



## Clinical trial results:

### A Phase 4, Open-Label, Randomized Study of two Inotuzumab Ozogamicin Dose Levels In Adult Participants With Relapsed Or Refractory B-Cell Acute Lymphoblastic Leukemia Eligible for Hematopoietic Stem Cell Transplantation and who Have Risk Factor(S) for Veno-Occlusive Disease

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2018-001557-27 |
| Trial protocol           | PL BE HU ES    |
| Global end of trial date | 26 May 2023    |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 08 June 2024 |
| First version publication date | 08 June 2024 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | B1931030 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03677596 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Pfizer Inc.   |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017  |
| Public contact               | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact           | Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 27 November 2023 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 26 May 2023      |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the rates of veno-occlusive disease (VOD) and hematologic remission (complete remission/complete remission with incomplete hematologic recovery [CR/Cri]) for 2 Inotuzumab Ozogamicin dose levels in adult subjects with relapsed or refractory B-cell Acute lymphocytic leukemia (ALL) who are eligible for hematopoietic stem cell transplant (HSCT) and who are at higher risk for developing VOD post-HSCT.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trials subjects were followed.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 01 July 2019 |
| Long term follow-up planned                               | Yes          |
| Long term follow-up rationale                             | Safety       |
| Long term follow-up duration                              | 2 Years      |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | Hungary: 1       |
| Country: Number of subjects enrolled | Spain: 17        |
| Country: Number of subjects enrolled | India: 14        |
| Country: Number of subjects enrolled | Poland: 13       |
| Country: Number of subjects enrolled | Singapore: 5     |
| Country: Number of subjects enrolled | Türkiye: 43      |
| Country: Number of subjects enrolled | Taiwan: 4        |
| Country: Number of subjects enrolled | United States: 5 |
| Worldwide total number of subjects   | 102              |
| EEA total number of subjects         | 31               |

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)                      | 95 |
| From 65 to 84 years                       | 7  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 102 were enrolled and treated. In Run-in Phase, 22 subjects were enrolled and treated. In Randomised Phase, 80 subjects were enrolled and treated.

### Period 1

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

### Arms

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes   |
| <b>Arm title</b>             | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in + Randomized) |

Arm description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After complete remission (CR)/complete remission with incomplete hematologic recovery (CRi) is achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Day 1, 8 and 15). The maximum treatment duration was approximately 26 weeks.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Inotuzumab Ozogamicin |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Injection             |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

1.2 mg/m<sup>2</sup>/cycle administered in 3 divided doses (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously.

|                  |  |
|------------------|--|
| <b>Arm title</b> | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomized Phase) |
|------------------|--|

Arm description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m<sup>2</sup>/cycle administered in 3 divided doses (0.8 mg/m<sup>2</sup> on Day 1, 0.5 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 1.5 mg/m<sup>2</sup>/cycle (0.5 mg/m<sup>2</sup> on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | Inotuzumab Ozogamicin |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Injection             |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

1.8 mg/m<sup>2</sup>/cycle administered in 3 divided doses (0.8 mg/m<sup>2</sup> on Day 1, 0.5 mg/m<sup>2</sup> on Days 8 and 15) intravenously.

| <b>Number of subjects in period 1</b> | <b>1.2 mg/m<sup>2</sup>/cycle<br/>(Dose Level 2 Run-in + Randomized)</b> | <b>1.8 mg/m<sup>2</sup>/cycle<br/>(Dose Level 1 Randomized Phase)</b> |
|---------------------------------------|--|---|
| Started                               | 64   | 38  |
| Completed                             | 41   | 19  |
| Not completed                         | 23   | 19  |
| Adverse event, serious fatal          | 10   | 6   |
| Consent withdrawn by subject          | 3  | -   |
| Disease Relapse                       | 2  | 2   |
| Adverse event, non-fatal              | -  | 1   |
| Progressive Disease                   | 8  | 8   |
| Unspecified                           | -  | 1   |
| Lost to follow-up                     | -  | 1   |

## Baseline characteristics

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in + Randomized) |
|-----------------------|---|

Reporting group description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After complete remission (CR)/complete remission with incomplete hematologic recovery (CRi) is achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Day 1, 8 and 15). The maximum treatment duration was approximately 26 weeks.

|                       |  |
|-----------------------|--|
| Reporting group title | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomized Phase) |
|-----------------------|--|

Reporting group description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m<sup>2</sup>/cycle administered in 3 divided doses (0.8 mg/m<sup>2</sup> on Day 1, 0.5 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 1.5 mg/m<sup>2</sup>/cycle (0.5 mg/m<sup>2</sup> on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

| Reporting group values  | 1.2 mg/m <sup>2</sup> /cycle<br>(Dose Level 2 Run-in + Randomized) | 1.8 mg/m <sup>2</sup> /cycle<br>(Dose Level 1 Randomized Phase) | Total |
|---|--|---|-------|
| Number of subjects  | 64   | 38  | 102   |
| Age Categorical   |  |   |       |
| Units: Subjects   |  |   |       |
| <=18 years  | 0  | 0   | 0     |
| Between 18 and 65 years   | 59   | 36  | 95    |
| >=65 years  | 5  | 2   | 7     |
| Age continuous  |  |   |       |
| Units: years  |  |   |       |
| arithmetic mean   | 43.27  | 39.47   |       |
| standard deviation  | ± 14.85  | ± 15.26   | -     |
| Sex: Female, Male   |  |   |       |
| Units: Subjects   |  |   |       |
| Female  | 28   | 18  | 46    |
| Male  | 36   | 20  | 56    |
| Race (NIH/OMB)  |  |   |       |
| Units: Subjects   |  |   |       |
| American Indian or Alaska Native  | 0  | 0   | 0     |
| Asian   | 11   | 11  | 22    |
| Native Hawaiian or Other Pacific Islander   | 0  | 0   | 0     |
| Black or African American   | 0  | 0   | 0     |
| White   | 51   | 25  | 76    |
| More than one race  | 0  | 0   | 0     |
| Unknown or Not Reported   | 2  | 2   | 4     |
| Ethnicity (NIH/OMB)   |  |   |       |
| Units: Subjects   |  |   |       |
| Hispanic or Latino  | 7  | 3   | 10    |
| Not Hispanic or Latino  | 56   | 35  | 91    |
| Unknown or Not Reported   | 1  | 0   | 1     |
| ECOG Performance Status   |  |   |       |
| Eastern Cooperative Oncology Group (ECOG) Performance Status is defined as: ECOG=0: Fully active, able to carry on all predisease performance without restriction; ECOG=1: Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, ie, light |  |   |       |

|   |          |          |    |
|---|----------|----------|----|
| house work, office work; ECOG=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. |          |          |    |
| Units: Subjects   |          |          |    |
| ECOG = 0  | 28       | 20       | 48 |
| ECOG = 1  | 33       | 13       | 46 |
| ECOG = 2  | 3        | 5        | 8  |
| Body Mass Index (BMI)   |          |          |    |
| BMI (kg/m <sup>2</sup> ) was computed as Height (cm)/Weight (kg) x 100.   |          |          |    |
| Units: kg/m <sup>2</sup>  |          |          |    |
| median  | 25.26    | 24.78    |    |
| full range (min-max)  | 16 to 39 | 16 to 41 | -  |
| Body Surface Area (BSA)   |          |          |    |
| BSA (m <sup>2</sup> ) will be computed using Du Bois Formula: 0.007184 x Weight (kg) <sup>0.425</sup> x Height (cm) <sup>0.725</sup> .                            |          |          |    |
| Units: m <sup>2</sup>   |          |          |    |
| median  | 1.84     | 1.79     |    |
| full range (min-max)  | 1 to 3   | 1 to 3   | -  |

### Subject analysis sets

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in) |
| Subject analysis set type  | Safety analysis                                    |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.6 mg/m<sup>2</sup> on Day1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised Phase) |
| Subject analysis set type  | Safety analysis  |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised) |
| Subject analysis set type  | Safety analysis  |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomised) |
| Subject analysis set type  | Safety analysis  |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m<sup>2</sup>/cycle (0.8 mg/m<sup>2</sup> on Day 1, 0.5 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m<sup>2</sup>/cycle (0.5 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in) |
| Subject analysis set type  | Safety analysis                                    |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.6 mg/m<sup>2</sup> on Day1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|  |  |
|--|--|
| Subject analysis set title   | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised) |
| Subject analysis set type  | Safety analysis  |
| Subject analysis set description:  |  |
| Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m <sup>2</sup> /cycle (0.6 mg/m <sup>2</sup> on Day 1, 0.3 mg/m <sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m <sup>2</sup> /cycle (0.3 mg/m <sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.   |  |
| Subject analysis set title   | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomised) |
| Subject analysis set type  | Safety analysis  |
| Subject analysis set description:  |  |
| Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m <sup>2</sup> /cycle (0.8 mg/m <sup>2</sup> on Day 1, 0.5 mg/m <sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m <sup>2</sup> /cycle (0.5 mg/m <sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.   |  |
| Subject analysis set title   | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in)     |
| Subject analysis set type  | Safety analysis  |
| Subject analysis set description:  |  |
| Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m <sup>2</sup> /cycle administrated in 3 divided doses (0.6 mg/m <sup>2</sup> on Day1, 0.3 mg/m <sup>2</sup> on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m <sup>2</sup> /cycle (0.3 mg/m <sup>2</sup> on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks. |  |
| Subject analysis set title   | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in)     |
| Subject analysis set type  | Safety analysis  |
| Subject analysis set description:  |  |
| Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m <sup>2</sup> /cycle administrated in 3 divided doses (0.6 mg/m <sup>2</sup> on Day1, 0.3 mg/m <sup>2</sup> on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m <sup>2</sup> /cycle (0.3 mg/m <sup>2</sup> on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks. |  |
| Subject analysis set title   | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomized) |
| Subject analysis set type  | Safety analysis  |
| Subject analysis set description:  |  |
| Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m <sup>2</sup> /cycle (0.6 mg/m <sup>2</sup> on Day 1, 0.3 mg/m <sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m <sup>2</sup> /cycle (0.3 mg/m <sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.   |  |
| Subject analysis set title   | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomised) |
| Subject analysis set type  | Safety analysis  |
| Subject analysis set description:  |  |
| Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m <sup>2</sup> /cycle (0.8 mg/m <sup>2</sup> on Day 1, 0.5 mg/m <sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m <sup>2</sup> /cycle (0.5 mg/m <sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.   |  |
| Subject analysis set title   | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomized) |
| Subject analysis set type  | Safety analysis  |
| Subject analysis set description:  |  |
| Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m <sup>2</sup> /cycle (0.6 mg/m <sup>2</sup> on Day 1, 0.3 mg/m <sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m <sup>2</sup> /cycle (0.3 mg/m <sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.   |  |
| Subject analysis set title   | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in)     |
| Subject analysis set type  | Safety analysis  |
| Subject analysis set description:  |  |
| Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m <sup>2</sup> /cycle administrated in 3 divided doses (0.6 mg/m <sup>2</sup> on Day1, 0.3 mg/m <sup>2</sup> on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m <sup>2</sup> /cycle (0.3 mg/m <sup>2</sup> on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks. |  |



