| Dyspnoea  |                 |                  |                 |
| subjects affected / exposed                     | 5 / 38 (13.16%) | 3 / 41 (7.32%)   | 4 / 50 (8.00%)  |
| occurrences (all)                               | 5               | 3                | 5               |
| Wheezing  |                 |                  |                 |
| subjects affected / exposed                     | 1 / 38 (2.63%)  | 0 / 41 (0.00%)   | 0 / 50 (0.00%)  |
| occurrences (all)                               | 1               | 0                | 0               |
| Pulmonary oedema                                |                 |                  |                 |
| subjects affected / exposed                     | 0 / 38 (0.00%)  | 0 / 41 (0.00%)   | 0 / 50 (0.00%)  |
| occurrences (all)                               | 0               | 0                | 0               |
| Upper-airway cough syndrome                     |                 |                  |                 |
| subjects affected / exposed                     | 1 / 38 (2.63%)  | 0 / 41 (0.00%)   | 0 / 50 (0.00%)  |
| occurrences (all)                               | 1               | 0                | 0               |
| Tachypnoea                                      |                 |                  |                 |



|                             |                  |                |                 |
|-----------------------------|------------------|----------------|-----------------|
| subjects affected / exposed | 3 / 38 (7.89%)   | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 3                | 0              | 0               |
| Hiccups                     |                  |                |                 |
| subjects affected / exposed | 0 / 38 (0.00%)   | 0 / 41 (0.00%) | 1 / 50 (2.00%)  |
| occurrences (all)           | 0                | 0              | 1               |
| Laryngeal haemorrhage       |                  |                |                 |
| subjects affected / exposed | 0 / 38 (0.00%)   | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0               |
| Rhinitis allergic           |                  |                |                 |
| subjects affected / exposed | 0 / 38 (0.00%)   | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0               |
| Rhinorrhoea                 |                  |                |                 |
| subjects affected / exposed | 0 / 38 (0.00%)   | 1 / 41 (2.44%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 0                | 1              | 0               |
| Atelectasis                 |                  |                |                 |
| subjects affected / exposed | 0 / 38 (0.00%)   | 1 / 41 (2.44%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 0                | 1              | 0               |
| Paranasal cyst              |                  |                |                 |
| subjects affected / exposed | 0 / 38 (0.00%)   | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0               |
| Psychiatric disorders       |                  |                |                 |
| Anxiety                     |                  |                |                 |
| subjects affected / exposed | 4 / 38 (10.53%)  | 0 / 41 (0.00%) | 2 / 50 (4.00%)  |
| occurrences (all)           | 4                | 0              | 2               |
| Insomnia                    |                  |                |                 |
| subjects affected / exposed | 4 / 38 (10.53%)  | 2 / 41 (4.88%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 4                | 2              | 0               |
| Confusional state           |                  |                |                 |
| subjects affected / exposed | 16 / 38 (42.11%) | 4 / 41 (9.76%) | 6 / 50 (12.00%) |
| occurrences (all)           | 19               | 6              | 8               |
| Agitation                   |                  |                |                 |
| subjects affected / exposed | 0 / 38 (0.00%)   | 1 / 41 (2.44%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 0                | 1              | 0               |
| Hallucination               |                  |                |                 |
| subjects affected / exposed | 1 / 38 (2.63%)   | 2 / 41 (4.88%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 1                | 2              | 0               |

|                                  |                  |                  |                  |
|----------------------------------|------------------|------------------|------------------|
| Mental status changes            |                  |                  |                  |
| subjects affected / exposed      | 1 / 38 (2.63%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                | 1                | 0                | 0                |
| Delirium                         |                  |                  |                  |
| subjects affected / exposed      | 2 / 38 (5.26%)   | 0 / 41 (0.00%)   | 2 / 50 (4.00%)   |
| occurrences (all)                | 2                | 0                | 2                |
| Bradyphrenia                     |                  |                  |                  |
| subjects affected / exposed      | 2 / 38 (5.26%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                | 2                | 0                | 0                |
| Disorientation                   |                  |                  |                  |
| subjects affected / exposed      | 1 / 38 (2.63%)   | 1 / 41 (2.44%)   | 0 / 50 (0.00%)   |
| occurrences (all)                | 1                | 1                | 0                |
| Depression                       |                  |                  |                  |
| subjects affected / exposed      | 0 / 38 (0.00%)   | 1 / 41 (2.44%)   | 0 / 50 (0.00%)   |
| occurrences (all)                | 0                | 1                | 0                |
| Restlessness                     |                  |                  |                  |
| subjects affected / exposed      | 1 / 38 (2.63%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                | 1                | 0                | 0                |
| Mood altered                     |                  |                  |                  |
| subjects affected / exposed      | 0 / 38 (0.00%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                | 0                | 0                | 0                |
| Investigations                   |                  |                  |                  |
| White blood cell count decreased |                  |                  |                  |
| subjects affected / exposed      | 10 / 38 (26.32%) | 6 / 41 (14.63%)  | 14 / 50 (28.00%) |
| occurrences (all)                | 13               | 13               | 24               |
| Platelet count decreased         |                  |                  |                  |
| subjects affected / exposed      | 9 / 38 (23.68%)  | 10 / 41 (24.39%) | 17 / 50 (34.00%) |
| occurrences (all)                | 16               | 17               | 20               |
| Neutrophil count decreased       |                  |                  |                  |
| subjects affected / exposed      | 11 / 38 (28.95%) | 13 / 41 (31.71%) | 25 / 50 (50.00%) |
| occurrences (all)                | 18               | 29               | 49               |
| Lymphocyte count decreased       |                  |                  |                  |
| subjects affected / exposed      | 4 / 38 (10.53%)  | 4 / 41 (9.76%)   | 8 / 50 (16.00%)  |
| occurrences (all)                | 4                | 4                | 12               |
| C-reactive protein increased     |                  |                  |                  |

|                                      |                 |                 |                 |
|--------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed          | 2 / 38 (5.26%)  | 5 / 41 (12.20%) | 7 / 50 (14.00%) |
| occurrences (all)                    | 2               | 6               | 7               |
| Weight decreased                     |                 |                 |                 |
| subjects affected / exposed          | 1 / 38 (2.63%)  | 0 / 41 (0.00%)  | 4 / 50 (8.00%)  |
| occurrences (all)                    | 1               | 0               | 4               |
| Aspartate aminotransferase increased |                 |                 |                 |
| subjects affected / exposed          | 7 / 38 (18.42%) | 4 / 41 (9.76%)  | 7 / 50 (14.00%) |
| occurrences (all)                    | 10              | 4               | 9               |
| Alanine aminotransferase increased   |                 |                 |                 |
| subjects affected / exposed          | 8 / 38 (21.05%) | 5 / 41 (12.20%) | 7 / 50 (14.00%) |
| occurrences (all)                    | 12              | 6               | 8               |
| Blood creatinine increased           |                 |                 |                 |
| subjects affected / exposed          | 0 / 38 (0.00%)  | 3 / 41 (7.32%)  | 1 / 50 (2.00%)  |
| occurrences (all)                    | 0               | 3               | 1               |
| Blood alkaline phosphatase increased |                 |                 |                 |
| subjects affected / exposed          | 4 / 38 (10.53%) | 1 / 41 (2.44%)  | 1 / 50 (2.00%)  |
| occurrences (all)                    | 4               | 1               | 1               |
| Serum ferritin increased             |                 |                 |                 |
| subjects affected / exposed          | 2 / 38 (5.26%)  | 3 / 41 (7.32%)  | 5 / 50 (10.00%) |
| occurrences (all)                    | 2               | 3               | 5               |
| Weight increased                     |                 |                 |                 |
| subjects affected / exposed          | 1 / 38 (2.63%)  | 4 / 41 (9.76%)  | 4 / 50 (8.00%)  |
| occurrences (all)                    | 1               | 4               | 4               |
| Blood bilirubin increased            |                 |                 |                 |
| subjects affected / exposed          | 2 / 38 (5.26%)  | 0 / 41 (0.00%)  | 1 / 50 (2.00%)  |
| occurrences (all)                    | 5               | 0               | 1               |
| Gamma-glutamyltransferase increased  |                 |                 |                 |
| subjects affected / exposed          | 0 / 38 (0.00%)  | 3 / 41 (7.32%)  | 4 / 50 (8.00%)  |
| occurrences (all)                    | 0               | 5               | 6               |
| Blood immunoglobulin G decreased     |                 |                 |                 |
| subjects affected / exposed          | 1 / 38 (2.63%)  | 0 / 41 (0.00%)  | 3 / 50 (6.00%)  |
| occurrences (all)                    | 1               | 0               | 3               |
| Blood potassium decreased            |                 |                 |                 |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 4 / 50 (8.00%) |
| occurrences (all)                              | 0              | 0              | 6              |
| Urine output decreased                         |                |                |                |
| subjects affected / exposed                    | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Immunoglobulins decreased                      |                |                |                |
| subjects affected / exposed                    | 0 / 38 (0.00%) | 3 / 41 (7.32%) | 0 / 50 (0.00%) |
| occurrences (all)                              | 0              | 3              | 0              |
| Blood fibrinogen decreased                     |                |                |                |
| subjects affected / exposed                    | 2 / 38 (5.26%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                              | 5              | 0              | 0              |
| Oxygen saturation decreased                    |                |                |                |
| subjects affected / exposed                    | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 3 / 50 (6.00%) |
| occurrences (all)                              | 0              | 0              | 3              |
| Blood albumin decreased                        |                |                |                |
| subjects affected / exposed                    | 1 / 38 (2.63%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0              |
| Blood magnesium decreased                      |                |                |                |
| subjects affected / exposed                    | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Injury, poisoning and procedural complications |                |                |                |
| Skin abrasion                                  |                |                |                |
| subjects affected / exposed                    | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Infusion related reaction                      |                |                |                |
| subjects affected / exposed                    | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Fall   |                |                |                |
| subjects affected / exposed                    | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 1 / 50 (2.00%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Head injury                                    |                |                |                |
| subjects affected / exposed                    | 0 / 38 (0.00%) | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                              | 0              | 0              | 0              |
| Procedural pain                                |                |                |                |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 38 (0.00%)<br>0 | 0 / 41 (0.00%)<br>0 | 0 / 50 (0.00%)<br>0 |
| Cardiac disorders                                |                     |                     |                     |
| Atrial fibrillation                              |                     |                     |                     |
| subjects affected / exposed                      | 1 / 38 (2.63%)      | 1 / 41 (2.44%)      | 2 / 50 (4.00%)      |
| occurrences (all)                                | 1                   | 1                   | 2                   |
| Sinus bradycardia                                |                     |                     |                     |
| subjects affected / exposed                      | 1 / 38 (2.63%)      | 1 / 41 (2.44%)      | 0 / 50 (0.00%)      |
| occurrences (all)                                | 1                   | 1                   | 0                   |
| Ventricular arrhythmia                           |                     |                     |                     |
| subjects affected / exposed                      | 0 / 38 (0.00%)      | 0 / 41 (0.00%)      | 0 / 50 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Sinus tachycardia                                |                     |                     |                     |
| subjects affected / exposed                      | 4 / 38 (10.53%)     | 2 / 41 (4.88%)      | 3 / 50 (6.00%)      |
| occurrences (all)                                | 5                   | 2                   | 3                   |
| Tachycardia                                      |                     |                     |                     |
| subjects affected / exposed                      | 6 / 38 (15.79%)     | 7 / 41 (17.07%)     | 7 / 50 (14.00%)     |
| occurrences (all)                                | 7                   | 8                   | 8                   |
| Bradycardia                                      |                     |                     |                     |
| subjects affected / exposed                      | 2 / 38 (5.26%)      | 0 / 41 (0.00%)      | 0 / 50 (0.00%)      |
| occurrences (all)                                | 2                   | 0                   | 0                   |
| Acute left ventricular failure                   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 38 (0.00%)      | 0 / 41 (0.00%)      | 0 / 50 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Ventricular tachycardia                          |                     |                     |                     |
| subjects affected / exposed                      | 2 / 38 (5.26%)      | 0 / 41 (0.00%)      | 0 / 50 (0.00%)      |
| occurrences (all)                                | 2                   | 0                   | 0                   |
| Nervous system disorders                         |                     |                     |                     |
| Tremor   |                     |                     |                     |
| subjects affected / exposed                      | 16 / 38 (42.11%)    | 5 / 41 (12.20%)     | 11 / 50 (22.00%)    |
| occurrences (all)                                | 16                  | 5                   | 12                  |
| Headache   |                     |                     |                     |
| subjects affected / exposed                      | 19 / 38 (50.00%)    | 16 / 41 (39.02%)    | 17 / 50 (34.00%)    |
| occurrences (all)                                | 21                  | 20                  | 20                  |
| Encephalopathy                                   |                     |                     |                     |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 9 / 38 (23.68%) | 5 / 41 (12.20%) | 5 / 50 (10.00%) |
| occurrences (all)           | 10              | 6               | 5               |
| Dysarthria                  |                 |                 |                 |
| subjects affected / exposed | 3 / 38 (7.89%)  | 2 / 41 (4.88%)  | 1 / 50 (2.00%)  |
| occurrences (all)           | 3               | 4               | 1               |
| Somnolence                  |                 |                 |                 |
| subjects affected / exposed | 3 / 38 (7.89%)  | 5 / 41 (12.20%) | 5 / 50 (10.00%) |
| occurrences (all)           | 6               | 5               | 5               |
| Aphasia                     |                 |                 |                 |
| subjects affected / exposed | 8 / 38 (21.05%) | 4 / 41 (9.76%)  | 9 / 50 (18.00%) |
| occurrences (all)           | 10              | 4               | 9               |
| Dizziness                   |                 |                 |                 |
| subjects affected / exposed | 5 / 38 (13.16%) | 7 / 41 (17.07%) | 8 / 50 (16.00%) |
| occurrences (all)           | 6               | 8               | 9               |
| Memory impairment           |                 |                 |                 |
| subjects affected / exposed | 0 / 38 (0.00%)  | 1 / 41 (2.44%)  | 1 / 50 (2.00%)  |
| occurrences (all)           | 0               | 1               | 1               |
| Paraesthesia                |                 |                 |                 |
| subjects affected / exposed | 4 / 38 (10.53%) | 2 / 41 (4.88%)  | 1 / 50 (2.00%)  |
| occurrences (all)           | 5               | 3               | 1               |
| Dysgeusia                   |                 |                 |                 |
| subjects affected / exposed | 0 / 38 (0.00%)  | 0 / 41 (0.00%)  | 0 / 50 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Dyskinesia                  |                 |                 |                 |
| subjects affected / exposed | 2 / 38 (5.26%)  | 0 / 41 (0.00%)  | 0 / 50 (0.00%)  |
| occurrences (all)           | 2               | 0               | 0               |
| Dysgraphia                  |                 |                 |                 |
| subjects affected / exposed | 0 / 38 (0.00%)  | 0 / 41 (0.00%)  | 3 / 50 (6.00%)  |
| occurrences (all)           | 0               | 0               | 3               |
| Seizure                     |                 |                 |                 |
| subjects affected / exposed | 2 / 38 (5.26%)  | 0 / 41 (0.00%)  | 0 / 50 (0.00%)  |
| occurrences (all)           | 2               | 0               | 0               |
| Disturbance in attention    |                 |                 |                 |
| subjects affected / exposed | 0 / 38 (0.00%)  | 1 / 41 (2.44%)  | 1 / 50 (2.00%)  |
| occurrences (all)           | 0               | 1               | 1               |
| Post herpetic neuralgia     |                 |                 |                 |

|                                      |                  |                  |                  |
|--------------------------------------|------------------|------------------|------------------|
| subjects affected / exposed          | 0 / 38 (0.00%)   | 0 / 41 (0.00%)   | 1 / 50 (2.00%)   |
| occurrences (all)                    | 0                | 0                | 1                |
| Head discomfort                      |                  |                  |                  |
| subjects affected / exposed          | 0 / 38 (0.00%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                    | 0                | 0                | 0                |
| Dementia                             |                  |                  |                  |
| subjects affected / exposed          | 0 / 38 (0.00%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                    | 0                | 0                | 0                |
| Peripheral sensory neuropathy        |                  |                  |                  |
| subjects affected / exposed          | 1 / 38 (2.63%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                    | 1                | 0                | 0                |
| Apraxia                              |                  |                  |                  |
| subjects affected / exposed          | 0 / 38 (0.00%)   | 0 / 41 (0.00%)   | 1 / 50 (2.00%)   |
| occurrences (all)                    | 0                | 0                | 1                |
| Muscle contractions involuntary      |                  |                  |                  |
| subjects affected / exposed          | 2 / 38 (5.26%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                    | 2                | 0                | 0                |
| Poor sucking reflex                  |                  |                  |                  |
| subjects affected / exposed          | 0 / 38 (0.00%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                    | 0                | 0                | 0                |
| Peripheral motor neuropathy          |                  |                  |                  |
| subjects affected / exposed          | 0 / 38 (0.00%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                    | 0                | 0                | 0                |
| Presyncope                           |                  |                  |                  |
| subjects affected / exposed          | 0 / 38 (0.00%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                    | 0                | 0                | 0                |
| Sensory loss                         |                  |                  |                  |
| subjects affected / exposed          | 0 / 38 (0.00%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                    | 0                | 0                | 0                |
| Blood and lymphatic system disorders |                  |                  |                  |
| Anaemia                              |                  |                  |                  |
| subjects affected / exposed          | 22 / 38 (57.89%) | 19 / 41 (46.34%) | 19 / 50 (38.00%) |
| occurrences (all)                    | 34               | 27               | 47               |
| Neutropenia                          |                  |                  |                  |
| subjects affected / exposed          | 18 / 38 (47.37%) | 16 / 41 (39.02%) | 16 / 50 (32.00%) |
| occurrences (all)                    | 30               | 24               | 25               |

|   |                        |                       |                       |
|---|------------------------|-----------------------|-----------------------|
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                        | 12 / 38 (31.58%)<br>21 | 7 / 41 (17.07%)<br>9  | 9 / 50 (18.00%)<br>10 |
| Febrile neutropenia<br>subjects affected / exposed<br>occurrences (all)                     | 10 / 38 (26.32%)<br>10 | 3 / 41 (7.32%)<br>3   | 2 / 50 (4.00%)<br>2   |
| Pancytopenia<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 38 (0.00%)<br>0    | 4 / 41 (9.76%)<br>4   | 2 / 50 (4.00%)<br>3   |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)                              | 4 / 38 (10.53%)<br>4   | 7 / 41 (17.07%)<br>14 | 8 / 50 (16.00%)<br>11 |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 38 (0.00%)<br>0    | 3 / 41 (7.32%)<br>7   | 0 / 50 (0.00%)<br>0   |
| Ear and labyrinth disorders<br>Tinnitus<br>subjects affected / exposed<br>occurrences (all) | 1 / 38 (2.63%)<br>1    | 1 / 41 (2.44%)<br>1   | 0 / 50 (0.00%)<br>0   |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 38 (0.00%)<br>0    | 0 / 41 (0.00%)<br>0   | 0 / 50 (0.00%)<br>0   |
| Hypoacusis<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 38 (0.00%)<br>0    | 0 / 41 (0.00%)<br>0   | 0 / 50 (0.00%)<br>0   |
| Eye disorders<br>Vision blurred<br>subjects affected / exposed<br>occurrences (all)         | 2 / 38 (5.26%)<br>2    | 1 / 41 (2.44%)<br>1   | 1 / 50 (2.00%)<br>1   |
| Vitreous floaters<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 38 (0.00%)<br>0    | 0 / 41 (0.00%)<br>0   | 1 / 50 (2.00%)<br>1   |
| Eyelid function disorder<br>subjects affected / exposed<br>occurrences (all)                | 0 / 38 (0.00%)<br>0    | 0 / 41 (0.00%)<br>0   | 0 / 50 (0.00%)<br>0   |
| Gastrointestinal disorders  |                        |                       |                       |



|                                  |                  |                  |                  |
|----------------------------------|------------------|------------------|------------------|
| Vomiting                         |                  |                  |                  |
| subjects affected / exposed      | 9 / 38 (23.68%)  | 6 / 41 (14.63%)  | 7 / 50 (14.00%)  |
| occurrences (all)                | 10               | 8                | 7                |
| Constipation                     |                  |                  |                  |
| subjects affected / exposed      | 7 / 38 (18.42%)  | 6 / 41 (14.63%)  | 8 / 50 (16.00%)  |
| occurrences (all)                | 7                | 6                | 8                |
| Nausea                           |                  |                  |                  |
| subjects affected / exposed      | 15 / 38 (39.47%) | 12 / 41 (29.27%) | 12 / 50 (24.00%) |
| occurrences (all)                | 18               | 17               | 14               |
| Diarrhoea                        |                  |                  |                  |
| subjects affected / exposed      | 16 / 38 (42.11%) | 25 / 41 (60.98%) | 11 / 50 (22.00%) |
| occurrences (all)                | 25               | 29               | 11               |
| Abdominal pain                   |                  |                  |                  |
| subjects affected / exposed      | 3 / 38 (7.89%)   | 2 / 41 (4.88%)   | 5 / 50 (10.00%)  |
| occurrences (all)                | 3                | 2                | 5                |
| Gastrooesophageal reflux disease |                  |                  |                  |
| subjects affected / exposed      | 1 / 38 (2.63%)   | 0 / 41 (0.00%)   | 0 / 50 (0.00%)   |
| occurrences (all)                | 1                | 0                | 0                |
| Anal incontinence                |                  |                  |                  |
| subjects affected / exposed      | 0 / 38 (0.00%)   | 2 / 41 (4.88%)   | 1 / 50 (2.00%)   |
| occurrences (all)                | 0                | 2                | 1                |
| Stomatitis                       |                  |                  |                  |
| subjects affected / exposed      | 2 / 38 (5.26%)   | 1 / 41 (2.44%)   | 4 / 50 (8.00%)   |
| occurrences (all)                | 2                | 1                | 4                |
| Dry mouth                        |                  |                  |                  |
| subjects affected / exposed      | 3 / 38 (7.89%)   | 2 / 41 (4.88%)   | 0 / 50 (0.00%)   |
| occurrences (all)                | 3                | 5                | 0                |
| Dyspepsia                        |                  |                  |                  |
| subjects affected / exposed      | 0 / 38 (0.00%)   | 2 / 41 (4.88%)   | 3 / 50 (6.00%)   |
| occurrences (all)                | 0                | 2                | 3                |
| Abdominal distension             |                  |                  |                  |
| subjects affected / exposed      | 1 / 38 (2.63%)   | 0 / 41 (0.00%)   | 1 / 50 (2.00%)   |
| occurrences (all)                | 1                | 0                | 1                |
| Abdominal pain upper             |                  |                  |                  |
| subjects affected / exposed      | 3 / 38 (7.89%)   | 1 / 41 (2.44%)   | 2 / 50 (4.00%)   |
| occurrences (all)                | 3                | 1                | 2                |

|  |                 |                |                |
|--|-----------------|----------------|----------------|
| Dysphagia                              |                 |                |                |
| subjects affected / exposed            | 5 / 38 (13.16%) | 3 / 41 (7.32%) | 2 / 50 (4.00%) |
| occurrences (all)                      | 5               | 3              | 2              |
| Toothache                              |                 |                |                |
| subjects affected / exposed            | 0 / 38 (0.00%)  | 1 / 41 (2.44%) | 0 / 50 (0.00%) |
| occurrences (all)                      | 0               | 1              | 0              |
| Rectal haemorrhage                     |                 |                |                |
| subjects affected / exposed            | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                      | 0               | 0              | 0              |
| Flatulence                             |                 |                |                |
| subjects affected / exposed            | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                      | 0               | 0              | 0              |
| Ascites                                |                 |                |                |
| subjects affected / exposed            | 1 / 38 (2.63%)  | 1 / 41 (2.44%) | 0 / 50 (0.00%) |
| occurrences (all)                      | 1               | 1              | 0              |
| Odynophagia                            |                 |                |                |
| subjects affected / exposed            | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                      | 0               | 0              | 0              |
| Skin and subcutaneous tissue disorders |                 |                |                |
| Dry skin                               |                 |                |                |
| subjects affected / exposed            | 2 / 38 (5.26%)  | 2 / 41 (4.88%) | 0 / 50 (0.00%) |
| occurrences (all)                      | 2               | 2              | 0              |
| Rash                                   |                 |                |                |
| subjects affected / exposed            | 2 / 38 (5.26%)  | 1 / 41 (2.44%) | 2 / 50 (4.00%) |
| occurrences (all)                      | 2               | 1              | 2              |
| Pruritus                               |                 |                |                |
| subjects affected / exposed            | 1 / 38 (2.63%)  | 1 / 41 (2.44%) | 3 / 50 (6.00%) |
| occurrences (all)                      | 1               | 1              | 3              |
| Hyperhidrosis                          |                 |                |                |
| subjects affected / exposed            | 2 / 38 (5.26%)  | 2 / 41 (4.88%) | 2 / 50 (4.00%) |
| occurrences (all)                      | 2               | 2              | 2              |
| Alopecia                               |                 |                |                |
| subjects affected / exposed            | 0 / 38 (0.00%)  | 1 / 41 (2.44%) | 1 / 50 (2.00%) |
| occurrences (all)                      | 0               | 1              | 1              |
| Erythema                               |                 |                |                |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 38 (0.00%)  | 1 / 41 (2.44%) | 0 / 50 (0.00%) |
| occurrences (all)                               | 0               | 1              | 0              |
| Night sweats                                    |                 |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 2 / 50 (4.00%) |
| occurrences (all)                               | 0               | 0              | 2              |
| Renal and urinary disorders                     |                 |                |                |
| Dysuria   |                 |                |                |
| subjects affected / exposed                     | 3 / 38 (7.89%)  | 1 / 41 (2.44%) | 0 / 50 (0.00%) |
| occurrences (all)                               | 3               | 1              | 0              |
| Pollakiuria                                     |                 |                |                |
| subjects affected / exposed                     | 2 / 38 (5.26%)  | 2 / 41 (4.88%) | 1 / 50 (2.00%) |
| occurrences (all)                               | 2               | 2              | 1              |
| Acute kidney injury                             |                 |                |                |
| subjects affected / exposed                     | 2 / 38 (5.26%)  | 2 / 41 (4.88%) | 1 / 50 (2.00%) |
| occurrences (all)                               | 2               | 2              | 1              |
| Urinary incontinence                            |                 |                |                |
| subjects affected / exposed                     | 4 / 38 (10.53%) | 1 / 41 (2.44%) | 3 / 50 (6.00%) |
| occurrences (all)                               | 4               | 1              | 3              |
| Urinary retention                               |                 |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%)  | 1 / 41 (2.44%) | 0 / 50 (0.00%) |
| occurrences (all)                               | 0               | 1              | 0              |
| Haematuria                                      |                 |                |                |
| subjects affected / exposed                     | 0 / 38 (0.00%)  | 1 / 41 (2.44%) | 0 / 50 (0.00%) |
| occurrences (all)                               | 0               | 1              | 0              |
| Urinary tract obstruction                       |                 |                |                |
| subjects affected / exposed                     | 2 / 38 (5.26%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                               | 2               | 0              | 0              |
| Bladder spasm                                   |                 |                |                |
| subjects affected / exposed                     | 2 / 38 (5.26%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all)                               | 2               | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                 |                |                |
| Myalgia   |                 |                |                |
| subjects affected / exposed                     | 5 / 38 (13.16%) | 2 / 41 (4.88%) | 1 / 50 (2.00%) |
| occurrences (all)                               | 6               | 4              | 1              |
| Pain in extremity                               |                 |                |                |

|                                   |                 |                 |                |
|-----------------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed       | 1 / 38 (2.63%)  | 4 / 41 (9.76%)  | 1 / 50 (2.00%) |
| occurrences (all)                 | 1               | 4               | 1              |
| Muscular weakness                 |                 |                 |                |
| subjects affected / exposed       | 4 / 38 (10.53%) | 1 / 41 (2.44%)  | 2 / 50 (4.00%) |
| occurrences (all)                 | 4               | 1               | 2              |
| Arthralgia                        |                 |                 |                |
| subjects affected / exposed       | 1 / 38 (2.63%)  | 4 / 41 (9.76%)  | 4 / 50 (8.00%) |
| occurrences (all)                 | 1               | 4               | 4              |
| Back pain                         |                 |                 |                |
| subjects affected / exposed       | 1 / 38 (2.63%)  | 5 / 41 (12.20%) | 4 / 50 (8.00%) |
| occurrences (all)                 | 1               | 5               | 4              |
| Muscle spasms                     |                 |                 |                |
| subjects affected / exposed       | 2 / 38 (5.26%)  | 1 / 41 (2.44%)  | 1 / 50 (2.00%) |
| occurrences (all)                 | 3               | 1               | 1              |
| Flank pain                        |                 |                 |                |
| subjects affected / exposed       | 2 / 38 (5.26%)  | 0 / 41 (0.00%)  | 0 / 50 (0.00%) |
| occurrences (all)                 | 2               | 0               | 0              |
| Bone pain                         |                 |                 |                |
| subjects affected / exposed       | 2 / 38 (5.26%)  | 1 / 41 (2.44%)  | 0 / 50 (0.00%) |
| occurrences (all)                 | 3               | 1               | 0              |
| Neck pain                         |                 |                 |                |
| subjects affected / exposed       | 1 / 38 (2.63%)  | 2 / 41 (4.88%)  | 0 / 50 (0.00%) |
| occurrences (all)                 | 1               | 2               | 0              |
| Tenosynovitis stenosaurs          |                 |                 |                |
| subjects affected / exposed       | 0 / 38 (0.00%)  | 0 / 41 (0.00%)  | 0 / 50 (0.00%) |
| occurrences (all)                 | 0               | 0               | 0              |
| Groin pain                        |                 |                 |                |
| subjects affected / exposed       | 0 / 38 (0.00%)  | 0 / 41 (0.00%)  | 1 / 50 (2.00%) |
| occurrences (all)                 | 0               | 0               | 1              |
| Infections and infestations       |                 |                 |                |
| Upper respiratory tract infection |                 |                 |                |
| subjects affected / exposed       | 7 / 38 (18.42%) | 3 / 41 (7.32%)  | 1 / 50 (2.00%) |
| occurrences (all)                 | 7               | 3               | 1              |
| Herpes zoster                     |                 |                 |                |
| subjects affected / exposed       | 1 / 38 (2.63%)  | 4 / 41 (9.76%)  | 1 / 50 (2.00%) |
| occurrences (all)                 | 1               | 5               | 1              |

|                                       |                 |                 |                |
|---------------------------------------|-----------------|-----------------|----------------|
| Sinusitis                             |                 |                 |                |
| subjects affected / exposed           | 2 / 38 (5.26%)  | 2 / 41 (4.88%)  | 0 / 50 (0.00%) |
| occurrences (all)                     | 2               | 2               | 0              |
| Urinary tract infection               |                 |                 |                |
| subjects affected / exposed           | 0 / 38 (0.00%)  | 1 / 41 (2.44%)  | 2 / 50 (4.00%) |
| occurrences (all)                     | 0               | 1               | 3              |
| Pneumonia                             |                 |                 |                |
| subjects affected / exposed           | 1 / 38 (2.63%)  | 6 / 41 (14.63%) | 4 / 50 (8.00%) |
| occurrences (all)                     | 1               | 7               | 4              |
| Candida infection                     |                 |                 |                |
| subjects affected / exposed           | 4 / 38 (10.53%) | 0 / 41 (0.00%)  | 2 / 50 (4.00%) |
| occurrences (all)                     | 4               | 0               | 2              |
| Oral candidiasis                      |                 |                 |                |
| subjects affected / exposed           | 1 / 38 (2.63%)  | 2 / 41 (4.88%)  | 0 / 50 (0.00%) |
| occurrences (all)                     | 1               | 2               | 0              |
| Clostridium difficile infection       |                 |                 |                |
| subjects affected / exposed           | 0 / 38 (0.00%)  | 1 / 41 (2.44%)  | 0 / 50 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0              |
| Covid-19                              |                 |                 |                |
| subjects affected / exposed           | 1 / 38 (2.63%)  | 0 / 41 (0.00%)  | 1 / 50 (2.00%) |
| occurrences (all)                     | 1               | 0               | 1              |
| Nasopharyngitis                       |                 |                 |                |
| subjects affected / exposed           | 0 / 38 (0.00%)  | 3 / 41 (7.32%)  | 0 / 50 (0.00%) |
| occurrences (all)                     | 0               | 3               | 0              |
| Conjunctivitis                        |                 |                 |                |
| subjects affected / exposed           | 0 / 38 (0.00%)  | 1 / 41 (2.44%)  | 0 / 50 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0              |
| Clostridium difficile colitis         |                 |                 |                |
| subjects affected / exposed           | 2 / 38 (5.26%)  | 0 / 41 (0.00%)  | 0 / 50 (0.00%) |
| occurrences (all)                     | 2               | 0               | 0              |
| Respiratory syncytial virus infection |                 |                 |                |
| subjects affected / exposed           | 0 / 38 (0.00%)  | 1 / 41 (2.44%)  | 1 / 50 (2.00%) |
| occurrences (all)                     | 0               | 1               | 1              |
| Tooth infection                       |                 |                 |                |
| subjects affected / exposed           | 1 / 38 (2.63%)  | 0 / 41 (0.00%)  | 0 / 50 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0              |

|   |                  |                 |                  |
|---|------------------|-----------------|------------------|
| Oral herpes                             |                  |                 |                  |
| subjects affected / exposed             | 0 / 38 (0.00%)   | 0 / 41 (0.00%)  | 0 / 50 (0.00%)   |
| occurrences (all)                       | 0                | 0               | 0                |
| Folliculitis                            |                  |                 |                  |
| subjects affected / exposed             | 1 / 38 (2.63%)   | 0 / 41 (0.00%)  | 0 / 50 (0.00%)   |
| occurrences (all)                       | 1                | 0               | 0                |
| Rhinitis                                |                  |                 |                  |
| subjects affected / exposed             | 0 / 38 (0.00%)   | 0 / 41 (0.00%)  | 0 / 50 (0.00%)   |
| occurrences (all)                       | 0                | 0               | 0                |
| Ear infection                           |                  |                 |                  |
| subjects affected / exposed             | 0 / 38 (0.00%)   | 0 / 41 (0.00%)  | 0 / 50 (0.00%)   |
| occurrences (all)                       | 0                | 0               | 0                |
| Tinea versicolour                       |                  |                 |                  |
| subjects affected / exposed             | 0 / 38 (0.00%)   | 0 / 41 (0.00%)  | 0 / 50 (0.00%)   |
| occurrences (all)                       | 0                | 0               | 0                |
| Viral upper respiratory tract infection |                  |                 |                  |
| subjects affected / exposed             | 0 / 38 (0.00%)   | 0 / 41 (0.00%)  | 0 / 50 (0.00%)   |
| occurrences (all)                       | 0                | 0               | 0                |
| Wound infection                         |                  |                 |                  |
| subjects affected / exposed             | 0 / 38 (0.00%)   | 0 / 41 (0.00%)  | 0 / 50 (0.00%)   |
| occurrences (all)                       | 0                | 0               | 0                |
| Metabolism and nutrition disorders      |                  |                 |                  |
| Hypokalaemia                            |                  |                 |                  |
| subjects affected / exposed             | 6 / 38 (15.79%)  | 6 / 41 (14.63%) | 10 / 50 (20.00%) |
| occurrences (all)                       | 9                | 7               | 13               |
| Decreased appetite                      |                  |                 |                  |
| subjects affected / exposed             | 10 / 38 (26.32%) | 3 / 41 (7.32%)  | 6 / 50 (12.00%)  |
| occurrences (all)                       | 10               | 4               | 6                |
| Hypophosphataemia                       |                  |                 |                  |
| subjects affected / exposed             | 5 / 38 (13.16%)  | 6 / 41 (14.63%) | 5 / 50 (10.00%)  |
| occurrences (all)                       | 5                | 7               | 7                |
| Hyponatraemia                           |                  |                 |                  |
| subjects affected / exposed             | 2 / 38 (5.26%)   | 2 / 41 (4.88%)  | 1 / 50 (2.00%)   |
| occurrences (all)                       | 3                | 3               | 1                |
| Hypoalbuminaemia                        |                  |                 |                  |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 4 / 38 (10.53%) | 2 / 41 (4.88%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 4               | 2              | 0               |
| Hypocalcaemia               |                 |                |                 |
| subjects affected / exposed | 4 / 38 (10.53%) | 1 / 41 (2.44%) | 1 / 50 (2.00%)  |
| occurrences (all)           | 4               | 1              | 2               |
| Hypernatraemia              |                 |                |                 |
| subjects affected / exposed | 2 / 38 (5.26%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 2               | 0              | 0               |
| Hyperglycaemia              |                 |                |                 |
| subjects affected / exposed | 2 / 38 (5.26%)  | 1 / 41 (2.44%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 3               | 2              | 0               |
| Hypomagnesaemia             |                 |                |                 |
| subjects affected / exposed | 6 / 38 (15.79%) | 2 / 41 (4.88%) | 5 / 50 (10.00%) |
| occurrences (all)           | 7               | 3              | 9               |
| Dehydration                 |                 |                |                 |
| subjects affected / exposed | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Hyperkalaemia               |                 |                |                 |
| subjects affected / exposed | 1 / 38 (2.63%)  | 0 / 41 (0.00%) | 1 / 50 (2.00%)  |
| occurrences (all)           | 1               | 0              | 1               |
| Hypermagnesaemia            |                 |                |                 |
| subjects affected / exposed | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Malnutrition                |                 |                |                 |
| subjects affected / exposed | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Metabolic acidosis          |                 |                |                 |
| subjects affected / exposed | 0 / 38 (0.00%)  | 0 / 41 (0.00%) | 0 / 50 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |

| <b>Non-serious adverse events</b>                                      | Retreatment<br>Axicabtagene<br>Ciloleucel: Phase 2<br>Cohort 5 | Retreatment<br>Axicabtagene<br>Ciloleucel: Phase 1 | Retreatment<br>Axicabtagene<br>Ciloleucel: Phase 2<br>Cohort 1 |
|--|--|--|--|
| Total subjects affected by non-serious<br>adverse events               |  |  |  |
| subjects affected / exposed  | 2 / 2 (100.00%)  | 1 / 1 (100.00%)                                    | 9 / 9 (100.00%)  |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps) |  |  |  |

|  |                     |                      |                     |
|--|---------------------|----------------------|---------------------|
| Squamous cell carcinoma<br>subjects affected / exposed<br>occurrences (all)    | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Myelodysplastic syndrome<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Cancer pain<br>subjects affected / exposed<br>occurrences (all)                | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 |
| Vascular disorders   |                     |                      |                     |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)                | 1 / 2 (50.00%)<br>1 | 1 / 1 (100.00%)<br>3 | 1 / 9 (11.11%)<br>1 |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)               | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Capillary leak syndrome<br>subjects affected / exposed<br>occurrences (all)    | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Deep vein thrombosis<br>subjects affected / exposed<br>occurrences (all)       | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Hot flush<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 2 (50.00%)<br>1 | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Embolism<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 |
| Subclavian vein thrombosis<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| General disorders and administration<br>site conditions                        |                     |                      |                     |
| Chills<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 2 (0.00%)<br>0  | 1 / 1 (100.00%)<br>1 | 2 / 9 (22.22%)<br>2 |
| Fatigue  |                     |                      |                     |



|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 1 (0.00%)   | 3 / 9 (33.33%)  |
| occurrences (all)           | 0               | 0               | 3               |
| Pyrexia                     |                 |                 |                 |
| subjects affected / exposed | 2 / 2 (100.00%) | 1 / 1 (100.00%) | 9 / 9 (100.00%) |
| occurrences (all)           | 2               | 1               | 13              |
| Asthenia                    |                 |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 1 (0.00%)   | 1 / 9 (11.11%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Pain                        |                 |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 1 (0.00%)   | 1 / 9 (11.11%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Malaise                     |                 |                 |                 |
| subjects affected / exposed | 1 / 2 (50.00%)  | 0 / 1 (0.00%)   | 1 / 9 (11.11%)  |
| occurrences (all)           | 1               | 0               | 1               |
| Non-cardiac chest pain      |                 |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 1 (0.00%)   | 0 / 9 (0.00%)   |
| occurrences (all)           | 0               | 0               | 0               |
| Gait disturbance            |                 |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 1 (0.00%)   | 0 / 9 (0.00%)   |
| occurrences (all)           | 0               | 0               | 0               |
| Influenza like illness      |                 |                 |                 |
| subjects affected / exposed | 1 / 2 (50.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)   |
| occurrences (all)           | 2               | 0               | 0               |
| Oedema                      |                 |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 1 (0.00%)   | 1 / 9 (11.11%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Oedema peripheral           |                 |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 1 (0.00%)   | 1 / 9 (11.11%)  |
| occurrences (all)           | 0               | 0               | 1               |
| Chest pain                  |                 |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 1 (0.00%)   | 0 / 9 (0.00%)   |
| occurrences (all)           | 0               | 0               | 0               |
| Peripheral swelling         |                 |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 1 (0.00%)   | 0 / 9 (0.00%)   |
| occurrences (all)           | 0               | 0               | 0               |
| Swelling                    |                 |                 |                 |

|  |                    |                    |                     |
|--|--------------------|--------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Puncture site pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Catheter site pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Hernia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Immune system disorders<br>Hypogammaglobulinaemia<br>subjects affected / exposed<br>occurrences (all)          | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Graft versus host disease<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Scrotal oedema<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Perineal pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Respiratory, thoracic and mediastinal disorders<br>Hypoxia<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 2 / 9 (22.22%)<br>2 |
| Cough<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 5 / 9 (55.56%)<br>5 |
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0  |
| Oropharyngeal pain   |                    |                    |                     |

|                             |               |               |               |
|-----------------------------|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Pleural effusion            |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Dyspnoea                    |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Wheezing                    |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Pulmonary oedema            |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Upper-airway cough syndrome |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Tachypnoea                  |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Hiccups                     |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Laryngeal haemorrhage       |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Rhinitis allergic           |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Rhinorrhoea                 |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Atelectasis                 |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Paranasal cyst              |               |               |               |

|  |                    |                    |                    |
|--|--------------------|--------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 |
| Psychiatric disorders                            |                    |                    |                    |
| Anxiety  |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 1 (0.00%)      | 2 / 9 (22.22%)     |
| occurrences (all)                                | 0                  | 0                  | 2                  |
| Insomnia   |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 1 / 1 (100.00%)    | 3 / 9 (33.33%)     |
| occurrences (all)                                | 0                  | 1                  | 3                  |
| Confusional state                                |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 1 (0.00%)      | 2 / 9 (22.22%)     |
| occurrences (all)                                | 0                  | 0                  | 2                  |
| Agitation  |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Hallucination                                    |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Mental status changes                            |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Delirium   |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Bradyphrenia                                     |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Disorientation                                   |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Depression                                       |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Restlessness                                     |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 1 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |

|  |                     |                      |                      |
|--|---------------------|----------------------|----------------------|
| Mood altered<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0   |
| Investigations   |                     |                      |                      |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all)     | 1 / 2 (50.00%)<br>1 | 1 / 1 (100.00%)<br>1 | 3 / 9 (33.33%)<br>9  |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)             | 1 / 2 (50.00%)<br>1 | 1 / 1 (100.00%)<br>1 | 3 / 9 (33.33%)<br>8  |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 4 / 9 (44.44%)<br>11 |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 1 / 1 (100.00%)<br>3 | 3 / 9 (33.33%)<br>8  |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)         | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0   |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 2 / 9 (22.22%)<br>6  |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0   |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0   |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 1 / 9 (11.11%)<br>2  |
| Serum ferritin increased   |                     |                      |                      |

|                                     |               |               |                |
|-------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Weight increased                    |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                   | 0             | 0             | 1              |
| Blood bilirubin increased           |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Gamma-glutamyltransferase increased |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Blood immunoglobulin G decreased    |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Blood potassium decreased           |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Urine output decreased              |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Immunoglobulins decreased           |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Blood fibrinogen decreased          |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Oxygen saturation decreased         |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Blood albumin decreased             |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Blood magnesium decreased           |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |

|  |               |               |                |
|--|---------------|---------------|----------------|
| Injury, poisoning and procedural complications |               |               |                |
| Skin abrasion                                  |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Infusion related reaction                      |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Fall   |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Head injury                                    |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Procedural pain                                |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Cardiac disorders                              |               |               |                |
| Atrial fibrillation                            |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Sinus bradycardia                              |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Ventricular arrhythmia                         |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Sinus tachycardia                              |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 4 / 9 (44.44%) |
| occurrences (all)                              | 0             | 0             | 11             |
| Tachycardia                                    |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                              | 0             | 0             | 1              |
| Bradycardia                                    |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Acute left ventricular failure                 |               |               |                |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Ventricular tachycardia     |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Nervous system disorders    |                |               |                |
| Tremor                      |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 4 / 9 (44.44%) |
| occurrences (all)           | 0              | 0             | 5              |
| Headache                    |                |               |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 3 / 9 (33.33%) |
| occurrences (all)           | 2              | 0             | 4              |
| Encephalopathy              |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all)           | 0              | 0             | 2              |
| Dysarthria                  |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Somnolence                  |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 0              | 0             | 1              |
| Aphasia                     |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Dizziness                   |                |               |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 2              | 0             | 1              |
| Memory impairment           |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Paraesthesia                |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Dysgeusia                   |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 0              | 0             | 1              |



|                                 |               |               |               |
|---------------------------------|---------------|---------------|---------------|
| Dyskinesia                      |               |               |               |
| subjects affected / exposed     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)               | 0             | 0             | 0             |
| Dysgraphia                      |               |               |               |
| subjects affected / exposed     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)               | 0             | 0             | 0             |
| Seizure                         |               |               |               |
| subjects affected / exposed     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)               | 0             | 0             | 0             |
| Disturbance in attention        |               |               |               |
| subjects affected / exposed     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)               | 0             | 0             | 0             |
| Post herpetic neuralgia         |               |               |               |
| subjects affected / exposed     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)               | 0             | 0             | 0             |
| Head discomfort                 |               |               |               |
| subjects affected / exposed     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)               | 0             | 0             | 0             |
| Dementia                        |               |               |               |
| subjects affected / exposed     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)               | 0             | 0             | 0             |
| Peripheral sensory neuropathy   |               |               |               |
| subjects affected / exposed     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)               | 0             | 0             | 0             |
| Apraxia                         |               |               |               |
| subjects affected / exposed     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)               | 0             | 0             | 0             |
| Muscle contractions involuntary |               |               |               |
| subjects affected / exposed     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)               | 0             | 0             | 0             |
| Poor sucking reflex             |               |               |               |
| subjects affected / exposed     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)               | 0             | 0             | 0             |
| Peripheral motor neuropathy     |               |               |               |
| subjects affected / exposed     | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%) |
| occurrences (all)               | 0             | 0             | 0             |

|   |                     |                      |                     |
|---|---------------------|----------------------|---------------------|
| Presyncope<br>subjects affected / exposed<br>occurrences (all)          | 1 / 2 (50.00%)<br>1 | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Sensory loss<br>subjects affected / exposed<br>occurrences (all)        | 1 / 2 (50.00%)<br>1 | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Blood and lymphatic system disorders                                    |                     |                      |                     |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)             | 0 / 2 (0.00%)<br>0  | 1 / 1 (100.00%)<br>1 | 3 / 9 (33.33%)<br>9 |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)    | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Febrile neutropenia<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 3 / 9 (33.33%)<br>4 |
| Pancytopenia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)          | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 2 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Ear and labyrinth disorders   |                     |                      |                     |
| Tinnitus<br>subjects affected / exposed<br>occurrences (all)            | 0 / 2 (0.00%)<br>0  | 1 / 1 (100.00%)<br>1 | 0 / 9 (0.00%)<br>0  |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)            | 1 / 2 (50.00%)<br>1 | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Hypoacusis  |                     |                      |                     |

|  |                      |                      |                     |
|--|----------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                     | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Eye disorders  |                      |                      |                     |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Vitreous floaters<br>subjects affected / exposed<br>occurrences (all)                | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Eyelid function disorder<br>subjects affected / exposed<br>occurrences (all)         | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 |
| Gastrointestinal disorders   |                      |                      |                     |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 2 (50.00%)<br>1  | 0 / 1 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 |
| Constipation<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 2 (50.00%)<br>1  | 1 / 1 (100.00%)<br>1 | 3 / 9 (33.33%)<br>3 |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                           | 2 / 2 (100.00%)<br>2 | 1 / 1 (100.00%)<br>1 | 4 / 9 (44.44%)<br>4 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0   | 2 / 9 (22.22%)<br>2 |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0   | 1 / 1 (100.00%)<br>1 | 0 / 9 (0.00%)<br>0  |
| Anal incontinence<br>subjects affected / exposed<br>occurrences (all)                | 0 / 2 (0.00%)<br>0   | 0 / 1 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Stomatitis   |                      |                      |                     |

|  |                |               |                |
|--|----------------|---------------|----------------|
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Dry mouth                              |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 2 / 9 (22.22%) |
| occurrences (all)                      | 0              | 0             | 2              |
| Dyspepsia                              |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Abdominal distension                   |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Abdominal pain upper                   |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Dysphagia                              |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Toothache                              |                |               |                |
| subjects affected / exposed            | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 1              | 0             | 0              |
| Rectal haemorrhage                     |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Flatulence                             |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Ascites                                |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Odynophagia                            |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Skin and subcutaneous tissue disorders |                |               |                |
| Dry skin                               |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| Rash                        |                |               |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 1              | 0             | 1              |
| Pruritus                    |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hyperhidrosis               |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Alopecia                    |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Erythema                    |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Night sweats                |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 0              | 0             | 1              |
| Renal and urinary disorders |                |               |                |
| Dysuria                     |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Pollakiuria                 |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Acute kidney injury         |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Urinary incontinence        |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Urinary retention           |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Haematuria                  |                |               |                |

|   |                |               |                |
|---|----------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Urinary tract obstruction                       |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Bladder spasm                                   |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Musculoskeletal and connective tissue disorders |                |               |                |
| Myalgia   |                |               |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                               | 1              | 0             | 1              |
| Pain in extremity                               |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Muscular weakness                               |                |               |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 3 / 9 (33.33%) |
| occurrences (all)                               | 1              | 0             | 3              |
| Arthralgia                                      |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Back pain                                       |                |               |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                               | 1              | 0             | 1              |
| Muscle spasms                                   |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Flank pain                                      |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Bone pain                                       |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 3 / 9 (33.33%) |
| occurrences (all)                               | 0              | 0             | 3              |
| Neck pain                                       |                |               |                |

|                                   |                |               |                |
|-----------------------------------|----------------|---------------|----------------|
| subjects affected / exposed       | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                 | 1              | 0             | 0              |
| Tenosynovitis stenosans           |                |               |                |
| subjects affected / exposed       | 1 / 2 (50.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                 | 1              | 0             | 0              |
| Groin pain                        |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                 | 0              | 0             | 1              |
| Infections and infestations       |                |               |                |
| Upper respiratory tract infection |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Herpes zoster                     |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Sinusitis                         |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Urinary tract infection           |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Pneumonia                         |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                 | 0              | 0             | 1              |
| Candida infection                 |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Oral candidiasis                  |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Clostridium difficile infection   |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Covid-19                          |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Nasopharyngitis                         |               |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                       | 0             | 0             | 0              |
| Conjunctivitis                          |               |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                       | 0             | 0             | 0              |
| Clostridium difficile colitis           |               |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                       | 0             | 0             | 0              |
| Respiratory syncytial virus infection   |               |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                       | 0             | 0             | 0              |
| Tooth infection                         |               |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                       | 0             | 0             | 0              |
| Oral herpes                             |               |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                       | 0             | 0             | 0              |
| Folliculitis                            |               |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                       | 0             | 0             | 1              |
| Rhinitis                                |               |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                       | 0             | 0             | 0              |
| Ear infection                           |               |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                       | 0             | 0             | 0              |
| Tinea versicolour                       |               |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                       | 0             | 0             | 0              |
| Viral upper respiratory tract infection |               |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)                       | 0             | 0             | 0              |
| Wound infection                         |               |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)                       | 0             | 0             | 1              |



|                                    |                |                 |                |
|------------------------------------|----------------|-----------------|----------------|
| Metabolism and nutrition disorders |                |                 |                |
| Hypokalaemia                       |                |                 |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 1 (0.00%)   | 2 / 9 (22.22%) |
| occurrences (all)                  | 0              | 0               | 5              |
| Decreased appetite                 |                |                 |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 1 (0.00%)   | 4 / 9 (44.44%) |
| occurrences (all)                  | 0              | 0               | 5              |
| Hypophosphataemia                  |                |                 |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 1 / 1 (100.00%) | 1 / 9 (11.11%) |
| occurrences (all)                  | 0              | 1               | 3              |
| Hyponatraemia                      |                |                 |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 1 / 1 (100.00%) | 3 / 9 (33.33%) |
| occurrences (all)                  | 0              | 1               | 4              |
| Hypoalbuminaemia                   |                |                 |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 1 (0.00%)   | 3 / 9 (33.33%) |
| occurrences (all)                  | 0              | 0               | 7              |
| Hypocalcaemia                      |                |                 |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Hypernatraemia                     |                |                 |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)                  | 0              | 0               | 1              |
| Hyperglycaemia                     |                |                 |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 1 (0.00%)   | 3 / 9 (33.33%) |
| occurrences (all)                  | 0              | 0               | 9              |
| Hypomagnesaemia                    |                |                 |                |
| subjects affected / exposed        | 1 / 2 (50.00%) | 0 / 1 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                  | 1              | 0               | 0              |
| Dehydration                        |                |                 |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 1 / 1 (100.00%) | 2 / 9 (22.22%) |
| occurrences (all)                  | 0              | 1               | 5              |
| Hyperkalaemia                      |                |                 |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 1 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)                  | 0              | 0               | 1              |
| Hypermagnesaemia                   |                |                 |                |

|                             |               |               |                |
|-----------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 0             | 0             | 2              |
| Malnutrition                |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Metabolic acidosis          |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 1 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |

| <b>Non-serious adverse events</b>                                   | Retreatment<br>Axicabtagene<br>Ciloleucel: Phase 2<br>Cohort 2 | Retreatment<br>Axicabtagene<br>Ciloleucel: Phase 2<br>Cohort 3 | Retreatment<br>Axicabtagene<br>Ciloleucel: Phase 2<br>Cohort 4 |
|---|--|--|--|
| Total subjects affected by non-serious adverse events               |  |  |  |
| subjects affected / exposed   | 2 / 2 (100.00%)  | 2 / 2 (100.00%)  | 2 / 2 (100.00%)  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |
| Squamous cell carcinoma   |  |  |  |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)   | 0  | 0  | 0  |
| Myelodysplastic syndrome  |  |  |  |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 1 / 2 (50.00%)   |
| occurrences (all)   | 0  | 0  | 1  |
| Cancer pain   |  |  |  |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)   | 0  | 0  | 0  |
| Vascular disorders  |  |  |  |
| Hypotension   |  |  |  |
| subjects affected / exposed   | 1 / 2 (50.00%)   | 0 / 2 (0.00%)  | 1 / 2 (50.00%)   |
| occurrences (all)   | 1  | 0  | 1  |
| Hypertension  |  |  |  |
| subjects affected / exposed   | 1 / 2 (50.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)   | 1  | 0  | 0  |
| Capillary leak syndrome   |  |  |  |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)   | 0  | 0  | 0  |
| Deep vein thrombosis  |  |  |  |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)   | 0  | 0  | 0  |

|  |                 |                |                 |
|--|-----------------|----------------|-----------------|
| Hot flush  |                 |                |                 |
| subjects affected / exposed                          | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                                    | 0               | 0              | 0               |
| Embolism   |                 |                |                 |
| subjects affected / exposed                          | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                                    | 0               | 0              | 0               |
| Subclavian vein thrombosis                           |                 |                |                 |
| subjects affected / exposed                          | 1 / 2 (50.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                                    | 1               | 0              | 0               |
| General disorders and administration site conditions |                 |                |                 |
| Chills   |                 |                |                 |
| subjects affected / exposed                          | 2 / 2 (100.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                                    | 3               | 0              | 0               |
| Fatigue  |                 |                |                 |
| subjects affected / exposed                          | 0 / 2 (0.00%)   | 1 / 2 (50.00%) | 1 / 2 (50.00%)  |
| occurrences (all)                                    | 0               | 1              | 1               |
| Pyrexia  |                 |                |                 |
| subjects affected / exposed                          | 2 / 2 (100.00%) | 1 / 2 (50.00%) | 2 / 2 (100.00%) |
| occurrences (all)                                    | 3               | 1              | 2               |
| Asthenia   |                 |                |                 |
| subjects affected / exposed                          | 1 / 2 (50.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                                    | 1               | 0              | 0               |
| Pain   |                 |                |                 |
| subjects affected / exposed                          | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                                    | 0               | 0              | 0               |
| Malaise  |                 |                |                 |
| subjects affected / exposed                          | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                                    | 0               | 0              | 0               |
| Non-cardiac chest pain                               |                 |                |                 |
| subjects affected / exposed                          | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                                    | 0               | 0              | 0               |
| Gait disturbance                                     |                 |                |                 |
| subjects affected / exposed                          | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                                    | 0               | 0              | 0               |
| Influenza like illness                               |                 |                |                 |

|  |                |               |                |
|--|----------------|---------------|----------------|
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0              | 0             | 0              |
| Oedema                                   |                |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                        | 0              | 0             | 1              |
| Oedema peripheral                        |                |               |                |
| subjects affected / exposed              | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                        | 1              | 0             | 0              |
| Chest pain                               |                |               |                |
| subjects affected / exposed              | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                        | 1              | 0             | 0              |
| Peripheral swelling                      |                |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0              | 0             | 0              |
| Swelling                                 |                |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0              | 0             | 0              |
| Puncture site pain                       |                |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0              | 0             | 0              |
| Catheter site pain                       |                |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                        | 0              | 0             | 1              |
| Hernia                                   |                |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0              | 0             | 0              |
| Immune system disorders                  |                |               |                |
| Hypogammaglobulinaemia                   |                |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                        | 0              | 0             | 2              |
| Graft versus host disease                |                |               |                |
| subjects affected / exposed              | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                        | 2              | 0             | 0              |
| Reproductive system and breast disorders |                |               |                |

|   |                |               |                |
|---|----------------|---------------|----------------|
| Scrotal oedema                                  |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Perineal pain                                   |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Respiratory, thoracic and mediastinal disorders |                |               |                |
| Hypoxia   |                |               |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                               | 2              | 0             | 1              |
| Cough   |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Nasal congestion                                |                |               |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 1              | 0             | 0              |
| Oropharyngeal pain                              |                |               |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 1              | 0             | 0              |
| Pleural effusion                                |                |               |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 1              | 0             | 0              |
| Dyspnoea  |                |               |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 1              | 0             | 0              |
| Wheezing  |                |               |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 1              | 0             | 0              |
| Pulmonary oedema                                |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Upper-airway cough syndrome                     |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Tachypnoea                                      |                |               |                |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hiccups                     |                |                |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Laryngeal haemorrhage       |                |                |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Rhinitis allergic           |                |                |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Rhinorrhoea                 |                |                |               |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Atelectasis                 |                |                |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Paranasal cyst              |                |                |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Psychiatric disorders       |                |                |               |
| Anxiety                     |                |                |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Insomnia                    |                |                |               |
| subjects affected / exposed | 1 / 2 (50.00%) | 1 / 2 (50.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 1              | 1              | 0             |
| Confusional state           |                |                |               |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 1              | 0              | 0             |
| Agitation                   |                |                |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hallucination               |                |                |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |

|                                  |                 |                |                |
|----------------------------------|-----------------|----------------|----------------|
| Mental status changes            |                 |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              | 0              |
| Delirium                         |                 |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              | 0              |
| Bradyphrenia                     |                 |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              | 0              |
| Disorientation                   |                 |                |                |
| subjects affected / exposed      | 1 / 2 (50.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 2               | 0              | 0              |
| Depression                       |                 |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 0              | 0              |
| Restlessness                     |                 |                |                |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 1 / 2 (50.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                | 0               | 1              | 0              |
| Mood altered                     |                 |                |                |
| subjects affected / exposed      | 1 / 2 (50.00%)  | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                | 1               | 0              | 0              |
| Investigations                   |                 |                |                |
| White blood cell count decreased |                 |                |                |
| subjects affected / exposed      | 2 / 2 (100.00%) | 0 / 2 (0.00%)  | 1 / 2 (50.00%) |
| occurrences (all)                | 6               | 0              | 2              |
| Platelet count decreased         |                 |                |                |
| subjects affected / exposed      | 1 / 2 (50.00%)  | 0 / 2 (0.00%)  | 1 / 2 (50.00%) |
| occurrences (all)                | 2               | 0              | 1              |
| Neutrophil count decreased       |                 |                |                |
| subjects affected / exposed      | 2 / 2 (100.00%) | 0 / 2 (0.00%)  | 1 / 2 (50.00%) |
| occurrences (all)                | 2               | 0              | 2              |
| Lymphocyte count decreased       |                 |                |                |
| subjects affected / exposed      | 2 / 2 (100.00%) | 0 / 2 (0.00%)  | 1 / 2 (50.00%) |
| occurrences (all)                | 2               | 0              | 1              |
| C-reactive protein increased     |                 |                |                |

|                                      |                |               |                |
|--------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                    | 0              | 0             | 1              |
| Weight decreased                     |                |               |                |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 2              | 0             | 0              |
| Aspartate aminotransferase increased |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Alanine aminotransferase increased   |                |               |                |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 1              | 0             | 0              |
| Blood creatinine increased           |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                    | 0              | 0             | 1              |
| Blood alkaline phosphatase increased |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Serum ferritin increased             |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Weight increased                     |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                    | 0              | 0             | 1              |
| Blood bilirubin increased            |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Gamma-glutamyltransferase increased  |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Blood immunoglobulin G decreased     |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Blood potassium decreased            |                |               |                |



|  |                |               |               |
|--|----------------|---------------|---------------|
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Urine output decreased                         |                |               |               |
| subjects affected / exposed                    | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                              | 1              | 0             | 0             |
| Immunoglobulins decreased                      |                |               |               |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Blood fibrinogen decreased                     |                |               |               |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Oxygen saturation decreased                    |                |               |               |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Blood albumin decreased                        |                |               |               |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Blood magnesium decreased                      |                |               |               |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Injury, poisoning and procedural complications |                |               |               |
| Skin abrasion                                  |                |               |               |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Infusion related reaction                      |                |               |               |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Fall   |                |               |               |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Head injury                                    |                |               |               |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                              | 0              | 0             | 0             |
| Procedural pain                                |                |               |               |

|  |                    |                    |                    |
|--|--------------------|--------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Cardiac disorders                                |                    |                    |                    |
| Atrial fibrillation                              |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Sinus bradycardia                                |                    |                    |                    |
| subjects affected / exposed                      | 1 / 2 (50.00%)     | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                | 1                  | 0                  | 0                  |
| Ventricular arrhythmia                           |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Sinus tachycardia                                |                    |                    |                    |
| subjects affected / exposed                      | 1 / 2 (50.00%)     | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                | 1                  | 0                  | 0                  |
| Tachycardia                                      |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Bradycardia                                      |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Acute left ventricular failure                   |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Ventricular tachycardia                          |                    |                    |                    |
| subjects affected / exposed                      | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                | 0                  | 0                  | 0                  |
| Nervous system disorders                         |                    |                    |                    |
| Tremor   |                    |                    |                    |
| subjects affected / exposed                      | 1 / 2 (50.00%)     | 0 / 2 (0.00%)      | 0 / 2 (0.00%)      |
| occurrences (all)                                | 1                  | 0                  | 0                  |
| Headache   |                    |                    |                    |
| subjects affected / exposed                      | 1 / 2 (50.00%)     | 0 / 2 (0.00%)      | 2 / 2 (100.00%)    |
| occurrences (all)                                | 2                  | 0                  | 4                  |
| Encephalopathy                                   |                    |                    |                    |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Dysarthria                  |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Somnolence                  |                |               |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)           | 1              | 0             | 0              |
| Aphasia                     |                |               |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)           | 1              | 0             | 1              |
| Dizziness                   |                |               |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)           | 1              | 0             | 0              |
| Memory impairment           |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Paraesthesia                |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Dysgeusia                   |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)           | 0              | 0             | 1              |
| Dyskinesia                  |                |               |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)           | 1              | 0             | 0              |
| Dysgraphia                  |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Seizure                     |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Disturbance in attention    |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Post herpetic neuralgia     |                |               |                |

|                                      |                |               |                |
|--------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Head discomfort                      |                |               |                |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 1              | 0             | 0              |
| Dementia                             |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Peripheral sensory neuropathy        |                |               |                |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 1              | 0             | 0              |
| Apraxia                              |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Muscle contractions involuntary      |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Poor sucking reflex                  |                |               |                |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 1              | 0             | 0              |
| Peripheral motor neuropathy          |                |               |                |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 1              | 0             | 0              |
| Presyncope                           |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Sensory loss                         |                |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0             | 0              |
| Blood and lymphatic system disorders |                |               |                |
| Anaemia                              |                |               |                |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                    | 1              | 0             | 1              |
| Neutropenia                          |                |               |                |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                    | 1              | 0             | 0              |

|   |                     |                    |                     |
|---|---------------------|--------------------|---------------------|
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Febrile neutropenia<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 2 (50.00%)<br>1 | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Pancytopenia<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Ear and labyrinth disorders<br>Tinnitus<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Hypoacusis<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 1 / 2 (50.00%)<br>1 |
| Eye disorders<br>Vision blurred<br>subjects affected / exposed<br>occurrences (all)         | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Vitreous floaters<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Eyelid function disorder<br>subjects affected / exposed<br>occurrences (all)                | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Gastrointestinal disorders  |                     |                    |                     |

|                                  |                 |                |                 |
|----------------------------------|-----------------|----------------|-----------------|
| Vomiting                         |                 |                |                 |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 2 / 2 (100.00%) |
| occurrences (all)                | 0               | 0              | 2               |
| Constipation                     |                 |                |                 |
| subjects affected / exposed      | 2 / 2 (100.00%) | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 2               | 0              | 0               |
| Nausea                           |                 |                |                 |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 1 / 2 (50.00%) | 2 / 2 (100.00%) |
| occurrences (all)                | 0               | 1              | 2               |
| Diarrhoea                        |                 |                |                 |
| subjects affected / exposed      | 2 / 2 (100.00%) | 0 / 2 (0.00%)  | 1 / 2 (50.00%)  |
| occurrences (all)                | 3               | 0              | 1               |
| Abdominal pain                   |                 |                |                 |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0               | 0              | 0               |
| Gastrooesophageal reflux disease |                 |                |                 |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0               | 0              | 0               |
| Anal incontinence                |                 |                |                 |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0               | 0              | 0               |
| Stomatitis                       |                 |                |                 |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0               | 0              | 0               |
| Dry mouth                        |                 |                |                 |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0               | 0              | 0               |
| Dyspepsia                        |                 |                |                 |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0               | 0              | 0               |
| Abdominal distension             |                 |                |                 |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0               | 0              | 0               |
| Abdominal pain upper             |                 |                |                 |
| subjects affected / exposed      | 0 / 2 (0.00%)   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0               | 0              | 0               |

|  |                |               |               |
|--|----------------|---------------|---------------|
| Dysphagia                              |                |               |               |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Toothache                              |                |               |               |
| subjects affected / exposed            | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 1              | 0             | 0             |
| Rectal haemorrhage                     |                |               |               |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Flatulence                             |                |               |               |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Ascites                                |                |               |               |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Odynophagia                            |                |               |               |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Skin and subcutaneous tissue disorders |                |               |               |
| Dry skin                               |                |               |               |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Rash                                   |                |               |               |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Pruritus                               |                |               |               |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Hyperhidrosis                          |                |               |               |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Alopecia                               |                |               |               |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                      | 0              | 0             | 0             |
| Erythema                               |                |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Night sweats                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Renal and urinary disorders                     |               |               |               |
| Dysuria   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Pollakiuria                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Acute kidney injury                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Urinary incontinence                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Urinary retention                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Haematuria                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Urinary tract obstruction                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Bladder spasm                                   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Musculoskeletal and connective tissue disorders |               |               |               |
| Myalgia   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Pain in extremity                               |               |               |               |



|                                   |                |               |                |
|-----------------------------------|----------------|---------------|----------------|
| subjects affected / exposed       | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                 | 1              | 0             | 0              |
| Muscular weakness                 |                |               |                |
| subjects affected / exposed       | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                 | 1              | 0             | 0              |
| Arthralgia                        |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Back pain                         |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                 | 0              | 0             | 1              |
| Muscle spasms                     |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Flank pain                        |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Bone pain                         |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Neck pain                         |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Tenosynovitis stenosaurs          |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Groin pain                        |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Infections and infestations       |                |               |                |
| Upper respiratory tract infection |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |
| Herpes zoster                     |                |               |                |
| subjects affected / exposed       | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                 | 0              | 0             | 0              |

|                                       |               |               |                |
|---------------------------------------|---------------|---------------|----------------|
| Sinusitis                             |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Urinary tract infection               |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Pneumonia                             |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Candida infection                     |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Oral candidiasis                      |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                     | 0             | 0             | 1              |
| Clostridium difficile infection       |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Covid-19                              |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Nasopharyngitis                       |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Conjunctivitis                        |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Clostridium difficile colitis         |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Respiratory syncytial virus infection |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Tooth infection                       |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |

|   |                |               |                |
|---|----------------|---------------|----------------|
| Oral herpes                             |                |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                       | 0              | 0             | 0              |
| Folliculitis                            |                |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                       | 0              | 0             | 0              |
| Rhinitis                                |                |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                       | 0              | 0             | 0              |
| Ear infection                           |                |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                       | 0              | 0             | 0              |
| Tinea versicolour                       |                |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                       | 0              | 0             | 0              |
| Viral upper respiratory tract infection |                |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                       | 0              | 0             | 0              |
| Wound infection                         |                |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                       | 0              | 0             | 0              |
| Metabolism and nutrition disorders      |                |               |                |
| Hypokalaemia                            |                |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                       | 0              | 0             | 1              |
| Decreased appetite                      |                |               |                |
| subjects affected / exposed             | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                       | 0              | 0             | 0              |
| Hypophosphataemia                       |                |               |                |
| subjects affected / exposed             | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                       | 3              | 0             | 0              |
| Hyponatraemia                           |                |               |                |
| subjects affected / exposed             | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                       | 4              | 0             | 0              |
| Hypoalbuminaemia                        |                |               |                |

|                             |                |               |               |
|-----------------------------|----------------|---------------|---------------|
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 2              | 0             | 0             |
| Hypocalcaemia               |                |               |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Hypernatraemia              |                |               |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Hyperglycaemia              |                |               |               |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 2              | 0             | 0             |
| Hypomagnesaemia             |                |               |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Dehydration                 |                |               |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Hyperkalaemia               |                |               |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Hypermagnesaemia            |                |               |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Malnutrition                |                |               |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Metabolic acidosis          |                |               |               |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |

|   |   |  |  |
|---|---|--|--|
| <b>Non-serious adverse events</b>                                   | Phase 2 (Safety Management Study): Cohort 6 |  |  |
| Total subjects affected by non-serious adverse events               |   |  |  |
| subjects affected / exposed   | 40 / 40 (100.00%)                           |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |  |  |

|  |                        |  |  |
|--|------------------------|--|--|
| Squamous cell carcinoma<br>subjects affected / exposed<br>occurrences (all)    | 2 / 40 (5.00%)<br>2    |  |  |
| Myelodysplastic syndrome<br>subjects affected / exposed<br>occurrences (all)   | 0 / 40 (0.00%)<br>0    |  |  |
| Cancer pain<br>subjects affected / exposed<br>occurrences (all)                | 0 / 40 (0.00%)<br>0    |  |  |
| Vascular disorders   |                        |  |  |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)                | 21 / 40 (52.50%)<br>30 |  |  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)               | 4 / 40 (10.00%)<br>8   |  |  |
| Capillary leak syndrome<br>subjects affected / exposed<br>occurrences (all)    | 0 / 40 (0.00%)<br>0    |  |  |
| Deep vein thrombosis<br>subjects affected / exposed<br>occurrences (all)       | 3 / 40 (7.50%)<br>3    |  |  |
| Hot flush<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 40 (0.00%)<br>0    |  |  |
| Embolism<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 40 (5.00%)<br>2    |  |  |
| Subclavian vein thrombosis<br>subjects affected / exposed<br>occurrences (all) | 0 / 40 (0.00%)<br>0    |  |  |
| General disorders and administration<br>site conditions                        |                        |  |  |
| Chills<br>subjects affected / exposed<br>occurrences (all)                     | 8 / 40 (20.00%)<br>8   |  |  |
| Fatigue  |                        |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 18 / 40 (45.00%) |  |  |
| occurrences (all)           | 25               |  |  |
| Pyrexia                     |                  |  |  |
| subjects affected / exposed | 33 / 40 (82.50%) |  |  |
| occurrences (all)           | 41               |  |  |
| Asthenia                    |                  |  |  |
| subjects affected / exposed | 5 / 40 (12.50%)  |  |  |
| occurrences (all)           | 5                |  |  |
| Pain                        |                  |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Malaise                     |                  |  |  |
| subjects affected / exposed | 2 / 40 (5.00%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Non-cardiac chest pain      |                  |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Gait disturbance            |                  |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Influenza like illness      |                  |  |  |
| subjects affected / exposed | 2 / 40 (5.00%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Oedema                      |                  |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Oedema peripheral           |                  |  |  |
| subjects affected / exposed | 3 / 40 (7.50%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Chest pain                  |                  |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| Peripheral swelling         |                  |  |  |
| subjects affected / exposed | 2 / 40 (5.00%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Swelling                    |                  |  |  |

|  |  |  |  |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>0 / 40 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>   |  |  |  |
| <p>Puncture site pain</p> <p>subjects affected / exposed</p> <p>0 / 40 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>   |  |  |  |
| <p>Catheter site pain</p> <p>subjects affected / exposed</p> <p>0 / 40 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>   |  |  |  |
| <p>Hernia</p> <p>subjects affected / exposed</p> <p>0 / 40 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>   |  |  |  |
| <p>Immune system disorders</p> <p>Hypogammaglobulinaemia</p> <p>subjects affected / exposed</p> <p>8 / 40 (20.00%)</p> <p>occurrences (all)</p> <p>11</p> <p>Graft versus host disease</p> <p>subjects affected / exposed</p> <p>0 / 40 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>  |  |  |  |
| <p>Reproductive system and breast disorders</p> <p>Scrotal oedema</p> <p>subjects affected / exposed</p> <p>0 / 40 (0.00%)</p> <p>occurrences (all)</p> <p>0</p> <p>Perineal pain</p> <p>subjects affected / exposed</p> <p>0 / 40 (0.00%)</p> <p>occurrences (all)</p> <p>0</p>   |  |  |  |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Hypoxia</p> <p>subjects affected / exposed</p> <p>7 / 40 (17.50%)</p> <p>occurrences (all)</p> <p>8</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>6 / 40 (15.00%)</p> <p>occurrences (all)</p> <p>8</p> <p>Nasal congestion</p> <p>subjects affected / exposed</p> <p>4 / 40 (10.00%)</p> <p>occurrences (all)</p> <p>4</p> <p>Oropharyngeal pain</p> |  |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 2 / 40 (5.00%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Pleural effusion            |                 |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Dyspnoea                    |                 |  |  |
| subjects affected / exposed | 8 / 40 (20.00%) |  |  |
| occurrences (all)           | 12              |  |  |
| Wheezing                    |                 |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Pulmonary oedema            |                 |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Upper-airway cough syndrome |                 |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Tachypnoea                  |                 |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Hiccups                     |                 |  |  |
| subjects affected / exposed | 3 / 40 (7.50%)  |  |  |
| occurrences (all)           | 5               |  |  |
| Laryngeal haemorrhage       |                 |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Rhinitis allergic           |                 |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Rhinorrhoea                 |                 |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Atelectasis                 |                 |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)  |  |  |
| occurrences (all)           | 0               |  |  |
| Paranasal cyst              |                 |  |  |



|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| Psychiatric disorders       |                  |  |  |
| Anxiety                     |                  |  |  |
| subjects affected / exposed | 4 / 40 (10.00%)  |  |  |
| occurrences (all)           | 5                |  |  |
| Insomnia                    |                  |  |  |
| subjects affected / exposed | 6 / 40 (15.00%)  |  |  |
| occurrences (all)           | 6                |  |  |
| Confusional state           |                  |  |  |
| subjects affected / exposed | 12 / 40 (30.00%) |  |  |
| occurrences (all)           | 14               |  |  |
| Agitation                   |                  |  |  |
| subjects affected / exposed | 3 / 40 (7.50%)   |  |  |
| occurrences (all)           | 4                |  |  |
| Hallucination               |                  |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Mental status changes       |                  |  |  |
| subjects affected / exposed | 2 / 40 (5.00%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Delirium                    |                  |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Bradyphrenia                |                  |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| Disorientation              |                  |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| Depression                  |                  |  |  |
| subjects affected / exposed | 3 / 40 (7.50%)   |  |  |
| occurrences (all)           | 3                |  |  |
| Restlessness                |                  |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)   |  |  |
| occurrences (all)           | 1                |  |  |

|  |                        |  |  |
|--|------------------------|--|--|
| Mood altered<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 40 (0.00%)<br>0    |  |  |
| Investigations   |                        |  |  |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all)     | 10 / 40 (25.00%)<br>24 |  |  |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)             | 6 / 40 (15.00%)<br>6   |  |  |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)           | 14 / 40 (35.00%)<br>25 |  |  |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)           | 7 / 40 (17.50%)<br>11  |  |  |
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)         | 1 / 40 (2.50%)<br>1    |  |  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                     | 2 / 40 (5.00%)<br>2    |  |  |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 40 (0.00%)<br>0    |  |  |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)   | 1 / 40 (2.50%)<br>1    |  |  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)           | 1 / 40 (2.50%)<br>1    |  |  |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 40 (0.00%)<br>0    |  |  |
| Serum ferritin increased   |                        |  |  |

|                                     |                |  |  |
|-------------------------------------|----------------|--|--|
| subjects affected / exposed         | 1 / 40 (2.50%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Weight increased                    |                |  |  |
| subjects affected / exposed         | 0 / 40 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Blood bilirubin increased           |                |  |  |
| subjects affected / exposed         | 1 / 40 (2.50%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Gamma-glutamyltransferase increased |                |  |  |
| subjects affected / exposed         | 0 / 40 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Blood immunoglobulin G decreased    |                |  |  |
| subjects affected / exposed         | 0 / 40 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Blood potassium decreased           |                |  |  |
| subjects affected / exposed         | 0 / 40 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Urine output decreased              |                |  |  |
| subjects affected / exposed         | 0 / 40 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Immunoglobulins decreased           |                |  |  |
| subjects affected / exposed         | 0 / 40 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Blood fibrinogen decreased          |                |  |  |
| subjects affected / exposed         | 1 / 40 (2.50%) |  |  |
| occurrences (all)                   | 1              |  |  |
| Oxygen saturation decreased         |                |  |  |
| subjects affected / exposed         | 0 / 40 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Blood albumin decreased             |                |  |  |
| subjects affected / exposed         | 0 / 40 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |
| Blood magnesium decreased           |                |  |  |
| subjects affected / exposed         | 0 / 40 (0.00%) |  |  |
| occurrences (all)                   | 0              |  |  |

|  |                 |  |  |
|--|-----------------|--|--|
| Injury, poisoning and procedural complications |                 |  |  |
| Skin abrasion                                  |                 |  |  |
| subjects affected / exposed                    | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                              | 1               |  |  |
| Infusion related reaction                      |                 |  |  |
| subjects affected / exposed                    | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                              | 0               |  |  |
| Fall   |                 |  |  |
| subjects affected / exposed                    | 3 / 40 (7.50%)  |  |  |
| occurrences (all)                              | 4               |  |  |
| Head injury                                    |                 |  |  |
| subjects affected / exposed                    | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                              | 2               |  |  |
| Procedural pain                                |                 |  |  |
| subjects affected / exposed                    | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                              | 0               |  |  |
| Cardiac disorders                              |                 |  |  |
| Atrial fibrillation                            |                 |  |  |
| subjects affected / exposed                    | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                              | 1               |  |  |
| Sinus bradycardia                              |                 |  |  |
| subjects affected / exposed                    | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                              | 1               |  |  |
| Ventricular arrhythmia                         |                 |  |  |
| subjects affected / exposed                    | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                              | 0               |  |  |
| Sinus tachycardia                              |                 |  |  |
| subjects affected / exposed                    | 5 / 40 (12.50%) |  |  |
| occurrences (all)                              | 6               |  |  |
| Tachycardia                                    |                 |  |  |
| subjects affected / exposed                    | 6 / 40 (15.00%) |  |  |
| occurrences (all)                              | 8               |  |  |
| Bradycardia                                    |                 |  |  |
| subjects affected / exposed                    | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                              | 1               |  |  |
| Acute left ventricular failure                 |                 |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| Ventricular tachycardia     |                  |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |
| Nervous system disorders    |                  |  |  |
| Tremor                      |                  |  |  |
| subjects affected / exposed | 9 / 40 (22.50%)  |  |  |
| occurrences (all)           | 12               |  |  |
| Headache                    |                  |  |  |
| subjects affected / exposed | 13 / 40 (32.50%) |  |  |
| occurrences (all)           | 16               |  |  |
| Encephalopathy              |                  |  |  |
| subjects affected / exposed | 3 / 40 (7.50%)   |  |  |
| occurrences (all)           | 4                |  |  |
| Dysarthria                  |                  |  |  |
| subjects affected / exposed | 2 / 40 (5.00%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Somnolence                  |                  |  |  |
| subjects affected / exposed | 5 / 40 (12.50%)  |  |  |
| occurrences (all)           | 5                |  |  |
| Aphasia                     |                  |  |  |
| subjects affected / exposed | 4 / 40 (10.00%)  |  |  |
| occurrences (all)           | 4                |  |  |
| Dizziness                   |                  |  |  |
| subjects affected / exposed | 6 / 40 (15.00%)  |  |  |
| occurrences (all)           | 7                |  |  |
| Memory impairment           |                  |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)   |  |  |
| occurrences (all)           | 1                |  |  |
| Paraesthesia                |                  |  |  |
| subjects affected / exposed | 2 / 40 (5.00%)   |  |  |
| occurrences (all)           | 2                |  |  |
| Dysgeusia                   |                  |  |  |
| subjects affected / exposed | 0 / 40 (0.00%)   |  |  |
| occurrences (all)           | 0                |  |  |

|                                 |                |  |  |
|---------------------------------|----------------|--|--|
| Dyskinesia                      |                |  |  |
| subjects affected / exposed     | 0 / 40 (0.00%) |  |  |
| occurrences (all)               | 0              |  |  |
| Dysgraphia                      |                |  |  |
| subjects affected / exposed     | 1 / 40 (2.50%) |  |  |
| occurrences (all)               | 1              |  |  |
| Seizure                         |                |  |  |
| subjects affected / exposed     | 1 / 40 (2.50%) |  |  |
| occurrences (all)               | 1              |  |  |
| Disturbance in attention        |                |  |  |
| subjects affected / exposed     | 1 / 40 (2.50%) |  |  |
| occurrences (all)               | 1              |  |  |
| Post herpetic neuralgia         |                |  |  |
| subjects affected / exposed     | 1 / 40 (2.50%) |  |  |
| occurrences (all)               | 1              |  |  |
| Head discomfort                 |                |  |  |
| subjects affected / exposed     | 0 / 40 (0.00%) |  |  |
| occurrences (all)               | 0              |  |  |
| Dementia                        |                |  |  |
| subjects affected / exposed     | 2 / 40 (5.00%) |  |  |
| occurrences (all)               | 2              |  |  |
| Peripheral sensory neuropathy   |                |  |  |
| subjects affected / exposed     | 0 / 40 (0.00%) |  |  |
| occurrences (all)               | 0              |  |  |
| Apraxia                         |                |  |  |
| subjects affected / exposed     | 2 / 40 (5.00%) |  |  |
| occurrences (all)               | 2              |  |  |
| Muscle contractions involuntary |                |  |  |
| subjects affected / exposed     | 0 / 40 (0.00%) |  |  |
| occurrences (all)               | 0              |  |  |
| Poor sucking reflex             |                |  |  |
| subjects affected / exposed     | 0 / 40 (0.00%) |  |  |
| occurrences (all)               | 0              |  |  |
| Peripheral motor neuropathy     |                |  |  |
| subjects affected / exposed     | 0 / 40 (0.00%) |  |  |
| occurrences (all)               | 0              |  |  |

|   |                        |  |  |
|---|------------------------|--|--|
| Presyncope<br>subjects affected / exposed<br>occurrences (all)          | 0 / 40 (0.00%)<br>0    |  |  |
| Sensory loss<br>subjects affected / exposed<br>occurrences (all)        | 0 / 40 (0.00%)<br>0    |  |  |
| Blood and lymphatic system disorders                                    |                        |  |  |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)             | 13 / 40 (32.50%)<br>16 |  |  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)         | 20 / 40 (50.00%)<br>43 |  |  |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)    | 10 / 40 (25.00%)<br>18 |  |  |
| Febrile neutropenia<br>subjects affected / exposed<br>occurrences (all) | 2 / 40 (5.00%)<br>2    |  |  |
| Pancytopenia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 40 (0.00%)<br>0    |  |  |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)          | 7 / 40 (17.50%)<br>15  |  |  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)         | 4 / 40 (10.00%)<br>6   |  |  |
| Ear and labyrinth disorders   |                        |  |  |
| Tinnitus<br>subjects affected / exposed<br>occurrences (all)            | 0 / 40 (0.00%)<br>0    |  |  |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)            | 0 / 40 (0.00%)<br>0    |  |  |
| Hypoacusis  |                        |  |  |

|  |                        |  |  |
|--|------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)                                     | 0 / 40 (0.00%)<br>0    |  |  |
| Eye disorders  |                        |  |  |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 40 (5.00%)<br>2    |  |  |
| Vitreous floaters<br>subjects affected / exposed<br>occurrences (all)                | 2 / 40 (5.00%)<br>2    |  |  |
| Eyelid function disorder<br>subjects affected / exposed<br>occurrences (all)         | 0 / 40 (0.00%)<br>0    |  |  |
| Gastrointestinal disorders   |                        |  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                         | 8 / 40 (20.00%)<br>9   |  |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)                     | 15 / 40 (37.50%)<br>19 |  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                           | 14 / 40 (35.00%)<br>20 |  |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                        | 11 / 40 (27.50%)<br>14 |  |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                   | 5 / 40 (12.50%)<br>5   |  |  |
| Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all) | 1 / 40 (2.50%)<br>1    |  |  |
| Anal incontinence<br>subjects affected / exposed<br>occurrences (all)                | 2 / 40 (5.00%)<br>2    |  |  |
| Stomatitis   |                        |  |  |



|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed            | 1 / 40 (2.50%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Dry mouth                              |                |  |  |
| subjects affected / exposed            | 3 / 40 (7.50%) |  |  |
| occurrences (all)                      | 3              |  |  |
| Dyspepsia                              |                |  |  |
| subjects affected / exposed            | 1 / 40 (2.50%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Abdominal distension                   |                |  |  |
| subjects affected / exposed            | 0 / 40 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Abdominal pain upper                   |                |  |  |
| subjects affected / exposed            | 1 / 40 (2.50%) |  |  |
| occurrences (all)                      | 5              |  |  |
| Dysphagia                              |                |  |  |
| subjects affected / exposed            | 1 / 40 (2.50%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Toothache                              |                |  |  |
| subjects affected / exposed            | 1 / 40 (2.50%) |  |  |
| occurrences (all)                      | 1              |  |  |
| Rectal haemorrhage                     |                |  |  |
| subjects affected / exposed            | 2 / 40 (5.00%) |  |  |
| occurrences (all)                      | 2              |  |  |
| Flatulence                             |                |  |  |
| subjects affected / exposed            | 0 / 40 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Ascites                                |                |  |  |
| subjects affected / exposed            | 0 / 40 (0.00%) |  |  |
| occurrences (all)                      | 0              |  |  |
| Odynophagia                            |                |  |  |
| subjects affected / exposed            | 2 / 40 (5.00%) |  |  |
| occurrences (all)                      | 2              |  |  |
| Skin and subcutaneous tissue disorders |                |  |  |
| Dry skin                               |                |  |  |
| subjects affected / exposed            | 2 / 40 (5.00%) |  |  |
| occurrences (all)                      | 2              |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| Rash                        |                 |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Pruritus                    |                 |  |  |
| subjects affected / exposed | 2 / 40 (5.00%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Hyperhidrosis               |                 |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Alopecia                    |                 |  |  |
| subjects affected / exposed | 2 / 40 (5.00%)  |  |  |
| occurrences (all)           | 2               |  |  |
| Erythema                    |                 |  |  |
| subjects affected / exposed | 3 / 40 (7.50%)  |  |  |
| occurrences (all)           | 4               |  |  |
| Night sweats                |                 |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Renal and urinary disorders |                 |  |  |
| Dysuria                     |                 |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Pollakiuria                 |                 |  |  |
| subjects affected / exposed | 4 / 40 (10.00%) |  |  |
| occurrences (all)           | 4               |  |  |
| Acute kidney injury         |                 |  |  |
| subjects affected / exposed | 1 / 40 (2.50%)  |  |  |
| occurrences (all)           | 1               |  |  |
| Urinary incontinence        |                 |  |  |
| subjects affected / exposed | 3 / 40 (7.50%)  |  |  |
| occurrences (all)           | 3               |  |  |
| Urinary retention           |                 |  |  |
| subjects affected / exposed | 3 / 40 (7.50%)  |  |  |
| occurrences (all)           | 3               |  |  |
| Haematuria                  |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                               | 2               |  |  |
| Urinary tract obstruction                       |                 |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                               | 0               |  |  |
| Bladder spasm                                   |                 |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                               | 0               |  |  |
| Musculoskeletal and connective tissue disorders |                 |  |  |
| Myalgia   |                 |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                               | 1               |  |  |
| Pain in extremity                               |                 |  |  |
| subjects affected / exposed                     | 3 / 40 (7.50%)  |  |  |
| occurrences (all)                               | 3               |  |  |
| Muscular weakness                               |                 |  |  |
| subjects affected / exposed                     | 6 / 40 (15.00%) |  |  |
| occurrences (all)                               | 6               |  |  |
| Arthralgia                                      |                 |  |  |
| subjects affected / exposed                     | 9 / 40 (22.50%) |  |  |
| occurrences (all)                               | 12              |  |  |
| Back pain                                       |                 |  |  |
| subjects affected / exposed                     | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                               | 2               |  |  |
| Muscle spasms                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                               | 1               |  |  |
| Flank pain                                      |                 |  |  |
| subjects affected / exposed                     | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                               | 0               |  |  |
| Bone pain                                       |                 |  |  |
| subjects affected / exposed                     | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                               | 2               |  |  |
| Neck pain                                       |                 |  |  |

|                                   |                 |  |  |
|-----------------------------------|-----------------|--|--|
| subjects affected / exposed       | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                 | 2               |  |  |
| Tenosynovitis stenosans           |                 |  |  |
| subjects affected / exposed       | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                 | 0               |  |  |
| Groin pain                        |                 |  |  |
| subjects affected / exposed       | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                 | 0               |  |  |
| Infections and infestations       |                 |  |  |
| Upper respiratory tract infection |                 |  |  |
| subjects affected / exposed       | 3 / 40 (7.50%)  |  |  |
| occurrences (all)                 | 4               |  |  |
| Herpes zoster                     |                 |  |  |
| subjects affected / exposed       | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                 | 1               |  |  |
| Sinusitis                         |                 |  |  |
| subjects affected / exposed       | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                 | 0               |  |  |
| Urinary tract infection           |                 |  |  |
| subjects affected / exposed       | 3 / 40 (7.50%)  |  |  |
| occurrences (all)                 | 3               |  |  |
| Pneumonia                         |                 |  |  |
| subjects affected / exposed       | 1 / 40 (2.50%)  |  |  |
| occurrences (all)                 | 1               |  |  |
| Candida infection                 |                 |  |  |
| subjects affected / exposed       | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                 | 0               |  |  |
| Oral candidiasis                  |                 |  |  |
| subjects affected / exposed       | 2 / 40 (5.00%)  |  |  |
| occurrences (all)                 | 2               |  |  |
| Clostridium difficile infection   |                 |  |  |
| subjects affected / exposed       | 0 / 40 (0.00%)  |  |  |
| occurrences (all)                 | 0               |  |  |
| Covid-19                          |                 |  |  |
| subjects affected / exposed       | 4 / 40 (10.00%) |  |  |
| occurrences (all)                 | 4               |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Nasopharyngitis                         |                |  |  |
| subjects affected / exposed             | 0 / 40 (0.00%) |  |  |
| occurrences (all)                       | 0              |  |  |
| Conjunctivitis                          |                |  |  |
| subjects affected / exposed             | 1 / 40 (2.50%) |  |  |
| occurrences (all)                       | 1              |  |  |
| Clostridium difficile colitis           |                |  |  |
| subjects affected / exposed             | 0 / 40 (0.00%) |  |  |
| occurrences (all)                       | 0              |  |  |
| Respiratory syncytial virus infection   |                |  |  |
| subjects affected / exposed             | 2 / 40 (5.00%) |  |  |
| occurrences (all)                       | 2              |  |  |
| Tooth infection                         |                |  |  |
| subjects affected / exposed             | 0 / 40 (0.00%) |  |  |
| occurrences (all)                       | 0              |  |  |
| Oral herpes                             |                |  |  |
| subjects affected / exposed             | 0 / 40 (0.00%) |  |  |
| occurrences (all)                       | 0              |  |  |
| Folliculitis                            |                |  |  |
| subjects affected / exposed             | 0 / 40 (0.00%) |  |  |
| occurrences (all)                       | 0              |  |  |
| Rhinitis                                |                |  |  |
| subjects affected / exposed             | 2 / 40 (5.00%) |  |  |
| occurrences (all)                       | 2              |  |  |
| Ear infection                           |                |  |  |
| subjects affected / exposed             | 0 / 40 (0.00%) |  |  |
| occurrences (all)                       | 0              |  |  |
| Tinea versicolour                       |                |  |  |
| subjects affected / exposed             | 0 / 40 (0.00%) |  |  |
| occurrences (all)                       | 0              |  |  |
| Viral upper respiratory tract infection |                |  |  |
| subjects affected / exposed             | 0 / 40 (0.00%) |  |  |
| occurrences (all)                       | 0              |  |  |
| Wound infection                         |                |  |  |
| subjects affected / exposed             | 0 / 40 (0.00%) |  |  |
| occurrences (all)                       | 0              |  |  |

|                                    |                  |  |  |
|------------------------------------|------------------|--|--|
| Metabolism and nutrition disorders |                  |  |  |
| Hypokalaemia                       |                  |  |  |
| subjects affected / exposed        | 11 / 40 (27.50%) |  |  |
| occurrences (all)                  | 14               |  |  |
| Decreased appetite                 |                  |  |  |
| subjects affected / exposed        | 8 / 40 (20.00%)  |  |  |
| occurrences (all)                  | 13               |  |  |
| Hypophosphataemia                  |                  |  |  |
| subjects affected / exposed        | 11 / 40 (27.50%) |  |  |
| occurrences (all)                  | 12               |  |  |
| Hyponatraemia                      |                  |  |  |
| subjects affected / exposed        | 6 / 40 (15.00%)  |  |  |
| occurrences (all)                  | 8                |  |  |
| Hypoalbuminaemia                   |                  |  |  |
| subjects affected / exposed        | 2 / 40 (5.00%)   |  |  |
| occurrences (all)                  | 2                |  |  |
| Hypocalcaemia                      |                  |  |  |
| subjects affected / exposed        | 2 / 40 (5.00%)   |  |  |
| occurrences (all)                  | 2                |  |  |
| Hypernatraemia                     |                  |  |  |
| subjects affected / exposed        | 1 / 40 (2.50%)   |  |  |
| occurrences (all)                  | 3                |  |  |
| Hyperglycaemia                     |                  |  |  |
| subjects affected / exposed        | 4 / 40 (10.00%)  |  |  |
| occurrences (all)                  | 6                |  |  |
| Hypomagnesaemia                    |                  |  |  |
| subjects affected / exposed        | 4 / 40 (10.00%)  |  |  |
| occurrences (all)                  | 6                |  |  |
| Dehydration                        |                  |  |  |
| subjects affected / exposed        | 2 / 40 (5.00%)   |  |  |
| occurrences (all)                  | 2                |  |  |
| Hyperkalaemia                      |                  |  |  |
| subjects affected / exposed        | 1 / 40 (2.50%)   |  |  |
| occurrences (all)                  | 1                |  |  |
| Hypermagnesaemia                   |                  |  |  |

|                             |                |  |  |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Malnutrition                |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |
| Metabolic acidosis          |                |  |  |
| subjects affected / exposed | 0 / 40 (0.00%) |  |  |
| occurrences (all)           | 0              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 20 January 2015  | <ul style="list-style-type: none"><li>• Visit windows for screening, leukapheresis, and Month 1 imaging were expanded to provide greater logistical flexibility for the subjects and study sites.</li><li>• Additional toxicity assessments prior to the infusion of axicabtagene ciloleucel were added.</li><li>• Recovery criteria for discharge of subject from hospital after Day 7 were expanded.</li><li>• Grade 3 or higher CRS was designated for expedited safety reporting.</li></ul>   |
| 27 February 2015 | <ul style="list-style-type: none"><li>• Total sample size of the study was increased from approximately 118–124 to 118–136 subjects based upon the contingency for additional cohort assessment in Phase 1.</li><li>• Exclusion criterion was added for subjects with a history of aminoglycoside hypersensitivity.</li><li>• Cyclophosphamide dose for the initial A1 cohort in Phase 1 was increased from 300 to 500 mg/m<sup>2</sup>/day.</li><li>• Contingency for an additional cohort (B1) added in the event that a more intensive lymphodepletion therapy is deemed warranted. Subjects would receive 30 mg/kg cyclophosphamide Days –7 and –6 and 25 mg/m<sup>2</sup> fludarabine Days –5 through –1.</li><li>• Objective response rate, the primary endpoint of Phase 2, was specified to be based on investigator assessment; response rate according to the central reviewer was designated as a secondary endpoint.</li></ul>  |
| 27 October 2015  | <ul style="list-style-type: none"><li>• Enrollment was aligned with the day of leukapheresis.</li><li>• Eligibility criteria governing renal, hepatic, cardiac, pulmonary function were revised (adding oxygen saturation of &gt; 92%, adding cardiac and pleural effusion criteria).</li><li>• Deep vein thrombosis and pulmonary embolism were added as exclusion criteria.</li><li>• Clarification that indwelling line or drain were exclusion criteria but Ommaya reservoir and dedicated central venous access catheters were permitted.</li><li>• Clarifications were made for the concomitant use of corticosteroids and other agents with immunosuppressive potential for the management of CRS and neurologic events.</li><li>• Expanded instructions were given for management of possible hypotension and renal insufficiency arising from CRS; specifically, use of IV saline was detailed.</li><li>• Blood samples were added for measurement of cytokine levels, CRP, and antibodies to axicabtagene ciloleucel or bovine serum albumin.</li><li>• Expanded instructions were given about subject requirements prior to initiating leukapheresis; namely, no significant infection before proceeding with leukapheresis.</li><li>• Instructions were added for subjects eligible to receive a second treatment with axicabtagene ciloleucel.</li></ul> |



|                 |  |
|-----------------|--|
| 18 April 2016   | <ul style="list-style-type: none"> <li>• IND and EudraCT numbers added to title page.</li> <li>• Several eligibility criteria in Section 5 were clarified as related to prior radiation or systemic therapy, history of hepatitis B or C, history of CNS lymphoma, and history of autoimmune disease.</li> <li>• Section 6 was updated with additional toxicity management guidance to include specific treatments for CRS, management of cardiac toxicity, management of neurologic events, deep vein thrombosis prophylaxis.</li> <li>• Description of histiocytosis haematophagic/hemophagocytic lymphohistiocytosis (HLH) was added.</li> <li>• Lumbar puncture when expect expansion, infiltration of the CAR T cells, and neurologic events were added.</li> <li>• Confirmation of eligibility with PET-CT.</li> <li>• Recommendation that CRP, ferritin, and LDH (if elevated at baseline) be monitored daily starting at Day 0 through hospitalization.</li> </ul> |
| 05 January 2022 | <ul style="list-style-type: none"> <li>• A Long-term Follow-up (LTFU) protocol, KT-US-982-5968 has been developed to allow for rollover of subjects to complete the 15-year follow-up after infusion of KTE-C19 on the KTE-C19-101/ZUMA-1 study. Subjects will be provided the opportunity to rollover to the LTFU protocol after a minimum of 24-months follow-up for safety follow-up and reduced burden of study-specific assessments.</li> </ul>   |
| 22 June 2022    | <ul style="list-style-type: none"> <li>• References to availability of retreatment with axicabtagene ciloleucel in the KT-US-982-5968 long-term follow-up (LTFU) have been removed following a separate amendment to the LTFU protocol.</li> </ul>   |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported