



## Clinical trial results:

### A Phase 1/2 Open-Label Study to Evaluate the Safety and Efficacy of Loncastuximab Tesirine and Ibrutinib in Patients with Advanced Diffuse Large B-Cell Lymphoma or Mantle Cell Lymphoma (LOTIS-3)

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2018-002625-38   |
| Trial protocol           | BE GB IT         |
| Global end of trial date | 08 November 2022 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 07 December 2023 |
| First version publication date | 07 December 2023 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | ADCT-402-103 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03684694 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | ADC Therapeutics SA   |
| Sponsor organisation address | Route de la Corniche, 3B, Epalinges, Switzerland, 1066                                  |
| Public contact               | Clinical Trials Information, ADC Therapeutics SA,<br>clinicaltrials@adctherapeutics.com |
| Scientific contact           | Clinical Trials Information, ADC Therapeutics SA,<br>clinicaltrials@adctherapeutics.com |

Notes:

##### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 08 November 2022 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 08 November 2022 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

Phase 1: To characterize the safety and tolerability of loncastuximab tesirine in combination with ibrutinib, and to identify the maximum tolerated dose (MTD) /recommended dose and schedule for future studies.

Phase 2: To evaluate the efficacy of loncastuximab tesirine in combination with ibrutinib in participants with relapsed or refractory diffuse large B-Cell lymphoma (DLBCL).

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki in place at the time of study conduct. The study was conducted in compliance with the International Conference on Harmonisation (ICH) E6 Guideline for Good Clinical Practice (GCP) (Committee for Proprietary Medicinal Products [CPMP] guideline CPMP/ICH/135/95) and the European Union Clinical Trial Directive (EU CTD): Directive 2001/20/EC.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 01 December 2018 |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety, Efficacy |
| Long term follow-up duration                              | 2 Years          |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Spain: 8          |
| Country: Number of subjects enrolled | Belgium: 24       |
| Country: Number of subjects enrolled | France: 16        |
| Country: Number of subjects enrolled | Italy: 58         |
| Country: Number of subjects enrolled | United States: 30 |
| Worldwide total number of subjects   | 136               |
| EEA total number of subjects         | 106               |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |

|  |    |
|--|----|
| Newborns (0-27 days)                     | 0  |
| Infants and toddlers (28 days-23 months) | 0  |
| Children (2-11 years)                    | 0  |
| Adolescents (12-17 years)                | 0  |
| Adults (18-64 years)                     | 43 |
| From 65 to 84 years                      | 93 |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details:

136 participants were enrolled into sites in the United States, Belgium, France, Italy, and Spain.

### Pre-assignment

Screening details:

Participants were screened for eligibility to enroll within 28 days prior to the start of treatment.

### 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: 60 µg/kg Loncastuximab Tesirine and Ibrutinib |

Arm description:

Participants with advanced diffuse large B-Cell lymphoma (DLBCL) or mantle cell lymphoma (MCL) were enrolled to receive 60 µg/kg of loncastuximab tesirine via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Loncastuximab Tesirine |
| Investigational medicinal product code | ADCT-402               |
| Other name                             | Zynlonta               |
| Pharmaceutical forms                   | Infusion               |
| Routes of administration               | Intravenous use        |

Dosage and administration details:

Loncastuximab tesirine was received as 60, 75 or 90 µg/kg via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) in Phase 1 arms. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

In Phase 2 arms, loncastuximab tesirine was received at the recommended phase 2 dose (RP2D) of 60 µg/kg on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10 (cycle is 4 weeks for Cycles 3 onwards).

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

Dosage and administration details:

Ibrutinib was received as 560 mg oral capsules once daily.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib |
|------------------|--|

Arm description:

Participants with advanced DLBCL or MCL were enrolled to receive 75 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab

tesirine given 4 weeks apart.

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Loncastuximab Tesirine |
| Investigational medicinal product code | ADCT-402               |
| Other name                             | Zynlonta               |
| Pharmaceutical forms                   | Infusion               |
| Routes of administration               | Intravenous use        |

Dosage and administration details:

Loncastuximab tesirine was received as 60, 75 or 90 µg/kg via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) in Phase 1 arms. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

In Phase 2 arms, loncastuximab tesirine was received at the recommended phase 2 dose (RP2D) of 60 µg/kg on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10 (cycle is 4 weeks for Cycles 3 onwards).

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

Dosage and administration details:

Ibrutinib was received as 560 mg oral capsules once daily.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib |
|------------------|--|

Arm description:

Participants with advanced DLBCL or MCL were enrolled to receive 90 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Loncastuximab Tesirine |
| Investigational medicinal product code | ADCT-402               |
| Other name                             | Zynlonta               |
| Pharmaceutical forms                   | Infusion               |
| Routes of administration               | Intravenous use        |

Dosage and administration details:

Loncastuximab tesirine was received as 60, 75 or 90 µg/kg via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) in Phase 1 arms. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

In Phase 2 arms, loncastuximab tesirine was received at the recommended phase 2 dose (RP2D) of 60 µg/kg on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10 (cycle is 4 weeks for Cycles 3 onwards).

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

Dosage and administration details:

Ibrutinib was received as 560 mg oral capsules once daily.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Phase 2: Non-Germinal Center B-cell (GCB) DLBCL |
|------------------|---|

**Arm description:**

Participants with non-germinal center B-cell (GCB) DLBCL received the recommended phase 2 dose (RP2D) of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Loncastuximab Tesirine |
| Investigational medicinal product code | ADCT-402               |
| Other name                             | Zynlonta               |
| Pharmaceutical forms                   | Infusion               |
| Routes of administration               | Intravenous use        |

**Dosage and administration details:**

Loncastuximab tesirine was received as 60, 75 or 90 µg/kg via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) in Phase 1 arms. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

In Phase 2 arms, loncastuximab tesirine was received at the recommended phase 2 dose (RP2D) of 60 µg/kg on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10 (cycle is 4 weeks for Cycles 3 onwards).

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

**Dosage and administration details:**

Ibrutinib was received as 560 mg oral capsules once daily.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL |
|------------------|--|

**Arm description:**

Participants with GCB DLBCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Loncastuximab Tesirine |
| Investigational medicinal product code | ADCT-402               |
| Other name                             | Zynlonta               |
| Pharmaceutical forms                   | Infusion               |
| Routes of administration               | Intravenous use        |

**Dosage and administration details:**

Loncastuximab tesirine was received as 60, 75 or 90 µg/kg via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) in Phase 1 arms. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

In Phase 2 arms, loncastuximab tesirine was received at the recommended phase 2 dose (RP2D) of 60 µg/kg on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10 (cycle is 4 weeks for Cycles 3 onwards).

|  |           |
|--|-----------|
| Investigational medicinal product name | Ibrutinib |
| Investigational medicinal product code |           |
| Other name                             |           |
| Pharmaceutical forms                   | Capsule   |

|                          |          |
|--------------------------|----------|
| Routes of administration | Oral use |
|--------------------------|----------|

Dosage and administration details:

Ibrutinib was received as 560 mg oral capsules once daily.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL |
|------------------|--|

Arm description:

Participants with MCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Loncastuximab Tesirine |
| Investigational medicinal product code | ADCT-402               |
| Other name                             | Zynlonta               |
| Pharmaceutical forms                   | Infusion               |
| Routes of administration               | Intravenous use        |

Dosage and administration details:

Loncastuximab tesirine was received as 60, 75 or 90 µg/kg via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) in Phase 1 arms. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

In Phase 2 arms, loncastuximab tesirine was received at the recommended phase 2 dose (RP2D) of 60 µg/kg on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10 (cycle is 4 weeks for Cycles 3 onwards).

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

Dosage and administration details:

Ibrutinib was received as 560 mg oral capsules once daily.

| <b>Number of subjects in period 1</b> | Phase 1: 60 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib | Phase 1: 75 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib | Phase 1: 90 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib |
|---------------------------------------|---|---|---|
| Started                               | 37  | 4   | 6   |
| Completed                             | 0   | 1   | 1   |
| Not completed                         | 37  | 3   | 5   |
| Consent withdrawn by subject          | 1   | -   | -   |
| Investigator/Sponsor Decision         | 12  | 2   | 1   |
| Death                                 | 24  | -   | 3   |
| Miscellaneous                         | -   | 1   | -   |
| Lost to follow-up                     | -   | -   | 1   |

| Number of subjects in period 1 | Phase 2: Non-Germinal Center B-cell (GCB) DLBCL | Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL | Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL |
|--------------------------------|---|--|--|
|                                |   |  |  |
| Started                        | 49  | 30   | 10   |
| Completed                      | 0   | 0  | 0  |
| Not completed                  | 49  | 30   | 10   |
| Consent withdrawn by subject   | -   | -  | 1  |
| Investigator/Sponsor Decision  | 17  | 16   | 6  |
| Death                          | 28  | 14   | 3  |
| Miscellaneous                  | 3   | -  | -  |
| Lost to follow-up              | 1   | -  | -  |



## Baseline characteristics

### Reporting groups

|  |  |
|--|--|
| Reporting group title  | Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib     |
| Reporting group description:   |  |
| Participants with advanced diffuse large B-Cell lymphoma (DLBCL) or mantle cell lymphoma (MCL) were enrolled to receive 60 µg/kg of loncastuximab tesirine via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.                          |  |
| Reporting group title  | Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib     |
| Reporting group description:   |  |
| Participants with advanced DLBCL or MCL were enrolled to receive 75 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.  |  |
| Reporting group title  | Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib     |
| Reporting group description:   |  |
| Participants with advanced DLBCL or MCL were enrolled to receive 90 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.  |  |
| Reporting group title  | Phase 2: Non-Germinal Center B-cell (GCB) DLBCL            |
| Reporting group description:   |  |
| Participants with non-germinal center B-cell (GCB) DLBCL received the recommended phase 2 dose (RP2D) of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10. |  |
| Reporting group title  | Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL |
| Reporting group description:   |  |
| Participants with GCB DLBCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.   |  |
| Reporting group title  | Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL       |
| Reporting group description:   |  |
| Participants with MCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.   |  |

| Reporting group values                             | Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib | Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib | Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib |
|--|--|--|--|
| Number of subjects                                 | 37   | 4  | 6  |
| Age categorical<br>Units: Subjects                 |  |  |  |
| In utero   | 0  | 0  | 0  |
| Preterm newborn infants (gestational age < 37 wks) | 0  | 0  | 0  |

|  |    |   |   |
|--|----|---|---|
| Newborns (0-27 days)                     | 0  | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0  | 0 | 0 |
| Children (2-11 years)                    | 0  | 0 | 0 |
| Adolescents (12-17 years)                | 0  | 0 | 0 |
| Adults (18-64 years)                     | 11 | 1 | 3 |
| From 65-84 years                         | 23 | 3 | 3 |
| 85 years and over                        | 3  | 0 | 0 |
| Gender categorical                       |    |   |   |
| Units: Subjects                          |    |   |   |
| Female                                   | 10 | 2 | 2 |
| Male                                     | 27 | 2 | 4 |
| Ethnicity (NIH/OMB)                      |    |   |   |
| Units: Subjects                          |    |   |   |
| Hispanic or Latino                       | 0  | 0 | 0 |
| Not Hispanic or Latino                   | 37 | 4 | 6 |
| Unknown or Not Reported                  | 0  | 0 | 0 |
| Race (NIH/OMB)                           |    |   |   |
| Units: Subjects                          |    |   |   |
| Asian                                    | 0  | 0 | 0 |
| Black or African American                | 1  | 0 | 0 |
| White                                    | 35 | 4 | 6 |
| Unknown or Not Reported                  | 1  | 0 | 0 |

| <b>Reporting group values</b>                      | Phase 2: Non-Germinal Center B-cell (GCB) DLBCL | Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL | Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL |
|--|---|--|--|
| Number of subjects                                 | 49  | 30   | 10   |
| Age categorical                                    |   |  |  |
| Units: Subjects                                    |   |  |  |
| In utero   | 0   | 0  | 0  |
| Preterm newborn infants (gestational age < 37 wks) | 0   | 0  | 0  |
| Newborns (0-27 days)                               | 0   | 0  | 0  |
| Infants and toddlers (28 days-23 months)           | 0   | 0  | 0  |
| Children (2-11 years)                              | 0   | 0  | 0  |
| Adolescents (12-17 years)                          | 0   | 0  | 0  |
| Adults (18-64 years)                               | 13  | 10   | 5  |
| From 65-84 years                                   | 36  | 18   | 4  |
| 85 years and over                                  | 0   | 2  | 1  |
| Gender categorical                                 |   |  |  |
| Units: Subjects                                    |   |  |  |
| Female   | 19  | 9  | 3  |
| Male   | 30  | 21   | 7  |
| Ethnicity (NIH/OMB)                                |   |  |  |
| Units: Subjects                                    |   |  |  |
| Hispanic or Latino                                 | 2   | 0  | 0  |
| Not Hispanic or Latino                             | 47  | 27   | 9  |
| Unknown or Not Reported                            | 0   | 3  | 1  |
| Race (NIH/OMB)                                     |   |  |  |
| Units: Subjects                                    |   |  |  |

|                           |    |    |    |
|---------------------------|----|----|----|
| Asian                     | 1  | 0  | 0  |
| Black or African American | 1  | 0  | 0  |
| White                     | 43 | 26 | 10 |
| Unknown or Not Reported   | 4  | 4  | 0  |

| <b>Reporting group values</b>                         | Total |  |  |
|---|-------|--|--|
| Number of subjects                                    | 136   |  |  |
| Age categorical<br>Units: Subjects                    |       |  |  |
| In utero  | 0     |  |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0     |  |  |
| Newborns (0-27 days)                                  | 0     |  |  |
| Infants and toddlers (28 days-23<br>months)           | 0     |  |  |
| Children (2-11 years)                                 | 0     |  |  |
| Adolescents (12-17 years)                             | 0     |  |  |
| Adults (18-64 years)                                  | 43    |  |  |
| From 65-84 years                                      | 87    |  |  |
| 85 years and over                                     | 6     |  |  |
| Gender categorical<br>Units: Subjects                 |       |  |  |
| Female  | 45    |  |  |
| Male  | 91    |  |  |
| Ethnicity (NIH/OMB)<br>Units: Subjects                |       |  |  |
| Hispanic or Latino                                    | 2     |  |  |
| Not Hispanic or Latino                                | 130   |  |  |
| Unknown or Not Reported                               | 4     |  |  |
| Race (NIH/OMB)<br>Units: Subjects                     |       |  |  |
| Asian   | 1     |  |  |
| Black or African American                             | 2     |  |  |
| White   | 124   |  |  |
| Unknown or Not Reported                               | 9     |  |  |

## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib     |
| Reporting group description:<br>Participants with advanced diffuse large B-Cell lymphoma (DLBCL) or mantle cell lymphoma (MCL) were enrolled to receive 60 µg/kg of loncastuximab tesirine via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.  |  |
| Reporting group title  | Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib     |
| Reporting group description:<br>Participants with advanced DLBCL or MCL were enrolled to receive 75 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.  |  |
| Reporting group title  | Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib     |
| Reporting group description:<br>Participants with advanced DLBCL or MCL were enrolled to receive 90 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.  |  |
| Reporting group title  | Phase 2: Non-Germinal Center B-cell (GCB) DLBCL            |
| Reporting group description:<br>Participants with non-germinal center B-cell (GCB) DLBCL received the recommended phase 2 dose (RP2D) of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.   |  |
| Reporting group title  | Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL |
| Reporting group description:<br>Participants with GCB DLBCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.   |  |
| Reporting group title  | Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL       |
| Reporting group description:<br>Participants with MCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.   |  |
| Subject analysis set title   | Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib     |
| Subject analysis set type  | Safety analysis  |
| Subject analysis set description:<br>Participants with advanced diffuse large B-Cell lymphoma (DLBCL) or mantle cell lymphoma (MCL) were enrolled to receive 60 µg/kg of loncastuximab tesirine via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart. Due to the constraints of the EudraCT system, this arm has had to be added as a subject analysis set. |  |
| Subject analysis set title   | Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib     |
| Subject analysis set type  | Safety analysis  |

#### Subject analysis set description:

Participants with advanced DLBCL or MCL were enrolled to receive 75 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart. Due to the constraints of the EudraCT system, this arm has had to be added as a subject analysis set.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib |
| Subject analysis set type  | Safety analysis  |

#### Subject analysis set description:

Participants with advanced DLBCL or MCL were enrolled to receive 90 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart. Due to the constraints of the EudraCT system, this arm has had to be added as a subject analysis set.

|                            |                        |
|----------------------------|------------------------|
| Subject analysis set title | Phase 2: Non-GCB DLBCL |
| Subject analysis set type  | Full analysis          |

#### Subject analysis set description:

Participants with non-germinal center B-cell (GCB) DLBCL received the recommended phase 2 dose (RP2D) of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10. Due to the constraints of the EudraCT system, this arm has had to be added as a subject analysis set.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL |
| Subject analysis set type  | Full analysis  |

#### Subject analysis set description:

Participants with GCB DLBCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10. Due to the constraints of the EudraCT system, this arm has had to be added as a subject analysis set.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL |
| Subject analysis set type  | Full analysis  |

#### Subject analysis set description:

Participants with MCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10. Due to the constraints of the EudraCT system, this arm has had to be added as a subject analysis set.

### **Primary: Phase 1: Number of Participants With Treatment-emergent Adverse Events (TEAEs)**

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

#### End point description:

A TEAE was defined as an adverse event (AE) that occurred or worsened in the period extending from the first dose of study drug to 30 days after the last dose of study drug in this study or start of a new anticancer therapy, whichever is earlier. Any clinically significant changes from baseline in safety laboratory values, vital signs, Eastern Cooperative Oncology Group (ECOG) performance status, and 12-lead electrocardiograms (ECGs) which occurred after first dose of study drug were recorded as TEAEs.

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

#### End point timeframe:

Day 1 until 30 days after last dose; max duration of treatment was 686 days for Phase 1 (up to approximately 716 days total)

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 analyses were pre-specified for this endpoint. Descriptive statistics are presented.

| End point values            | Phase 1: 60 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib | Phase 1: 75 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib | Phase 1: 90 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib |  |
|-----------------------------|---|---|---|--|
| Subject group type          | Subject analysis set  | Subject analysis set  | Subject analysis set  |  |
| Number of subjects analysed | 37  | 4   | 6   |  |
| Units: participants         | 37  | 4   | 6   |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Phase 1: Number of Participants With Serious TEAEs

|                 |   |
|-----------------|---|
| End point title | Phase 1: Number of Participants With Serious TEAEs <sup>[2]</sup> |
|-----------------|---|

End point description:

A serious TEAE was defined as any AE which occurred after the first dose of study drug that resulted in death, was life threatening, required inpatient hospitalization or prolongation of existing hospitalization (hospitalization for elective procedures or for protocol compliance was not considered a serious adverse event), resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or important medical events that did not meet the preceding criteria but based on appropriate medical judgement may have jeopardized the participant or may have required medical or surgical intervention to prevent any of the outcomes listed above.

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

End point timeframe:

Day 1 until 30 days after last dose; max duration of treatment was 686 days for Phase 1 (up to approximately 716 days total)

Notes:

[2] - 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 analyses were pre-specified for this endpoint. Descriptive statistics are presented.

| End point values            | Phase 1: 60 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib | Phase 1: 75 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib | Phase 1: 90 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib |  |
|-----------------------------|---|---|---|--|
| Subject group type          | Subject analysis set  | Subject analysis set  | Subject analysis set  |  |
| Number of subjects analysed | 37  | 4   | 6   |  |
| Units: participants         | 19  | 0   | 3   |  |

## Statistical analyses

No statistical analyses for this end point

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

|                 |   |
|-----------------|---|
| End point title | Phase 1: Number of Participants With Dose-Limiting Toxicities (DLTs) <sup>[3]</sup> |
|-----------------|---|

End point description:

A DLT was defined as any of the following events which occur during the DLT Period (first 21 days of ibrutinib treatment), except those that are clearly due to underlying disease or extraneous causes: a hematologic DLT (grade  $\geq 3$  anaemia, grade 4/febrile neutropenia, grade  $\geq 3$  thrombocytopenia), a non-hematologic DLT (including aspartate aminotransferase [AST] and/or alanine aminotransferase [ALT]  $> 3 \times$  upper limit of normal (ULN) and bilirubin  $> 2 \times$  ULN), any other non-hematologic toxicities  $\geq$  Grade 3, with exceptions.

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

End point timeframe:

21 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 analyses were pre-specified for this endpoint. Descriptive statistics are presented.

| End point values            | Phase 1: 60 $\mu\text{g/kg}$ Loncastuximab Tesirine and Ibrutinib | Phase 1: 75 $\mu\text{g/kg}$ Loncastuximab Tesirine and Ibrutinib | Phase 1: 90 $\mu\text{g/kg}$ Loncastuximab Tesirine and Ibrutinib |  |
|-----------------------------|---|---|---|--|
| Subject group type          | Subject analysis set  | Subject analysis set  | Subject analysis set  |  |
| Number of subjects analysed | 37  | 4   | 6   |  |
| Units: participants         | 0   | 0   | 2   |  |

**Statistical analyses**

No statistical analyses for this end point

**Primary: Phase 1: Number of Participants With Dose Interruptions**

|                 |  |
|-----------------|--|
| End point title | Phase 1: Number of Participants With Dose Interruptions <sup>[4]</sup> |
|-----------------|--|

End point description:

Measured in the safety population, which included all participants who received study drug.

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

End point timeframe:

Up to a maximum of 686 days

Notes:

[4] - 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 analyses were pre-specified for this endpoint. Descriptive statistics are presented.

| End point values            | Phase 1: 60 $\mu\text{g/kg}$ Loncastuximab Tesirine and Ibrutinib | Phase 1: 75 $\mu\text{g/kg}$ Loncastuximab Tesirine and Ibrutinib | Phase 1: 90 $\mu\text{g/kg}$ Loncastuximab Tesirine and Ibrutinib |  |
|-----------------------------|---|---|---|--|
| Subject group type          | Subject analysis set  | Subject analysis set  | Subject analysis set  |  |
| Number of subjects analysed | 37  | 4   | 6   |  |
| Units: participants         | 1   | 0   | 0   |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Phase 1: Number of Participants With Dose Reductions

|                 |   |
|-----------------|---|
| End point title | Phase 1: Number of Participants With Dose Reductions <sup>[5]</sup> |
|-----------------|---|

End point description:

Measured in the safety population, which included all participants who received study drug.

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

End point timeframe:

Up to a maximum of 686 days

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 analyses were pre-specified for this endpoint. Descriptive statistics are presented.

| End point values            | Phase 1: 60 µg/kg<br>Loncastuximab<br>Tesarine and<br>Ibrutinib | Phase 1: 75 µg/kg<br>Loncastuximab<br>Tesarine and<br>Ibrutinib | Phase 1: 90 µg/kg<br>Loncastuximab<br>Tesarine and<br>Ibrutinib |  |
|-----------------------------|---|---|---|--|
| Subject group type          | Subject analysis set  | Subject analysis set  | Subject analysis set  |  |
| Number of subjects analysed | 37  | 4   | 6   |  |
| Units: participants         | 0   | 0   | 0   |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Phase 2: Complete Response Rate (CRR)

|                 |  |
|-----------------|--|
| End point title | Phase 2: Complete Response Rate (CRR) <sup>[6]</sup> |
|-----------------|--|

End point description:

CRR according to the 2014 Lugano classifications determined by Independent Review Committee (IRC). CRR was defined as the percentage of participants with a best overall response (BOR) of complete response (CR). Measured in the efficacy analysis set, which included all participants who received at least 1 dose of study drug, who had valid baseline disease assessment(s), and who had at least one valid post-baseline disease assessment. Participants who did not have a post-baseline assessment due to early clinical progression or death (after receiving study drug) were also included.

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

End point timeframe:

Up to approximately 38 months

Notes:

[6] - 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 analyses were pre-specified for this endpoint. Descriptive statistics are presented.



| <b>End point values</b>           | Phase 2: Non-GCB DLBCL | Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL | Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL |  |
|-----------------------------------|------------------------|--|--|--|
| Subject group type                | Subject analysis set   | Subject analysis set                                       | Subject analysis set                                 |  |
| Number of subjects analysed       | 48                     | 30   | 10   |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 27.1 (15.3 to 41.8)    | 26.7 (12.3 to 45.9)  | 90.0 (55.5 to 99.7)                                  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All-cause mortality from enrollment until approx. 4 years. For serious adverse events and other adverse events, from Day 1 until 30 days after last dose; max duration of treatment was 686 days for Phase 1 (up to approximately 716 days total)

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 22.0   |

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 1: 60 µg/kg Loncastuximab Tesirine and Ibrutinib |
|-----------------------|--|

Reporting group description:

Participants with advanced diffuse large B-Cell lymphoma (DLBCL) or mantle cell lymphoma (MCL) were enrolled to receive 60 µg/kg of loncastuximab tesirine via intravenous (IV) infusion once every 3 weeks (Q3W) for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 1: 75 µg/kg Loncastuximab Tesirine and Ibrutinib |
|-----------------------|--|

Reporting group description:

Participants with advanced DLBCL or MCL were enrolled to receive 75 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 1: 90 µg/kg Loncastuximab Tesirine and Ibrutinib |
|-----------------------|--|

Reporting group description:

Participants with advanced DLBCL or MCL were enrolled to receive 90 µg/kg of loncastuximab tesirine via IV infusion Q3W for 2 treatment cycles (cycle is 3 weeks for Cycles 1 and 2) with concurrent 560 mg ibrutinib orally via capsules once daily. Participants who had a response of partial response (PR) or stable disease (SD) at the 14-week assessment may have received 2 additional doses of loncastuximab tesirine given 4 weeks apart.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase 2: Non-Germinal Center B-cell (GCB) DLBCL |
|-----------------------|---|

Reporting group description:

Participants with non-germinal center B-cell (GCB) DLBCL received the recommended phase 2 dose (RP2D) of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of complete response (CR), partial response (PR), and stable disease (SD) received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL |
|-----------------------|--|

Reporting group description:

Participants with GCB DLBCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL |
|-----------------------|--|

Reporting group description:

Participants with MCL received the RP2D of 60 µg/kg loncastuximab tesirine via IV infusion with concurrent 560 mg ibrutinib orally via capsules once daily. Loncastuximab tesirine was administered on Day 1 of Cycles 1 and 2 (cycle is 3 weeks for Cycles 1 and 2, and 4 weeks for Cycles 3 onwards). Participants who had a response of CR, PR, and SD received additional doses of loncastuximab tesirine on Day 1 of Cycles 5, 6, 9 and 10.

| <b>Serious adverse events</b>                                       | Phase 1: 60 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib | Phase 1: 75 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib | Phase 1: 90 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib |
|---|---|---|---|
| Total subjects affected by serious adverse events                   |   |   |   |
| subjects affected / exposed   | 19 / 37 (51.35%)  | 0 / 4 (0.00%)   | 3 / 6 (50.00%)  |
| number of deaths (all causes)                                       | 24  | 0   | 3   |
| number of deaths resulting from adverse events                      |   |   |   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |   |   |
| Cancer pain   |   |   |   |
| subjects affected / exposed   | 1 / 37 (2.70%)  | 0 / 4 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 1   | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0   |
| Lymphoma  |   |   |   |
| subjects affected / exposed   | 0 / 37 (0.00%)  | 0 / 4 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0   |
| Tumour associated fever   |   |   |   |
| subjects affected / exposed   | 0 / 37 (0.00%)  | 0 / 4 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0   |
| Vascular disorders  |   |   |   |
| Deep vein thrombosis  |   |   |   |
| subjects affected / exposed   | 1 / 37 (2.70%)  | 0 / 4 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 1   | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0   |
| Hypotension   |   |   |   |
| subjects affected / exposed   | 1 / 37 (2.70%)  | 0 / 4 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 1   | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0   |
| General disorders and administration site conditions                |   |   |   |
| Asthenia  |   |   |   |

|   |                |               |                |
|---|----------------|---------------|----------------|
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Death   |                |               |                |
| subjects affected / exposed                     | 2 / 37 (5.41%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 2          | 0 / 0         | 0 / 1          |
| Disease progression                             |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| 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 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| 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                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |               |                |
| Acute pulmonary oedema                          |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| 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 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Haemoptysis                                     |                |               |                |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Lung disorder                                   |                |               |                |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Pleural effusion                                |                |               |               |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Pulmonary embolism                              |                |               |               |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| 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 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Psychiatric disorders                           |                |               |               |
| Delirium  |                |               |               |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Investigations                                  |                |               |               |
| Transaminases increased                         |                |               |               |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Injury, poisoning and procedural complications  |                |               |               |
| Fall  |                |               |               |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Humerus fracture                                |                |               |               |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |

|   |                |               |                |
|---|----------------|---------------|----------------|
| Cardiac disorders                               |                |               |                |
| Atrial fibrillation                             |                |               |                |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Cardiomyopathy                                  |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Cardiopulmonary failure                         |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Coronary artery disease                         |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pericardial disease                             |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pericardial effusion                            |                |               |                |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pericarditis                                    |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| 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                        |                |               |                |
| Ataxia  |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| 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 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 2 / 3          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Haemorrhagic disorder                           |                |               |               |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Lymph node pain                                 |                |               |               |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Neutropenia                                     |                |               |               |
| subjects affected / exposed                     | 2 / 37 (5.41%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 2 / 3          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Gastrointestinal disorders                      |                |               |               |
| Abdominal pain                                  |                |               |               |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Abdominal pain upper                            |                |               |               |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Ascites   |                |               |               |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Colitis   |                |               |               |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |

|   |                |               |                |
|---|----------------|---------------|----------------|
| Pneumatosis intestinalis                              |                |               |                |
| subjects affected / exposed                           | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         | 0 / 0          |
| Small intestinal obstruction                          |                |               |                |
| subjects affected / exposed                           | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         | 0 / 1          |
| Stomatitis  |                |               |                |
| subjects affected / exposed                           | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all       | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         | 0 / 0          |
| Vomiting  |                |               |                |
| subjects affected / exposed                           | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all       | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         | 0 / 0          |
| Hepatobiliary disorders                               |                |               |                |
| Cholecystitis acute                                   |                |               |                |
| subjects affected / exposed                           | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| 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                |                |               |                |
| Drug reaction with eosinophilia and systemic symptoms |                |               |                |
| subjects affected / exposed                           | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| 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                           | 2 / 37 (5.41%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all       | 0 / 2          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all            | 0 / 1          | 0 / 0         | 0 / 0          |
| Haematuria  |                |               |                |



|   |                |               |                |
|---|----------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Renal failure                                   |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Endocrine disorders                             |                |               |                |
| Inappropriate antidiuretic hormone secretion    |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| 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 |                |               |                |
| Bone swelling                                   |                |               |                |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Infections and infestations                     |                |               |                |
| Bacteraemia                                     |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Campylobacter infection                         |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Citrobacter infection                           |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Corona virus infection                          |                |               |                |

|   |                |               |                |
|---|----------------|---------------|----------------|
| subjects affected / exposed                     | 2 / 37 (5.41%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 4          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 0          |
| Enterococcal infection                          |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Escherichia sepsis                              |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Folliculitis                                    |                |               |                |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pneumocystis jirovecii infection                |                |               |                |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pneumonia                                       |                |               |                |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pneumonia fungal                                |                |               |                |
| subjects affected / exposed                     | 1 / 37 (2.70%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pneumonia parainfluenzae viral                  |                |               |                |
| subjects affected / exposed                     | 0 / 37 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pneumonia viral                                 |                |               |                |

|   |   |  |  |
|---|---|--|--|
| subjects affected / exposed                       | 0 / 37 (0.00%)                                  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 0   | 0 / 0  | 0 / 0  |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0  | 0 / 0  |
| Progressive multifocal leukoencephalopathy        |   |  |  |
| subjects affected / exposed                       | 1 / 37 (2.70%)                                  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 1   | 0 / 0  | 0 / 0  |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0  | 0 / 0  |
| Sepsis  |   |  |  |
| subjects affected / exposed                       | 0 / 37 (0.00%)                                  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| 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 / 37 (0.00%)                                  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| 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 bacterial                 |   |  |  |
| subjects affected / exposed                       | 1 / 37 (2.70%)                                  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all   | 0 / 1   | 0 / 0  | 0 / 0  |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0  | 0 / 0  |
| Urosepsis   |   |  |  |
| subjects affected / exposed                       | 0 / 37 (0.00%)                                  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| 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                |   |  |  |
| Hypercalcaemia                                    |   |  |  |
| subjects affected / exposed                       | 0 / 37 (0.00%)                                  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| 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: Non-Germinal Center B-cell (GCB) DLBCL | Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL | Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL |
| Total subjects affected by serious adverse events |   |  |  |
| subjects affected / exposed                       | 27 / 49 (55.10%)                                | 5 / 30 (16.67%)  | 5 / 10 (50.00%)                                      |

|   |                |                |                |
|---|----------------|----------------|----------------|
| number of deaths (all causes)                                       | 28             | 14             | 3              |
| number of deaths resulting from adverse events                      |                |                |                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |                |
| Cancer pain   |                |                |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Lymphoma  |                |                |                |
| subjects affected / exposed   | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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          |
| Tumour associated fever   |                |                |                |
| subjects affected / exposed   | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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          |
| Vascular disorders  |                |                |                |
| Deep vein thrombosis  |                |                |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypotension   |                |                |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions                |                |                |                |
| Asthenia  |                |                |                |
| subjects affected / exposed   | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Death   |                |                |                |
| subjects affected / exposed   | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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          |
| Disease progression   |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 30 (3.33%) | 0 / 10 (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          |
| General physical health deterioration           |                |                |                |
| subjects affected / exposed                     | 4 / 49 (8.16%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 3          | 0 / 0          | 0 / 0          |
| Oedema peripheral                               |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Acute pulmonary oedema                          |                |                |                |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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          |
| Dyspnoea  |                |                |                |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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          |
| Haemoptysis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lung disorder                                   |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| 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 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| 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                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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 failure                             |                |                |                |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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          |
| Psychiatric disorders                           |                |                |                |
| Delirium  |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| 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                                  |                |                |                |
| Transaminases increased                         |                |                |                |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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          |
| Injury, poisoning and procedural complications  |                |                |                |
| Fall  |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Humerus fracture                                |                |                |                |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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          |
| Cardiac disorders                               |                |                |                |
| Atrial fibrillation                             |                |                |                |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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          |
| Cardiomyopathy                                  |                |                |                |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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           |
| Cardiopulmonary failure                         |                |                |                 |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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           |
| Coronary artery disease                         |                |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Pericardial disease                             |                |                |                 |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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           |
| Pericardial effusion                            |                |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| 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                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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           |
| Nervous system disorders                        |                |                |                 |
| Ataxia  |                |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Blood and lymphatic system disorders            |                |                |                 |
| Febrile neutropenia                             |                |                |                 |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Haemorrhagic disorder                           |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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           |
| Lymph node pain                                 |                |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| 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 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Gastrointestinal disorders                      |                |                |                 |
| Abdominal pain                                  |                |                |                 |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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           |
| Abdominal pain upper                            |                |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| 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 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Colitis   |                |                |                 |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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           |
| Pneumatosis intestinalis                        |                |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Small intestinal obstruction                    |                |                |                 |



|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                           | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          | 0 / 0           |
| Stomatitis  |                |                |                 |
| subjects affected / exposed                           | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          | 0 / 0           |
| Vomiting  |                |                |                 |
| subjects affected / exposed                           | 0 / 49 (0.00%) | 1 / 30 (3.33%) | 0 / 10 (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           |
| Hepatobiliary disorders                               |                |                |                 |
| Cholecystitis acute                                   |                |                |                 |
| subjects affected / exposed                           | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          | 0 / 0           |
| Skin and subcutaneous tissue disorders                |                |                |                 |
| Drug reaction with eosinophilia and systemic symptoms |                |                |                 |
| subjects affected / exposed                           | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| 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 and urinary disorders                           |                |                |                 |
| Acute kidney injury                                   |                |                |                 |
| subjects affected / exposed                           | 0 / 49 (0.00%) | 1 / 30 (3.33%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 1          | 0 / 0           |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          | 0 / 0           |
| Haematuria  |                |                |                 |
| subjects affected / exposed                           | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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           |
| Renal failure   |                |                |                 |
| subjects affected / exposed                           | 0 / 49 (0.00%) | 1 / 30 (3.33%) | 0 / 10 (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           |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| Endocrine disorders                             |                |                |                 |
| Inappropriate antidiuretic hormone secretion    |                |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 30 (3.33%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Musculoskeletal and connective tissue disorders |                |                |                 |
| Bone swelling                                   |                |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| 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                     |                |                |                 |
| Bacteraemia                                     |                |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 1 / 30 (3.33%) | 0 / 10 (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           |
| Campylobacter infection                         |                |                |                 |
| subjects affected / exposed                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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           |
| Citrobacter infection                           |                |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Corona virus infection                          |                |                |                 |
| subjects affected / exposed                     | 2 / 49 (4.08%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1           |
| Enterococcal infection                          |                |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| 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                     | 1 / 49 (2.04%)  | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Folliculitis                                    |                 |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%)  | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| 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 / 49 (0.00%)  | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Pneumonia                                       |                 |                |                 |
| subjects affected / exposed                     | 1 / 49 (2.04%)  | 0 / 30 (0.00%) | 0 / 10 (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 fungal                                |                 |                |                 |
| subjects affected / exposed                     | 1 / 49 (2.04%)  | 0 / 30 (0.00%) | 0 / 10 (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 parainfluenzae viral                  |                 |                |                 |
| subjects affected / exposed                     | 1 / 49 (2.04%)  | 0 / 30 (0.00%) | 0 / 10 (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 viral                                 |                 |                |                 |
| subjects affected / exposed                     | 5 / 49 (10.20%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 8           | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 3           | 0 / 0          | 0 / 1           |
| Progressive multifocal leukoencephalopathy      |                 |                |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%)  | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Sepsis  |                 |                |                 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 2 / 49 (4.08%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 0          |
| Urinary tract infection                         |                |                |                |
| subjects affected / exposed                     | 2 / 49 (4.08%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary tract infection bacterial               |                |                |                |
| subjects affected / exposed                     | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| 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                     | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (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              |                |                |                |
| Hypercalcaemia                                  |                |                |                |
| subjects affected / exposed                     | 2 / 49 (4.08%) | 0 / 30 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

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

| <b>Non-serious adverse events</b>                     | Phase 1: 60 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib | Phase 1: 75 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib | Phase 1: 90 µg/kg<br>Loncastuximab<br>Tesirine and<br>Ibrutinib |
|---|---|---|---|
| Total subjects affected by non-serious adverse events |   |   |   |
| subjects affected / exposed                           | 37 / 37 (100.00%)   | 4 / 4 (100.00%)   | 6 / 6 (100.00%)   |
| Vascular disorders                                    |   |   |   |
| Flushing  |   |   |   |
| subjects affected / exposed                           | 0 / 37 (0.00%)  | 0 / 4 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences (all)                                     | 0   | 0   | 0   |
| Haematoma   |   |   |   |
| subjects affected / exposed                           | 3 / 37 (8.11%)  | 0 / 4 (0.00%)   | 0 / 6 (0.00%)   |
| occurrences (all)                                     | 4   | 0   | 0   |
| Hypertension  |   |   |   |

|  |                 |                |                |
|--|-----------------|----------------|----------------|
| subjects affected / exposed                          | 4 / 37 (10.81%) | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 4               | 0              | 0              |
| Phlebitis  |                 |                |                |
| subjects affected / exposed                          | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| General disorders and administration site conditions |                 |                |                |
| Asthenia   |                 |                |                |
| subjects affected / exposed                          | 6 / 37 (16.22%) | 1 / 4 (25.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 7               | 1              | 0              |
| Chest pain   |                 |                |                |
| subjects affected / exposed                          | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Chills   |                 |                |                |
| subjects affected / exposed                          | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 2               | 0              | 0              |
| Early satiety  |                 |                |                |
| subjects affected / exposed                          | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 2               | 0              | 0              |
| Fatigue  |                 |                |                |
| subjects affected / exposed                          | 9 / 37 (24.32%) | 0 / 4 (0.00%)  | 2 / 6 (33.33%) |
| occurrences (all)                                    | 10              | 0              | 3              |
| Generalised oedema                                   |                 |                |                |
| subjects affected / exposed                          | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 0               | 0              | 0              |
| Malaise  |                 |                |                |
| subjects affected / exposed                          | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 2               | 0              | 0              |
| Mucosal inflammation                                 |                 |                |                |
| subjects affected / exposed                          | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 2               | 0              | 0              |
| Oedema peripheral                                    |                 |                |                |
| subjects affected / exposed                          | 6 / 37 (16.22%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all)                                    | 10              | 2              | 1              |
| Pain   |                 |                |                |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                     | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 2               | 0              | 0              |
| Peripheral swelling                             |                 |                |                |
| subjects affected / exposed                     | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Pyrexia   |                 |                |                |
| subjects affected / exposed                     | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 2 / 6 (33.33%) |
| occurrences (all)                               | 2               | 0              | 3              |
| Sensation of foreign body                       |                 |                |                |
| subjects affected / exposed                     | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0               | 0              | 1              |
| Immune system disorders                         |                 |                |                |
| Hypogammaglobulinaemia                          |                 |                |                |
| subjects affected / exposed                     | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 2               | 0              | 0              |
| Respiratory, thoracic and mediastinal disorders |                 |                |                |
| Cough   |                 |                |                |
| subjects affected / exposed                     | 6 / 37 (16.22%) | 1 / 4 (25.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 9               | 1              | 0              |
| Dry throat                                      |                 |                |                |
| subjects affected / exposed                     | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0               | 0              | 1              |
| Dyspnoea  |                 |                |                |
| subjects affected / exposed                     | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 3               | 0              | 0              |
| Epistaxis                                       |                 |                |                |
| subjects affected / exposed                     | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 1               | 0              | 0              |
| Hiccups   |                 |                |                |
| subjects affected / exposed                     | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Oropharyngeal pain                              |                 |                |                |
| subjects affected / exposed                     | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 1               | 0              | 0              |
| Psychiatric disorders                           |                 |                |                |

|                                      |                 |                |                |
|--------------------------------------|-----------------|----------------|----------------|
| Agitation                            |                 |                |                |
| subjects affected / exposed          | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 2               | 0              | 0              |
| Anxiety                              |                 |                |                |
| subjects affected / exposed          | 4 / 37 (10.81%) | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 4               | 0              | 0              |
| Confusional state                    |                 |                |                |
| subjects affected / exposed          | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 1               | 0              | 0              |
| Depression                           |                 |                |                |
| subjects affected / exposed          | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                    | 0               | 0              | 1              |
| Insomnia                             |                 |                |                |
| subjects affected / exposed          | 3 / 37 (8.11%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 3               | 0              | 0              |
| Investigations                       |                 |                |                |
| Alanine aminotransferase increased   |                 |                |                |
| subjects affected / exposed          | 3 / 37 (8.11%)  | 0 / 4 (0.00%)  | 3 / 6 (50.00%) |
| occurrences (all)                    | 9               | 0              | 5              |
| Amylase increased                    |                 |                |                |
| subjects affected / exposed          | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 2               | 0              | 0              |
| Aspartate aminotransferase increased |                 |                |                |
| subjects affected / exposed          | 2 / 37 (5.41%)  | 1 / 4 (25.00%) | 2 / 6 (33.33%) |
| occurrences (all)                    | 3               | 1              | 3              |
| Blood bilirubin increased            |                 |                |                |
| subjects affected / exposed          | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                    | 1               | 0              | 1              |
| Blood creatinine increased           |                 |                |                |
| subjects affected / exposed          | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 3               | 0              | 0              |
| Blood iron decreased                 |                 |                |                |
| subjects affected / exposed          | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 2               | 0              | 0              |
| Coronavirus test positive            |                 |                |                |

|   |                       |                     |                     |
|---|-----------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 37 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Gamma-glutamyltransferase increased<br>subjects affected / exposed<br>occurrences (all) | 4 / 37 (10.81%)<br>11 | 0 / 4 (0.00%)<br>0  | 2 / 6 (33.33%)<br>3 |
| Lipase increased<br>subjects affected / exposed<br>occurrences (all)                    | 3 / 37 (8.11%)<br>4   | 0 / 4 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                    | 3 / 37 (8.11%)<br>3   | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Weight increased<br>subjects affected / exposed<br>occurrences (all)                    | 4 / 37 (10.81%)<br>5  | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Injury, poisoning and procedural complications  |                       |                     |                     |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 37 (2.70%)<br>1   | 0 / 4 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Fall<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 37 (2.70%)<br>3   | 1 / 4 (25.00%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Limb injury<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 37 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Skin abrasion<br>subjects affected / exposed<br>occurrences (all)                       | 2 / 37 (5.41%)<br>3   | 0 / 4 (0.00%)<br>0  | 1 / 6 (16.67%)<br>1 |
| Cardiac disorders   |                       |                     |                     |
| Acute coronary syndrome<br>subjects affected / exposed<br>occurrences (all)             | 0 / 37 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)                 | 2 / 37 (5.41%)<br>3   | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Bradycardia   |                       |                     |                     |



|                                      |                 |                |                |
|--------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed          | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Palpitations                         |                 |                |                |
| subjects affected / exposed          | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 2               | 0              | 0              |
| Sinus bradycardia                    |                 |                |                |
| subjects affected / exposed          | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 2               | 0              | 0              |
| Sinus tachycardia                    |                 |                |                |
| subjects affected / exposed          | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                    | 1               | 0              | 1              |
| Tachycardia                          |                 |                |                |
| subjects affected / exposed          | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Nervous system disorders             |                 |                |                |
| Ataxia                               |                 |                |                |
| subjects affected / exposed          | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0              |
| Dizziness                            |                 |                |                |
| subjects affected / exposed          | 1 / 37 (2.70%)  | 1 / 4 (25.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 1               | 1              | 0              |
| Headache                             |                 |                |                |
| subjects affected / exposed          | 2 / 37 (5.41%)  | 1 / 4 (25.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 2               | 1              | 0              |
| Neuropathy peripheral                |                 |                |                |
| subjects affected / exposed          | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 1               | 0              | 0              |
| Paraesthesia                         |                 |                |                |
| subjects affected / exposed          | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 2               | 0              | 0              |
| Blood and lymphatic system disorders |                 |                |                |
| Anaemia                              |                 |                |                |
| subjects affected / exposed          | 9 / 37 (24.32%) | 2 / 4 (50.00%) | 4 / 6 (66.67%) |
| occurrences (all)                    | 14              | 4              | 8              |
| Leukopenia                           |                 |                |                |

|                             |                  |                |                |
|-----------------------------|------------------|----------------|----------------|
| subjects affected / exposed | 2 / 37 (5.41%)   | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 3                | 4              | 1              |
| Lymphadenopathy             |                  |                |                |
| subjects affected / exposed | 0 / 37 (0.00%)   | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0              |
| Lymphopenia                 |                  |                |                |
| subjects affected / exposed | 1 / 37 (2.70%)   | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1                | 0              | 0              |
| Neutropenia                 |                  |                |                |
| subjects affected / exposed | 5 / 37 (13.51%)  | 3 / 4 (75.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 26               | 4              | 3              |
| Thrombocytopenia            |                  |                |                |
| subjects affected / exposed | 17 / 37 (45.95%) | 2 / 4 (50.00%) | 4 / 6 (66.67%) |
| occurrences (all)           | 38               | 3              | 8              |
| Ear and labyrinth disorders |                  |                |                |
| Vertigo                     |                  |                |                |
| subjects affected / exposed | 3 / 37 (8.11%)   | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 3                | 0              | 0              |
| Eye disorders               |                  |                |                |
| Cataract                    |                  |                |                |
| subjects affected / exposed | 0 / 37 (0.00%)   | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0                | 0              | 0              |
| Ocular hyperaemia           |                  |                |                |
| subjects affected / exposed | 1 / 37 (2.70%)   | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1                | 0              | 0              |
| Swelling of eyelid          |                  |                |                |
| subjects affected / exposed | 0 / 37 (0.00%)   | 1 / 4 (25.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0                | 1              | 0              |
| Vision blurred              |                  |                |                |
| subjects affected / exposed | 1 / 37 (2.70%)   | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1                | 0              | 0              |
| Gastrointestinal disorders  |                  |                |                |
| Abdominal pain              |                  |                |                |
| subjects affected / exposed | 2 / 37 (5.41%)   | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 2                | 0              | 2              |
| Abdominal pain upper        |                  |                |                |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Constipation                |                 |                |                |
| subjects affected / exposed | 4 / 37 (10.81%) | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 4               | 0              | 0              |
| Diarrhoea                   |                 |                |                |
| subjects affected / exposed | 9 / 37 (24.32%) | 2 / 4 (50.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 13              | 2              | 1              |
| Dry mouth                   |                 |                |                |
| subjects affected / exposed | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 2               | 0              | 0              |
| Dyspepsia                   |                 |                |                |
| subjects affected / exposed | 3 / 37 (8.11%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 3               | 0              | 2              |
| Dysphagia                   |                 |                |                |
| subjects affected / exposed | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Faeces soft                 |                 |                |                |
| subjects affected / exposed | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 2               | 0              | 0              |
| Gastritis                   |                 |                |                |
| subjects affected / exposed | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0               | 0              | 1              |
| Nausea                      |                 |                |                |
| subjects affected / exposed | 9 / 37 (24.32%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 9               | 1              | 1              |
| Odynophagia                 |                 |                |                |
| subjects affected / exposed | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Oral pain                   |                 |                |                |
| subjects affected / exposed | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Pancreatitis                |                 |                |                |
| subjects affected / exposed | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Stomatitis                  |                 |                |                |

|  |                 |                |                |
|--|-----------------|----------------|----------------|
| subjects affected / exposed            | 1 / 37 (2.70%)  | 1 / 4 (25.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 2               | 1              | 0              |
| Upper gastrointestinal haemorrhage     |                 |                |                |
| subjects affected / exposed            | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                      | 0               | 0              | 1              |
| Vomiting                               |                 |                |                |
| subjects affected / exposed            | 3 / 37 (8.11%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 6               | 0              | 0              |
| Hepatobiliary disorders                |                 |                |                |
| Bile duct stone                        |                 |                |                |
| subjects affected / exposed            | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Cholecystocholangitis                  |                 |                |                |
| subjects affected / exposed            | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Hepatocellular injury                  |                 |                |                |
| subjects affected / exposed            | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Hyperbilirubinaemia                    |                 |                |                |
| subjects affected / exposed            | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                      | 0               | 0              | 4              |
| Skin and subcutaneous tissue disorders |                 |                |                |
| Blister                                |                 |                |                |
| subjects affected / exposed            | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 2               | 0              | 0              |
| Blood blister                          |                 |                |                |
| subjects affected / exposed            | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0               | 0              | 0              |
| Dermatitis bullous                     |                 |                |                |
| subjects affected / exposed            | 4 / 37 (10.81%) | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 4               | 0              | 0              |
| Dry skin                               |                 |                |                |
| subjects affected / exposed            | 3 / 37 (8.11%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 4               | 0              | 0              |
| Ecchymosis                             |                 |                |                |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Erythema                    |                 |                |                |
| subjects affected / exposed | 2 / 37 (5.41%)  | 1 / 4 (25.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 4               | 1              | 0              |
| Lividity                    |                 |                |                |
| subjects affected / exposed | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Macule                      |                 |                |                |
| subjects affected / exposed | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Night sweats                |                 |                |                |
| subjects affected / exposed | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Onychoclasia                |                 |                |                |
| subjects affected / exposed | 0 / 37 (0.00%)  | 1 / 4 (25.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0              |
| Palmar erythema             |                 |                |                |
| subjects affected / exposed | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Petechiae                   |                 |                |                |
| subjects affected / exposed | 3 / 37 (8.11%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 3               | 0              | 0              |
| Photosensitivity reaction   |                 |                |                |
| subjects affected / exposed | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 2               | 0              | 1              |
| Pruritus                    |                 |                |                |
| subjects affected / exposed | 3 / 37 (8.11%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 5               | 0              | 1              |
| Purpura                     |                 |                |                |
| subjects affected / exposed | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 2               | 0              | 0              |
| Rash                        |                 |                |                |
| subjects affected / exposed | 7 / 37 (18.92%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 12              | 1              | 2              |
| Rash macular                |                 |                |                |

|   |                     |                     |                    |
|---|---------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 37 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)   | 1 / 37 (2.70%)<br>1 | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Rash vesicular<br>subjects affected / exposed<br>occurrences (all)  | 0 / 37 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Skin hyperpigmentation<br>subjects affected / exposed<br>occurrences (all)  | 0 / 37 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Skin ulcer<br>subjects affected / exposed<br>occurrences (all)  | 1 / 37 (2.70%)<br>1 | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Renal and urinary disorders<br>Dysuria<br>subjects affected / exposed<br>occurrences (all)                        | 2 / 37 (5.41%)<br>2 | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 3 / 37 (8.11%)<br>3 | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 37 (2.70%)<br>1 | 1 / 4 (25.00%)<br>1 | 0 / 6 (0.00%)<br>0 |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)   | 3 / 37 (8.11%)<br>3 | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 37 (0.00%)<br>0 | 1 / 4 (25.00%)<br>1 | 0 / 6 (0.00%)<br>0 |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)   | 2 / 37 (5.41%)<br>2 | 0 / 4 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Infections and infestations   |                     |                     |                    |

|                               |                 |                |                |
|-------------------------------|-----------------|----------------|----------------|
| Bronchitis                    |                 |                |                |
| subjects affected / exposed   | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)             | 1               | 0              | 0              |
| Clostridium difficile colitis |                 |                |                |
| subjects affected / exposed   | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)             | 1               | 0              | 0              |
| Conjunctivitis                |                 |                |                |
| subjects affected / exposed   | 6 / 37 (16.22%) | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)             | 7               | 0              | 0              |
| Corona virus infection        |                 |                |                |
| subjects affected / exposed   | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)             | 0               | 0              | 0              |
| Erysipelas                    |                 |                |                |
| subjects affected / exposed   | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)             | 0               | 0              | 0              |
| Eye infection                 |                 |                |                |
| subjects affected / exposed   | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)             | 0               | 0              | 0              |
| Furuncle                      |                 |                |                |
| subjects affected / exposed   | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)             | 2               | 0              | 0              |
| Genital infection fungal      |                 |                |                |
| subjects affected / exposed   | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)             | 0               | 0              | 0              |
| Herpes zoster                 |                 |                |                |
| subjects affected / exposed   | 0 / 37 (0.00%)  | 1 / 4 (25.00%) | 0 / 6 (0.00%)  |
| occurrences (all)             | 0               | 1              | 0              |
| Lung infection                |                 |                |                |
| subjects affected / exposed   | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)             | 0               | 0              | 1              |
| Oral candidiasis              |                 |                |                |
| subjects affected / exposed   | 3 / 37 (8.11%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)             | 3               | 0              | 0              |
| Oral fungal infection         |                 |                |                |
| subjects affected / exposed   | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)             | 0               | 0              | 1              |

|                                    |                 |                |                |
|------------------------------------|-----------------|----------------|----------------|
| Oral herpes                        |                 |                |                |
| subjects affected / exposed        | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 1               | 0              | 0              |
| Pharyngitis                        |                 |                |                |
| subjects affected / exposed        | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0              |
| Pneumonia                          |                 |                |                |
| subjects affected / exposed        | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 4               | 0              | 0              |
| Rhinitis                           |                 |                |                |
| subjects affected / exposed        | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0               | 0              | 0              |
| Sinusitis                          |                 |                |                |
| subjects affected / exposed        | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 2               | 0              | 0              |
| Upper respiratory tract infection  |                 |                |                |
| subjects affected / exposed        | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 1               | 0              | 0              |
| Urinary tract infection            |                 |                |                |
| subjects affected / exposed        | 3 / 37 (8.11%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 4               | 0              | 0              |
| Metabolism and nutrition disorders |                 |                |                |
| Decreased appetite                 |                 |                |                |
| subjects affected / exposed        | 5 / 37 (13.51%) | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                  | 5               | 0              | 1              |
| Hypercalcaemia                     |                 |                |                |
| subjects affected / exposed        | 1 / 37 (2.70%)  | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all)                  | 1               | 1              | 1              |
| Hyperglycaemia                     |                 |                |                |
| subjects affected / exposed        | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 2               | 0              | 0              |
| Hyperkalaemia                      |                 |                |                |
| subjects affected / exposed        | 3 / 37 (8.11%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 5               | 0              | 0              |
| Hypermagnesaemia                   |                 |                |                |



|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1               | 0              | 0              |
| Hyperuricaemia              |                 |                |                |
| subjects affected / exposed | 0 / 37 (0.00%)  | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0               | 0              | 1              |
| Hypoalbuminaemia            |                 |                |                |
| subjects affected / exposed | 0 / 37 (0.00%)  | 1 / 4 (25.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0              |
| Hypocalcaemia               |                 |                |                |
| subjects affected / exposed | 4 / 37 (10.81%) | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 8               | 0              | 0              |
| Hypokalaemia                |                 |                |                |
| subjects affected / exposed | 6 / 37 (16.22%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 8               | 1              | 1              |
| Hypomagnesaemia             |                 |                |                |
| subjects affected / exposed | 5 / 37 (13.51%) | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 5               | 0              | 0              |
| Hyponatraemia               |                 |                |                |
| subjects affected / exposed | 1 / 37 (2.70%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 3               | 0              | 0              |
| Hypophosphataemia           |                 |                |                |
| subjects affected / exposed | 4 / 37 (10.81%) | 0 / 4 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 5               | 0              | 1              |
| Musculoskeletal pain        |                 |                |                |
| subjects affected / exposed | 2 / 37 (5.41%)  | 0 / 4 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 2               | 0              | 0              |

| <b>Non-serious adverse events</b>                     | Phase 2: Non-Germinal Center B-cell (GCB) DLBCL | Phase 2: Loncastuximab Tesirine and Ibrutinib in GCB DLBCL | Phase 2: Loncastuximab Tesirine and Ibrutinib in MCL |
|---|---|--|--|
| Total subjects affected by non-serious adverse events |   |  |  |
| subjects affected / exposed                           | 48 / 49 (97.96%)                                | 30 / 30 (100.00%)  | 10 / 10 (100.00%)                                    |
| Vascular disorders                                    |   |  |  |
| Flushing  |   |  |  |
| subjects affected / exposed                           | 0 / 49 (0.00%)                                  | 2 / 30 (6.67%)   | 0 / 10 (0.00%)                                       |
| occurrences (all)                                     | 0   | 2  | 0  |
| Haematoma   |   |  |  |

|  |                  |                |                 |
|--|------------------|----------------|-----------------|
| subjects affected / exposed                          | 1 / 49 (2.04%)   | 2 / 30 (6.67%) | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 2                | 3              | 0               |
| Hypertension   |                  |                |                 |
| subjects affected / exposed                          | 2 / 49 (4.08%)   | 1 / 30 (3.33%) | 3 / 10 (30.00%) |
| occurrences (all)                                    | 2                | 2              | 3               |
| Phlebitis  |                  |                |                 |
| subjects affected / exposed                          | 0 / 49 (0.00%)   | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)                                    | 0                | 0              | 1               |
| General disorders and administration site conditions |                  |                |                 |
| Asthenia   |                  |                |                 |
| subjects affected / exposed                          | 5 / 49 (10.20%)  | 2 / 30 (6.67%) | 3 / 10 (30.00%) |
| occurrences (all)                                    | 8                | 2              | 4               |
| Chest pain   |                  |                |                 |
| subjects affected / exposed                          | 0 / 49 (0.00%)   | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)                                    | 0                | 0              | 2               |
| Chills   |                  |                |                 |
| subjects affected / exposed                          | 0 / 49 (0.00%)   | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 0                | 0              | 0               |
| Early satiety  |                  |                |                 |
| subjects affected / exposed                          | 0 / 49 (0.00%)   | 1 / 30 (3.33%) | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 0                | 1              | 0               |
| Fatigue  |                  |                |                 |
| subjects affected / exposed                          | 14 / 49 (28.57%) | 2 / 30 (6.67%) | 3 / 10 (30.00%) |
| occurrences (all)                                    | 20               | 3              | 3               |
| Generalised oedema                                   |                  |                |                 |
| subjects affected / exposed                          | 0 / 49 (0.00%)   | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)                                    | 0                | 0              | 1               |
| Malaise  |                  |                |                 |
| subjects affected / exposed                          | 0 / 49 (0.00%)   | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 0                | 0              | 0               |
| Mucosal inflammation                                 |                  |                |                 |
| subjects affected / exposed                          | 1 / 49 (2.04%)   | 1 / 30 (3.33%) | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 1                | 1              | 0               |
| Oedema peripheral                                    |                  |                |                 |

|   |                  |                 |                 |
|---|------------------|-----------------|-----------------|
| subjects affected / exposed                     | 12 / 49 (24.49%) | 3 / 30 (10.00%) | 1 / 10 (10.00%) |
| occurrences (all)                               | 16               | 3               | 1               |
| Pain  |                  |                 |                 |
| subjects affected / exposed                     | 2 / 49 (4.08%)   | 1 / 30 (3.33%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 2                | 2               | 0               |
| Peripheral swelling                             |                  |                 |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%)   | 2 / 30 (6.67%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 0                | 2               | 1               |
| Pyrexia   |                  |                 |                 |
| subjects affected / exposed                     | 10 / 49 (20.41%) | 1 / 30 (3.33%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 11               | 1               | 0               |
| Sensation of foreign body                       |                  |                 |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%)   | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0                | 0               | 0               |
| Immune system disorders                         |                  |                 |                 |
| Hypogammaglobulinaemia                          |                  |                 |                 |
| subjects affected / exposed                     | 1 / 49 (2.04%)   | 1 / 30 (3.33%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 1                | 1               | 0               |
| Respiratory, thoracic and mediastinal disorders |                  |                 |                 |
| Cough   |                  |                 |                 |
| subjects affected / exposed                     | 6 / 49 (12.24%)  | 1 / 30 (3.33%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 6                | 1               | 0               |
| Dry throat                                      |                  |                 |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%)   | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0                | 0               | 0               |
| Dyspnoea  |                  |                 |                 |
| subjects affected / exposed                     | 6 / 49 (12.24%)  | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 9                | 0               | 0               |
| Epistaxis                                       |                  |                 |                 |
| subjects affected / exposed                     | 1 / 49 (2.04%)   | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 1                | 0               | 1               |
| Hiccups   |                  |                 |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%)   | 2 / 30 (6.67%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0                | 2               | 0               |
| Oropharyngeal pain                              |                  |                 |                 |

|  |                     |                     |                      |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 49 (2.04%)<br>1 | 0 / 30 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 |
| Psychiatric disorders                            |                     |                     |                      |
| Agitation  |                     |                     |                      |
| subjects affected / exposed                      | 2 / 49 (4.08%)      | 0 / 30 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 2                   | 0                   | 0                    |
| Anxiety  |                     |                     |                      |
| subjects affected / exposed                      | 2 / 49 (4.08%)      | 2 / 30 (6.67%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 2                   | 2                   | 0                    |
| Confusional state                                |                     |                     |                      |
| subjects affected / exposed                      | 0 / 49 (0.00%)      | 1 / 30 (3.33%)      | 1 / 10 (10.00%)      |
| occurrences (all)                                | 0                   | 1                   | 1                    |
| Depression                                       |                     |                     |                      |
| subjects affected / exposed                      | 0 / 49 (0.00%)      | 0 / 30 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 0                   | 0                   | 0                    |
| Insomnia   |                     |                     |                      |
| subjects affected / exposed                      | 4 / 49 (8.16%)      | 1 / 30 (3.33%)      | 1 / 10 (10.00%)      |
| occurrences (all)                                | 4                   | 1                   | 1                    |
| Investigations                                   |                     |                     |                      |
| Alanine aminotransferase increased               |                     |                     |                      |
| subjects affected / exposed                      | 4 / 49 (8.16%)      | 3 / 30 (10.00%)     | 1 / 10 (10.00%)      |
| occurrences (all)                                | 8                   | 4                   | 1                    |
| Amylase increased                                |                     |                     |                      |
| subjects affected / exposed                      | 4 / 49 (8.16%)      | 3 / 30 (10.00%)     | 1 / 10 (10.00%)      |
| occurrences (all)                                | 6                   | 3                   | 2                    |
| Aspartate aminotransferase increased             |                     |                     |                      |
| subjects affected / exposed                      | 5 / 49 (10.20%)     | 3 / 30 (10.00%)     | 0 / 10 (0.00%)       |
| occurrences (all)                                | 9                   | 3                   | 0                    |
| Blood bilirubin increased                        |                     |                     |                      |
| subjects affected / exposed                      | 3 / 49 (6.12%)      | 1 / 30 (3.33%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 3                   | 1                   | 0                    |
| Blood creatinine increased                       |                     |                     |                      |
| subjects affected / exposed                      | 2 / 49 (4.08%)      | 0 / 30 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 2                   | 0                   | 0                    |
| Blood iron decreased                             |                     |                     |                      |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed                    | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0               |
| Coronavirus test positive                      |                |                |                 |
| subjects affected / exposed                    | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)                              | 0              | 0              | 1               |
| Gamma-glutamyltransferase increased            |                |                |                 |
| subjects affected / exposed                    | 3 / 49 (6.12%) | 2 / 30 (6.67%) | 2 / 10 (20.00%) |
| occurrences (all)                              | 4              | 2              | 11              |
| Lipase increased                               |                |                |                 |
| subjects affected / exposed                    | 2 / 49 (4.08%) | 2 / 30 (6.67%) | 1 / 10 (10.00%) |
| occurrences (all)                              | 2              | 4              | 7               |
| Weight decreased                               |                |                |                 |
| subjects affected / exposed                    | 0 / 49 (0.00%) | 1 / 30 (3.33%) | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0               |
| Weight increased                               |                |                |                 |
| subjects affected / exposed                    | 3 / 49 (6.12%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                              | 3              | 0              | 0               |
| Injury, poisoning and procedural complications |                |                |                 |
| Contusion                                      |                |                |                 |
| subjects affected / exposed                    | 0 / 49 (0.00%) | 2 / 30 (6.67%) | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0              | 2              | 0               |
| Fall   |                |                |                 |
| subjects affected / exposed                    | 1 / 49 (2.04%) | 1 / 30 (3.33%) | 0 / 10 (0.00%)  |
| occurrences (all)                              | 1              | 1              | 0               |
| Limb injury                                    |                |                |                 |
| subjects affected / exposed                    | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)                              | 0              | 0              | 1               |
| Skin abrasion                                  |                |                |                 |
| subjects affected / exposed                    | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0               |
| Cardiac disorders                              |                |                |                 |
| Acute coronary syndrome                        |                |                |                 |
| subjects affected / exposed                    | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)                              | 0              | 0              | 1               |
| Atrial fibrillation                            |                |                |                 |

|                                      |                |                |                 |
|--------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed          | 4 / 49 (8.16%) | 1 / 30 (3.33%) | 1 / 10 (10.00%) |
| occurrences (all)                    | 7              | 1              | 1               |
| Bradycardia                          |                |                |                 |
| subjects affected / exposed          | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)                    | 0              | 0              | 1               |
| Palpitations                         |                |                |                 |
| subjects affected / exposed          | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all)                    | 0              | 0              | 2               |
| Sinus bradycardia                    |                |                |                 |
| subjects affected / exposed          | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0               |
| Sinus tachycardia                    |                |                |                 |
| subjects affected / exposed          | 1 / 49 (2.04%) | 0 / 30 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0               |
| Tachycardia                          |                |                |                 |
| subjects affected / exposed          | 1 / 49 (2.04%) | 1 / 30 (3.33%) | 1 / 10 (10.00%) |
| occurrences (all)                    | 1              | 1              | 1               |
| Nervous system disorders             |                |                |                 |
| Ataxia                               |                |                |                 |
| subjects affected / exposed          | 0 / 49 (0.00%) | 0 / 30 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)                    | 0              | 0              | 3               |
| Dizziness                            |                |                |                 |
| subjects affected / exposed          | 1 / 49 (2.04%) | 1 / 30 (3.33%) | 1 / 10 (10.00%) |
| occurrences (all)                    | 1              | 1              | 1               |
| Headache                             |                |                |                 |
| subjects affected / exposed          | 4 / 49 (8.16%) | 1 / 30 (3.33%) | 1 / 10 (10.00%) |
| occurrences (all)                    | 4              | 1              | 1               |
| Neuropathy peripheral                |                |                |                 |
| subjects affected / exposed          | 0 / 49 (0.00%) | 1 / 30 (3.33%) | 2 / 10 (20.00%) |
| occurrences (all)                    | 0              | 1              | 2               |
| Paraesthesia                         |                |                |                 |
| subjects affected / exposed          | 2 / 49 (4.08%) | 1 / 30 (3.33%) | 0 / 10 (0.00%)  |
| occurrences (all)                    | 2              | 2              | 0               |
| Blood and lymphatic system disorders |                |                |                 |
| Anaemia                              |                |                |                 |

|                             |                  |                  |                 |
|-----------------------------|------------------|------------------|-----------------|
| subjects affected / exposed | 13 / 49 (26.53%) | 4 / 30 (13.33%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 15               | 5                | 2               |
| Leukopenia                  |                  |                  |                 |
| subjects affected / exposed | 4 / 49 (8.16%)   | 4 / 30 (13.33%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 7                | 11               | 1               |
| Lymphadenopathy             |                  |                  |                 |
| subjects affected / exposed | 0 / 49 (0.00%)   | 2 / 30 (6.67%)   | 0 / 10 (0.00%)  |
| occurrences (all)           | 0                | 2                | 0               |
| Lymphopenia                 |                  |                  |                 |
| subjects affected / exposed | 1 / 49 (2.04%)   | 2 / 30 (6.67%)   | 0 / 10 (0.00%)  |
| occurrences (all)           | 1                | 3                | 0               |
| Neutropenia                 |                  |                  |                 |
| subjects affected / exposed | 18 / 49 (36.73%) | 7 / 30 (23.33%)  | 4 / 10 (40.00%) |
| occurrences (all)           | 36               | 13               | 11              |
| Thrombocytopenia            |                  |                  |                 |
| subjects affected / exposed | 22 / 49 (44.90%) | 12 / 30 (40.00%) | 4 / 10 (40.00%) |
| occurrences (all)           | 56               | 21               | 14              |
| Ear and labyrinth disorders |                  |                  |                 |
| Vertigo                     |                  |                  |                 |
| subjects affected / exposed | 2 / 49 (4.08%)   | 0 / 30 (0.00%)   | 0 / 10 (0.00%)  |
| occurrences (all)           | 2                | 0                | 0               |
| Eye disorders               |                  |                  |                 |
| Cataract                    |                  |                  |                 |
| subjects affected / exposed | 0 / 49 (0.00%)   | 0 / 30 (0.00%)   | 1 / 10 (10.00%) |
| occurrences (all)           | 0                | 0                | 1               |
| Ocular hyperaemia           |                  |                  |                 |
| subjects affected / exposed | 0 / 49 (0.00%)   | 2 / 30 (6.67%)   | 0 / 10 (0.00%)  |
| occurrences (all)           | 0                | 2                | 0               |
| Swelling of eyelid          |                  |                  |                 |
| subjects affected / exposed | 0 / 49 (0.00%)   | 0 / 30 (0.00%)   | 0 / 10 (0.00%)  |
| occurrences (all)           | 0                | 0                | 0               |
| Vision blurred              |                  |                  |                 |
| subjects affected / exposed | 0 / 49 (0.00%)   | 2 / 30 (6.67%)   | 1 / 10 (10.00%) |
| occurrences (all)           | 0                | 2                | 1               |
| Gastrointestinal disorders  |                  |                  |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Abdominal pain              |                 |                 |                 |
| subjects affected / exposed | 3 / 49 (6.12%)  | 3 / 30 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 4               | 5               | 0               |
| Abdominal pain upper        |                 |                 |                 |
| subjects affected / exposed | 1 / 49 (2.04%)  | 3 / 30 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 1               | 3               | 0               |
| Constipation                |                 |                 |                 |
| subjects affected / exposed | 6 / 49 (12.24%) | 2 / 30 (6.67%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 6               | 2               | 0               |
| Diarrhoea                   |                 |                 |                 |
| subjects affected / exposed | 9 / 49 (18.37%) | 7 / 30 (23.33%) | 5 / 10 (50.00%) |
| occurrences (all)           | 16              | 8               | 10              |
| Dry mouth                   |                 |                 |                 |
| subjects affected / exposed | 2 / 49 (4.08%)  | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 2               | 0               | 0               |
| Dyspepsia                   |                 |                 |                 |
| subjects affected / exposed | 3 / 49 (6.12%)  | 2 / 30 (6.67%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 4               | 2               | 0               |
| Dysphagia                   |                 |                 |                 |
| subjects affected / exposed | 1 / 49 (2.04%)  | 1 / 30 (3.33%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 1               | 1               | 1               |
| Faeces soft                 |                 |                 |                 |
| subjects affected / exposed | 0 / 49 (0.00%)  | 1 / 30 (3.33%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Gastritis                   |                 |                 |                 |
| subjects affected / exposed | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Nausea                      |                 |                 |                 |
| subjects affected / exposed | 5 / 49 (10.20%) | 4 / 30 (13.33%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 6               | 5               | 0               |
| Odynophagia                 |                 |                 |                 |
| subjects affected / exposed | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0               | 1               |
| Oral pain                   |                 |                 |                 |
| subjects affected / exposed | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0               | 1               |



|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| Pancreatitis                           |                 |                 |                 |
| subjects affected / exposed            | 1 / 49 (2.04%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 1               | 0               | 1               |
| Stomatitis                             |                 |                 |                 |
| subjects affected / exposed            | 1 / 49 (2.04%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 1               | 0               | 1               |
| Upper gastrointestinal haemorrhage     |                 |                 |                 |
| subjects affected / exposed            | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Vomiting                               |                 |                 |                 |
| subjects affected / exposed            | 5 / 49 (10.20%) | 3 / 30 (10.00%) | 1 / 10 (10.00%) |
| occurrences (all)                      | 6               | 7               | 1               |
| Hepatobiliary disorders                |                 |                 |                 |
| Bile duct stone                        |                 |                 |                 |
| subjects affected / exposed            | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 0               | 0               | 1               |
| Cholecystocholangitis                  |                 |                 |                 |
| subjects affected / exposed            | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 0               | 0               | 1               |
| Hepatocellular injury                  |                 |                 |                 |
| subjects affected / exposed            | 1 / 49 (2.04%)  | 0 / 30 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)                      | 1               | 0               | 7               |
| Hyperbilirubinaemia                    |                 |                 |                 |
| subjects affected / exposed            | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Skin and subcutaneous tissue disorders |                 |                 |                 |
| Blister                                |                 |                 |                 |
| subjects affected / exposed            | 1 / 49 (2.04%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 1               | 0               | 1               |
| Blood blister                          |                 |                 |                 |
| subjects affected / exposed            | 0 / 49 (0.00%)  | 1 / 30 (3.33%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 0               | 1               | 2               |
| Dermatitis bullous                     |                 |                 |                 |
| subjects affected / exposed            | 1 / 49 (2.04%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                      | 1               | 0               | 1               |
| Dry skin                               |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)           | 0               | 0               | 2               |
| Ecchymosis                  |                 |                 |                 |
| subjects affected / exposed | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0               | 1               |
| Erythema                    |                 |                 |                 |
| subjects affected / exposed | 5 / 49 (10.20%) | 5 / 30 (16.67%) | 3 / 10 (30.00%) |
| occurrences (all)           | 11              | 5               | 7               |
| Lividity                    |                 |                 |                 |
| subjects affected / exposed | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0               | 2               |
| Macule                      |                 |                 |                 |
| subjects affected / exposed | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0               | 1               |
| Night sweats                |                 |                 |                 |
| subjects affected / exposed | 2 / 49 (4.08%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 2               | 0               | 1               |
| Onychoclasia                |                 |                 |                 |
| subjects affected / exposed | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Palmar erythema             |                 |                 |                 |
| subjects affected / exposed | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0               | 1               |
| Petechiae                   |                 |                 |                 |
| subjects affected / exposed | 0 / 49 (0.00%)  | 3 / 30 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 2               | 0               |
| Photosensitivity reaction   |                 |                 |                 |
| subjects affected / exposed | 2 / 49 (4.08%)  | 1 / 30 (3.33%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 3               | 2               | 3               |
| Pruritus                    |                 |                 |                 |
| subjects affected / exposed | 4 / 49 (8.16%)  | 1 / 30 (3.33%)  | 3 / 10 (30.00%) |
| occurrences (all)           | 7               | 1               | 6               |
| Purpura                     |                 |                 |                 |
| subjects affected / exposed | 2 / 49 (4.08%)  | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 2               | 0               | 0               |
| Rash                        |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 6 / 49 (12.24%) | 4 / 30 (13.33%) | 2 / 10 (20.00%) |
| occurrences (all)                               | 9               | 4               | 3               |
| Rash macular                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 0               | 0               | 4               |
| Rash maculo-papular                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%)  | 2 / 30 (6.67%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 0               | 3               | 1               |
| Rash vesicular                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 0               | 0               | 2               |
| Skin hyperpigmentation                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 0               | 0               | 1               |
| Skin ulcer                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 0               | 0               | 3               |
| Renal and urinary disorders                     |                 |                 |                 |
| Dysuria   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 49 (2.04%)  | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 1               | 0               | 0               |
| Musculoskeletal and connective tissue disorders |                 |                 |                 |
| Arthralgia                                      |                 |                 |                 |
| subjects affected / exposed                     | 2 / 49 (4.08%)  | 2 / 30 (6.67%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 2               | 4               | 0               |
| Back pain                                       |                 |                 |                 |
| subjects affected / exposed                     | 6 / 49 (12.24%) | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 8               | 0               | 0               |
| Muscle spasms                                   |                 |                 |                 |
| subjects affected / exposed                     | 6 / 49 (12.24%) | 2 / 30 (6.67%)  | 2 / 10 (20.00%) |
| occurrences (all)                               | 6               | 3               | 3               |
| Myalgia   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0               | 0               | 0               |
| Pain in extremity                               |                 |                 |                 |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 49 (0.00%)<br>0 | 2 / 30 (6.67%)<br>3 | 0 / 10 (0.00%)<br>0 |
| Infections and infestations                      |                     |                     |                     |
| Bronchitis                                       |                     |                     |                     |
| subjects affected / exposed                      | 1 / 49 (2.04%)      | 0 / 30 (0.00%)      | 1 / 10 (10.00%)     |
| occurrences (all)                                | 1                   | 0                   | 1                   |
| Clostridium difficile colitis                    |                     |                     |                     |
| subjects affected / exposed                      | 0 / 49 (0.00%)      | 0 / 30 (0.00%)      | 1 / 10 (10.00%)     |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Conjunctivitis                                   |                     |                     |                     |
| subjects affected / exposed                      | 1 / 49 (2.04%)      | 1 / 30 (3.33%)      | 2 / 10 (20.00%)     |
| occurrences (all)                                | 1                   | 2                   | 2                   |
| Corona virus infection                           |                     |                     |                     |
| subjects affected / exposed                      | 3 / 49 (6.12%)      | 1 / 30 (3.33%)      | 1 / 10 (10.00%)     |
| occurrences (all)                                | 8                   | 1                   | 4                   |
| Erysipelas                                       |                     |                     |                     |
| subjects affected / exposed                      | 0 / 49 (0.00%)      | 0 / 30 (0.00%)      | 1 / 10 (10.00%)     |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Eye infection                                    |                     |                     |                     |
| subjects affected / exposed                      | 1 / 49 (2.04%)      | 0 / 30 (0.00%)      | 1 / 10 (10.00%)     |
| occurrences (all)                                | 1                   | 0                   | 1                   |
| Furuncle   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 49 (0.00%)      | 0 / 30 (0.00%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Genital infection fungal                         |                     |                     |                     |
| subjects affected / exposed                      | 0 / 49 (0.00%)      | 0 / 30 (0.00%)      | 1 / 10 (10.00%)     |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Herpes zoster                                    |                     |                     |                     |
| subjects affected / exposed                      | 0 / 49 (0.00%)      | 1 / 30 (3.33%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Lung infection                                   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 49 (0.00%)      | 1 / 30 (3.33%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Oral candidiasis                                 |                     |                     |                     |
| subjects affected / exposed                      | 1 / 49 (2.04%)      | 1 / 30 (3.33%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 1                   | 1                   | 0                   |

|   |                     |                      |                      |
|---|---------------------|----------------------|----------------------|
| Oral fungal infection<br>subjects affected / exposed<br>occurrences (all)             | 1 / 49 (2.04%)<br>1 | 0 / 30 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Oral herpes<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 49 (0.00%)<br>0 | 1 / 30 (3.33%)<br>1  | 1 / 10 (10.00%)<br>1 |
| Pharyngitis<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 49 (0.00%)<br>0 | 1 / 30 (3.33%)<br>1  | 2 / 10 (20.00%)<br>2 |
| Pneumonia<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 49 (0.00%)<br>0 | 2 / 30 (6.67%)<br>2  | 0 / 10 (0.00%)<br>0  |
| Rhinitis<br>subjects affected / exposed<br>occurrences (all)                          | 1 / 49 (2.04%)<br>1 | 1 / 30 (3.33%)<br>1  | 1 / 10 (10.00%)<br>1 |
| Sinusitis<br>subjects affected / exposed<br>occurrences (all)                         | 1 / 49 (2.04%)<br>1 | 2 / 30 (6.67%)<br>3  | 0 / 10 (0.00%)<br>0  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 49 (0.00%)<br>0 | 0 / 30 (0.00%)<br>0  | 1 / 10 (10.00%)<br>1 |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)           | 1 / 49 (2.04%)<br>3 | 3 / 30 (10.00%)<br>3 | 2 / 10 (20.00%)<br>3 |
| Metabolism and nutrition disorders  |                     |                      |                      |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                | 4 / 49 (8.16%)<br>5 | 0 / 30 (0.00%)<br>0  | 2 / 10 (20.00%)<br>2 |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 49 (2.04%)<br>4 | 0 / 30 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 49 (2.04%)<br>1 | 1 / 30 (3.33%)<br>1  | 3 / 10 (30.00%)<br>3 |
| Hyperkalaemia   |                     |                      |                      |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 49 (0.00%)  | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Hypermagnesaemia            |                 |                 |                 |
| subjects affected / exposed | 0 / 49 (0.00%)  | 3 / 30 (10.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 3               | 0               |
| Hyperuricaemia              |                 |                 |                 |
| subjects affected / exposed | 1 / 49 (2.04%)  | 0 / 30 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1               | 0               | 0               |
| Hypoalbuminaemia            |                 |                 |                 |
| subjects affected / exposed | 1 / 49 (2.04%)  | 2 / 30 (6.67%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 1               | 4               | 1               |
| Hypocalcaemia               |                 |                 |                 |
| subjects affected / exposed | 5 / 49 (10.20%) | 4 / 30 (13.33%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 8               | 6               | 0               |
| Hypokalaemia                |                 |                 |                 |
| subjects affected / exposed | 6 / 49 (12.24%) | 3 / 30 (10.00%) | 1 / 10 (10.00%) |
| occurrences (all)           | 7               | 3               | 2               |
| Hypomagnesaemia             |                 |                 |                 |
| subjects affected / exposed | 6 / 49 (12.24%) | 2 / 30 (6.67%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 10              | 2               | 0               |
| Hyponatraemia               |                 |                 |                 |
| subjects affected / exposed | 3 / 49 (6.12%)  | 1 / 30 (3.33%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 3               | 1               | 0               |
| Hypophosphataemia           |                 |                 |                 |
| subjects affected / exposed | 7 / 49 (14.29%) | 6 / 30 (20.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 8               | 12              | 0               |
| Musculoskeletal pain        |                 |                 |                 |
| subjects affected / exposed | 4 / 49 (8.16%)  | 1 / 30 (3.33%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 4               | 1               | 0               |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 08 July 2019    | <ul style="list-style-type: none"><li>• Schedule of Events revised to for all participants to determine whether they met Exclusion Criterion 10.</li><li>• Exclusion Criteria was modified to remove the notation from Exclusion Criterion 10. Criterion 15 was modified to add the exclusion of participants with tuberculosis infection.</li><li>• Packaging and Storage was updated to match the ibrutinib Investigator's Brochure (IB).</li><li>• Preparation and Administration was updated to include precautions concerning extravasation of loncastuximab tesirine based on updated safety information.</li><li>• Loncastuximab Tesirine dosing was revised to clarify the criteria for using sequential dosing.</li><li>• Dose Escalation Design was revised to specify a minimum of 5 days between dosing the first and second patient at each dose level during dose escalation (Part 1), and was also revised to allow enrollment of additional participants during the dose escalation phase at the discretion of the Dose Escalation Steering Committee (DESC).</li><li>• Dose-Limiting Toxicity Definition was modified to clarify the non-hematologic DLT definition.</li><li>• Loncastuximab Tesirine was revised to clarify criteria for dose hold and resumption for non-hematologic and hematologic toxicity.</li><li>• Premedication for Loncastuximab Tesirine and Treatment and Prophylaxis of Infusion-Related to Hypersensitivity Reactions were modified to allow the use of intravenous (IV) dexamethasone.</li><li>• Adverse Events of Special Interest (AESIs) was added to provide information regarding reporting the AESI of major hemorrhage.</li><li>• Laboratory Tests added hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) testing.</li><li>• Table 9 was revised to show updated PK time points for C5 and C6</li><li>• Adverse Events was revised to clarify which treatment-emergent adverse events (TEAEs) were included in the statistical analysis.</li></ul> |
| 09 January 2020 | <ul style="list-style-type: none"><li>• Based on the observed complete response (CR) rate in participants who were enrolled and treated with loncastuximab tesirine and ibrutinib in Part 1, this trial was amended to a Phase 1/2 protocol.</li><li>• The trial expanded enrollment to allow GCB DLBCL patients on study treatment.</li><li>• The trial sample size was increased to approximately 161 patients, and Phase 2 evaluated efficacy in non-GCB DLBCL participants as its primary endpoint.</li><li>• Supplementary secondary endpoints were added.</li></ul>   |
| 14 May 2020     | <ul style="list-style-type: none"><li>• The trial was amended to allow for additional doses of loncastuximab tesirine to be administered on Day 1 of Cycles 5, 6, 9 and 10 in the Phase 2 portion of the study.</li><li>• In addition, the Sponsor on a case-by-case review could have allowed participants benefitting clinically at 1 year to receive additional doses of study drug(s).</li></ul>  |

|                |  |
|----------------|--|
| 26 March 2021  | <ul style="list-style-type: none"> <li>Extended the contraception duration for applicable participants to align with the current regulatory guidance; to update guidance to investigators regarding loncastuximab tesirine dose delays and modifications as well as prohibited medication for concurrent use with loncastuximab tesirine; and removed the loncastuximab tesirine dose adjustment for participants with a body mass index (BMI) <math>\geq 35\text{kg/m}^2</math>.</li> <li>Provided two clarifications: one regarding patient reported outcome (PRO) collection time points during the study follow-up and the other notifying that mantle cell lymphoma (MCL) participants enrolled into the Phase 2 part of the study will have central reviews of their scans.</li> <li>Incorporated all country specific amendments from the country specific protocols to a global protocol to eliminate country specific protocols going forward.</li> </ul> |
| 31 August 2021 | <ul style="list-style-type: none"> <li>Amended the study design for the Phase 2 by enrolling approximately 100 participants with relapsed or refractory Diffuse Large B-Cell Lymphoma (DLBCL) to a new treatment cohort in which loncastuximab tesirine will be given every cycle (rather than intermittently) in combination with ibrutinib.</li> </ul>   |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date             | Interruption   | Restart date |
|------------------|--|--------------|
| 08 November 2022 | The study was early terminated before enrolling participants into the new, planned treatment cohort. | -            |

Notes:

## Limitations and caveats

None reported