# Clinical trial results:
# An Open-label, Multicenter, Exploratory Phase II Study to Evaluate the Efficacy, Safety, and Tolerability of the BiTE® Antibody Blinatumomab in Adult Patients With Relapsed/Refractory B-Precursor Acute Lymphoblastic Leukemia (ALL)

## Summary

| | |
|---|---|
| EudraCT number | 2009-015989-62 |
| Trial protocol | DE |
| Global end of trial date | 14 October 2016 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 19 October 2017 |
| First version publication date | 19 October 2017 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | 0103206 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01209286 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Amgen Inc. |
| Sponsor organisation address | One Amgen Center Drive, Thousand Oaks, CA, United States, 01320 |
| Public contact | IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com |
| Scientific contact | IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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 | 14 October 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 14 October 2016 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to determine whether the bispecific T-cell engager blinatumomab is effective, safe and tolerable in the treatment of patients with relapsed/refractory B-precursor ALL.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) and country-specific national and local laws and regulations.
The study protocol including amendments, informed consent form (ICF), and any accompanying material provided to the subject was reviewed and approved by the Independent Ethics Committee (IEC). A copy of the written approval of the protocol and the ICF were collected by Amgen before recruitment of any study subjects and shipment of Amgen investigational product commenced. Amgen notified the IEC of any deviations from the protocol or of any serious adverse events that occurred.
The investigator or his/her designee informed the subject of all aspects pertaining to the subject's participation in the study. Subject informed consent was obtained in writing before enrollment into the study according to all applicable regulatory requirements. The written ICF was dated and signed by both the investigator (or designee) and the subject before any study-related procedure was initiated.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 12 October 2010 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 5 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Germany: 36 |
| Worldwide total number of subjects | 36 |
| EEA total number of subjects | 36 |

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 | 0 |

| | |
|---|---|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 31 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

This study was open to adult patients with relapsed / refractory B-precursor acute lymphoblastic leukemia (ALL). This study was conducted at 9 centers in Germany.

### Pre-assignment

Screening details:

This study consisted of a core study of up to 33 weeks, efficacy follow-up until 24 months after treatment start and survival follow-up until 5 years after treatment start.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Blinatumomab 15 µg |

Arm description:

Participants received blinatumomab 15 µg/m²/day as a continuous intravenous infusion at a constant flow rate over 4 weeks followed by a 2-week treatment-free interval for up to 5 consecutive cycles.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Blinatumomab |
| Investigational medicinal product code | AMG 103 |
| Other name | MT103, BLINCYTO™ |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Continuous intravenous infusion over four weeks per treatment cycle

| | |
|---|---|
| **Arm title** | Blinatumomab 5/15 µg |

Arm description:

Participants received blinatumomab by continuous intravenous infusion over 4 weeks followed by a treatment-free interval of 2 weeks for up to 5 consecutive cycles. The initial dose was 5 µg/m²/day for the first seven days of treatment, followed by 15 µg/m²/day starting from Week 2 of treatment.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Blinatumomab |
| Investigational medicinal product code | AMG 103 |
| Other name | MT103, BLINCYTO™ |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Continuous intravenous infusion over four weeks per treatment cycle

| | |
|---|---|
| **Arm title** | Blinatumomab 5/15/30 µg |

Arm description:

Participants received blinatumomab by continuous intravenous infusion over 4 weeks followed by a treatment-free interval of 2 weeks for up to 5 consecutive cycles. The initial dose was 5 µg/m²/day for the first seven days of treatment, a dose of 15 µg/m²/day in the subsequent 7 days, followed by 30 µg/m²/day starting from Week 3 of treatment.

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

| | |
|---|---|
| Investigational medicinal product name | Blinatumomab |
| Investigational medicinal product code | AMG 103 |
| Other name | MT103, BLINCYTO™ |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Continuous intravenous infusion over four weeks per treatment cycle

| **Number of subjects in period 1** | Blinatumomab 15 µg | Blinatumomab 5/15 µg | Blinatumomab 5/15/30 µg |
|---|---|---|---|
| Started | 7 | 23 | 6 |
| Completed | 2 | 13 | 3 |
| Not completed | 5 | 10 | 3 |
| Physician decision | - | 2 | - |
| Adverse event, non-fatal | 4 | 3 | 1 |
| Other | - | 1 | - |
| Hematological Relapse After Remission | - | 1 | 1 |
| Remission Not Achieved in 2 Cycles | 1 | 3 | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Blinatumomab 15 µg |
| Reporting group description: | |
| Participants received blinatumomab 15 µg/m²/day as a continuous intravenous infusion at a constant flow rate over 4 weeks followed by a 2-week treatment-free interval for up to 5 consecutive cycles. | |
| Reporting group title | Blinatumomab 5/15 µg |
| Reporting group description: | |
| Participants received blinatumomab by continuous intravenous infusion over 4 weeks followed by a treatment-free interval of 2 weeks for up to 5 consecutive cycles. The initial dose was 5 µg/m²/day for the first seven days of treatment, followed by 15 µg/m²/day starting from Week 2 of treatment. | |
| Reporting group title | Blinatumomab 5/15/30 µg |
| Reporting group description: | |
| Participants received blinatumomab by continuous intravenous infusion over 4 weeks followed by a treatment-free interval of 2 weeks for up to 5 consecutive cycles. The initial dose was 5 µg/m²/day for the first seven days of treatment, a dose of 15 µg/m²/day in the subsequent 7 days, followed by 30 µg/m²/day starting from Week 3 of treatment. | |

