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 Units: Subjects			
<=60 years	5	20	4
> 60 years	2	3	2
Age Continuous Units: years			
arithmetic mean	44.0	38.1	42.5
standard deviation	± 21.5	± 16.7	± 23.2
Gender Categorical Units: Subjects			
Female	3	9	2
Male	4	14	4
Race 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 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) 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 Units: Subjects			
<=60 years	29		
> 60 years	7		
Age Continuous Units: years arithmetic mean standard deviation	- -		
Gender Categorical Units: Subjects			
Female	14		
Male	22		
Race 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 Units: Subjects			
No relapes	3		
1 relapse	23		
2 relapses	9		
3 relapses	1		
Relapsed / refractory Status Units: Subjects			
Primary Refractory	3		
Relapsed	33		
Prior Allogeneic Hematopoietic Stem cell Transplantation (HSCT) 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			

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		

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 subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3		
Skin infection subjects affected / exposed occurrences (all)	1 / 36 (2.78%) 2		
Staphylococcal infection subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2		
Urinary tract infection subjects affected / exposed occurrences (all)	3 / 36 (8.33%) 3		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	2 / 36 (5.56%) 2		
Hyperglycaemia subjects affected / exposed occurrences (all)	4 / 36 (11.11%) 4		
Hypokalaemia subjects affected / exposed occurrences (all)	6 / 36 (16.67%) 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) - Implementation of possibility for re-treatment in case of medullary relapse after treatment start - Shortening of period for last dose of tyrosine kinase inhibitor and initiation of treatment with blinatumomab from 2 weeks to 72 hours - Exclusion of subjects with testicular involvement of acute lymphoblastic leukemia - Recommendation to obtain an additional bone marrow aspiration/biopsy on day 15 of the first treatment cycle - 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: - 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. - 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. - Dosing in re-treatment cycles had to be the same as in cohort 3 (5 to 15 µg/m²/day). - 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 - Permanent discontinuation of blinatumomab in case of occurrence of ≥ 1 seizure - Prophylactic measures for subjects with a high risk for cytomegalovirus infection - Prophylactic anticonvulsant treatment for subjects who had a seizure - 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