|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised) |
| Subject analysis set type  | Safety analysis  |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomised) |
| Subject analysis set type  | Safety analysis  |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m<sup>2</sup>/cycle (0.8 mg/m<sup>2</sup> on Day 1, 0.5 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m<sup>2</sup>/cycle (0.5 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

| Reporting group values  | 1.2 mg/m <sup>2</sup> /cycle<br>(Dose Level 2 Run-in) | 1.2 mg/m <sup>2</sup> /cycle<br>(Dose Level 2 Randomised Phase) | 1.2 mg/m <sup>2</sup> /cycle<br>(Dose Level 2 Randomised) |
|---|---|---|---|
| Number of subjects  | 22  | 42  | 42  |
| Age Categorical<br>Units: Subjects  |   |   |   |
| <=18 years  |   |   |   |
| Between 18 and 65 years   |   |   |   |
| >=65 years  |   |   |   |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation   | ±   | ±   | ±   |
| Sex: Female, Male<br>Units: Subjects  |   |   |   |
| Female  |   |   |   |
| Male  |   |   |   |
| Race (NIH/OMB)<br>Units: Subjects   |   |   |   |
| American Indian or Alaska Native  |   |   |   |
| Asian   |   |   |   |
| Native Hawaiian or Other Pacific Islander   |   |   |   |
| Black or African American   |   |   |   |
| White   |   |   |   |
| More than one race  |   |   |   |
| Unknown or Not Reported   |   |   |   |
| Ethnicity (NIH/OMB)<br>Units: Subjects  |   |   |   |
| Hispanic or Latino  |   |   |   |
| Not Hispanic or Latino  |   |   |   |
| Unknown or Not Reported   |   |   |   |
| ECOG Performance Status   |   |   |   |
| Eastern Cooperative Oncology Group (ECOG) Performance Status is defined as: ECOG=0: Fully active, able to carry on all predisease performance without restriction; ECOG=1: Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, ie, light house work, office work; ECOG=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. |   |   |   |
| Units: Subjects   |   |   |   |
| ECOG = 0  |   |   |   |

|          |  |  |  |
|----------|--|--|--|
| ECOG = 1 |  |  |  |
| ECOG = 2 |  |  |  |

|  |  |  |  |
|--|--|--|--|
| Body Mass Index (BMI)  |  |  |  |
| BMI (kg/m <sup>2</sup> ) was computed as Height (cm)/Weight (kg) x 100.  |  |  |  |
| Units: kg/m <sup>2</sup>   |  |  |  |
| median   |  |  |  |
| full range (min-max)   |  |  |  |
| Body Surface Area (BSA)  |  |  |  |
| BSA (m <sup>2</sup> ) will be computed using Du Bois Formula: 0.007184 x Weight (kg) <sup>0.425</sup> x Height (cm) <sup>0.725</sup> . |  |  |  |
| Units: m <sup>2</sup>  |  |  |  |
| median   |  |  |  |
| full range (min-max)   |  |  |  |

| Reporting group values  | 1.8 mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) | 1.2 mg/m <sup>2</sup> /cycle<br>(Dose Level 2 Run-<br>in) | 1.2 mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised) |
|---|--|---|--|
| Number of subjects  | 38   | 10  | 21   |
| Age Categorical   |  |   |  |
| Units: Subjects   |  |   |  |
| <=18 years  |  |   |  |
| Between 18 and 65 years   |  |   |  |
| >=65 years  |  |   |  |
| Age continuous  |  |   |  |
| Units: years  |  |   |  |
| arithmetic mean   |  |   |  |
| standard deviation  | ±  | ±   | ±  |
| Sex: Female, Male   |  |   |  |
| Units: Subjects   |  |   |  |
| Female  |  |   |  |
| Male  |  |   |  |
| Race (NIH/OMB)  |  |   |  |
| Units: Subjects   |  |   |  |
| American Indian or Alaska Native  |  |   |  |
| Asian   |  |   |  |
| Native Hawaiian or Other Pacific<br>Islander  |  |   |  |
| Black or African American   |  |   |  |
| White   |  |   |  |
| More than one race  |  |   |  |
| Unknown or Not Reported   |  |   |  |
| Ethnicity (NIH/OMB)   |  |   |  |
| Units: Subjects   |  |   |  |
| Hispanic or Latino  |  |   |  |
| Not Hispanic or Latino  |  |   |  |
| Unknown or Not Reported   |  |   |  |
| ECOG Performance Status   |  |   |  |
| Eastern Cooperative Oncology Group (ECOG) Performance Status is defined as: ECOG=0: Fully active, able to carry on all predisease performance without restriction; ECOG=1: Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, ie, light house work, office work; ECOG=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. |  |   |  |
| Units: Subjects   |  |   |  |

|  |  |  |  |
|--|--|--|--|
| ECOG = 0<br>ECOG = 1<br>ECOG = 2   |  |  |  |
| Body Mass Index (BMI)  |  |  |  |
| BMI (kg/m <sup>2</sup> ) was computed as Height (cm)/Weight (kg) x 100.  |  |  |  |
| Units: kg/m <sup>2</sup><br>median<br>full range (min-max)   |  |  |  |
| Body Surface Area (BSA)  |  |  |  |
| BSA (m <sup>2</sup> ) will be computed using Du Bois Formula: 0.007184 x Weight (kg) <sup>0.425</sup> x Height (cm) <sup>0.725</sup> . |  |  |  |
| Units: m <sup>2</sup><br>median<br>full range (min-max)  |  |  |  |

| <b>Reporting group values</b>   | 1.8 mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) | 1.2 mg/m <sup>2</sup> /cycle<br>(Dose Level 2 Run-<br>in) | 1.2 mg/m <sup>2</sup> /cycle<br>(Dose Level 2 Run-<br>in) |
|---|--|---|---|
| Number of subjects  | 12   | 22  | 11  |
| Age Categorical<br>Units: Subjects  |  |   |   |
| <=18 years<br>Between 18 and 65 years<br>>=65 years   |  |   |   |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation   | ±  | ±   | ±   |
| Sex: Female, Male<br>Units: Subjects  |  |   |   |
| Female<br>Male  |  |   |   |
| Race (NIH/OMB)<br>Units: Subjects   |  |   |   |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific<br>Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported  |  |   |   |
| Ethnicity (NIH/OMB)<br>Units: Subjects  |  |   |   |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |  |   |   |
| ECOG Performance Status   |  |   |   |
| Eastern Cooperative Oncology Group (ECOG) Performance Status is defined as: ECOG=0: Fully active, able to carry on all predisease performance without restriction; ECOG=1: Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, ie, light house work, office work; ECOG=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. |  |   |   |
| Units: Subjects   |  |   |   |

|  |  |  |  |
|--|--|--|--|
| ECOG = 0<br>ECOG = 1<br>ECOG = 2   |  |  |  |
| Body Mass Index (BMI)  |  |  |  |
| BMI (kg/m <sup>2</sup> ) was computed as Height (cm)/Weight (kg) x 100.  |  |  |  |
| Units: kg/m <sup>2</sup><br>median<br>full range (min-max)   |  |  |  |
| Body Surface Area (BSA)  |  |  |  |
| BSA (m <sup>2</sup> ) will be computed using Du Bois Formula: 0.007184 x Weight (kg) <sup>0.425</sup> x Height (cm) <sup>0.725</sup> . |  |  |  |
| Units: m <sup>2</sup><br>median<br>full range (min-max)  |  |  |  |

| <b>Reporting group values</b>   | 1.2 mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomized) | 1.8 mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) | 1.2 mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomized) |
|---|--|--|--|
| Number of subjects  | 35   | 26   | 41   |
| Age Categorical<br>Units: Subjects  |  |  |  |
| <=18 years<br>Between 18 and 65 years<br>>=65 years   |  |  |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation   | ±  | ±  | ±  |
| Sex: Female, Male<br>Units: Subjects  |  |  |  |
| Female<br>Male  |  |  |  |
| Race (NIH/OMB)<br>Units: Subjects   |  |  |  |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific<br>Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported  |  |  |  |
| Ethnicity (NIH/OMB)<br>Units: Subjects  |  |  |  |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |  |  |  |
| ECOG Performance Status   |  |  |  |
| Eastern Cooperative Oncology Group (ECOG) Performance Status is defined as: ECOG=0: Fully active, able to carry on all predisease performance without restriction; ECOG=1: Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, ie, light house work, office work; ECOG=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. |  |  |  |
| Units: Subjects   |  |  |  |

|  |  |    |  |
|--|--|----|--|
| ECOG = 0<br>ECOG = 1<br>ECOG = 2   |  |    |  |
| Body Mass Index (BMI)  |  |    |  |
| BMI (kg/m <sup>2</sup> ) was computed as Height (cm)/Weight (kg) x 100.  |  |    |  |
| Units: kg/m <sup>2</sup><br>median<br>full range (min-max)   |  |    |  |
| Body Surface Area (BSA)  |  |    |  |
| BSA (m <sup>2</sup> ) will be computed using Du Bois Formula: 0.007184 x Weight (kg) <sup>0.425</sup> x Height (cm) <sup>0.725</sup> . |  |    |  |
| Units: m <sup>2</sup><br>median<br>full range (min-max)  |  | 18 |  |

| <b>Reporting group values</b>   | 1.2 mg/m <sup>2</sup> /cycle<br>(Dose Level 2 Run-in) | 1.2 mg/m <sup>2</sup> /cycle<br>(Dose Level 2 Randomised) | 1.8 mg/m <sup>2</sup> /cycle<br>(Dose Level 1 Randomised) |
|---|---|---|---|
| Number of subjects  | 2   | 3   | 3   |
| Age Categorical<br>Units: Subjects  |   |   |   |
| <=18 years<br>Between 18 and 65 years<br>>=65 years   |   |   |   |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation   | ±   | ±   | ±   |
| Sex: Female, Male<br>Units: Subjects  |   |   |   |
| Female<br>Male  |   |   |   |
| Race (NIH/OMB)<br>Units: Subjects   |   |   |   |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported   |   |   |   |
| Ethnicity (NIH/OMB)<br>Units: Subjects  |   |   |   |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |   |   |   |
| ECOG Performance Status   |   |   |   |
| Eastern Cooperative Oncology Group (ECOG) Performance Status is defined as: ECOG=0: Fully active, able to carry on all predisease performance without restriction; ECOG=1: Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature, ie, light house work, office work; ECOG=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. |   |   |   |
| Units: Subjects   |   |   |   |

|  |  |  |  |
|--|--|--|--|
| ECOG = 0<br>ECOG = 1<br>ECOG = 2   |  |  |  |
| Body Mass Index (BMI)  |  |  |  |
| BMI (kg/m <sup>2</sup> ) was computed as Height (cm)/Weight (kg) x 100.  |  |  |  |
| Units: kg/m <sup>2</sup><br>median<br>full range (min-max)   |  |  |  |
| Body Surface Area (BSA)  |  |  |  |
| BSA (m <sup>2</sup> ) will be computed using Du Bois Formula: 0.007184 x Weight (kg) <sup>0.425</sup> x Height (cm) <sup>0.725</sup> . |  |  |  |
| Units: m <sup>2</sup><br>median<br>full range (min-max)  |  |  |  |

---

## End points

### End points reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in + Randomized) |
|-----------------------|---|

Reporting group description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After complete remission (CR)/complete remission with incomplete hematologic recovery (CRi) is achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Day 1, 8 and 15). The maximum treatment duration was approximately 26 weeks.

|                       |  |
|-----------------------|--|
| Reporting group title | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomized Phase) |
|-----------------------|--|

Reporting group description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.8 mg/m<sup>2</sup> on Day 1, 0.5 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 1.5 mg/m<sup>2</sup>/cycle (0.5 mg/m<sup>2</sup> on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in) |
|----------------------------|--|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.6 mg/m<sup>2</sup> on Day1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised Phase) |
|----------------------------|--|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised) |
|----------------------------|--|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomised) |
|----------------------------|--|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m<sup>2</sup>/cycle (0.8 mg/m<sup>2</sup> on Day 1, 0.5 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m<sup>2</sup>/cycle (0.5 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in) |
|----------------------------|--|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.6 mg/m<sup>2</sup> on Day1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised) |
|----------------------------|--|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The

maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomised) |
| Subject analysis set type  | Safety analysis  |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m<sup>2</sup>/cycle (0.8 mg/m<sup>2</sup> on Day 1, 0.5 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m<sup>2</sup>/cycle (0.5 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in) |
| Subject analysis set type  | Safety analysis                                    |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.6 mg/m<sup>2</sup> on Day1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in) |
| Subject analysis set type  | Safety analysis                                    |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.6 mg/m<sup>2</sup> on Day1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomized) |
| Subject analysis set type  | Safety analysis  |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomised) |
| Subject analysis set type  | Safety analysis  |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m<sup>2</sup>/cycle (0.8 mg/m<sup>2</sup> on Day 1, 0.5 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m<sup>2</sup>/cycle (0.5 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomized) |
| Subject analysis set type  | Safety analysis  |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in) |
| Subject analysis set type  | Safety analysis                                    |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.6 mg/m<sup>2</sup> on Day1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised) |
| Subject analysis set type  | Safety analysis  |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The



maximum treatment duration was approximately 26 weeks.

|                            |  |
|----------------------------|--|
| Subject analysis set title | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomised) |
| Subject analysis set type  | Safety analysis  |

Subject analysis set description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m<sup>2</sup>/cycle (0.8 mg/m<sup>2</sup> on Day 1, 0.5 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m<sup>2</sup>/cycle (0.5 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 26 weeks.

### Primary: Percentage of Subjects With Veno-occlusive Disease (VOD)

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With Veno-occlusive Disease (VOD) <sup>[1][2]</sup> |
|-----------------|--|

End point description:

VOD happened when the small blood vessels that lead into the liver and were inside the liver become blocked. VOD is defined as: a. Classical VOD (first 21 days after HSCT): Bilirubin  $\geq$  2 mg/dL and 2 (or more) of the following criteria must also be present: 1. Painful hepatomegaly; 2. Weight gain  $>$ 5%; 3. Ascites. b. Late onset VOD ( $>$ 21 days after HSCT): Classical VOD beyond Day 21; or Histologically proven VOD; or Two or more of the following criteria must be present: 1. Bilirubin  $>$ 2 mg/dL; 2. Painful hepatomegaly; 3. Weight gain  $>$ 5%; 4. Ascites. and hemodynamical and/or ultrasound evidence of VOD. All randomised subjects who received at least 1 dose of study drug.

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

End point timeframe:

From consent up to follow-up (up to 2 years)

Notes:

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

Justification: No statistical analysis was planned for this endpoint

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

Justification: Only descriptive analysis was planned for this endpoint.

| End point values              | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in + Randomized) | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in) | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised) | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomised) |
|-------------------------------|---|--|--|--|
| Subject group type            | Reporting group   | Subject analysis set                               | Subject analysis set                                   | Subject analysis set                                   |
| Number of subjects analysed   | 64  | 22   | 42   | 38   |
| Units: Percentage of subjects |   |  |  |  |
| number (not applicable)       | 12.5  | 9.1  | 14.3   | 5.3  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Rate of Hematologic Remission (Complete Response [CR] / Complete Response with Incomplete Hematologic Recovery[CRi])

|                 |  |
|-----------------|--|
| End point title | Rate of Hematologic Remission (Complete Response [CR] / Complete Response with Incomplete Hematologic Recovery[CRi]) <sup>[3][4]</sup> |
|-----------------|--|

End point description:

CR=disappearance of leukemia indicated by  $<$ 5% marrow blasts, absence of peripheral blood leukemic blasts, recovery of hematopoiesis defined by absolute neutrophil count (ANC)  $\geq$  1000/ $\mu$ L and platelets  $\geq$  100000/ $\mu$ L. C1 extramedullary disease status is required. CRi = CR except with ANC  $<$  1000/ $\mu$ L and/or platelets  $<$  100000/ $\mu$ L. Subjects randomised into study with study drug assignment based on randomisation.

|   |   |   |   |   |                      |
|---|---|---|---|---|----------------------|
| End point type  | Primary   |   |   |   |                      |
| End point timeframe:  |   |   |   |   |                      |
| From first dose of study treatment till follow-up of up to 2 years  |   |   |   |   |                      |
| 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 analysis was planned for this endpoint  |   |   |   |   |                      |
| [4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. |   |   |   |   |                      |
| Justification: Only descriptive analysis was planned for this endpoint.   |   |   |   |   |                      |
| End point values  | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) |                      |
|   | Subject group type  | Reporting group   | Subject analysis set  | Subject analysis set  | Subject analysis set |
|   | Number of subjects analysed   | 64  | 22  | 42  | 38                   |
|   | Units: Percentage of subjects   |   |   |   |                      |
|   | number (not applicable)   | 71.9  | 50.0  | 83.3  | 68.4                 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Treatment-Emergent Adverse Events (Treatment-related)

|  |  |   |   |   |
|--|--|---|---|---|
| End point title  | Number of Subjects With Treatment-Emergent Adverse Events (Treatment-related) <sup>[5]</sup> |   |   |   |
| End point description:   |  |   |   |   |
| Adverse event (AE) = any untoward medical occurrence in subject who received study treatment without regard to possibility of causal relationship. Treatment emergent AEs (TEAEs) were defined as AEs that reported the period starting with the first dose of study treatment drug through 63 days after last dose or 1 day before start day of new anticancer therapy, whichever occurred first. A SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Grades of severity were defined by CTCAE v3.0. Grade 3 = severe adverse event; Grade 4 = life-threatening consequences; urgent intervention indicated. Grade 5 = death related to AE. Causality of TEAEs were assessed by the Investigator. All randomised subjects who received at least 1 dose of study drug. |  |   |   |   |
| End point type   | Secondary  |   |   |   |
| End point timeframe:   |  |   |   |   |
| From first dose of study treatment drug through 63 days after last dose (approximately 52 weeks)   |  |   |   |   |
| Notes:   |  |   |   |   |
| [5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only descriptive analysis was planned for this endpoint.  |  |   |   |   |
| End point values   | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized)                  | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) |
| Subject group type   | Reporting group  | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed  | 64   | 22  | 42  | 38  |
| Units: Subjects  |  |   |   |   |

|  |    |    |    |    |
|--|----|----|----|----|
| Participants with AEs                      | 31 | 13 | 18 | 22 |
| Participants with SAEs                     | 15 | 7  | 8  | 10 |
| Participants with Maximum Grade 3 or 4 AEs | 20 | 9  | 11 | 11 |
| Participants with Maximum Grade 5 AEs      | 2  | 1  | 1  | 4  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Treatment-Emergent Adverse Events (All Causalities)

|                 |  |
|-----------------|--|
| End point title | Number of Subjects With Treatment-Emergent Adverse Events (All Causalities) <sup>[6]</sup> |
|-----------------|--|

End point description:

Adverse event (AE) = any untoward medical occurrence in subject who received study treatment without regard to possibility of causal relationship. On-treatment period was defined as the period starting with the 1st dose of study treatment through 63 days after last dose or 1 day before start day of new anticancer therapy, whichever occurred first. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. All VOD cases were reported as SAE. Grades of severity were defined by Common terminology criteria for adverse events (CTCAE) v3.0. Grade 3=severe adverse event; Grade 4=life-threatening consequences; urgent intervention indicated. Grade 5=death related to AE. All randomised subjects who received at least 1 dose of study drug.

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

End point timeframe:

From first dose of study treatment drug through 63 days after last dose (approximately 52 weeks)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only descriptive analysis was planned for this endpoint.

| End point values                             | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) |
|--|---|---|---|---|
| Subject group type                           | Reporting group   | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed                  | 64  | 22  | 42  | 38  |
| Units: Subjects                              |   |   |   |   |
| Subjects with AE                             | 60  | 21  | 39  | 35  |
| Subjects with SAEs                           | 43  | 15  | 28  | 21  |
| Subjects with Maximum Grade 3 or 4 AE        | 30  | 9   | 21  | 18  |
| Subjects with Maximum Grade 5 adverse events | 19  | 7   | 12  | 10  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Shift Summary of Hematology Laboratory Test

## Results from Grade Less Than or Equal to ( $\leq$ ) 2 at Baseline to Grade 3 or 4 Post-Baseline

|                 |  |
|-----------------|--|
| End point title | Number of Subjects With Shift Summary of Hematology Laboratory Test Results from Grade Less Than or Equal to ( $\leq$ ) 2 at Baseline to Grade 3 or 4 Post-Baseline <sup>[7]</sup> |
|-----------------|--|

End point description:

Baseline assessment was defined as the last assessment performed on or prior to the date of the first dose of study treatment. Following Parameters were analyzed for laboratory assessment: Hematology (Activated partial thromboplastin time prolonged, Anemia, Hemoglobin increased, International normalization rate (INR) increased, Leukocytosis, Lymphocyte count decreased, Lymphocyte count increased, Neutrophil count decreased, Platelet count decreased, White blood cell decreased). Grades of severity were defined by CTCAE v3.0. Grade 2 = moderate adverse event; Grade 3= severe adverse event; Grade 4 = life-threatening consequences; urgent intervention indicated. All randomised subjects who received at least 1 dose of study drug and with at least 1 postbaseline assessment in each treatment group. 'Number analysed' = subjects evaluable for this endpoint for each specified row. '99999'=Grade4 was not applicable for the test.

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

End point timeframe:

From first dose of study treatment drug through 63 days after last dose (approximately 52 weeks)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only descriptive analysis was planned for this endpoint.

| End point values                                     | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) |
|--|---|---|---|---|
| Subject group type                                   | Reporting group   | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed                          | 64  | 22  | 42  | 38  |
| Units: Subjects                                      |   |   |   |   |
| APT time prolonged - Grade 3<br>(n=51,19,32,27)      | 0   | 0   | 0   | 0   |
| APT time prolonged - Grade 4<br>(n=51,19,32,27)      | 99999   | 99999   | 99999   | 99999   |
| Anemia - Grade 3 (n=37,15,22,20)                     | 21  | 8   | 13  | 11  |
| Anemia - Grade 4 (n=37,15,22,20)                     | 99999   | 99999   | 99999   | 99999   |
| Hemoglobin increased - Grade<br>3(n=18,6,12,13)      | 0   | 0   | 0   | 0   |
| Hemoglobin increased - Grade<br>4(n=18,6,12,13)      | 99999   | 99999   | 99999   | 99999   |
| INR increased - Grade<br>3(n=27,11,16,12)            | 0   | 0   | 0   | 0   |
| INR increased - Grade<br>4(n=27,11,16,12)            | 99999   | 99999   | 99999   | 99999   |
| Leukocytosis - Grade 3(n=18,7,11,13)                 | 1   | 1   | 0   | 0   |
| Leukocytosis - Grade 4(n=18,7,11,13)                 | 99999   | 99999   | 99999   | 99999   |
| Lymphocyte count decreased-Grade<br>3(n=51,16,35,28) | 16  | 1   | 15  | 7   |
| Lymphocyte count decreased-Grade<br>4(n=51,16,35,28) | 6   | 4   | 2   | 4   |
| Lymphocyte count increased-Grade<br>3(n=27,13,14,17) | 3   | 2   | 1   | 3   |
| Lymphocyte count increased-Grade<br>4(n=27,13,14,17) | 99999   | 99999   | 99999   | 99999   |
| Neutrophil count decreased-Grade<br>3(n=51,17,34,27) | 8   | 2   | 6   | 7   |
| Neutrophil count decreased-Grade<br>4(n=51,17,34,27) | 21  | 11  | 10  | 9   |

|   |    |   |    |    |
|---|----|---|----|----|
| Platelet count decreased-Grade 3(n=41,13,28,28)   | 7  | 1 | 6  | 5  |
| Platelet count decreased - Grade 4(n=41,13,28,28) | 7  | 4 | 3  | 7  |
| White blood cell decreased-Grade 3(n=56,18,38,29) | 18 | 5 | 13 | 9  |
| White blood cell decreased-Grade 4(n=56,18,38,29) | 17 | 7 | 10 | 11 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Treatment-Emergent Serious Adverse Events (Post-HSCT)

|                 |  |
|-----------------|--|
| End point title | Number of Subjects With Treatment-Emergent Serious Adverse Events (Post-HSCT) <sup>[8]</sup> |
|-----------------|--|

End point description:

A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. All SAEs occurred after HSCT were reported in this endpoint. All randomised subjects who received at least 1 dose of study drug.

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

End point timeframe:

Starting from the first transplant after inotuzumab ozogamicin treatment and including the entire duration of subsequent follow up (approximately 52 weeks)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only descriptive analysis was planned for this endpoint.

| End point values            | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in + Randomized) | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in) | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised Phase) | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomised) |
|-----------------------------|---|--|--|--|
| Subject group type          | Reporting group   | Subject analysis set                               | Subject analysis set   | Subject analysis set                                   |
| Number of subjects analysed | 64  | 22   | 42   | 38   |
| Units: Subjects             | 14  | 6  | 8  | 2  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Shift Summary of Chemistry Laboratory Test Results from Grade ≤2 at Baseline to Grade 3 or 4 Post-Baseline

|                 |   |
|-----------------|---|
| End point title | Number of Subjects With Shift Summary of Chemistry Laboratory Test Results from Grade ≤2 at Baseline to Grade 3 or 4 Post-Baseline <sup>[9]</sup> |
|-----------------|---|

End point description:

Baseline assessment=last assessment performed on or prior to date of first dose of study treatment.

Parameters analysed for laboratory assessment: Chemistry (Alanine aminotransferase [ALT] increased, Alkaline phosphatase [ALP] increased, Aspartate aminotransferase [AST] increased, Blood bilirubin increased, Chronic kidney disease, Creatinine increased, Gamma glutamyl transpeptidase [GGT] increased, Hypercalcemia, Hyperglycemia, Hyperkalemia, Hypermagnesemia, Hyponatremia, Hypoalbuminemia, Hypocalcemia, Hypoglycemia, Hypokalemia, Hypomagnesemia, Hyponatremia, Hypophosphatemia, Lipase increased, Serum amylase increased). Grades of severity defined by CTCAE v3.0. Grade 2=moderate AE ; Grade 3=severe AE ; Grade 4= life-threatening consequences; urgent intervention indicated. All randomised subjects who received at least 1 dose of study drug with at least 1 postbaseline assessment in each treatment group. 'Number analysed' = subjects evaluable for each specified row. '99999' = Grade 4 was not applicable for the test.

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

End point timeframe:

From first dose of study treatment drug through 63 days after last dose (approximately 52 weeks)

Notes:

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

Justification: Only descriptive analysis was planned for this endpoint.

| End point values                                       | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) |
|--|---|---|---|---|
| Subject group type                                     | Reporting group   | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed                            | 64  | 22  | 42  | 38  |
| Units: Subjects  |   |   |   |   |
| ALT increased - Grade 3<br>(n=29,14,15,23)             | 1   | 1   | 0   | 0   |
| ALT increased - Grade 4<br>(n=29,14,15,23)             | 0   | 0   | 0   | 0   |
| ALP increased - Grade 3<br>(n=42,14,28,22)             | 1   | 1   | 0   | 1   |
| ALP increased - Grade 4<br>(n=42,14,28,22)             | 0   | 0   | 0   | 0   |
| AST increased - Grade 3<br>(n=42,16,26,26)             | 4   | 1   | 3   | 0   |
| AST increased - Grade 4<br>(n=42,16,26,26)             | 0   | 0   | 0   | 0   |
| Blood bilirubin increased - Grade 3<br>(n=31,14,17,20) | 2   | 1   | 1   | 0   |
| Blood bilirubin increased - Grade 4<br>(n=31,14,17,20) | 0   | 0   | 0   | 0   |
| Chronic kidney disease - Grade 3<br>(n=9,2,7,7)        | 0   | 0   | 0   | 0   |
| Chronic kidney disease - Grade 4<br>(n=9,2,7,7)        | 0   | 0   | 0   | 0   |
| Creatinine increased - Grade 3<br>(n=50,19,31,26)      | 0   | 0   | 0   | 0   |
| Creatinine increased - Grade 4<br>(n=50,19,31,26)      | 0   | 0   | 0   | 0   |
| GGT increased - Grade 3<br>(n=37,15,22,26)             | 3   | 1   | 2   | 3   |
| GGT increased - Grade 4<br>(n=37,15,22,26)             | 0   | 0   | 0   | 0   |
| Hypercalcemia - Grade 3<br>(n=22,10,12,15)             | 0   | 0   | 0   | 0   |
| Hypercalcemia - Grade 4<br>(n=22,10,12,15)             | 0   | 0   | 0   | 0   |
| Hyperglycemia - Grade 3<br>(n=37,13,24,21)             | 4   | 2   | 2   | 2   |
| Hyperglycemia - Grade 4<br>(n=37,13,24,21)             | 0   | 0   | 0   | 0   |

|  |       |       |       |       |
|--|-------|-------|-------|-------|
| Hyperkalemia - Grade 3(n=21,10,11,14)            | 0     | 0     | 0     | 0     |
| Hyperkalemia - Grade 4(n=21,10,11,14)            | 1     | 1     | 0     | 0     |
| Hypermagnesemia - Grade 3(n=21,11,10,15)         | 1     | 1     | 0     | 1     |
| Hypermagnesemia - Grade 4(n=21,11,10,15)         | 0     | 0     | 0     | 0     |
| Hypernatremia - Grade 3(n=19,9,10,15)            | 0     | 0     | 0     | 0     |
| Hypernatremia - Grade 4(n=19,9,10,15)            | 1     | 0     | 1     | 0     |
| Hypoalbuminemia - Grade 3 (n=31,16,15,21)        | 4     | 1     | 3     | 3     |
| Hypoalbuminemia - Grade 4(n=31,16,15,21)         | 99999 | 99999 | 99999 | 99999 |
| Hypocalcemia - Grade 3(n=28,12,16,15)            | 1     | 1     | 0     | 0     |
| Hypocalcemia - Grade 4(n=28,12,16,15)            | 0     | 0     | 0     | 0     |
| Hypoglycemia - Grade 3(n=22,10,12,16)            | 0     | 0     | 0     | 0     |
| Hypoglycemia - Grade 4(n=22,10,12,16)            | 0     | 0     | 0     | 0     |
| Hypokalemia - Grade 3(n=32,13,19,24)             | 3     | 1     | 2     | 1     |
| Hypokalemia - Grade 4(n=32,13,19,24)             | 1     | 1     | 0     | 0     |
| Hypomagnesemia - Grade 3(n=30,14,16,18)          | 1     | 1     | 0     | 1     |
| Hypomagnesemia - Grade 4(n=30,14,16,18)          | 0     | 0     | 0     | 1     |
| Hyponatremia - Grade 3(n=27,13,14,19)            | 1     | 1     | 0     | 0     |
| Hyponatremia - Grade 4(n=27,13,14,19)            | 0     | 0     | 0     | 0     |
| Hypophosphatemia- Grade 3(n=26,13,13,18)         | 2     | 2     | 0     | 1     |
| Hypophosphatemia - Grade 4(n=26,13,13,18)        | 0     | 0     | 0     | 1     |
| Lipase increased - Grade 3(n=38,15,23,24)        | 6     | 3     | 3     | 2     |
| Lipase increased - Grade 4(n=38,15,23,24)        | 2     | 0     | 2     | 0     |
| Serum amylase increased - Grade 3(n=32,14,18,22) | 2     | 1     | 1     | 0     |
| Serum amylase increased - Grade 4(n=32,14,18,22) | 0     | 0     | 0     | 0     |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Remission (DoR) in Subjects who Achieved CR/CRi

|                 |  |
|-----------------|--|
| End point title | Duration of Remission (DoR) in Subjects who Achieved |
|-----------------|--|

End point description:

DoR was defined as time from date of first response in responders (CR/CRi) to the date of disease progression (i.e., objective progression, relapse from CR/CRi, including post-study treatment follow-up disease assessments) or death due to any cause, whichever occurs first. DoR was estimated using Kaplan-Meier methods. 99999 indicates upper limit was not estimated due to fewer number of subjects

with event. Subjects who were randomised into the study and with a remission (CR/CRi).

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| From date of first response (subjects who achieved CR/CRi) to the date of disease progression or death due to any cause  |           |
| Notes:   |           |
| [10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. |           |
| Justification: Only descriptive analysis was planned for this endpoint.  |           |

| End point values                 | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in + Randomized) | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in) | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised Phase) | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomised) |
|----------------------------------|---|--|--|--|
| Subject group type               | Reporting group   | Subject analysis set                               | Subject analysis set   | Subject analysis set                                   |
| Number of subjects analysed      | 46  | 11   | 35   | 26   |
| Units: Months                    |   |  |  |  |
| median (confidence interval 95%) | 5.5 (4.7 to 13.4)   | 5.2 (1.9 to 99999)                                 | 6.5 (4.6 to 20.9)  | 6.8 (4.7 to 8.7)                                       |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects Achieving a CR/CRi with Minimal Residual Disease (MRD) Negativity

|   |  |
|---|--|
| End point title   | Number of Subjects Achieving a CR/CRi with Minimal Residual Disease (MRD) Negativity <sup>[11]</sup> |
| End point description:  |  |
| Subjects who achieved CR/CRi, a patient was considered to be MRD negative if the minimum MRD (%) between the date of achieving CR/CRi and end of treatment test is <0.01%. All subjects who were randomised into the study and achieved CR/CRi. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| At screening, once at Day 16-28 of Cycles 1 and 2, or until CR/CRi and MRD negativity were achieved, then after every 1-2 cycles as clinically indicated, and at EOT visit  |  |
| Notes:  |  |
| [11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.                        |  |
| Justification: Only descriptive analysis was planned for this endpoint.   |  |

| End point values            | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in + Randomized) | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in) | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised Phase) | 1.8 mg/m <sup>2</sup> /cycle (Dose Level 1 Randomised) |
|-----------------------------|---|--|--|--|
| Subject group type          | Reporting group   | Subject analysis set                               | Subject analysis set   | Subject analysis set                                   |
| Number of subjects analysed | 46  | 11   | 35   | 26   |
| Units: Subjects             | 33  | 8  | 25   | 18   |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Progression Free Survival (PFS)

|                 |   |
|-----------------|---|
| End point title | Progression Free Survival (PFS) <sup>[12]</sup> |
|-----------------|---|

End point description:

PFS was defined as time from date of randomisation to the date of disease progression (i.e., objective progression, relapse from CR/CRi, including post-study treatment follow-up disease assessments), death due to any cause, or starting new induction therapy/post-therapy HSCT without achieving CR/CRi, whichever occurred first. PFS was estimated using Kaplan-Meier methods. Results were reported as of the data cutoff date on 21 Sep 2022. All subjects who were randomised into the study with study drug assignment based on randomisation.

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

End point timeframe:

From date of randomisation to date of disease progression, death, or starting new induction therapy/post-therapy HSCT without achieving CR/CRi

Notes:

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

Justification: Only descriptive analysis was planned for this endpoint.

| End point values                 | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) |
|----------------------------------|---|---|---|---|
| Subject group type               | Reporting group   | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed      | 64  | 22  | 42  | 38  |
| Units: Months                    |   |   |   |   |
| median (confidence interval 95%) | 5.3 (3.4 to 7.2)  | 2.9 (1.7 to 5.8)  | 6.4 (4.8 to 16.0)   | 6.3 (2.8 to 8.0)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Overall Survival

|                 |                                  |
|-----------------|----------------------------------|
| End point title | Overall Survival <sup>[13]</sup> |
|-----------------|----------------------------------|

End point description:

Overall survival was defined as the time from date of first dose of study treatment to death due to any cause. Subjects without confirmation of death were censored at the date that the subject was last known to be alive. 99999 indicates upper limit was not estimable due to fewer number of subjects with event. All subjects who were randomised into the study with study drug assignment based on randomisation.

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

End point timeframe:

From date of randomisation to death due to any cause

Notes:

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

Justification: Only descriptive analysis was planned for this endpoint.

| End point values                 | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) |
|----------------------------------|---|---|---|---|
| Subject group type               | Reporting group   | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed      | 64  | 22  | 42  | 38  |
| Units: Months                    |   |   |   |   |
| median (confidence interval 95%) | 7.6 (5.8 to<br>10.0)  | 4.5 (3.2 to 8.6)  | 9.6 (6.4 to<br>99999)   | 8.1 (5.4 to<br>10.4)  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects who Received HSCT Post Inotuzumab Ozogamicin Treatment

|                 |   |
|-----------------|---|
| End point title | Number of Subjects who Received HSCT Post Inotuzumab Ozogamicin Treatment <sup>[14]</sup> |
|-----------------|---|

End point description:

Subjects who underwent HSCT after inotuzumab ozogamicin treatment. All subjects who were randomised into the study with study drug assignment based on randomisation.

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

End point timeframe:

From first dose of study treatment till follow-up of up to 2 years

Notes:

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

Justification: No statistical analysis was planned for this endpoint

| End point values            | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) |
|-----------------------------|---|---|---|---|
| Subject group type          | Reporting group   | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed | 64  | 22  | 42  | 38  |
| Units: Subjects             | 31  | 10  | 21  | 12  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Post-HSCT Mortality

|  |   |
|--|---|
| End point title  | Number of Subjects With Post-HSCT Mortality <sup>[15]</sup> |
| End point description:<br>Post-HSCT Mortality was defined as the time from date of first HSCT after inotuzumab ozogamicin treatment to death due to any cause. All subjects who were randomised into the study with study drug assignment based on randomisation and who were post HSCT. |   |
| End point type   | Secondary   |
| End point timeframe:<br>From date of HSCT to the date of death due to any cause (approximately 4 years)  |   |

Notes:

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

Justification: Only descriptive analysis was planned for this endpoint.

| End point values            | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised<br>Phase) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) |
|-----------------------------|---|---|--|---|
| Subject group type          | Reporting group   | Subject analysis set  | Subject analysis set   | Subject analysis set  |
| Number of subjects analysed | 31  | 10  | 21   | 12  |
| Units: Subjects             | 14  | 6   | 8  | 6   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cumulative Incidence Rate of Post-HSCT Relapse at Month 12

|  |   |
|--|---|
| End point title  | Cumulative Incidence Rate of Post-HSCT Relapse at Month |
| End point description:<br>Post-HSCT relapse is defined as the time from date of first HSCT after inotuzumab ozogamicin treatment to the date of first relapse post-HSCT. Cumulative incidence rates of an event at a particular timepoint were estimated with the CI calculated based on the cumulative incidence function using the method described by Kalbfleisch RL and Prentice JD. All subjects who were randomised into the study with study drug assignment based on randomisation and who were post HSCT. |   |
| End point type   | Secondary   |
| End point timeframe:<br>From date of HSCT to the date of first relapse post-HSCT to Month 12   |   |

Notes:

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

Justification: Only descriptive analysis was planned for this endpoint.

| End point values                 | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) |
|----------------------------------|---|---|---|---|
| Subject group type               | Reporting group   | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed      | 31  | 10  | 21  | 12  |
| Units: Percentages of subjects   |   |   |   |   |
| number (confidence interval 95%) | 17.58 (6.17 to  | 11.11 (0.40 to  | 20.51 (6.00 to  | 16.67 (2.26 to  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects with Post HSCT Relapse-Related Mortality

|                 |   |
|-----------------|---|
| End point title | Number of Subjects with Post HSCT Relapse-Related |
|-----------------|---|

End point description:

Post HSCT Relapse-Related Mortality was defined as time from date of first HSCT after inotuzumab ozogamicin treatment to death due to any cause with prior relapse. All subjects who were randomised into the study with study drug assignment based on randomisation and who underwent HSCT after inotuzumab ozogamicin treatment.

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

End point timeframe:

From date of HSCT to the date of death due to any cause with prior relapse/progression post-HSCT (approximately 4 years)

Notes:

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

Justification: Only descriptive analysis was planned for this endpoint.

| End point values            | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in + Randomized) | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Run-in) | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised Phase) | 1.2 mg/m <sup>2</sup> /cycle (Dose Level 2 Randomised) |
|-----------------------------|---|--|--|--|
| Subject group type          | Reporting group   | Subject analysis set                               | Subject analysis set   | Subject analysis set                                   |
| Number of subjects analysed | 31  | 10   | 21   | 12   |
| Units: Subjects             | 4   | 1  | 3  | 2  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Mean Predose Concentrations (Ctough) of Inotuzumab Ozogamicin

|                 |   |
|-----------------|---|
| End point title | Mean Predose Concentrations (Ctough) of Inotuzumab Ozogamicin <sup>[18]</sup> |
|-----------------|---|

End point description:

Ctough was defined as the mean Predose concentration of study treatment. All treated subjects who received at least 1 dose of study drug and had at least one PK sample collected and analysed. 'Number analysed' = Subjects evaluable for this endpoint for each specified row.

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

End point timeframe:

Pre-dose on Cycle 1 Day 1, 8 and 15, and on Day1 and 8 of Cycle 2, 3 and 4.

Notes:

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

Justification: Only descriptive analysis was planned for this endpoint.

| End point values                     | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) |
|--------------------------------------|---|---|---|---|
| Subject group type                   | Reporting group   | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed          | 64  | 22  | 42  | 38  |
| Units: Nanogram per milliliter       |   |   |   |   |
| arithmetic mean (standard deviation) |   |   |   |   |
| Cycle 1 Day 1 (C1D1) n=61,22,39,37   | 0.8 (± 5.56)  | 1.9 (± 9.10)  | 0.2 (± 1.38)  | 0.1 (± 0.35)  |
| C1D8 (n=60,22,38,36)                 | 8.1 (± 21.24)   | 7.7 (± 20.53)   | 8.3 (± 21.91)   | 4.3 (± 6.05)  |
| C1D15 (n=60,21,39,33)                | 15.8 (± 31.34)  | 8.9 (± 11.14)   | 19.5 (± 37.67)  | 25.8 (± 32.89)  |
| C2D1 (n=54,17,37,24)                 | 15.6 (± 24.95)  | 16.4 (± 21.43)  | 15.2 (± 26.67)  | 22.0 (± 47.15)  |
| C2D8 (n=51,18,33,22)                 | 42.7 (± 46.93)  | 42.6 (± 56.57)  | 42.8 (± 41.73)  | 48.6 (± 24.99)  |
| C3D1 (n=17,5,12,11)                  | 30.2 (± 43.39)  | 21.4 (± 18.46)  | 33.9 (± 50.64)  | 37.1 (± 34.03)  |
| C3D8 (n=19,5,14,9)                   | 36.2 (± 18.20)  | 31.9 (± 25.43)  | 37.8 (± 15.82)  | 68.8 (± 39.22)  |
| C4D1 (n=6,2,4,0)                     | 29.4 (± 18.12)  | 50.0 (± 14.64)  | 19.2 (± 7.42)   | 99999 (± 99999)   |
| C4D8 (n=6,2,4,1)                     | 47.7 (± 10.63)  | 48.7 (± 7.99)   | 47.2 (± 12.88)  | 90.4 (± 99999)  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Post HSCT non-Relapse Mortality

|                 |   |
|-----------------|---|
| End point title | Number of Subjects With Post HSCT non-Relapse Mortality <sup>[19]</sup> |
|-----------------|---|

End point description:

Post HSCT non-relapse mortality was defined as time from date of first HSCT after inotuzumab ozogamicin treatment to death due to any cause without prior relapse. All subjects who were randomised into the study with study drug assignment based on randomisation and who underwent HSCT after inotuzumab ozogamicin treatment.

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

End point timeframe:

From date of HSCT to the date of death due to any cause without prior relapse/progression post-HSCT (approximately 4 years)

Notes:

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

Justification: Only descriptive analysis was planned for this endpoint.

| End point values            | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised<br>Phase) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised) |
|-----------------------------|---|---|--|---|
| Subject group type          | Reporting group   | Subject analysis set  | Subject analysis set   | Subject analysis set  |
| Number of subjects analysed | 31  | 10  | 21   | 12  |
| Units: Subjects             | 10  | 5   | 5  | 4   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Positive Anti-Drug Antibody (ADA)

|                 |   |
|-----------------|---|
| End point title | Number of Subjects With Positive Anti-Drug Antibody (ADA) <sup>[20]</sup> |
|-----------------|---|

End point description:

ADA incidence is defined as combined results of treatment-boosted and treatment-induced ADA-positive subjects. The immunogenicity of inotuzumab ozogamicin was evaluated using a validated electrochemiluminescence (ECL)-based immunoassay. Subjects who received at least 1 dose of study drug and had at least 1 ADA sample collected and analysed for immunogenicity.

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

End point timeframe:

At Day 1 of every cycle prior to the beginning of inotuzumab ozogamicin infusion and at the EOT visit, up to approximately 4 years

Notes:

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

Justification: Only descriptive analysis was planned for this endpoint.

| End point values            | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomized) |
|-----------------------------|---|---|---|---|
| Subject group type          | Reporting group   | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed | 63  | 22  | 38  | 41  |
| Units: Subjects             |   |   |   |   |
| Positive Predose ADA        | 4   | 1   | 2   | 3   |
| Treatment-induced ADA       | 1   | 1   | 1   | 0   |
| Treatment-boosted ADA       | 0   | 0   | 0   | 0   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Positive Neutralizing Antibody (NAb)

|                 |  |
|-----------------|--|
| End point title | Number of Subjects With Positive Neutralizing Antibody |
|-----------------|--|

End point description:

NAb incidence is defined as combined results of treatment-boosted and treatment-induced NAb-positive

subjects. The immunogenicity of inotuzumab ozogamicin was evaluated using a validated electrochemiluminescence (ECL)-based immunoassay. Subjects who received at least 1 dose of study drug and had at least 1 Nab sample collected and analysed for immunogenicity.

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

End point timeframe:

At Day 1 of every cycle prior to the beginning of inotuzumab ozogamicin infusion and at the EOT visit, up to approximately 4 years.

Notes:

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

Justification: Only descriptive analysis was planned for this endpoint.

| End point values            | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in +<br>Randomized) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Run-in) | 1.2<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 2<br>Randomised<br>Phase) | 1.8<br>mg/m <sup>2</sup> /cycle<br>(Dose Level 1<br>Randomised) |
|-----------------------------|---|---|--|---|
| Subject group type          | Reporting group   | Subject analysis set  | Subject analysis set   | Subject analysis set  |
| Number of subjects analysed | 5   | 2   | 3  | 3   |
| Units: Subjects             |   |   |  |   |
| Positive Predose NAb        | 0   | 0   | 0  | 0   |
| Treatment-induced NAb       | 0   | 0   | 0  | 0   |
| Treatment-boosted NAb       | 0   | 0   | 0  | 0   |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the time of consent including a minimum of 9 weeks after the last dose

Adverse event reporting additional description:

Same event may appear as both an AE and SAE. However, what is presented are distinct events. An event may be categorized as serious in one participant and as non-serious in another, or a participant may have experienced both a serious and non-serious event. Analysis performed on safety set.

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

### Dictionary used

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

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

### Reporting groups

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | 1.2 mg/m <sup>2</sup> /cycle (Run-in) |
|-----------------------|---------------------------------------|

Reporting group description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.6 mg/m<sup>2</sup> on Day1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After complete response (CR)/complete remission with incomplete hematologic recovery (CRi) was achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Days 1, 8 and 15). The cycle length was 21-28 days. The maximum treatment duration was approximately 4 years.

|                       |   |
|-----------------------|---|
| Reporting group title | 1.8 mg/m <sup>2</sup> /cycle (Randomized) |
|-----------------------|---|

Reporting group description:

Subjects received a starting dose of inotuzumab ozogamicin 1.8 mg/m<sup>2</sup>/cycle (0.8 mg/m<sup>2</sup> on Day 1, 0.5 mg/m<sup>2</sup> on Day 8 and 15) intravenously. After CR/CRi is achieved, the dose was reduced to 1.5 mg/m<sup>2</sup>/cycle (0.5 mg/m<sup>2</sup> on Day 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 4 years.

|                       |  |
|-----------------------|--|
| Reporting group title | 1.2 mg/m <sup>2</sup> /cycle (Run-in + Randomized) |
|-----------------------|--|

Reporting group description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.8 mg/m<sup>2</sup> on Day 1, 0.5 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 1.5 mg/m<sup>2</sup>/cycle (0.5 mg/m<sup>2</sup> on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 4 years.

|                       |   |
|-----------------------|---|
| Reporting group title | 1.2 mg/m <sup>2</sup> /cycle (Randomized) |
|-----------------------|---|

Reporting group description:

Subjects received a starting dose of inotuzumab ozogamicin 1.2 mg/m<sup>2</sup>/cycle administrated in 3 divided doses (0.6 mg/m<sup>2</sup> on Day 1, 0.3 mg/m<sup>2</sup> on Days 8 and 15) intravenously. After CR/CRi was achieved, the dose was reduced to 0.9 mg/m<sup>2</sup>/cycle (0.3 mg/m<sup>2</sup> on Days 1, 8 and 15) for 2-3 cycles. The cycle length was 21-28 days. The maximum treatment duration was approximately 4 years.

| Serious adverse events  | 1.2 mg/m <sup>2</sup> /cycle (Run-in) | 1.8 mg/m <sup>2</sup> /cycle (Randomized) | 1.2 mg/m <sup>2</sup> /cycle (Run-in + Randomized) |
|---|---------------------------------------|---|--|
| Total subjects affected by serious adverse events                   |                                       |   |  |
| subjects affected / exposed   | 15 / 22 (68.18%)                      | 21 / 38 (55.26%)                          | 43 / 64 (67.19%)                                   |
| number of deaths (all causes)                                       | 16                                    | 26  | 40   |
| number of deaths resulting from adverse events                      | 7                                     | 10  | 19   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                       |   |  |
| Neoplasm recurrence   |                                       |   |  |



|  |                 |                |                |
|--|-----------------|----------------|----------------|
| subjects affected / exposed                          | 0 / 22 (0.00%)  | 1 / 38 (2.63%) | 0 / 64 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 1          | 0 / 0          |
| Neoplasm progression                                 |                 |                |                |
| subjects affected / exposed                          | 0 / 22 (0.00%)  | 2 / 38 (5.26%) | 0 / 64 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 3          | 0 / 0          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 2          | 0 / 0          |
| Myelodysplastic syndrome                             |                 |                |                |
| subjects affected / exposed                          | 1 / 22 (4.55%)  | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all      | 1 / 1           | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions |                 |                |                |
| Disease progression                                  |                 |                |                |
| subjects affected / exposed                          | 3 / 22 (13.64%) | 2 / 38 (5.26%) | 4 / 64 (6.25%) |
| occurrences causally related to treatment / all      | 0 / 3           | 2 / 4          | 0 / 4          |
| deaths causally related to treatment / all           | 0 / 2           | 1 / 2          | 0 / 3          |
| Pyrexia  |                 |                |                |
| subjects affected / exposed                          | 1 / 22 (4.55%)  | 3 / 38 (7.89%) | 3 / 64 (4.69%) |
| occurrences causally related to treatment / all      | 0 / 1           | 2 / 3          | 2 / 3          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Death  |                 |                |                |
| subjects affected / exposed                          | 0 / 22 (0.00%)  | 1 / 38 (2.63%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all      | 0 / 0           | 1 / 1          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0           | 1 / 1          | 0 / 1          |
| Immune system disorders                              |                 |                |                |
| Graft versus host disease in liver                   |                 |                |                |
| subjects affected / exposed                          | 0 / 22 (0.00%)  | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders      |                 |                |                |
| Sinus polyp  |                 |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Investigations                                  |                |                |                |
| SARS-CoV-2 test positive                        |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Klebsiella test positive                        |                |                |                |
| subjects affected / exposed                     | 1 / 22 (4.55%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Injury, poisoning and procedural complications  |                |                |                |
| Subdural haematoma                              |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Post procedural inflammation                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fall  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |                |                |                |
| Coronary artery thrombosis                      |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (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          |
| Nervous system disorders                        |                |                |                |
| Central nervous system lesion                   |                |                |                |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 0 / 38 (0.00%)  | 1 / 64 (1.56%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Focal dyscognitive seizures                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 22 (4.55%)  | 0 / 38 (0.00%)  | 1 / 64 (1.56%)  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Loss of consciousness                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 1 / 38 (2.63%)  | 0 / 64 (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           |
| Haemorrhage intracranial                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 2 / 38 (5.26%)  | 1 / 64 (1.56%)  |
| occurrences causally related to treatment / all | 0 / 0           | 3 / 4           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 1 / 1           | 0 / 0           |
| Blood and lymphatic system disorders            |                 |                 |                 |
| Anaemia megaloblastic                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 22 (4.55%)  | 0 / 38 (0.00%)  | 1 / 64 (1.56%)  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Febrile neutropenia                             |                 |                 |                 |
| subjects affected / exposed                     | 3 / 22 (13.64%) | 4 / 38 (10.53%) | 7 / 64 (10.94%) |
| occurrences causally related to treatment / all | 4 / 4           | 4 / 6           | 7 / 8           |
| deaths causally related to treatment / all      | 0 / 0           | 1 / 2           | 0 / 0           |
| Thrombocytopenia                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 22 (4.55%)  | 0 / 38 (0.00%)  | 2 / 64 (3.13%)  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Pancreatitis acute                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%)  | 0 / 38 (0.00%)  | 1 / 64 (1.56%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal haemorrhage                    |                 |                 |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Enterocolitis                                   |                |                |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (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                                   |                |                |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (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           |
| Drug-induced liver injury                       |                |                |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (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           |
| Venoocclusive liver disease                     |                |                |                 |
| subjects affected / exposed                     | 2 / 22 (9.09%) | 2 / 38 (5.26%) | 8 / 64 (12.50%) |
| occurrences causally related to treatment / all | 5 / 5          | 1 / 2          | 6 / 12          |
| deaths causally related to treatment / all      | 1 / 1          | 0 / 0          | 1 / 2           |
| Skin and subcutaneous tissue disorders          |                |                |                 |
| Dermatitis contact                              |                |                |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 38 (0.00%) | 1 / 64 (1.56%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Infections and infestations                     |                |                |                 |
| Bacteraemia                                     |                |                |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 38 (0.00%) | 1 / 64 (1.56%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1           |
| COVID-19  |                |                |                 |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 2 / 64 (3.13%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0           |

|   |                |                |                |
|---|----------------|----------------|----------------|
| COVID-19 pneumonia                              |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 38 (0.00%) | 3 / 64 (4.69%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 5          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 2          |
| Hepatosplenic candidiasis                       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Device related infection                        |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| 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 infection                           |                |                |                |
| subjects affected / exposed                     | 1 / 22 (4.55%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fungal infection                                |                |                |                |
| subjects affected / exposed                     | 2 / 22 (9.09%) | 0 / 38 (0.00%) | 2 / 64 (3.13%) |
| occurrences causally related to treatment / all | 1 / 2          | 0 / 0          | 1 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fungal sepsis                                   |                |                |                |
| subjects affected / exposed                     | 1 / 22 (4.55%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 1          |
| Cellulitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Neutropenic sepsis                              |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Klebsiella sepsis                               |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| Infection                                       |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (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          |
| Pneumocystis jirovecii pneumonia                |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 2 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 1 / 1          |
| Septic shock                                    |                |                |                |
| subjects affected / exposed                     | 1 / 22 (4.55%) | 0 / 38 (0.00%) | 4 / 64 (6.25%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 0 / 6          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 0 / 3          |
| Sepsis  |                |                |                |
| subjects affected / exposed                     | 2 / 22 (9.09%) | 1 / 38 (2.63%) | 6 / 64 (9.38%) |
| occurrences causally related to treatment / all | 0 / 3          | 2 / 2          | 0 / 8          |
| deaths causally related to treatment / all      | 0 / 1          | 1 / 1          | 0 / 4          |
| Pneumonia klebsiella                            |                |                |                |
| subjects affected / exposed                     | 1 / 22 (4.55%) | 0 / 38 (0.00%) | 2 / 64 (3.13%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 2 / 4          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0          | 1 / 2          |
| Pneumonia fungal                                |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 1 / 1          | 0 / 0          |
| Pneumonia bacterial                             |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 1 / 1          | 0 / 0          |
| Pneumonia                                       |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 22 (4.55%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tooth abscess                                   |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Tuberculosis                                    |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (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          |
| Urinary tract infection                         |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (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          |
| Upper respiratory tract infection               |                |                |                |
| subjects affected / exposed                     | 1 / 22 (4.55%) | 0 / 38 (0.00%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Hypercalcaemia                                  |                |                |                |
| subjects affected / exposed                     | 0 / 22 (0.00%) | 1 / 38 (2.63%) | 0 / 64 (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          |
| Tumour lysis syndrome                           |                |                |                |
| subjects affected / exposed                     | 1 / 22 (4.55%) | 3 / 38 (7.89%) | 1 / 64 (1.56%) |
| occurrences causally related to treatment / all | 0 / 1          | 2 / 3          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                                 |  |  |
|---|---------------------------------|--|--|
| <b>Serious adverse events</b>                     | 1.2 mg/m2/cycle<br>(Randomized) |  |  |
| Total subjects affected by serious adverse events |                                 |  |  |
| subjects affected / exposed                       | 28 / 42 (66.67%)                |  |  |
| number of deaths (all causes)                     | 24                              |  |  |
| number of deaths resulting from adverse events    | 12                              |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |  |  |
| Neoplasm recurrence   |                |  |  |
| subjects affected / exposed   | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 0          |  |  |
| deaths causally related to treatment / all                          | 0 / 0          |  |  |
| Neoplasm progression  |                |  |  |
| subjects affected / exposed   | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 0          |  |  |
| deaths causally related to treatment / all                          | 0 / 0          |  |  |
| Myelodysplastic syndrome  |                |  |  |
| subjects affected / exposed   | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 0          |  |  |
| deaths causally related to treatment / all                          | 0 / 0          |  |  |
| General disorders and administration site conditions                |                |  |  |
| Disease progression   |                |  |  |
| subjects affected / exposed   | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 1          |  |  |
| deaths causally related to treatment / all                          | 0 / 1          |  |  |
| Pyrexia   |                |  |  |
| subjects affected / exposed   | 2 / 42 (4.76%) |  |  |
| occurrences causally related to treatment / all                     | 2 / 2          |  |  |
| deaths causally related to treatment / all                          | 0 / 0          |  |  |
| Death   |                |  |  |
| subjects affected / exposed   | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 1          |  |  |
| deaths causally related to treatment / all                          | 0 / 1          |  |  |
| Immune system disorders   |                |  |  |
| Graft versus host disease in liver                                  |                |  |  |
| subjects affected / exposed   | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all                     | 0 / 1          |  |  |
| deaths causally related to treatment / all                          | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders                     |                |  |  |
| Sinus polyp   |                |  |  |



|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Investigations                                  |                |  |  |
| SARS-CoV-2 test positive                        |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Klebsiella test positive                        |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Injury, poisoning and procedural complications  |                |  |  |
| Subdural haematoma                              |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Post procedural inflammation                    |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Fall  |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac disorders                               |                |  |  |
| Coronary artery thrombosis                      |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nervous system disorders                        |                |  |  |
| Central nervous system lesion                   |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Focal dyscognitive seizures                     |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Loss of consciousness                           |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Haemorrhage intracranial                        |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Blood and lymphatic system disorders            |                |  |  |
| Anaemia megaloblastic                           |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Febrile neutropenia                             |                |  |  |
| subjects affected / exposed                     | 4 / 42 (9.52%) |  |  |
| occurrences causally related to treatment / all | 3 / 4          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Thrombocytopenia                                |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal disorders                      |                |  |  |
| Pancreatitis acute                              |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal haemorrhage                    |                |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 42 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Enterocolitis                                   |                 |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hepatobiliary disorders                         |                 |  |  |
| Cholecystitis                                   |                 |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Drug-induced liver injury                       |                 |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%)  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Venoocclusive liver disease                     |                 |  |  |
| subjects affected / exposed                     | 6 / 42 (14.29%) |  |  |
| occurrences causally related to treatment / all | 1 / 7           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Skin and subcutaneous tissue disorders          |                 |  |  |
| Dermatitis contact                              |                 |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infections and infestations                     |                 |  |  |
| Bacteraemia                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%)  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| COVID-19  |                 |  |  |
| subjects affected / exposed                     | 2 / 42 (4.76%)  |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| COVID-19 pneumonia                              |                |  |  |  |
| subjects affected / exposed                     | 3 / 42 (7.14%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 5          |  |  |  |
| deaths causally related to treatment / all      | 0 / 2          |  |  |  |
| Hepatosplenic candidiasis                       |                |  |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Device related infection                        |                |  |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Escherichia infection                           |                |  |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Fungal infection                                |                |  |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Fungal sepsis                                   |                |  |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Cellulitis                                      |                |  |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Neutropenic sepsis                              |                |  |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Klebsiella sepsis                               |                |  |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |  |
| Infection                                       |                |  |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumocystis jirovecii pneumonia                |                |  |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |  |
| occurrences causally related to treatment / all | 2 / 2          |  |  |  |
| deaths causally related to treatment / all      | 1 / 1          |  |  |  |
| Septic shock                                    |                |  |  |  |
| subjects affected / exposed                     | 3 / 42 (7.14%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 4          |  |  |  |
| deaths causally related to treatment / all      | 0 / 2          |  |  |  |
| Sepsis  |                |  |  |  |
| subjects affected / exposed                     | 4 / 42 (9.52%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 5          |  |  |  |
| deaths causally related to treatment / all      | 0 / 3          |  |  |  |
| Pneumonia klebsiella                            |                |  |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |  |
| occurrences causally related to treatment / all | 2 / 2          |  |  |  |
| deaths causally related to treatment / all      | 1 / 1          |  |  |  |
| Pneumonia fungal                                |                |  |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumonia bacterial                             |                |  |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumonia                                       |                |  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Tooth abscess                                   |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Tuberculosis                                    |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Urinary tract infection                         |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Upper respiratory tract infection               |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |
| Hypercalcaemia                                  |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Tumour lysis syndrome                           |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                     | 1.2 mg/m2/cycle<br>(Run-in) | 1.8 mg/m2/cycle<br>(Randomized) | 1.2 mg/m2/cycle<br>(Run-in +<br>Randomized) |
|---|-----------------------------|---------------------------------|---|
| Total subjects affected by non-serious adverse events |                             |                                 |   |
| subjects affected / exposed                           | 18 / 22 (81.82%)            | 29 / 38 (76.32%)                | 50 / 64 (78.13%)                            |
| Investigations  |                             |                                 |   |
| Platelet count decreased                              |                             |                                 |   |
| subjects affected / exposed                           | 3 / 22 (13.64%)             | 3 / 38 (7.89%)                  | 3 / 64 (4.69%)                              |
| occurrences (all)                                     | 3                           | 12                              | 3   |
| Neutrophil count decreased                            |                             |                                 |   |
| subjects affected / exposed                           | 4 / 22 (18.18%)             | 4 / 38 (10.53%)                 | 5 / 64 (7.81%)                              |
| occurrences (all)                                     | 9                           | 17                              | 15  |
| Gamma-glutamyltransferase increased                   |                             |                                 |   |
| subjects affected / exposed                           | 1 / 22 (4.55%)              | 6 / 38 (15.79%)                 | 5 / 64 (7.81%)                              |
| occurrences (all)                                     | 1                           | 6                               | 6   |
| Blood lactate dehydrogenase increased                 |                             |                                 |   |
| subjects affected / exposed                           | 2 / 22 (9.09%)              | 4 / 38 (10.53%)                 | 5 / 64 (7.81%)                              |
| occurrences (all)                                     | 2                           | 4                               | 5   |
| Blood alkaline phosphatase increased                  |                             |                                 |   |
| subjects affected / exposed                           | 1 / 22 (4.55%)              | 3 / 38 (7.89%)                  | 3 / 64 (4.69%)                              |
| occurrences (all)                                     | 2                           | 3                               | 5   |
| Aspartate aminotransferase increased                  |                             |                                 |   |
| subjects affected / exposed                           | 4 / 22 (18.18%)             | 8 / 38 (21.05%)                 | 7 / 64 (10.94%)                             |
| occurrences (all)                                     | 7                           | 10                              | 11  |
| Alanine aminotransferase increased                    |                             |                                 |   |
| subjects affected / exposed                           | 5 / 22 (22.73%)             | 3 / 38 (7.89%)                  | 10 / 64 (15.63%)                            |
| occurrences (all)                                     | 8                           | 6                               | 14  |
| SARS-CoV-2 test positive                              |                             |                                 |   |
| subjects affected / exposed                           | 0 / 22 (0.00%)              | 2 / 38 (5.26%)                  | 2 / 64 (3.13%)                              |
| occurrences (all)                                     | 0                           | 2                               | 2   |
| Vascular disorders                                    |                             |                                 |   |
| Hypertension  |                             |                                 |   |
| subjects affected / exposed                           | 2 / 22 (9.09%)              | 0 / 38 (0.00%)                  | 2 / 64 (3.13%)                              |
| occurrences (all)                                     | 2                           | 0                               | 2   |
| Nervous system disorders                              |                             |                                 |   |

|  |                       |                        |                        |
|--|-----------------------|------------------------|------------------------|
| Headache<br>subjects affected / exposed<br>occurrences (all)             | 0 / 22 (0.00%)<br>0   | 4 / 38 (10.53%)<br>4   | 4 / 64 (6.25%)<br>4    |
| Blood and lymphatic system disorders                                     |                       |                        |                        |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)     | 5 / 22 (22.73%)<br>10 | 13 / 38 (34.21%)<br>29 | 19 / 64 (29.69%)<br>40 |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)           | 2 / 22 (9.09%)<br>3   | 6 / 38 (15.79%)<br>10  | 8 / 64 (12.50%)<br>9   |
| Febrile neutropenia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 22 (4.55%)<br>1   | 4 / 38 (10.53%)<br>5   | 3 / 64 (4.69%)<br>4    |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)              | 2 / 22 (9.09%)<br>6   | 6 / 38 (15.79%)<br>9   | 11 / 64 (17.19%)<br>23 |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)          | 4 / 22 (18.18%)<br>6  | 10 / 38 (26.32%)<br>26 | 20 / 64 (31.25%)<br>43 |
| General disorders and administration<br>site conditions                  |                       |                        |                        |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)              | 5 / 22 (22.73%)<br>13 | 1 / 38 (2.63%)<br>1    | 10 / 64 (15.63%)<br>22 |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)              | 2 / 22 (9.09%)<br>2   | 1 / 38 (2.63%)<br>1    | 4 / 64 (6.25%)<br>4    |
| Asthenia<br>subjects affected / exposed<br>occurrences (all)             | 0 / 22 (0.00%)<br>0   | 2 / 38 (5.26%)<br>3    | 1 / 64 (1.56%)<br>1    |
| Gastrointestinal disorders   |                       |                        |                        |
| Constipation<br>subjects affected / exposed<br>occurrences (all)         | 1 / 22 (4.55%)<br>2   | 4 / 38 (10.53%)<br>4   | 3 / 64 (4.69%)<br>4    |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all) | 0 / 22 (0.00%)<br>0   | 3 / 38 (7.89%)<br>3    | 1 / 64 (1.56%)<br>1    |



|   |  |  |  |
|---|--|--|--|
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)  | 2 / 22 (9.09%)<br>3                            | 1 / 38 (2.63%)<br>1                            | 7 / 64 (10.94%)<br>8                           |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)   | 0 / 22 (0.00%)<br>0                            | 1 / 38 (2.63%)<br>1                            | 3 / 64 (4.69%)<br>4                            |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)  | 1 / 22 (4.55%)<br>2                            | 3 / 38 (7.89%)<br>5                            | 6 / 64 (9.38%)<br>9                            |
| Stomatitis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 22 (4.55%)<br>1                            | 2 / 38 (5.26%)<br>4                            | 2 / 64 (3.13%)<br>2                            |
| Nausea<br>subjects affected / exposed<br>occurrences (all)  | 0 / 22 (0.00%)<br>0                            | 3 / 38 (7.89%)<br>4                            | 5 / 64 (7.81%)<br>5                            |
| Respiratory, thoracic and mediastinal disorders<br>Epistaxis<br>subjects affected / exposed<br>occurrences (all)  | 3 / 22 (13.64%)<br>4                           | 4 / 38 (10.53%)<br>4                           | 5 / 64 (7.81%)<br>7                            |
| Skin and subcutaneous tissue disorders<br>Rash papular<br>subjects affected / exposed<br>occurrences (all)<br><br>Pruritus<br>subjects affected / exposed<br>occurrences (all)                | 1 / 22 (4.55%)<br>1<br><br>0 / 22 (0.00%)<br>0 | 2 / 38 (5.26%)<br>2<br><br>0 / 38 (0.00%)<br>0 | 1 / 64 (1.56%)<br>1<br><br>3 / 64 (4.69%)<br>3 |
| Musculoskeletal and connective tissue disorders<br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all)<br><br>Bone pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 22 (0.00%)<br>0<br><br>0 / 22 (0.00%)<br>0 | 2 / 38 (5.26%)<br>2<br><br>3 / 38 (7.89%)<br>4 | 1 / 64 (1.56%)<br>1<br><br>1 / 64 (1.56%)<br>1 |
| Infections and infestations<br>Pneumonia  |  |  |  |

|  |                      |                     |                     |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 3 / 22 (13.64%)<br>3 | 0 / 38 (0.00%)<br>0 | 4 / 64 (6.25%)<br>4 |
| Influenza<br>subjects affected / exposed<br>occurrences (all)  | 2 / 22 (9.09%)<br>2  | 0 / 38 (0.00%)<br>0 | 2 / 64 (3.13%)<br>2 |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 22 (0.00%)<br>0  | 2 / 38 (5.26%)<br>2 | 2 / 64 (3.13%)<br>2 |
| Metabolism and nutrition disorders<br>Hypokalaemia<br>subjects affected / exposed<br>occurrences (all) | 2 / 22 (9.09%)<br>2  | 1 / 38 (2.63%)<br>1 | 4 / 64 (6.25%)<br>6 |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)                                    | 1 / 22 (4.55%)<br>1  | 1 / 38 (2.63%)<br>1 | 4 / 64 (6.25%)<br>5 |

|  |                                 |  |  |
|--|---------------------------------|--|--|
| <b>Non-serious adverse events</b>  | 1.2 mg/m2/cycle<br>(Randomized) |  |  |
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed        | 32 / 42 (76.19%)                |  |  |
| Investigations<br>Platelet count decreased<br>subjects affected / exposed<br>occurrences (all) | 0 / 42 (0.00%)<br>0             |  |  |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 42 (2.38%)<br>6             |  |  |
| Gamma-glutamyltransferase<br>increased<br>subjects affected / exposed<br>occurrences (all)     | 4 / 42 (9.52%)<br>5             |  |  |
| Blood lactate dehydrogenase<br>increased<br>subjects affected / exposed<br>occurrences (all)   | 3 / 42 (7.14%)<br>3             |  |  |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)       | 2 / 42 (4.76%)<br>3             |  |  |
| Aspartate aminotransferase   |                                 |  |  |

|  |                        |  |  |
|--|------------------------|--|--|
| increased<br>subjects affected / exposed<br>occurrences (all)  | 3 / 42 (7.14%)<br>4    |  |  |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                       | 5 / 42 (11.90%)<br>6   |  |  |
| SARS-CoV-2 test positive<br>subjects affected / exposed<br>occurrences (all)                                 | 2 / 42 (4.76%)<br>2    |  |  |
| Vascular disorders<br>Hypertension<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 42 (0.00%)<br>0    |  |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                     | 4 / 42 (9.52%)<br>4    |  |  |
| Blood and lymphatic system disorders<br>Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all) | 14 / 42 (33.33%)<br>30 |  |  |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)   | 6 / 42 (14.29%)<br>6   |  |  |
| Febrile neutropenia<br>subjects affected / exposed<br>occurrences (all)                                      | 2 / 42 (4.76%)<br>3    |  |  |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)  | 9 / 42 (21.43%)<br>17  |  |  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)  | 16 / 42 (38.10%)<br>37 |  |  |
| General disorders and administration<br>site conditions<br>Pyrexia   |                        |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 5 / 42 (11.90%) |  |  |
| occurrences (all)                               | 9               |  |  |
| Fatigue   |                 |  |  |
| subjects affected / exposed                     | 2 / 42 (4.76%)  |  |  |
| occurrences (all)                               | 2               |  |  |
| Asthenia  |                 |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%)  |  |  |
| occurrences (all)                               | 1               |  |  |
| Gastrointestinal disorders                      |                 |  |  |
| Constipation                                    |                 |  |  |
| subjects affected / exposed                     | 2 / 42 (4.76%)  |  |  |
| occurrences (all)                               | 2               |  |  |
| Abdominal pain upper                            |                 |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%)  |  |  |
| occurrences (all)                               | 1               |  |  |
| Abdominal pain                                  |                 |  |  |
| subjects affected / exposed                     | 5 / 42 (11.90%) |  |  |
| occurrences (all)                               | 5               |  |  |
| Diarrhoea                                       |                 |  |  |
| subjects affected / exposed                     | 3 / 42 (7.14%)  |  |  |
| occurrences (all)                               | 4               |  |  |
| Vomiting  |                 |  |  |
| subjects affected / exposed                     | 5 / 42 (11.90%) |  |  |
| occurrences (all)                               | 7               |  |  |
| Stomatitis                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%)  |  |  |
| occurrences (all)                               | 1               |  |  |
| Nausea  |                 |  |  |
| subjects affected / exposed                     | 5 / 42 (11.90%) |  |  |
| occurrences (all)                               | 5               |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Epistaxis                                       |                 |  |  |
| subjects affected / exposed                     | 2 / 42 (4.76%)  |  |  |
| occurrences (all)                               | 3               |  |  |
| Skin and subcutaneous tissue disorders          |                 |  |  |

|  |   |  |  |
|--|---|--|--|
| Rash papular<br>subjects affected / exposed<br>occurrences (all)<br><br>Pruritus<br>subjects affected / exposed<br>occurrences (all)   | 0 / 42 (0.00%)<br>0<br><br>3 / 42 (7.14%)<br>3                            |  |  |
| Musculoskeletal and connective tissue disorders<br>Pain in extremity<br>subjects affected / exposed<br>occurrences (all)<br><br>Bone pain<br>subjects affected / exposed<br>occurrences (all)  | 1 / 42 (2.38%)<br>1<br><br>1 / 42 (2.38%)<br>1                            |  |  |
| Infections and infestations<br>Pneumonia<br>subjects affected / exposed<br>occurrences (all)<br><br>Influenza<br>subjects affected / exposed<br>occurrences (all)<br><br>Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 42 (2.38%)<br>1<br><br>0 / 42 (0.00%)<br>0<br><br>2 / 42 (4.76%)<br>2 |  |  |
| Metabolism and nutrition disorders<br>Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)<br><br>Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)  | 2 / 42 (4.76%)<br>4<br><br>3 / 42 (7.14%)<br>4                            |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported