



## Clinical trial results:

### A Phase 2 Open-Label Single-Arm Study to Evaluate the Efficacy and Safety of Loncastuximab Tesirine in Patients with Relapsed or Refractory Diffuse Large B-Cell Lymphoma (DLBCL) (LOTIS-2)

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-004288-11 |
| Trial protocol           | GB IT          |
| Global end of trial date | 09 August 2022 |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 19 August 2023 |
| First version publication date | 19 August 2023 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | ADCT-402-201 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03589469 |
| 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                       | 15 September 2022 |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 09 August 2022    |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of single agent loncastuximab tesirine in participants with relapsed or refractory diffuse large B-cell lymphoma (r/r DLBCL).

Protection of trial subjects:

This study was conducted in compliance with the Declaration of Helsinki and with Good Clinical Practices.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 01 August 2018   |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Efficacy, Safety |
| Long term follow-up duration                              | 3 Years          |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United Kingdom: 31 |
| Country: Number of subjects enrolled | Italy: 53          |
| Country: Number of subjects enrolled | United States: 59  |
| Country: Number of subjects enrolled | Switzerland: 2     |
| Worldwide total number of subjects   | 145                |
| EEA total number of subjects         | 53                 |

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)                      | 65 |

|                     |    |
|---------------------|----|
| From 65 to 84 years | 78 |
| 85 years and over   | 2  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Participants were enrolled at 28 study sites in Italy, Switzerland, the United Kingdom, and the United States from 01 August 2018 to 09 August 2022.

### Period 1

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

### Arms

|           |                        |
|-----------|------------------------|
| Arm title | Loncastuximab Tesirine |
|-----------|------------------------|

Arm description:

Participants received loncastuximab tesirine as an intravenous (IV) infusion over 30 minutes on Day 1 of each cycle (every 3 weeks) at a dose of 150 µg/kg once every 3 weeks (Q3W) for 2 cycles, then 75 µg/kg Q3W for subsequent cycles for up to one year or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurred first.

|  |  |
|--|--|
| Arm type                               | Experimental                                     |
| Investigational medicinal product name | Loncastuximab tesirine                           |
| Investigational medicinal product code | ADCT-402   |
| Other name                             | Zynlonta   |
| Pharmaceutical forms                   | Powder for concentrate for solution for infusion |
| Routes of administration               | Intravenous use                                  |

Dosage and administration details:

intravenous infusion

| Number of subjects in period 1 | Loncastuximab Tesirine |
|--------------------------------|------------------------|
| Started                        | 145                    |
| Completed                      | 11                     |
| Not completed                  | 134                    |
| Physician decision             | 20                     |
| Consent withdrawn by subject   | 8                      |
| Death                          | 97                     |
| Miscellaneous                  | 1                      |
| Lost to follow-up              | 8                      |

## Baseline characteristics

### Reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Loncastuximab Tesirine |
|-----------------------|------------------------|

Reporting group description:

Participants received loncastuximab tesirine as an intravenous (IV) infusion over 30 minutes on Day 1 of each cycle (every 3 weeks) at a dose of 150 µg/kg once every 3 weeks (Q3W) for 2 cycles, then 75 µg/kg Q3W for subsequent cycles for up to one year or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurred first.

| Reporting group values             | Loncastuximab<br>Tesirine | Total |  |
|------------------------------------|---------------------------|-------|--|
| Number of subjects                 | 145                       | 145   |  |
| Age categorical<br>Units: Subjects |                           |       |  |

|   |                 |     |  |
|---|-----------------|-----|--|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 62.7<br>± 13.63 | -   |  |
| Gender categorical<br>Units: Subjects                                   |                 |     |  |
| Female  | 60              | 60  |  |
| Male  | 85              | 85  |  |
| Ethnicity<br>Units: Subjects  |                 |     |  |
| Hispanic or Latino  | 13              | 13  |  |
| Not Hispanic or Latino  | 132             | 132 |  |
| Unknown or Not Reported   | 0               | 0   |  |
| Race<br>Units: Subjects   |                 |     |  |
| White   | 130             | 130 |  |
| Black or African American   | 5               | 5   |  |
| Asian   | 3               | 3   |  |
| American Indian or Alaskan Native                                       | 1               | 1   |  |
| Native Hawaiian or Pacific Islander                                     | 1               | 1   |  |
| Other   | 5               | 5   |  |

## End points

### End points reporting groups

|  |                        |
|--|------------------------|
| Reporting group title  | Loncastuximab Tesirine |
| Reporting group description:<br>Participants received loncastuximab tesirine as an intravenous (IV) infusion over 30 minutes on Day 1 of each cycle (every 3 weeks) at a dose of 150 µg/kg once every 3 weeks (Q3W) for 2 cycles, then 75 µg/kg Q3W for subsequent cycles for up to one year or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurred first. |                        |

### Primary: Overall Response Rate (ORR)

|   |  |
|---|--|
| End point title   | Overall Response Rate (ORR) <sup>[1]</sup> |
| End point description:<br>ORR, as determined by central review according to the 2014 Lugano classification, defined as the percentage of participants with a best overall response (BOR) of complete response (CR) or partial response (PR). All-treated population - all participants who received at least 1 dose of treatment. |  |
| End point type  | Primary                                    |
| End point timeframe:<br>Up to 21.5 months   |  |

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 additional statistical analyses were pre-specified for this endpoint.

|                                   |                           |  |  |  |
|-----------------------------------|---------------------------|--|--|--|
| <b>End point values</b>           | Loncastuximab<br>Tesirine |  |  |  |
| Subject group type                | Reporting group           |  |  |  |
| Number of subjects analysed       | 145                       |  |  |  |
| Units: percentage of participants |                           |  |  |  |
| number (confidence interval 95%)  | 48.3 (39.9 to 56.7)       |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Response (DOR)

|   |                            |
|---|----------------------------|
| End point title   | Duration of Response (DOR) |
| End point description:<br>DOR defined as the time from the first documentation of tumor response to disease progression or death. Participants in the all-treated population who achieved a CR or PR.<br><br>Values of "99999" indicate the upper confidence interval could not be calculated due to insufficient number of participants with events. |                            |
| End point type  | Secondary                  |
| End point timeframe:<br>Up to 39 months   |                            |

|                                  |                           |  |  |  |
|----------------------------------|---------------------------|--|--|--|
| <b>End point values</b>          | Loncastuximab<br>Tesirine |  |  |  |
| Subject group type               | Reporting group           |  |  |  |
| Number of subjects analysed      | 70                        |  |  |  |
| Units: months                    |                           |  |  |  |
| median (confidence interval 95%) | 13.37 (6.87 to<br>99999)  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Progression-free Survival (PFS)

|   |                                 |
|---|---------------------------------|
| End point title   | Progression-free Survival (PFS) |
| End point description:<br>PFS was defined as the time between start of treatment and the first documentation of recurrence, progression, or death. All-treated population - all participants who received at least 1 dose of treatment. |                                 |
| End point type  | Secondary                       |
| End point timeframe:<br>Up to 40 months   |                                 |

|                                  |                           |  |  |  |
|----------------------------------|---------------------------|--|--|--|
| <b>End point values</b>          | Loncastuximab<br>Tesirine |  |  |  |
| Subject group type               | Reporting group           |  |  |  |
| Number of subjects analysed      | 145                       |  |  |  |
| Units: months                    |                           |  |  |  |
| median (confidence interval 95%) | 4.93 (2.89 to<br>8.31)    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Overall Survival (OS)

|  |                       |
|--|-----------------------|
| End point title  | Overall Survival (OS) |
| End point description:<br>OS was defined as the time between the start of treatment and death from any cause. All-treated population - all participants who received at least 1 dose of treatment. |                       |
| End point type   | Secondary             |
| End point timeframe:<br>Up to 43 months  |                       |

| End point values                 | Loncastuximab<br>Tesirine |  |  |  |
|----------------------------------|---------------------------|--|--|--|
| Subject group type               | Reporting group           |  |  |  |
| Number of subjects analysed      | 145                       |  |  |  |
| Units: months                    |                           |  |  |  |
| median (confidence interval 95%) | 9.53 (6.74 to<br>11.47)   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product that did not necessarily have to have a causal relationship with treatment. A TEAE was an adverse event with an onset that began or worsened on or after the first dose date and until 30 days after the last dose date, or start of a new anticancer therapy/procedure, whichever came earlier. TEAE assessments also included those per the Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 Grade  $\geq 3$  AEs and serious TEAEs.

AEs were graded using CTCAE version 4 and according to the following: Grade 1 = mild AE, Grade 2 = Moderate AE, Grade 3 = a severe AE, Grade 4 = life-threatening AE, and Grade 5 = death due to AE. For events not listed in the CTCAE criteria, the same grading was used. All-treated population - all participants who received at least 1 dose of treatment.

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

End point timeframe:

Up to 599 days

| End point values            | Loncastuximab<br>Tesirine |  |  |  |
|-----------------------------|---------------------------|--|--|--|
| Subject group type          | Reporting group           |  |  |  |
| Number of subjects analysed | 145                       |  |  |  |
| Units: participants         |                           |  |  |  |
| Any TEAE                    | 143                       |  |  |  |
| Grade $\geq 3$ TEAE         | 107                       |  |  |  |
| Serious TEAE                | 57                        |  |  |  |

## Statistical analyses

No statistical analyses for this end point



## Secondary: Relapse-free Survival (RFS)

|                 |                             |
|-----------------|-----------------------------|
| End point title | Relapse-free Survival (RFS) |
|-----------------|-----------------------------|

End point description:

RFS was defined as the time from the documentation of CR to disease progression or death. Participants in the all-treated population who achieved CR.

Values of "99999" indicate the median, lower and upper confidence interval could not be calculated due to insufficient number of participants with events.

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

End point timeframe:

Up to 39 months

|                                  |                           |  |  |  |
|----------------------------------|---------------------------|--|--|--|
| <b>End point values</b>          | Loncastuximab<br>Tesirine |  |  |  |
| Subject group type               | Reporting group           |  |  |  |
| Number of subjects analysed      | 36                        |  |  |  |
| Units: months                    |                           |  |  |  |
| median (confidence interval 95%) | 99999 (99999<br>to 99999) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Complete Response (CR) Rate

|                 |                             |
|-----------------|-----------------------------|
| End point title | Complete Response (CR) Rate |
|-----------------|-----------------------------|

End point description:

CR rate defined as the percentage of treated participants with a BOR of CR. All-treated population - all participants who received at least 1 dose of treatment.

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

End point timeframe:

Up to 39 months

|                                   |                           |  |  |  |
|-----------------------------------|---------------------------|--|--|--|
| <b>End point values</b>           | Loncastuximab<br>Tesirine |  |  |  |
| Subject group type                | Reporting group           |  |  |  |
| Number of subjects analysed       | 145                       |  |  |  |
| Units: percentage of participants |                           |  |  |  |
| number (confidence interval 95%)  | 24.8 (18.0 to<br>32.7)    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Clinically Significant Changes From Baseline in Clinical Laboratory Tests

|                 |   |
|-----------------|---|
| End point title | Number of Participants With Clinically Significant Changes From Baseline in Clinical Laboratory Tests |
|-----------------|---|

End point description:

Clinical laboratory tests included hematology and chemistry. Clinically significant changes were determined by the Investigator. All-treated population - all participants who received at least 1 dose of treatment.

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

End point timeframe:

Baseline up to 599 days

|                             |                           |  |  |  |
|-----------------------------|---------------------------|--|--|--|
| <b>End point values</b>     | Loncastuximab<br>Tesirine |  |  |  |
| Subject group type          | Reporting group           |  |  |  |
| Number of subjects analysed | 145                       |  |  |  |
| Units: participants         | 83                        |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Clinically Significant Change From Baseline in Vital Signs

|                 |  |
|-----------------|--|
| End point title | Number of Participants With Clinically Significant Change From Baseline in Vital Signs |
|-----------------|--|

End point description:

Vital sign measurements included arterial blood pressure, heart rate, respiratory rate, and body temperature. Clinical significance was determined by the investigator. All-treated population - all participants who received at least 1 dose of treatment.

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

End point timeframe:

Baseline up to 599 days

|                             |                           |  |  |  |
|-----------------------------|---------------------------|--|--|--|
| <b>End point values</b>     | Loncastuximab<br>Tesirine |  |  |  |
| Subject group type          | Reporting group           |  |  |  |
| Number of subjects analysed | 145                       |  |  |  |
| Units: participants         | 0                         |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Eastern Cooperative Oncology Group (ECOG) Performance Status at Baseline and End of Treatment

|                 |   |
|-----------------|---|
| End point title | Eastern Cooperative Oncology Group (ECOG) Performance Status at Baseline and End of Treatment |
|-----------------|---|

End point description:

ECOG (Eastern Cooperative Oncology Group) Performance Status is scored on a 6-point scale where higher scores indicate a worse outcome. ECOG scores include the following:

- 0 = fully active, able to carry on all pre-disease performance without restriction
- 1 = restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
- 2 = ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours
- 3 = capable of only limited self-care; confined to bed or chair more than 50% of waking hours
- 4 = completely disabled; cannot carry on any self-care; totally confined to bed or chair
- 5 = dead.

All-treated population - all participants who received at least 1 dose of treatment. Results are presented for participants with data available for analysis at end of treatment.

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

End point timeframe:

Baseline and end of treatment (up to 599 days)

|                                |                           |  |  |  |
|--------------------------------|---------------------------|--|--|--|
| <b>End point values</b>        | Loncastuximab<br>Tesirine |  |  |  |
| Subject group type             | Reporting group           |  |  |  |
| Number of subjects analysed    | 145 <sup>[2]</sup>        |  |  |  |
| Units: participants            |                           |  |  |  |
| Baseline: ECOG score 0         | 58                        |  |  |  |
| Baseline: ECOG score 1         | 78                        |  |  |  |
| Baseline: ECOG score 2         | 9                         |  |  |  |
| Baseline: ECOG score 3         | 0                         |  |  |  |
| Baseline: ECOG score 4         | 0                         |  |  |  |
| Baseline: ECOG score 5         | 0                         |  |  |  |
| End of treatment: ECOG score 0 | 44                        |  |  |  |
| End of treatment: ECOG score 1 | 50                        |  |  |  |
| End of treatment: ECOG score 2 | 14                        |  |  |  |
| End of treatment: ECOG score 3 | 2                         |  |  |  |
| End of treatment: ECOG score 4 | 1                         |  |  |  |
| End of treatment: ECOG score 5 | 0                         |  |  |  |

Notes:

[2] - Baseline n = 145; End of treatment n = 111.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Clinically Significant Change From Baseline in 12-lead Electrocardiograms (ECGs)

|                 |  |
|-----------------|--|
| End point title | Number of Participants With Clinically Significant Change From Baseline in 12-lead Electrocardiograms (ECGs) |
|-----------------|--|

End point description:

Clinically significant changes from baseline for 12-lead ECGs were measured as abnormal QT interval corrected by Fridericia formula (QTcF) and QT interval corrected by Bazett formula (QTcB) values. All-treated population - all participants who received at least 1 dose of treatment.

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

End point timeframe:

Baseline up to 599 days

| End point values                                    | Loncastuximab<br>Tesirine |  |  |  |
|---|---------------------------|--|--|--|
| Subject group type                                  | Reporting group           |  |  |  |
| Number of subjects analysed                         | 145                       |  |  |  |
| Units: participants                                 |                           |  |  |  |
| QTcB maximum change from baseline:<br>>30, ≤60 msec | 30                        |  |  |  |
| QTcB maximum change from baseline:<br>>60 msec      | 4                         |  |  |  |
| QTcF maximum change from baseline:<br>>30, ≤60 msec | 23                        |  |  |  |
| QTcF maximum change from baseline:<br>>60 msec      | 1                         |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Concentration (Cmax) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

|                 |   |
|-----------------|---|
| End point title | Maximum Concentration (Cmax) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199 |
|-----------------|---|

End point description:

Pharmacokinetic (PK) population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

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

End point timeframe:

Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose and end of infusion.

| End point values                                       | Loncastuximab<br>Tesirine |  |  |  |
|--|---------------------------|--|--|--|
| Subject group type                                     | Reporting group           |  |  |  |
| Number of subjects analysed                            | 142                       |  |  |  |
| Units: ng/mL   |                           |  |  |  |
| geometric mean (geometric coefficient<br>of variation) |                           |  |  |  |
| Conjugated Antibody Cycle 1 (n = 142)                  | 2430 (± 38.8)             |  |  |  |
| Conjugated Antibody Cycle 2 (n = 117)                  | 2734 (± 35.8)             |  |  |  |

|                                      |                 |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Conjugated Antibody Cycle 3 (n = 83) | 1694 (± 47.6)   |  |  |  |
| Total Antibody Cycle 1 (n = 142)     | 3267 (± 36.7)   |  |  |  |
| Total Antibody Cycle 2 (n = 117)     | 3756 (± 31.3)   |  |  |  |
| Total Antibody Cycle 3 (n = 81)      | 2581 (± 41.9)   |  |  |  |
| SG3199 Cycle 1 (n = 8)               | 0.0410 (± 56.6) |  |  |  |
| SG3199 Cycle 2 (n = 5)               | 0.0490 (± 78.8) |  |  |  |
| SG3199 Cycle 3 (n = 3)               | 0.0320 (± 20.3) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Concentration-time Curve From Time Zero to the Last Quantifiable Concentration (AUC0-last) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

|                 |  |
|-----------------|--|
| End point title | Area Under the Concentration-time Curve From Time Zero to the Last Quantifiable Concentration (AUC0-last) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199 |
|-----------------|--|

End point description:

PK population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

Values of "99999" indicate n = 0.

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

End point timeframe:

Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose

| End point values                                    | Loncastuximab Tesirine |  |  |  |
|---|------------------------|--|--|--|
| Subject group type                                  | Reporting group        |  |  |  |
| Number of subjects analysed                         | 143                    |  |  |  |
| Units: day*ng/mL                                    |                        |  |  |  |
| geometric mean (geometric coefficient of variation) |                        |  |  |  |
| Conjugated Antibody Cycle 1 (n = 143)               | 15850 (± 105)          |  |  |  |
| Conjugated Antibody Cycle 2 (n = 116)               | 23913 (± 67.1)         |  |  |  |
| Conjugated Antibody Cycle 3 (n = 0)                 | 99999 (± 99999)        |  |  |  |
| Total Antibody Cycle 1 (n = 143)                    | 22160 (± 106)          |  |  |  |
| Total Antibody Cycle 2 (n = 116)                    | 33762 (± 67.2)         |  |  |  |
| Total Antibody Cycle 3 (n = 0)                      | 99999 (± 99999)        |  |  |  |
| SG3199 Cycle 1 (n = 8)                              | 0.00400 (± 576)        |  |  |  |
| SG3199 Cycle 2 (n = 5)                              | 0.00100 (± 204)        |  |  |  |

|                        |                 |  |  |  |
|------------------------|-----------------|--|--|--|
| SG3199 Cycle 3 (n = 0) | 99999 (± 99999) |  |  |  |
|------------------------|-----------------|--|--|--|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Area Under the Concentration-time Curve From Time Zero to Infinity (AUC<sub>0-∞</sub>) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

|                 |   |
|-----------------|---|
| End point title | Area Under the Concentration-time Curve From Time Zero to Infinity (AUC <sub>0-∞</sub> ) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199 |
|-----------------|---|

End point description:

PK population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

Values of "99999" indicate n = 0.

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

End point timeframe:

Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose

| End point values                                    | Loncastuximab Tesirine |  |  |  |
|---|------------------------|--|--|--|
| Subject group type                                  | Reporting group        |  |  |  |
| Number of subjects analysed                         | 99                     |  |  |  |
| Units: day*ng/mL                                    |                        |  |  |  |
| geometric mean (geometric coefficient of variation) |                        |  |  |  |
| Conjugated Antibody Cycle 1 (n = 32)                | 19825 (± 52.9)         |  |  |  |
| Conjugated Antibody Cycle 2 (n = 99)                | 26902 (± 33.4)         |  |  |  |
| Conjugated Antibody Cycle 3 (n = 0)                 | 99999 (± 99999)        |  |  |  |
| Total Antibody Cycle 1 (n = 27)                     | 25778 (± 61.3)         |  |  |  |
| Total Antibody Cycle 2 (n = 97)                     | 37761 (± 30.4)         |  |  |  |
| Total Antibody Cycle 3 (n = 0)                      | 99999 (± 99999)        |  |  |  |
| SG3199 Cycle 1 (n = 0)                              | 99999 (± 99999)        |  |  |  |
| SG3199 Cycle 2 (n = 0)                              | 99999 (± 99999)        |  |  |  |
| SG3199 Cycle 3 (n = 0)                              | 99999 (± 99999)        |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Apparent Terminal Half-life (Thalf) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

|                 |  |
|-----------------|--|
| End point title | Apparent Terminal Half-life (Thalf) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199 |
|-----------------|--|

End point description:

PK population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

Values of "99999" indicate n = 0.

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

End point timeframe:

Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose

| End point values                                    | Loncastuximab Tesirine |  |  |  |
|---|------------------------|--|--|--|
| Subject group type                                  | Reporting group        |  |  |  |
| Number of subjects analysed                         | 90                     |  |  |  |
| Units: days   |                        |  |  |  |
| geometric mean (geometric coefficient of variation) |                        |  |  |  |
| Conjugated Antibody Cycle 1 (n = 32)                | 8.85 (± 53.5)          |  |  |  |
| Conjugated Antibody Cycle 2 (n = 90)                | 15.2 (± 31.7)          |  |  |  |
| Conjugated Antibody Cycle 3 (n = 0)                 | 99999 (± 99999)        |  |  |  |
| Total Antibody Cycle 1 (n = 27)                     | 8.66 (± 54.6)          |  |  |  |
| Total Antibody Cycle 2 (n = 63)                     | 20.9 (± 56.5)          |  |  |  |
| Total Antibody Cycle 3 (n = 0)                      | 99999 (± 99999)        |  |  |  |
| SG3199 Cycle 1 (n = 0)                              | 99999 (± 99999)        |  |  |  |
| SG3199 Cycle 2 (n = 0)                              | 99999 (± 99999)        |  |  |  |
| SG3199 Cycle 3 (n = 0)                              | 99999 (± 99999)        |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Apparent Clearance (CL) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

|                 |  |
|-----------------|--|
| End point title | Apparent Clearance (CL) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199 |
|-----------------|--|

End point description:

PK population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

Values of "99999" indicate n = 0.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose |           |

|   |                           |  |  |  |
|---|---------------------------|--|--|--|
| <b>End point values</b>                             | Loncastuximab<br>Tesirine |  |  |  |
| Subject group type                                  | Reporting group           |  |  |  |
| Number of subjects analysed                         | 99                        |  |  |  |
| Units: L/day  |                           |  |  |  |
| geometric mean (geometric coefficient of variation) |                           |  |  |  |
| Conjugated Antibody Cycle 1 (n = 32)                | 0.458 (± 47.6)            |  |  |  |
| Conjugated Antibody Cycle 2 (n = 99)                | 0.331 (± 32.0)            |  |  |  |
| Total Antibody Cycle 1 (n = 27)                     | 0.418 (± 56.5)            |  |  |  |
| Total Antibody Cycle 2 (n = 97)                     | 0.285 (± 31.3)            |  |  |  |
| SG3199 Cycle 1 (n = 0)                              | 99999 (± 99999)           |  |  |  |
| SG3199 Cycle 2 (n = 0)                              | 99999 (± 99999)           |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Apparent Volume of Distribution at Steady State (Vss) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

|                 |  |
|-----------------|--|
| End point title | Apparent Volume of Distribution at Steady State (Vss) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199 |
|-----------------|--|

End point description:

PK population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

Values of "99999" indicate n = 0.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose |           |

|   |                           |  |  |  |
|---|---------------------------|--|--|--|
| <b>End point values</b>                             | Loncastuximab<br>Tesirine |  |  |  |
| Subject group type                                  | Reporting group           |  |  |  |
| Number of subjects analysed                         | 90                        |  |  |  |
| Units: liters                                       |                           |  |  |  |
| geometric mean (geometric coefficient of variation) |                           |  |  |  |



|                                      |                 |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Conjugated Antibody Cycle 1 (n = 32) | 4.24 (± 39.6)   |  |  |  |
| Conjugated Antibody Cycle 2 (n = 90) | 6.40 (± 36.5)   |  |  |  |
| Conjugated Antibody Cycle 3 (n = 0)  | 99999 (± 99999) |  |  |  |
| Total Antibody Cycle 1 (n = 27)      | 4.10 (± 36.4)   |  |  |  |
| Total Antibody Cycle 2 (n = 63)      | 7.54 (± 58.9)   |  |  |  |
| Total Antibody Cycle 3 (n = 0)       | 99999 (± 99999) |  |  |  |
| SG3199 Cycle 1 (n = 0)               | 99999 (± 99999) |  |  |  |
| SG3199 Cycle 2 (n = 0)               | 99999 (± 99999) |  |  |  |
| SG3199 Cycle 3 (n = 0)               | 99999 (± 99999) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Accumulation Index (AI) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199

|                 |  |
|-----------------|--|
| End point title | Accumulation Index (AI) of Loncastuximab Tesirine Conjugated Antibody, Total Antibody and Warhead SG3199 |
|-----------------|--|

End point description:

AI is the ratio of AUC<sub>0-last</sub> for each cycle divided by AUC<sub>0-last</sub> of the previous cycle. PK population: All participants in the per-protocol population (all participants in the all-treated population without major protocol deviations) with at least 1 pre- Cycle 1 Day 1 and 1 post-dose valid assessment. Only participants with data available for analysis are presented.

Values of "99999" indicate n = 0.

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

End point timeframe:

Cycles 1 and 2: Day 1 pre-dose, and at 0, 4, 168 and 336 hours post-dose; Cycle 3: Day 1 pre-dose

| End point values                                    | Loncastuximab Tesirine |  |  |  |
|---|------------------------|--|--|--|
| Subject group type                                  | Reporting group        |  |  |  |
| Number of subjects analysed                         | 90                     |  |  |  |
| Units: ratio  |                        |  |  |  |
| geometric mean (geometric coefficient of variation) |                        |  |  |  |
| Conjugated Antibody Cycle 1 (n = 0)                 | 99999 (± 99999)        |  |  |  |
| Conjugated Antibody Cycle 2 (n = 90)                | 1.65 (± 18.5)          |  |  |  |
| Conjugated Antibody Cycle 3 (n = 0)                 | 99999 (± 99999)        |  |  |  |
| Total Antibody Cycle 1 (n = 0)                      | 99999 (± 99999)        |  |  |  |
| Total Antibody Cycle 2 (n = 63)                     | 2.07 (± 38.1)          |  |  |  |
| Total Antibody Cycle 3 (n = 0)                      | 99999 (± 99999)        |  |  |  |

|                        |                 |  |  |  |
|------------------------|-----------------|--|--|--|
| SG3199 Cycle 1 (n = 0) | 99999 (± 99999) |  |  |  |
| SG3199 Cycle 2 (n = 0) | 99999 (± 99999) |  |  |  |
| SG3199 Cycle 3 (n = 0) | 99999 (± 99999) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With an Anti-drug Antibody (ADA) Response to Loncastuximab Tesirine

|                        |  |
|------------------------|--|
| End point title        | Number of Participants With an Anti-drug Antibody (ADA) Response to Loncastuximab Tesirine |
| End point description: | All-treated population - all participants who received at least 1 dose of treatment.       |
| End point type         | Secondary  |
| End point timeframe:   | Up to 599 days   |

|                                       |                        |  |  |  |
|---------------------------------------|------------------------|--|--|--|
| <b>End point values</b>               | Loncastuximab Tesirine |  |  |  |
| Subject group type                    | Reporting group        |  |  |  |
| Number of subjects analysed           | 145                    |  |  |  |
| Units: participants                   |                        |  |  |  |
| Confirmed Positive ADA Pre-dose       | 1                      |  |  |  |
| Confirmed Positive ADA Post-dose Only | 0                      |  |  |  |
| Confirmed Positive ADA Anytime        | 1                      |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline Score in the EuroQol-5 Dimensions-5 Levels (EQ-5D-5L) Visual Analogue Scale (VAS)

|                        |   |
|------------------------|---|
| End point title        | Change From Baseline Score in the EuroQol-5 Dimensions-5 Levels (EQ-5D-5L) Visual Analogue Scale (VAS)  |
| End point description: | EQ-5D-5L is designed as an international, standardized, instrument for describing and evaluating quality of life (QoL). In the EQ-5D-5L VAS participants are asked to indicate their health state today on a VAS with the endpoints labeled 'the best health you can imagine' (score 100) and 'the worst health you can imagine' (score 0).<br><br>A higher score on the VAS indicates better health related QoL. A positive change from baseline indicates an improvement in health related QoL. Patient reported outcome (PRO) population. Only participants with data available for analysis are included. Number of subjects analysed represents all participants who contributed data to this assessment, though not all participants contributed data to each time point. |

Values of "99999" indicate standard deviation could not be calculated as n = 1.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| Baseline, Day 1 of Cycles 2 to 26 (cycle duration of 3 weeks), and end of treatment (up to 599 days) |           |

| End point values                     | Loncastuximab<br>Tesirine |  |  |  |
|--------------------------------------|---------------------------|--|--|--|
| Subject group type                   | Reporting group           |  |  |  |
| Number of subjects analysed          | 130                       |  |  |  |
| Units: score on a scale              |                           |  |  |  |
| arithmetic mean (standard deviation) |                           |  |  |  |
| Cycle 2 Day 1 (n = 108)              | -0.1 (± 15.97)            |  |  |  |
| Cycle 3 Day 1 (n = 76)               | 1.3 (± 16.85)             |  |  |  |
| Cycle 4 Day 1 (n = 58)               | 2.8 (± 15.00)             |  |  |  |
| Cycle 5 Day 1 (n = 44)               | 2.8 (± 13.50)             |  |  |  |
| Cycle 6 Day 1 (n = 33)               | 3.0 (± 17.45)             |  |  |  |
| Cycle 7 Day 1 (n = 28)               | 4.0 (± 12.91)             |  |  |  |
| Cycle 8 Day 1 (n = 22)               | 7.3 (± 12.87)             |  |  |  |
| Cycle 9 Day 1 (n = 20)               | 7.7 (± 15.69)             |  |  |  |
| Cycle 10 Day 1 (n = 13)              | 12.2 (± 15.64)            |  |  |  |
| Cycle 11 Day 1 (n = 12)              | 11.8 (± 17.62)            |  |  |  |
| Cycle 12 Day 1 (n = 10)              | 16.3 (± 16.06)            |  |  |  |
| Cycle 13 Day 1 (n = 8)               | 6.0 (± 16.54)             |  |  |  |
| Cycle 14 Day 1 (n = 6)               | 12.2 (± 15.43)            |  |  |  |
| Cycle 15 Day 1 (n = 5)               | 6.6 (± 12.36)             |  |  |  |
| Cycle 16 Day 1 (n = 4)               | 5.5 (± 13.70)             |  |  |  |
| Cycle 17 Day 1 (n = 4)               | 8.3 (± 13.62)             |  |  |  |
| Cycle 18 Day 1 (n = 3)               | 11.0 (± 11.53)            |  |  |  |
| Cycle 19 Day 1 (n = 2)               | 11.5 (± 16.26)            |  |  |  |
| Cycle 20 Day 1 (n = 1)               | 23.0 (± 99999)            |  |  |  |
| Cycle 21 Day 1 (n = 2)               | 16.5 (± 9.19)             |  |  |  |
| Cycle 22 Day 1 (n = 2)               | 16.5 (± 9.19)             |  |  |  |
| Cycle 23 Day 1 (n = 1)               | 23.0 (± 99999)            |  |  |  |
| Cycle 24 Day 1 (n = 1)               | 23.0 (± 99999)            |  |  |  |
| Cycle 25 Day 1 (n = 1)               | 23.0 (± 99999)            |  |  |  |
| Cycle 26 Day 1 (n = 1)               | 23.0 (± 99999)            |  |  |  |
| End of treatment (n = 98)            | -8.3 (± 19.85)            |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline Score in the Functional Assessment of Cancer Therapy - Lymphoma (FACT-Lym) - Lymphoma Subscale (LymS)

|                 |  |
|-----------------|--|
| End point title | Change From Baseline Score in the Functional Assessment of Cancer Therapy - Lymphoma (FACT-Lym) - Lymphoma Subscale (LymS) |
|-----------------|--|

**End point description:**

Composed of the Functional Assessment of Cancer Therapy - General (FACT-G) plus the 15-item LymS. The FACTG questionnaire contains 27 items covering 4 core health related quality of life (QoL) subscales: Physical Wellbeing (7 items), Social/Family Wellbeing (7), Emotional Wellbeing (6), and Functional Wellbeing (7). The LymS addresses issues including pain, itching, night sweats, trouble sleeping, fatigue and trouble concentrating. Score range for the LymS was 0 - 60, where a higher score indicates less symptoms. The LymS score is reported. A positive change from baseline indicates an improvement in health related QoL. PRO population. Only participants with data available for analysis are included. Number of subjects analysed represents all participants who contributed data to this assessment, though not all participants contributed data to each time point.

Values of "9999" indicate n = 0; "99999" indicate standard deviation could not be calculated as n = 1.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| Baseline, Day 1 of Cycles 2 to 25 (cycle duration of 3 weeks), and end of treatment (up to 599 days) |           |

| End point values                     | Loncastuximab<br>Tesirine |  |  |  |
|--------------------------------------|---------------------------|--|--|--|
| Subject group type                   | Reporting group           |  |  |  |
| Number of subjects analysed          | 130                       |  |  |  |
| Units: score on a scale              |                           |  |  |  |
| arithmetic mean (standard deviation) |                           |  |  |  |
| Cycle 2 Day 1 (n = 110)              | 0.95 (± 7.114)            |  |  |  |
| Cycle 3 Day 1 (n = 78)               | 1.34 (± 8.764)            |  |  |  |
| Cycle 4 Day 1 (n = 60)               | 2.09 (± 8.832)            |  |  |  |
| Cycle 5 Day 1 (n = 47)               | 0.16 (± 8.506)            |  |  |  |
| Cycle 6 Day 1 (n = 33)               | 1.16 (± 9.918)            |  |  |  |
| Cycle 7 Day 1 (n = 29)               | 1.00 (± 11.474)           |  |  |  |
| Cycle 8 Day 1 (n = 22)               | 3.43 (± 10.141)           |  |  |  |
| Cycle 9 Day 1 (n = 20)               | 2.17 (± 9.498)            |  |  |  |
| Cycle 10 Day 1 (n = 13)              | 3.18 (± 11.769)           |  |  |  |
| Cycle 11 Day 1 (n = 12)              | 4.35 (± 13.053)           |  |  |  |
| Cycle 12 Day 1 (n = 10)              | 4.90 (± 11.140)           |  |  |  |
| Cycle 13 Day 1 (n = 9)               | 2.01 (± 16.871)           |  |  |  |
| Cycle 14 Day 1 (n = 6)               | 0.63 (± 17.442)           |  |  |  |
| Cycle 15 Day 1 (n = 5)               | -3.27 (± 7.691)           |  |  |  |
| Cycle 16 Day 1 (n = 4)               | -8.04 (± 10.561)          |  |  |  |
| Cycle 17 Day 1 (n = 4)               | -6.88 (± 9.360)           |  |  |  |
| Cycle 18 Day 1 (n = 3)               | -5.00 (± 7.937)           |  |  |  |
| Cycle 19 Day 1 (n = 2)               | -1.00 (± 4.243)           |  |  |  |
| Cycle 20 Day 1 (n = 2)               | -2.25 (± 4.596)           |  |  |  |
| Cycle 21 Day 1 (n = 2)               | -0.50 (± 2.121)           |  |  |  |

|                           |                 |  |  |  |
|---------------------------|-----------------|--|--|--|
| Cycle 22 Day 1 (n = 2)    | -1.00 (± 2.828) |  |  |  |
| Cycle 23 Day 1 (n = 1)    | 1.00 (± 99999)  |  |  |  |
| Cycle 24 Day 1 (n = 0)    | 9999 (± 9999)   |  |  |  |
| Cycle 25 Day 1 (n = 1)    | 1.00 (± 99999)  |  |  |  |
| End of treatment (n = 98) | -1.19 (± 9.042) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 43 months

Adverse event reporting additional description:

All non-serious AEs at a frequency threshold of  $\geq 5\%$  and all SAEs, regardless of relationship to study drug, were collected from the time the participant signs the ICF until 30 days after the last dose of study drug or start of new anti-cancer therapy, whichever is earlier; thereafter, only related SAEs were collected, with two exceptions.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

### Reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Loncastuximab Tesirine |
|-----------------------|------------------------|

Reporting group description:

Participants received loncastuximab tesirine as an IV infusion over 30 minutes on Day 1 of each cycle (every 3 weeks) at a dose of 150 µg/kg once Q3W for 2 cycles, then 75 µg/kg Q3W for subsequent cycles for up to one year or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurred first.

| Serious adverse events  | Loncastuximab<br>Tesirine |  |  |
|---|---------------------------|--|--|
| Total subjects affected by serious adverse events                   |                           |  |  |
| subjects affected / exposed   | 57 / 145 (39.31%)         |  |  |
| number of deaths (all causes)                                       | 97                        |  |  |
| number of deaths resulting from adverse events                      | 8                         |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                           |  |  |
| Diffuse large B-cell lymphoma                                       |                           |  |  |
| alternative assessment type: Systematic                             |                           |  |  |
| subjects affected / exposed   | 1 / 145 (0.69%)           |  |  |
| occurrences causally related to treatment / all                     | 0 / 1                     |  |  |
| deaths causally related to treatment / all                          | 0 / 1                     |  |  |
| Vascular disorders  |                           |  |  |
| Thrombosis  |                           |  |  |
| alternative assessment type: Systematic                             |                           |  |  |
| subjects affected / exposed   | 1 / 145 (0.69%)           |  |  |
| occurrences causally related to treatment / all                     | 0 / 1                     |  |  |
| deaths causally related to treatment / all                          | 0 / 0                     |  |  |
| Haematoma   |                           |  |  |
| alternative assessment type:  |                           |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| Systematic   |                 |  |  |  |
| subjects affected / exposed                          | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to treatment / all      | 1 / 1           |  |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |  |
| Embolism   |                 |  |  |  |
| alternative assessment type: Systematic              |                 |  |  |  |
| subjects affected / exposed                          | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |  |
| Deep vein thrombosis                                 |                 |  |  |  |
| alternative assessment type: Systematic              |                 |  |  |  |
| subjects affected / exposed                          | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |  |
| General disorders and administration site conditions |                 |  |  |  |
| Disease progression                                  |                 |  |  |  |
| alternative assessment type: Systematic              |                 |  |  |  |
| subjects affected / exposed                          | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |  |
| deaths causally related to treatment / all           | 0 / 1           |  |  |  |
| Fatigue  |                 |  |  |  |
| alternative assessment type: Systematic              |                 |  |  |  |
| subjects affected / exposed                          | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |  |
| Face oedema  |                 |  |  |  |
| alternative assessment type: Systematic              |                 |  |  |  |
| subjects affected / exposed                          | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to treatment / all      | 0 / 1           |  |  |  |
| deaths causally related to treatment / all           | 0 / 0           |  |  |  |
| Pyrexia  |                 |  |  |  |
| alternative assessment type: Systematic              |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 4 / 145 (2.76%) |  |  |
| occurrences causally related to treatment / all | 1 / 4           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pain  |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Oedema peripheral                               |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Non-cardiac chest pain                          |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 2 / 145 (1.38%) |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Cough   |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Dyspnoea  |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Haemoptysis                                     |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |



|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Pneumonitis                                     |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pleuritic pain                                  |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pleural effusion                                |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 3 / 145 (2.07%) |  |  |
| occurrences causally related to treatment / all | 4 / 5           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychiatric disorders                           |                 |  |  |
| Confusional state                               |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Intentional self-injury                         |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Mental status changes                           |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 2 / 145 (1.38%) |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Injury, poisoning and procedural complications  |                 |  |  |
| Fall  |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Postoperative hypotension                       |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac disorders                               |                 |  |  |
| Pericarditis                                    |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pericardial effusion                            |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 2 / 145 (1.38%) |  |  |
| occurrences causally related to treatment / all | 3 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Nervous system disorders                        |                 |  |  |
| Headache  |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 2 / 145 (1.38%) |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychomotor skills impaired                     |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Syncope   |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Facial nerve disorder                           |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Blood and lymphatic system disorders            |                 |  |  |
| Neutropenia                                     |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Febrile neutropenia                             |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 5 / 145 (3.45%) |  |  |
| occurrences causally related to treatment / all | 4 / 6           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Anaemia   |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 2 / 145 (1.38%) |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrointestinal disorders                      |                 |  |  |
| Small intestinal obstruction                    |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Intestinal obstruction                          |                 |  |  |  |
| alternative assessment type: Systematic         |                 |  |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Dysphagia                                       |                 |  |  |  |
| alternative assessment type: Systematic         |                 |  |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Diarrhoea                                       |                 |  |  |  |
| alternative assessment type: Systematic         |                 |  |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Ascites   |                 |  |  |  |
| alternative assessment type: Systematic         |                 |  |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Abdominal pain                                  |                 |  |  |  |
| alternative assessment type: Systematic         |                 |  |  |  |
| subjects affected / exposed                     | 3 / 145 (2.07%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 3           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Small intestinal perforation                    |                 |  |  |  |
| alternative assessment type: Systematic         |                 |  |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Renal and urinary disorders                     |                 |  |  |
| Acute kidney injury                             |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 2 / 145 (1.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Hydronephrosis                                  |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Ureterolithiasis                                |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Musculoskeletal and connective tissue disorders |                 |  |  |
| Neck pain                                       |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infections and infestations                     |                 |  |  |
| Sepsis  |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Rhinovirus infection                            |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumonia fungal                                |                 |  |  |

|  |                 |  |  |  |
|--|-----------------|--|--|--|
| alternative assessment type:<br>Systematic         |                 |  |  |  |
| subjects affected / exposed                        | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| Pneumonia  |                 |  |  |  |
| alternative assessment type:<br>Systematic         |                 |  |  |  |
| subjects affected / exposed                        | 2 / 145 (1.38%) |  |  |  |
| occurrences causally related to<br>treatment / all | 1 / 3           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 1           |  |  |  |
| Metapneumovirus infection                          |                 |  |  |  |
| alternative assessment type:<br>Systematic         |                 |  |  |  |
| subjects affected / exposed                        | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to<br>treatment / all | 1 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| Lung infection                                     |                 |  |  |  |
| alternative assessment type:<br>Systematic         |                 |  |  |  |
| subjects affected / exposed                        | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to<br>treatment / all | 1 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| Klebsiella infection                               |                 |  |  |  |
| alternative assessment type:<br>Systematic         |                 |  |  |  |
| subjects affected / exposed                        | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to<br>treatment / all | 1 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| Influenza  |                 |  |  |  |
| alternative assessment type:<br>Systematic         |                 |  |  |  |
| subjects affected / exposed                        | 1 / 145 (0.69%) |  |  |  |
| occurrences causally related to<br>treatment / all | 0 / 1           |  |  |  |
| deaths causally related to<br>treatment / all      | 0 / 0           |  |  |  |
| Escherichia sepsis                                 |                 |  |  |  |
| alternative assessment type:<br>Systematic         |                 |  |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Septic shock                                    |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Urinary tract infection bacterial               |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Soft tissue infection                           |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Metabolism and nutrition disorders              |                 |  |  |
| Hyponatraemia                                   |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hypercalcaemia                                  |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |
| subjects affected / exposed                     | 6 / 145 (4.14%) |  |  |
| occurrences causally related to treatment / all | 1 / 6           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Dehydration                                     |                 |  |  |
| alternative assessment type: Systematic         |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 145 (0.69%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

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

| <b>Non-serious adverse events</b>                     | Loncastuximab<br>Tesarine |  |  |
|---|---------------------------|--|--|
| Total subjects affected by non-serious adverse events |                           |  |  |
| subjects affected / exposed                           | 139 / 145 (95.86%)        |  |  |
| Investigations  |                           |  |  |
| Blood alkaline phosphatase increased                  |                           |  |  |
| subjects affected / exposed                           | 29 / 145 (20.00%)         |  |  |
| occurrences (all)                                     | 35                        |  |  |
| Aspartate aminotransferase increased                  |                           |  |  |
| subjects affected / exposed                           | 23 / 145 (15.86%)         |  |  |
| occurrences (all)                                     | 36                        |  |  |
| Alanine aminotransferase increased                    |                           |  |  |
| subjects affected / exposed                           | 22 / 145 (15.17%)         |  |  |
| occurrences (all)                                     | 27                        |  |  |
| Weight increased                                      |                           |  |  |
| subjects affected / exposed                           | 10 / 145 (6.90%)          |  |  |
| occurrences (all)                                     | 11                        |  |  |
| Gamma-glutamyltransferase increased                   |                           |  |  |
| subjects affected / exposed                           | 61 / 145 (42.07%)         |  |  |
| occurrences (all)                                     | 74                        |  |  |
| Vascular disorders                                    |                           |  |  |
| Hypotension   |                           |  |  |
| subjects affected / exposed                           | 10 / 145 (6.90%)          |  |  |
| occurrences (all)                                     | 12                        |  |  |
| Hypertension  |                           |  |  |
| subjects affected / exposed                           | 8 / 145 (5.52%)           |  |  |
| occurrences (all)                                     | 12                        |  |  |
| Cardiac disorders                                     |                           |  |  |
| Tachycardia   |                           |  |  |



|   |                        |  |  |
|---|------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)        | 11 / 145 (7.59%)<br>12 |  |  |
| Nervous system disorders                                |                        |  |  |
| Dizziness   |                        |  |  |
| subjects affected / exposed                             | 9 / 145 (6.21%)        |  |  |
| occurrences (all)                                       | 9                      |  |  |
| Headache  |                        |  |  |
| subjects affected / exposed                             | 15 / 145 (10.34%)      |  |  |
| occurrences (all)                                       | 20                     |  |  |
| Blood and lymphatic system disorders                    |                        |  |  |
| Lymphopenia   |                        |  |  |
| subjects affected / exposed                             | 11 / 145 (7.59%)       |  |  |
| occurrences (all)                                       | 18                     |  |  |
| Leukopenia  |                        |  |  |
| subjects affected / exposed                             | 21 / 145 (14.48%)      |  |  |
| occurrences (all)                                       | 34                     |  |  |
| Anaemia   |                        |  |  |
| subjects affected / exposed                             | 38 / 145 (26.21%)      |  |  |
| occurrences (all)                                       | 54                     |  |  |
| Thrombocytopenia  |                        |  |  |
| subjects affected / exposed                             | 48 / 145 (33.10%)      |  |  |
| occurrences (all)                                       | 73                     |  |  |
| Neutropenia   |                        |  |  |
| subjects affected / exposed                             | 58 / 145 (40.00%)      |  |  |
| occurrences (all)                                       | 100                    |  |  |
| General disorders and administration<br>site conditions |                        |  |  |
| Asthenia  |                        |  |  |
| subjects affected / exposed                             | 14 / 145 (9.66%)       |  |  |
| occurrences (all)                                       | 16                     |  |  |
| Pyrexia   |                        |  |  |
| subjects affected / exposed                             | 25 / 145 (17.24%)      |  |  |
| occurrences (all)                                       | 38                     |  |  |
| Oedema peripheral                                       |                        |  |  |
| subjects affected / exposed                             | 28 / 145 (19.31%)      |  |  |
| occurrences (all)                                       | 33                     |  |  |
| Fatigue   |                        |  |  |

|   |                   |  |  |
|---|-------------------|--|--|
| subjects affected / exposed                     | 40 / 145 (27.59%) |  |  |
| occurrences (all)                               | 44                |  |  |
| Gastrointestinal disorders                      |                   |  |  |
| Diarrhoea                                       |                   |  |  |
| subjects affected / exposed                     | 25 / 145 (17.24%) |  |  |
| occurrences (all)                               | 34                |  |  |
| Nausea  |                   |  |  |
| subjects affected / exposed                     | 34 / 145 (23.45%) |  |  |
| occurrences (all)                               | 42                |  |  |
| Abdominal pain                                  |                   |  |  |
| subjects affected / exposed                     | 16 / 145 (11.03%) |  |  |
| occurrences (all)                               | 18                |  |  |
| Constipation                                    |                   |  |  |
| subjects affected / exposed                     | 17 / 145 (11.72%) |  |  |
| occurrences (all)                               | 17                |  |  |
| Vomiting  |                   |  |  |
| subjects affected / exposed                     | 19 / 145 (13.10%) |  |  |
| occurrences (all)                               | 22                |  |  |
| Respiratory, thoracic and mediastinal disorders |                   |  |  |
| Pleural effusion                                |                   |  |  |
| subjects affected / exposed                     | 14 / 145 (9.66%)  |  |  |
| occurrences (all)                               | 15                |  |  |
| Dyspnoea  |                   |  |  |
| subjects affected / exposed                     | 17 / 145 (11.72%) |  |  |
| occurrences (all)                               | 17                |  |  |
| Cough   |                   |  |  |
| subjects affected / exposed                     | 32 / 145 (22.07%) |  |  |
| occurrences (all)                               | 33                |  |  |
| Nasal congestion                                |                   |  |  |
| subjects affected / exposed                     | 8 / 145 (5.52%)   |  |  |
| occurrences (all)                               | 8                 |  |  |
| Skin and subcutaneous tissue disorders          |                   |  |  |
| Rash maculo-papular                             |                   |  |  |
| subjects affected / exposed                     | 8 / 145 (5.52%)   |  |  |
| occurrences (all)                               | 8                 |  |  |
| Photosensitivity reaction                       |                   |  |  |

|   |   |  |  |
|---|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Erythema</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pruritus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                                 | <p>15 / 145 (10.34%)</p> <p>18</p> <p>15 / 145 (10.34%)</p> <p>27</p> <p>19 / 145 (13.10%)</p> <p>20</p> <p>19 / 145 (13.10%)</p> <p>20</p> |  |  |
| <p>Psychiatric disorders</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>16 / 145 (11.03%)</p> <p>16</p>  |  |  |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Neck pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain in extremity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                       | <p>8 / 145 (5.52%)</p> <p>8</p> <p>9 / 145 (6.21%)</p> <p>9</p> <p>9 / 145 (6.21%)</p> <p>9</p>   |  |  |
| <p>Metabolism and nutrition disorders</p> <p>Hypokalaemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypophosphataemia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Decreased appetite</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Hypomagnesaemia</p> | <p>23 / 145 (15.86%)</p> <p>30</p> <p>23 / 145 (15.86%)</p> <p>33</p> <p>22 / 145 (15.17%)</p> <p>22</p>                                    |  |  |

|                             |                   |  |  |
|-----------------------------|-------------------|--|--|
| subjects affected / exposed | 20 / 145 (13.79%) |  |  |
| occurrences (all)           | 23                |  |  |
| Hypocalcaemia               |                   |  |  |
| subjects affected / exposed | 12 / 145 (8.28%)  |  |  |
| occurrences (all)           | 16                |  |  |
| Hyperglycaemia              |                   |  |  |
| subjects affected / exposed | 11 / 145 (7.59%)  |  |  |
| occurrences (all)           | 14                |  |  |
| Hyponatraemia               |                   |  |  |
| subjects affected / exposed | 9 / 145 (6.21%)   |  |  |
| occurrences (all)           | 10                |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 05 April 2018     | <p>The original protocol was finalized on 09 Mar 2018 and was amended before implementation in response to United States Food and Drug Administration recommendations.</p> <p>The purposes of the amendment were the following:</p> <ul style="list-style-type: none"><li>- The study design was changed to a single cohort with the primary endpoint being ORR in all-treated participants, resulting in changes to primary and secondary objectives and endpoints, and statistical considerations.</li><li>- For eligibility, pathologic diagnosis was clarified to align with the 2016 World Health Organization classification, the requirement for participants to be ineligible or have failed stem cell transplant (SCT) was removed (as the Agency felt that loncastuximab tesirine was potentially suitable for third line therapy in participants who were potentially eligible for SCT), and the specific requirement for rituximab therapy was deleted as it was expected that all participants would have received this in at least 1 prior line of therapy.</li><li>- For participants whose disease was not positron-emission tomography (PET)-avid, bone marrow biopsy was added as part of baseline staging and disease assessment if clinically appropriate to fully align with the 2014 Lugano Classification.</li><li>- Safety follow-up was extended to 180 days after transplant for participants who had responded to loncastuximab tesirine and gone on to SCT to monitor for possible increased transplant-related toxicity in participants who had been treated with loncastuximab tesirine.</li></ul> |
| 24 September 2018 | <p>The purposes of the amendment were the following:</p> <ul style="list-style-type: none"><li>- Participants with bulky disease (defined as at least 1 lymph node <math>\geq 10</math> cm in longest diameter) were excluded based on analysis of Phase 1 data showing that these participants had an ORR of 11%. Based on an interim analysis this was the ORR at the time of this analysis.</li><li>- The inclusion criterion regarding hepatic function was revised to no longer allow participants with alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transferase <math>\leq 5 \times</math> upper limit of normal if there was liver involvement, to be consistent with the requirement to hold the dose of loncastuximab tesirine for participants with Grade <math>\geq 2</math> liver function test abnormalities as specified in Section 9.4.5.1.2.</li><li>- Participants who were clinically benefiting were allowed to continue treatment beyond 1 year with Sponsor review and approval.</li><li>- A requirement for dose discontinuation for dose delays <math>&gt; 5</math> weeks due to toxicity at least possibly related to loncastuximab tesirine was added.</li><li>- The requirement for IV contrast for PET-computer tomography (CT) was removed and the type and timing of efficacy assessments were clarified.</li></ul>   |
| 09 July 2019      | <p>The purposes of the amendment were the following:</p> <ul style="list-style-type: none"><li>- The text was updated to include information regarding monitoring for extravasation during or after loncastuximab tesirine infusion because of updated safety information.</li><li>- Efficacy assessments were updated to allow for capture of response information during the follow-up period for participants who received chimeric antigen receptor T-cell (CAR-T) therapy after loncastuximab tesirine treatment.</li><li>- AE/serious AE reporting requirements for participants who received CAR-T therapy after loncastuximab tesirine discontinuation were added.</li></ul>   |

Notes:

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## **Interruptions (globally)**

Were there any global interruptions to the trial? No

## **Limitations and caveats**

None reported