| Reporting group values | Blinatumomab 15 µg | Blinatumomab 5/15 µg | Blinatumomab 5/15/30 µg |
|---|---|---|---|
| Number of subjects | 7 | 23 | 6 |
| Age Categorical<br>Units: Subjects | | | |
| <=60 years | 5 | 20 | 4 |
| > 60 years | 2 | 3 | 2 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 44.0 | 38.1 | 42.5 |
| standard deviation | ± 21.5 | ± 16.7 | ± 23.2 |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 3 | 9 | 2 |
| Male | 4 | 14 | 4 |
| Race<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 1 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 0 |
| White | 7 | 22 | 6 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Number of Prior Relapses<br>Units: Subjects | | | |
| No relapes | 0 | 2 | 1 |
| 1 relapse | 5 | 15 | 3 |
| 2 relapses | 2 | 6 | 1 |
| 3 relapses | 0 | 0 | 1 |
| Relapsed / refractory Status | | | |

| | | | |
|---|---|---|---|
| Units: Subjects | | | |
| Primary Refractory | 0 | 2 | 1 |
| Relapsed | 7 | 21 | 5 |
| Prior Allogeneic Hematopoietic Stem cell Transplantation (HSCT)<br>Units: Subjects | | | |
| Yes, Sibling | 1 | 1 | 1 |
| Yes, Unrelated | 2 | 9 | 1 |
| Yes, Haploidentical (mother/father) | 0 | 0 | 0 |
| No prior allogeneic HSCT | 4 | 13 | 4 |

| **Reporting group values** | Total | | |
|---|---|---|---|
| Number of subjects | 36 | | |
| Age Categorical<br>Units: Subjects | | | |
| <=60 years | 29 | | |
| > 60 years | 7 | | |
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -<br>- | | |
| Gender Categorical<br>Units: Subjects | | | |
| Female | 14 | | |
| Male | 22 | | |
| Race<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | | |
| Asian | 1 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 0 | | |
| White | 35 | | |
| More than one race | 0 | | |
| Unknown or Not Reported | 0 | | |
| Number of Prior Relapses<br>Units: Subjects | | | |
| No relapes | 3 | | |
| 1 relapse | 23 | | |
| 2 relapses | 9 | | |
| 3 relapses | 1 | | |
| Relapsed / refractory Status<br>Units: Subjects | | | |
| Primary Refractory | 3 | | |
| Relapsed | 33 | | |
| Prior Allogeneic Hematopoietic Stem cell Transplantation (HSCT)<br>Units: Subjects | | | |
| Yes, Sibling | 3 | | |
| Yes, Unrelated | 12 | | |
| Yes, Haploidentical (mother/father) | 0 | | |
| No prior allogeneic HSCT | 21 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Blinatumomab 15 µg |
| Reporting group description: | |
| Participants received blinatumomab 15 µg/m²/day as a continuous intravenous infusion at a constant flow rate over 4 weeks followed by a 2-week treatment-free interval for up to 5 consecutive cycles. | |
| Reporting group title | Blinatumomab 5/15 µg |
| Reporting group description: | |
| Participants received blinatumomab by continuous intravenous infusion over 4 weeks followed by a treatment-free interval of 2 weeks for up to 5 consecutive cycles. The initial dose was 5 µg/m²/day for the first seven days of treatment, followed by 15 µg/m²/day starting from Week 2 of treatment. | |
| Reporting group title | Blinatumomab 5/15/30 µg |
| Reporting group description: | |
| Participants received blinatumomab by continuous intravenous infusion over 4 weeks followed by a treatment-free interval of 2 weeks for up to 5 consecutive cycles. The initial dose was 5 µg/m²/day for the first seven days of treatment, a dose of 15 µg/m²/day in the subsequent 7 days, followed by 30 µg/m²/day starting from Week 3 of treatment. | |
| Subject analysis set title | Blinatumomab Overall |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Participants received blinatumomab as a continuous intravenous infusion at a constant flow rate over 4 weeks followed by a 2-week treatment-free interval for up to 5 consecutive cycles. | |
| Subject analysis set title | Blinatumomab 5 µg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Participants receiving blinatumomab 5 µg/m²/day. | |
| Subject analysis set title | Blinatumomab 15 µg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Participants receiving blinatumomab 15 µg/m²/day. | |
| Subject analysis set title | Blinatumomab 30 µg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Participants receiving blinatumomab 30 µg/m²/day. | |

### Primary: Percentage of Participants With a Best Response of Complete Remission or Complete Remission With Only Partial Hematological Recovery Within 2 Cycles of Treatment

| | |
|---|---|
| End point title | Percentage of Participants With a Best Response of Complete Remission or Complete Remission With Only Partial Hematological Recovery Within 2 Cycles of Treatment[1] |

End point description:

At the end of each infusion period, a bone marrow aspiration/biopsy was performed to evaluate the efficacy of blinatumomab. All hematological assessments of bone marrow were reviewed in a central reference laboratory. Hematological remissions were defined by the following criteria:

Complete Response/Remission (CR):
- Less than or equal to 5% blasts in the bone marrow
- No evidence of circulating blasts or extramedullar disease
- Full recovery of peripheral blood counts:
  - Platelets > 100,000/µL
  - Hemoglobin ≥ 11 g/dL
  - Absolute neutrophil count (ANC) > 1,500/µL

Complete Remission with only Partial Hematological Recovery (CRh*):
- Less than or equal to 5% blasts in the bone marrow

- No evidence of circulating blasts or extramedullar disease
- Partial recovery of peripheral blood counts:
  - Platelets > 50,000/µL
  - Hemoglobin ≥ 7 g/dL
  - ANC > 500/µL

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

End point timeframe:

Within the first 2 cycles of treatment, 12 weeks

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: The study efficacy objectives were evaluated using descriptive methods. Confirmatory analyses were not performed.

| **End point values** | Blinatumomab 15 µg | Blinatumomab 5/15 µg | Blinatumomab 5/15/30 µg | Blinatumomab Overall |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 7 | 23 | 6 | 36 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 71.4 (29.0 to 96.3) | 69.6 (47.1 to 86.8) | 66.7 (22.3 to 95.7) | 69.4 (51.9 to 83.7) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With a Best Response of Complete Remission Within 2 Cycles of Treatment

| End point title | Percentage of Participants With a Best Response of Complete Remission Within 2 Cycles of Treatment |
|---|---|

End point description:

At the end of each infusion period, a bone marrow aspiration/biopsy was performed to evaluate the efficacy of blinatumomab. All hematological assessments of bone marrow were reviewed in a central reference laboratory. Complete Response/Remission (CR) was defined by the following criteria:

- Less than or equal to 5% blasts in the bone marrow
- No evidence of circulating blasts or extramedullar disease
- Full recovery of peripheral blood counts:
  - Platelets > 100,000/µL
  - Hemoglobin ≥ 11 g/dL
  - Absolute neutrophil count (ANC) > 1,500/µL

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

End point timeframe:

Within the first 2 cycles of treatment, 12 weeks

| **End point values** | Blinatumomab 15 µg | Blinatumomab 5/15 µg | Blinatumomab 5/15/30 µg | Blinatumomab Overall |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 7 | 23 | 6 | 36 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 14.3 (0.4 to 57.9) | 43.5 (23.2 to 65.5) | 66.7 (22.3 to 95.7) | 41.7 (25.5 to 59.2) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With a Best Response of Complete Remission With Only Partial Hematological Recovery Within 2 Cycles of Treatment

| End point title | Percentage of Participants With a Best Response of Complete Remission With Only Partial Hematological Recovery Within 2 Cycles of Treatment |
|---|---|

End point description:

At the end of each infusion period, a bone marrow aspiration/biopsy was performed to evaluate the efficacy of blinatumomab. All hematological assessments of bone marrow were reviewed in a central reference laboratory. Complete remission with only partial hematological recovery (CRh*) was defined by the following criteria:
- Less than or equal to 5% blasts in the bone marrow
- No evidence of circulating blasts or extramedullar disease
- Partial recovery of peripheral blood counts:
  - Platelets > 50,000/µL
  - Hemoglobin ≥ 7 g/dL
  - ANC > 500/µL.

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

End point timeframe:

Within the first 2 cycles of treatment, 12 weeks

| End point values | Blinatumomab 15 µg | Blinatumomab 5/15 µg | Blinatumomab 5/15/30 µg | Blinatumomab Overall |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 7 | 23 | 6 | 36 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 57.1 (18.4 to 90.1) | 26.1 (10.2 to 48.4) | 0.0 (0.0 to 45.9) | 27.8 (14.2 to 45.2) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With a Best Response of Partial Remission Within 2 Cycles of Treatment

| End point title | Percentage of Participants With a Best Response of Partial Remission Within 2 Cycles of Treatment |
|---|---|

End point description:

At the end of each infusion period, a bone marrow aspiration/biopsy was performed to evaluate the efficacy of blinatumomab. All hematological assessments of bone marrow were reviewed in a central reference laboratory. Partial remission was defined by the following criteria:
- Bone marrow blasts ≤ 25%

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

End point timeframe:

Within the first 2 cycles of treatment, 12 weeks

| End point values | Blinatumomab 15 µg | Blinatumomab 5/15 µg | Blinatumomab 5/15/30 µg | Blinatumomab Overall |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 7 | 23 | 6 | 36 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 0.0 (0.0 to 41.0) | 8.7 (1.1 to 28.0) | 0.0 (0.0 to 45.9) | 5.6 (0.7 to 18.7) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With a Minimal Residual Disease (MRD) Response During the Core Study

| End point title | Percentage of Participants With a Minimal Residual Disease (MRD) Response During the Core Study |
|---|---|

End point description:

A minimal residual disease (MRD) response is defined as MRD < 10^-4 blasts/nucleated cells based on polymerase chain reaction (PCR) evaluation of individual rearrangements of immunoglobulin or T cell receptor genes.

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

End point timeframe:

During the core study treatment period (up to 30 weeks).

| End point values | Blinatumomab 15 µg | Blinatumomab 5/15 µg | Blinatumomab 5/15/30 µg | Blinatumomab Overall |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 7 | 23 | 6 | 36 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 71.4 (29.0 to 96.3) | 73.9 (51.6 to 89.8) | 50.0 (11.8 to 88.2) | 69.4 (51.9 to 83.7) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants Who Received an Allogeneic Hematopoietic Stem Cell Transplant (HSCT) After Treatment With Blinatumomab

| End point title | Percentage of Participants Who Received an Allogeneic Hematopoietic Stem Cell Transplant (HSCT) After Treatment |
|---|---|

| | With Blinatumomab |
|---|---|

End point description:

The percentage of participants who underwent immediate allogeneic HSCT (defined as those in remission who undergo HSCT without receiving any other treatments) after having discontinued or completed the core study.

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

End point timeframe:

Up to the data cut-off date of 15 October 2012; maximum follow up time was 459 days

| **End point values** | Blinatumomab 15 µg | Blinatumomab 5/15 µg | Blinatumomab 5/15/30 µg | Blinatumomab Overall |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 7 | 23 | 6 | 36 |
| Units: percentage of participants | | | | |
| number (not applicable) | 42.9 | 60.9 | 16.7 | 50.0 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Hematological Relapse

| End point title | Time to Hematological Relapse |
|---|---|

End point description:

Time to hematological relapse was measured for participants who achieved a CR or CRh* during the core study and was measured from the time the participant first achieved remission until first documented relapse or death due to disease progression. Participants without a documented relapse (hematological or extramedullary) and who did not die were censored at the time of their last bone marrow assessment or their last survival follow-up visit confirming remission. Participants who died without having reported hematological relapse or without showing any clinical sign of disease progression were censored on their day of death.
Hematological Relapse was defined as:
• Proportion of blasts in bone marrow > 5%
• Extramedullary relapse.
Time to hematological relapse was analyzed by Kaplan-Meier methods. "99999" indicates data not estimable due to the low number of events.

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

End point timeframe:

From remission during the core study until the end of follow-up period; median time on study was 404.5 days.

| **End point values** | Blinatumomab 15 µg | Blinatumomab 5/15 µg | Blinatumomab 5/15/30 µg | Blinatumomab Overall |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 5 | 16 | 4 | 25 |
| Units: days | | | | |
| median (confidence interval 95%) | 240.0 (63.0 to 270.0) | 1535.0 (275.0 to 99999) | 373.0 (15.0 to 99999) | 352.0 (240.0 to 99999) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Relapse-free Survival

| End point title | Relapse-free Survival |
|---|---|

End point description:

Relapse-free survival was measured only for participants who achieved a CR or CRh* during the core study and was measured from the time the participant first achieved remission until first documented relapse or death due to any cause. Participants without a documented relapse (hematological or extramedullary) or who did not die were censored at the time of their last bone marrow assessment or their last survival follow-up visit confirming remission. Relapse-free survival was estimated using Kaplan-Meier methods. "99999" indicates data not estimable due to the low number of events.

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

End point timeframe:

From remission during the core study until the end of follow-up period; median time on study was 404.5 days.

| End point values | Blinatumomab 15 µg | Blinatumomab 5/15 µg | Blinatumomab 5/15/30 µg | Blinatumomab Overall |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 5 | 16 | 4 | 25 |
| Units: days | | | | |
| median (confidence interval 95%) | 137.0 (63.0 to 270.0) | 283.0 (226.0 to 1535.0) | 373.0 (15.0 to 99999) | 268.0 (175.0 to 403.0) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Survival

| End point title | Overall Survival |
|---|---|

End point description:

Overall survival was measured for all subjects from the date of first infusion of blinatumomab until the date of death because of any cause. Subjects who did not die were censored on the last documented visit date. Overall survival was estimated using Kaplan-Meier methods. "99999" indicates data not estimable due to the low number of events.

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

End point timeframe:

From first dose until the end of follow-up period; median time on study was 404.5 days.

| End point values | Blinatumomab 15 µg | Blinatumomab 5/15 µg | Blinatumomab 5/15/30 µg | Blinatumomab Overall |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 7 | 23 | 6 | 36 |
| Units: days | | | | |
| median (confidence interval 95%) | 269.0 (165.0 to 482.0) | 361.0 (258.0 to 973.0) | 584.0 (276.0 to 99999) | 396.0 (262.0 to 667.0) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Treatment-emergent Adverse Events

| End point title | Number of Participants With Treatment-emergent Adverse Events |
|---|---|

End point description:

Adverse events were evaluated for severity according to the grading scale provided in the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), version 3.0 and according to the following:
Grade I (mild); Grade 2 (moderate); Grade 3 (severe - significantly limits the patient's ability to perform routine activities despite symptomatic therapy; Grade 4 (life-threatening); Grade 5 (death).
The investigator used medical judgment to determine if there was a causal relationship (ie, certain, probable, possible, unlikely, not related) between an adverse event and blinatumomab.
A serious adverse event is any untoward medical occurrence or effect, that at any dose: resulted in death, was life-threatening, required or prolonged hospitalization, resulted in persistent or significant disability or incapacity, is a congenital anomaly or birth defect or is a medically important condition.

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

End point timeframe:

From the first infusion to 30 days after the last infusion in the core study or from the first retreatment cycle infusion to 30 days after the last retreatment cycle; Median treatment duration was 44, 56 and 75 days in each cohort respectively.

| End point values | Blinatumomab 15 µg | Blinatumomab 5/15 µg | Blinatumomab 5/15/30 µg | Blinatumomab Overall |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 7 | 23 | 6 | 36 |
| Units: participants | | | | |
| Any adverse event (AE) | 7 | 23 | 6 | 36 |
| Adverse events of at least CTC grade 3 | 7 | 15 | 5 | 27 |
| Treatment-related adverse events | 7 | 23 | 6 | 36 |
| Related adverse events of at least CTC grade 3 | 7 | 12 | 4 | 23 |
| Serious adverse events | 6 | 14 | 5 | 25 |
| Serious adverse events of at least CTC grade 3 | 6 | 12 | 4 | 22 |
| Serious related adverse events | 4 | 10 | 4 | 18 |
| AEs leading to interruption of blinatumomab | 3 | 6 | 3 | 12 |

| | | | | |
|---|---|---|---|---|
| AEs leading to discontinuation of blinatumomab | 4 | 5 | 1 | 10 |
| AEs leading to death | 1 | 4 | 1 | 6 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Steady State Blinatumomab Concentration

| End point title | Steady State Blinatumomab Concentration |
|---|---|

End point description:

The steady state concentration of blinatumomab was summarized as the observed concentrations collected at least 10 hours after the intravenous infusion was started for cycle 1 and cycle 2, respectively. Actual doses administered were used in the analysis.
Concentrations below the limit of detection (3 pg/mL) were set to zero before data analysis and concentrations below the lower limit of quantitation (50 pg/mL) were excluded from analysis.

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

End point timeframe:

Samples were collected at predose and at 48 hours following start of infusion, when dose is escalated and on Days 8, 15, 22, and 29 of the first 2 cycles.

| End point values | Blinatumomab 5 µg | Blinatumomab 15 µg | Blinatumomab 30 µg | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 31 | 34 | 5 | |
| Units: pg/mL | | | | |
| arithmetic mean (standard deviation) | 167 (± 66) | 553 (± 238) | 1180 (± 820) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Clearance of Blinatumomab

| End point title | Clearance of Blinatumomab |
|---|---|

End point description:

Clearance was calculated as R0/Css; where R0 is the infusion rate (µg/m²/hr) and Css is the steady state concentration.

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

End point timeframe:

Samples were collected at predose and at 48 hours following start of infusion, when dose is escalated and on Days 8, 15, 22, and 29 of the first 2 cycles.

| End point values | Blinatumomab Overall | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 36 | | | |
| Units: L/m²/hr | | | | |
| arithmetic mean (standard deviation) | 1.34 (± 0.61) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Serum Cytokine Peak Levels

| End point title | Serum Cytokine Peak Levels |
|---|---|

End point description:

The activation of immune effector cells was monitored by the measurement of peripheral blood cytokine levels including interleukin (IL)-2, IL-6, IL-10, tumor necrosis factor (TNF)-α and interferon gamma (IFN-γ) using multiplex cytometric bead assays. The lower limit of quantification (LLOQ) is 125 pg/mL and the limit of detection (LOD) is 20 pg/mL. "99999" indicates values below detection level of the assay.

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

End point timeframe:

Samples were collected prior to treatment start (baseline), and at 2, 6, 24, and 48 hours after drug infusion start, and at these same time points when dose is escalated in each treatment cycle.

| End point values | Blinatumomab Overall | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 36 | | | |
| Units: pg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| IL-6: Cycle 1 (N=35) | 2563 (± 5231) | | | |
| IL-6: Cycle 2 (N=22) | 212 (± 477) | | | |
| IL-6: Cycle 3 (N=11) | 21 (± 26) | | | |
| IL-10: Cycle 1 (N=35) | 1302 (± 2563) | | | |
| IL-10: Cycle 2 (N=22) | 351 (± 582) | | | |
| IL-10: Cycle 3 (N=11) | 419 (± 730) | | | |
| IFN-: Cycle 1 (N=35) | 467 (± 1824) | | | |
| IFN-: Cycle 2 (N=22) | 25 (± 28) | | | |
| IFN-: Cycle 3 (N=11) | 99999 (± 99999) | | | |
| IL-2: Cycle 1 (N=35) | 36 (± 49) | | | |
| IL-2: Cycle 2 (N=22) | 99999 (± 99999) | | | |
| IL-2: Cycle 3 (N=11) | 99999 (± 99999) | | | |
| TNF-α: Cycle 1 (N=35) | 60 (± 122) | | | |
| TNF-α: Cycle 2 (N=22) | 99999 (± 99999) | | | |
| TNF-α: Cycle 3 (N=11) | 99999 (± 99999) | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the first infusion to 30 days after the last infusion in the core study or from the first retreatment cycle infusion to 30 days after the last retreatment cycle; Median treatment duration was 44, 56 and 75 days in each cohort respectively.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 19.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Blinatumomab 15 µg/m²/day |

Reporting group description:

Participants received blinatumomab 15 µg/m²/day as a continuous intravenous infusion at a constant flow rate over 4 weeks followed by a 2-week treatment-free interval for up to 5 consecutive cycles.

| | |
|---|---|
| Reporting group title | Blinatumomab 5/15 µg/m²/day |

Reporting group description:

Participants received blinatumomab by continuous intravenous infusion over 4 weeks followed by a treatment-free interval of 2 weeks for up to 5 consecutive cycles. The initial dose was 5 µg/m²/day for the first seven days of treatment, followed by 15 µg/m²/day starting from Week 2 of treatment.

| | |
|---|---|
| Reporting group title | Blinatumomab 5/15/30 µg/m²/day |

Reporting group description:

Participants received blinatumomab by continuous intravenous infusion over 4 weeks followed by a treatment-free interval of 2 weeks for up to 5 consecutive cycles. The initial dose was 5 µg/m²/day for the first seven days of treatment, a dose of 15 µg/m²/day in the subsequent 7 days, followed by 30 µg/m²/day starting from Week 3 of treatment.

| | |
|---|---|
| Reporting group title | Blinatumomab Overall |

Reporting group description:

All participants who received blinatumomab by continuous intravenous infusion during the study.

| Serious adverse events | Blinatumomab 15 µg/m²/day | Blinatumomab 5/15 µg/m²/day | Blinatumomab 5/15/30 µg/m²/day |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 7 (85.71%) | 14 / 23 (60.87%) | 5 / 6 (83.33%) |
| number of deaths (all causes) | 7 | 17 | 4 |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| C-reactive protein increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute lymphocytic leukaemia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Subdural haemorrhage | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular procedure complication | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysgraphia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 3 / 3 | 2 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Cytopenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphadenitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Graft versus host disease | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Disorientation | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychotic disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Candida sepsis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Catheter site infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 7 (42.86%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Central nervous system infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Febrile infection | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pneumonia fungal | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Sinusitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Blinatumomab Overall | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 25 / 36 (69.44%) | | |
| number of deaths (all causes) | 28 | | |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute lymphocytic leukaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Subdural haemorrhage | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular procedure complication | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dysgraphia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Encephalopathy | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences causally related to treatment / all | 6 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epilepsy | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Seizure | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| Tremor | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| **Blood and lymphatic system disorders** | | | |
| Cytopenia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphadenitis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| **General disorders and administration site conditions** | | | |
| Asthenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences causally related to treatment / all | 4 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Graft versus host disease | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|---|---|---|---|
| Mouth haemorrhage | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nausea | | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vomiting | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Psychiatric disorders | | | | |
| Disorientation | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Psychotic disorder | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infections and infestations | | | | |
| Candida sepsis | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Catheter site infection | | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | | |
| occurrences causally related to treatment / all | 0 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Central nervous system infection | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |

| | | | |
|---|---|---|---|
| Febrile infection | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infection | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Pneumonia fungal | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---|---|---|
| Dehydration | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Blinatumomab 15 µg/m²/day | Blinatumomab 5/15 µg/m²/day | Blinatumomab 5/15/30 µg/m²/day |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 7 / 7 (100.00%) | 23 / 23 (100.00%) | 6 / 6 (100.00%) |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 1 | 1 |
| Flushing | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertension | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 5 / 23 (21.74%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 7 | 1 |
| Hypotension | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 5 | 0 | 3 |
| General disorders and administration site conditions | | | |
| Catheter site haematoma | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Catheter site haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Catheter site pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 3 / 23 (13.04%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 3 / 23 (13.04%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Chills | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 2 / 23 (8.70%) | 3 / 6 (50.00%) |
| occurrences (all) | 2 | 2 | 7 |
| Face oedema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 5 / 7 (71.43%) | 8 / 23 (34.78%) | 5 / 6 (83.33%) |
| occurrences (all) | 7 | 10 | 7 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Localised oedema | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 23 (8.70%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 3 | 1 |
| Oedema peripheral | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 6 / 7 (85.71%) | 5 / 23 (21.74%) | 3 / 6 (50.00%) |
| occurrences (all) | 8 | 8 | 6 |
| Pyrexia | | | |
| subjects affected / exposed | 5 / 7 (71.43%) | 18 / 23 (78.26%) | 6 / 6 (100.00%) |
| occurrences (all) | 16 | 36 | 25 |
| Immune system disorders | | | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Graft versus host disease in skin | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Breast mass | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vulvovaginal dryness | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 5 / 23 (21.74%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 5 | 2 |
| Dry throat | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 6 / 23 (26.09%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 7 | 2 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperventilation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Mediastinal haemorrhage | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 3 / 23 (13.04%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Depression | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Disorientation | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fear | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 3 / 23 (13.04%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Organic brain syndrome | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 2 | 2 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 1 | 1 |
| Amylase increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 2 / 23 (8.70%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 3 | 1 |
| Blood albumin decreased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Blood calcium decreased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood fibrinogen decreased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood fibrinogen increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 4 / 23 (17.39%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Blood immunoglobulin A decreased | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 4 / 23 (17.39%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 4 | 2 |
| Blood immunoglobulin G decreased | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 3 / 23 (13.04%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 3 | 3 |
| Blood immunoglobulin M decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 7 (42.86%) | 2 / 23 (8.70%) | 2 / 6 (33.33%) |
| occurrences (all) | 3 | 2 | 2 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood magnesium decreased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood potassium decreased | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 3 / 23 (13.04%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 4 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 5 / 23 (21.74%) | 2 / 6 (33.33%) |
| occurrences (all) | 5 | 6 | 2 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fibrin D dimer increased | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 4 / 23 (17.39%) | 2 / 6 (33.33%) |
| occurrences (all) | 3 | 4 | 3 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 4 / 7 (57.14%) | 3 / 23 (13.04%) | 0 / 6 (0.00%) |
| occurrences (all) | 5 | 3 | 0 |
| Immunoglobulins decreased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Prothrombin time prolonged | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Reticulocyte count increased | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Vital capacity abnormal | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 4 / 7 (57.14%) | 2 / 23 (8.70%) | 2 / 6 (33.33%) |
| occurrences (all) | 4 | 2 | 2 |
| Weight increased | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 7 / 23 (30.43%) | 3 / 6 (50.00%) |
| occurrences (all) | 6 | 7 | 6 |
| pH urine decreased | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Injury, poisoning and procedural complications | | | |
| Allergic transfusion reaction | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Laceration | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tachycardia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 7 (28.57%) | 5 / 23 (21.74%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 7 | 2 |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Apraxia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 4 / 23 (17.39%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Formication | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Headache | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 11 / 23 (47.83%) | 4 / 6 (66.67%) |
| occurrences (all) | 5 | 22 | 6 |
| Intention tremor | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 2 | 1 |
| Neurotoxicity | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 3 / 23 (13.04%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 4 | 1 |
| Polyneuropathy | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| | | | |
|---|---|---|---|
| Tremor | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 8 / 23 (34.78%) | 2 / 6 (33.33%) |
| occurrences (all) | 3 | 11 | 3 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Coagulopathy | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 1 / 23 (4.35%) | 2 / 6 (33.33%) |
| occurrences (all) | 4 | 4 | 4 |
| Lymphopenia | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Monocytosis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Splenomegaly | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 3 / 23 (13.04%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 3 | 1 |
| Ear and labyrinth disorders | | | |

| | | | |
|---|---|---|---|
| Vertigo | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Eye disorders | | | |
| Conjunctival haemorrhage | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dry eye | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 2 | 1 |
| Eye pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eyelid oedema | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Lacrimation increased | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Periorbital oedema | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Visual acuity reduced | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Anal incontinence | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 4 / 23 (17.39%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 6 | 2 |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 7 (42.86%) | 6 / 23 (26.09%) | 3 / 6 (50.00%) |
| occurrences (all) | 5 | 7 | 3 |
| Dry mouth | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 23 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 3 | 0 | 2 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 2 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Nausea | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 5 / 23 (21.74%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 7 | 3 |
| Proctitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 23 (8.70%) | 2 / 6 (33.33%) |
| occurrences (all) | 3 | 2 | 3 |
| Hepatobiliary disorders | | | |
| Hepatic failure | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Cold sweat | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Dry skin | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 3 / 23 (13.04%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 3 | 1 |
| Erythema | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 1 | 1 |
| Hirsutism | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 3 / 23 (13.04%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Petechiae | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 2 | 3 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Psoriasis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 7 (14.29%) | 6 / 23 (26.09%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 10 | 1 |
| Rash generalised | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Incontinence | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal failure | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary tract pain | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Back pain | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 3 / 23 (13.04%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 3 | 1 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 4 / 23 (17.39%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 6 | 0 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Muscle spasms | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 3 | 2 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 3 / 23 (13.04%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 3 |
| Myopathy | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 5 / 23 (21.74%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Infections and infestations | | | |
| Adenovirus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Candida infection | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Cytomegalovirus chorioretinitis | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---|---|---|
| Infection | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 1 |
| JC virus infection | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 4 / 23 (17.39%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 5 | 2 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 3 / 23 (13.04%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Paronychia | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Pneumonia fungal | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 1 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 0 / 23 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |

| | | | |
|---|---|---|---|
| Staphylococcal infection | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 7 (14.29%) | 1 / 23 (4.35%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 1 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 7 (0.00%) | 2 / 23 (8.70%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 4 / 7 (57.14%) | 0 / 23 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 7 (28.57%) | 3 / 23 (13.04%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 3 | 1 |

| **Non-serious adverse events** | Blinatumomab Overall | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 36 / 36 (100.00%) | | |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 4 | | |
| Flushing | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Hypertension | | | |
| subjects affected / exposed | 8 / 36 (22.22%) | | |
| occurrences (all) | 11 | | |
| Hypotension | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 8 | | |
| General disorders and administration | | | |

| | | | | |
|---|---|---|---|---|
| site conditions | | | | |
| Catheter site haematoma | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Catheter site haemorrhage | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Catheter site pain | | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | | |
| occurrences (all) | 3 | | | |
| Chest pain | | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | | |
| occurrences (all) | 5 | | | |
| Chills | | | | |
| subjects affected / exposed | 7 / 36 (19.44%) | | | |
| occurrences (all) | 11 | | | |
| Face oedema | | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | | |
| occurrences (all) | 2 | | | |
| Fatigue | | | | |
| subjects affected / exposed | 18 / 36 (50.00%) | | | |
| occurrences (all) | 24 | | | |
| General physical health deterioration | | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | | |
| occurrences (all) | 2 | | | |
| Influenza like illness | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 2 | | | |
| Injection site erythema | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Localised oedema | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Malaise | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 5 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 14 / 36 (38.89%) | | |
| occurrences (all) | 22 | | |
| Pyrexia | | | |
| subjects affected / exposed | 29 / 36 (80.56%) | | |
| occurrences (all) | 77 | | |
| Immune system disorders | | | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Graft versus host disease in skin | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Reproductive system and breast disorders | | | |
| Breast mass | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Vulvovaginal dryness | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 8 / 36 (22.22%) | | |
| occurrences (all) | 8 | | |
| Dry throat | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 4 | | |
| Epistaxis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 9 / 36 (25.00%) | | |
| occurrences (all) | 11 | | |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Hyperventilation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Mediastinal haemorrhage | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 4 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 2 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Depression | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Disorientation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Fear | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |

| | | | |
|---|---|---|---|
| Insomnia | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 4 | | |
| Organic brain syndrome | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Sleep disorder | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 4 | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 4 | | |
| Amylase increased | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 6 | | |
| Blood albumin decreased | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Blood calcium decreased | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Blood fibrinogen decreased | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Blood fibrinogen increased | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 5 | | |
| Blood immunoglobulin A decreased | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 8 / 36 (22.22%) | | | |
| occurrences (all) | 8 | | | |
| Blood immunoglobulin G decreased | | | | |
| subjects affected / exposed | 7 / 36 (19.44%) | | | |
| occurrences (all) | 8 | | | |
| Blood immunoglobulin M decreased | | | | |
| subjects affected / exposed | 7 / 36 (19.44%) | | | |
| occurrences (all) | 7 | | | |
| Blood lactate dehydrogenase increased | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Blood magnesium decreased | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Blood potassium decreased | | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | | |
| occurrences (all) | 6 | | | |
| C-reactive protein increased | | | | |
| subjects affected / exposed | 10 / 36 (27.78%) | | | |
| occurrences (all) | 13 | | | |
| Electrocardiogram QT prolonged | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Fibrin D dimer increased | | | | |
| subjects affected / exposed | 9 / 36 (25.00%) | | | |
| occurrences (all) | 10 | | | |
| Gamma-glutamyltransferase increased | | | | |
| subjects affected / exposed | 7 / 36 (19.44%) | | | |
| occurrences (all) | 8 | | | |
| Immunoglobulins decreased | | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | | |
| occurrences (all) | 2 | | | |
| Lipase increased | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 2 | | |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Prothrombin time prolonged | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Reticulocyte count increased | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Vital capacity abnormal | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Weight decreased | | | |
| subjects affected / exposed | 8 / 36 (22.22%) | | |
| occurrences (all) | 8 | | |
| Weight increased | | | |
| subjects affected / exposed | 13 / 36 (36.11%) | | |
| occurrences (all) | 19 | | |
| pH urine decreased | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 4 | | |
| Injury, poisoning and procedural complications | | | |
| Allergic transfusion reaction | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Laceration | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Bradycardia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Tachycardia | | | |
| subjects affected / exposed | 9 / 36 (25.00%) | | |
| occurrences (all) | 11 | | |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Apraxia | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Balance disorder | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Dizziness | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 5 | | |
| Formication | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Headache | | | |
| subjects affected / exposed | 17 / 36 (47.22%) | | |
| occurrences (all) | 33 | | |
| Intention tremor | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Memory impairment | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Neurotoxicity | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |

| | | | |
|---|---|---|---|
| Paraesthesia | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 6 | | |
| Polyneuropathy | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 2 | | |
| Tremor | | | |
| subjects affected / exposed | 12 / 36 (33.33%) | | |
| occurrences (all) | 17 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Coagulopathy | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Leukocytosis | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Leukopenia | | | |
| subjects affected / exposed | 6 / 36 (16.67%) | | |
| occurrences (all) | 12 | | |
| Lymphopenia | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 4 | | |
| Monocytosis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 2 | | |
| Splenomegaly | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 7 / 36 (19.44%) | | |
| occurrences (all) | 7 | | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Eye disorders | | | |
| Conjunctival haemorrhage | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Dry eye | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Eye pain | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Eyelid oedema | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Lacrimation increased | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Periorbital oedema | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Visual acuity reduced | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Abdominal pain | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 2 / 36 (5.56%) | | | |
| occurrences (all) | 2 | | | |
| Abdominal pain upper | | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | | |
| occurrences (all) | 3 | | | |
| Anal incontinence | | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | | |
| occurrences (all) | 2 | | | |
| Aphthous ulcer | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Constipation | | | | |
| subjects affected / exposed | 7 / 36 (19.44%) | | | |
| occurrences (all) | 10 | | | |
| Diarrhoea | | | | |
| subjects affected / exposed | 12 / 36 (33.33%) | | | |
| occurrences (all) | 15 | | | |
| Dry mouth | | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | | |
| occurrences (all) | 5 | | | |
| Dyspepsia | | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | | |
| occurrences (all) | 3 | | | |
| Dysphagia | | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | | |
| occurrences (all) | 2 | | | |
| Gastrooesophageal reflux disease | | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | | |
| occurrences (all) | 2 | | | |
| Gingival bleeding | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Nausea | | | | |
| subjects affected / exposed | 8 / 36 (22.22%) | | | |
| occurrences (all) | 11 | | | |
| Proctitis | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 8 | | |
| Hepatobiliary disorders | | | |
| Hepatic failure | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Hepatotoxicity | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Cold sweat | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Dry skin | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 5 | | |
| Erythema | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 4 | | |
| Hirsutism | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Petechiae | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 8 | | |
| Pruritus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Psoriasis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Rash | | | |
| subjects affected / exposed | 8 / 36 (22.22%) | | |
| occurrences (all) | 12 | | |
| Rash generalised | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Incontinence | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Renal failure | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Urinary tract pain | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 4 | | |
| Back pain | | | |
| subjects affected / exposed | 6 / 36 (16.67%) | | |
| occurrences (all) | 6 | | |
| Bone pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 6 | | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 5 | | |
| Muscular weakness | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 4 | | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 3 | | |
| Myopathy | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 3 | | |
| Neck pain | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 5 | | |
| Infections and infestations | | | |
| Adenovirus infection | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences (all) | 1 | | |
| Candida infection | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 5 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 4 | | |

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|---|---|---|---|---|
| Cystitis | | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | | |
| occurrences (all) | 2 | | | |
| Cytomegalovirus chorioretinitis | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Infection | | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | | |
| occurrences (all) | 3 | | | |
| JC virus infection | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Nasopharyngitis | | | | |
| subjects affected / exposed | 7 / 36 (19.44%) | | | |
| occurrences (all) | 8 | | | |
| Oral herpes | | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | | |
| occurrences (all) | 4 | | | |
| Otitis media | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Paronychia | | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | | |
| occurrences (all) | 2 | | | |
| Pharyngitis | | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | | |
| occurrences (all) | 2 | | | |
| Pneumonia fungal | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Respiratory syncytial virus infection | | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | | |
| occurrences (all) | 1 | | | |
| Rhinitis | | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | | |
| occurrences (all) | 3 | | | |

| | | | |
|---|---|---|---|
| Sinusitis<br>subjects affected / exposed<br>occurrences (all) | 3 / 36 (8.33%)<br>3 | | |
| Skin infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 36 (2.78%)<br>2 | | |
| Staphylococcal infection<br>subjects affected / exposed<br>occurrences (all) | 2 / 36 (5.56%)<br>2 | | |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 3 / 36 (8.33%)<br>3 | | |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 2 / 36 (5.56%)<br>2 | | |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all) | 4 / 36 (11.11%)<br>4 | | |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all) | 6 / 36 (16.67%)<br>6 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 08 July 2010 | - Reduce the highest dose explored in the study from 60 µg/m²/day to 30 µg/m²/day |
| 27 January 2011 | - Implementation of an interim cohort 2a with a lower initial dose of 5 µg/m²/day for the first week and with the maintenance dose of 15 µg/m²/day for the remaining 3 weeks of the first cycle on the basis of recommendation of the Data Monitoring Committee (DMC)<br>- Implementation of possibility for re-treatment in case of medullary relapse after treatment start<br>- Shortening of period for last dose of tyrosine kinase inhibitor and initiation of treatment with blinatumomab from 2 weeks to 72 hours<br>- Exclusion of subjects with testicular involvement of acute lymphoblastic leukemia<br>- Recommendation to obtain an additional bone marrow aspiration/biopsy on day 15 of the first treatment cycle<br>- Outsourcing of analyses of lymphocyte subpopulation (cohorts 1 and 2a were performed at Amgen Research [Munich]); cohorts 2b and 3 analyses were outsourced to a central laboratory (Labor München Zentrum). Reduction of blood sampling time points and change of marker panel in connection with the change in laboratory. |
| 02 September 2011 | - Implementation of decisions made at investigator meeting (03 March 2011) and DMC meetings (08 March 2011 and 15 July 2011) concerning dose modification in case of relevant central nervous system (CNS) events and dosing in re-treatment cycles:<br>- No dose increase to 30 µg/m²/day for subjects treated in cohort 2b who experience clinically-relevant CNS events at a dose of 15 µg/m²/day.<br>- For subjects experiencing a clinically-relevant CNS event leading to treatment stop at a dose of 15 µg/m²/day, the infusion could be restarted at a constant dose of 5 µg/m²/day for the remaining treatment duration in the core study after a temporary interruption for up to 2 weeks.<br>- Dosing in re-treatment cycles had to be the same as in cohort 3 (5 to 15 µg/m²/day).<br>- Increase in the number of subjects for ethical and operational reasons: subjects who already were in the screening phase at the time the 25th potentially evaluable subject started treatment, had to be allowed to receive treatment as well. Therefore, an over running of subject recruitment up to a total of approximately 30 subjects could be possible. |
| 16 February 2012 | - Antifungal prophylaxis for subjects with active graft-versus-host disease in their medical history after allogeneic hematopoietic stem cell transplantation<br>- Permanent discontinuation of blinatumomab in case of occurrence of ≥ 1 seizure<br>- Prophylactic measures for subjects with a high risk for cytomegalovirus infection<br>- Prophylactic anticonvulsant treatment for subjects who had a seizure<br>- Diagnostic measures to exclude potential infectious causes after CNS events Common Terminology Criteria for Adverse Events grade ≥ 3 |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported