Clinical trial results:
A Single-Arm Multicenter Phase II Study preceded by Dose Evaluation to Investigate the Efficacy, Safety, and Tolerability of the BiTE® Antibody Blinatumomab (MT103) in Pediatric and Adolescent Patients with Relapsed/Refractory B-Precursor Acute Lymphoblastic Leukemia (ALL)

Summary

EudraCT number	2010-024264-18
Trial protocol	DE AT NL IT GB Outside EU/EEA
Global end of trial date	24 May 2016

Results information

Result version number	v1 (current)
This version publication date	08 December 2016
First version publication date	08 December 2016

Trial information

Trial identification

Sponsor protocol code	MT103-205

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01471782
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen, Inc
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000574-PIP02-12
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 May 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 the dose of the bispecific T cell engager blinatumomab (MT103) in pediatric and adolescent patients with relapsed/refractory acute lymphoblastic leukemia (ALL) and to assess whether this dose of blinatumomab is effective.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines, the GCPs applicable to any region where the study is conducted and in accordance with the ethical principles set forth in the Declaration of Helsinki.
All subject/the subject's legal representative provided written informed consent before undergoing any study-related procedures, including screening procedures.
The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs). No subjects were recruited into the study and no investigational product (IP) was shipped until the IRB/IEC gave written approval of the protocol and ICF and Amgen received copies of these approvals.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 January 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 29
Country: Number of subjects enrolled	Italy: 28
Country: Number of subjects enrolled	United States: 28
Worldwide total number of subjects	93
EEA total number of subjects	65

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	10
Children (2-11 years)	59
Adolescents (12-17 years)	24
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in 26 centers in Germany, France, Italy, the Netherlands, the United Kingdom, and the United States of America.

Pre-assignment

Screening details:

The phase 1 part of the study comprised 2 parts:
• A dose evaluation/escalation part in patients aged 2 to 17 years to define the recommended phase 2 dose of blinatumomab,
• An expansion part in patients less than 18 years to assess pharmacokinetics.
The Phase 2 efficacy part enrolled patients at the recommended dose determined in phase 1.

Period 1

Period 1 title	Overall 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	Phase 1: Blinatumomab 5 µg/m²/Day

Arm description:

Blinatumomab was administered as a continuous intravenous (cIV) infusion at a constant daily flow rate of 5 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.

Arm type	Experimental
Investigational medicinal product name	Blinatumomab
Investigational medicinal product code	MT103
Other name	BLINCYTO®, AMG 103
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered by continuous intravenous infusion

Arm title	Phase 1: Blinatumomab 15 µg/m²/Day

Arm description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 15 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.

Arm type	Experimental
Investigational medicinal product name	Blinatumomab
Investigational medicinal product code	MT103
Other name	BLINCYTO®, AMG 103
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered by continuous intravenous infusion

Arm title	Phase 1: Blinatumomab 30 µg/m²/Day

Arm description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 30 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.

Arm type	Experimental
Investigational medicinal product name	Blinatumomab
Investigational medicinal product code	MT103
Other name	BLINCYTO®, AMG 103
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered by continuous intravenous infusion

Arm title	Phase 1: Blinatumomab 15/30 µg/m²/Day

Arm description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 15 µg/m²/day for the first week of cycle 1 and then at 30 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 30 µg/m²/day for up to five cycles of treatment.

Arm type	Experimental
Investigational medicinal product name	Blinatumomab
Investigational medicinal product code	MT103
Other name	BLINCYTO®, AMG 103
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered by continuous intravenous infusion

Arm title	Phase 1: Blinatumomab 5/15 µg/m²/Day

Arm description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 5 µg/m²/day for the first week of cycle 1 and then at 15 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 15 µg/m²/day for up to five cycles of treatment.

Arm type	Experimental
Investigational medicinal product name	Blinatumomab
Investigational medicinal product code	MT103
Other name	BLINCYTO®, AMG 103
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered by continuous intravenous infusion

Arm title	Phase 2: Blinatumomab 5/15 µg/m²/Day

Arm description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 5 µg/m²/day for the first week of cycle 1 and then at 15 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 15 µg/m²/day for up to five cycles of treatment.

Arm type	Experimental
Investigational medicinal product name	Blinatumomab
Investigational medicinal product code	MT103
Other name	BLINCYTO®, AMG 103
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Administered by continuous intravenous infusion

Number of subjects in period 1	Phase 1: Blinatumomab 5 µg/m²/Day	Phase 1: Blinatumomab 15 µg/m²/Day	Phase 1: Blinatumomab 30 µg/m²/Day
Started	5	7	5
Completed	0	1	0
Not completed	5	6	5
Disease Relapse	-	-	-
Physician decision	-	-	-
Adverse event, non-fatal	1	1	2
Other	-	-	1
Death	-	-	-
Withdrawal by Parent/Guardian	-	-	-
Hematopoietic Stem Cell Transplantation	2	2	1
Change of Chemotherapy	1	1	-
Lack of efficacy	1	2	1

Number of subjects in period 1	Phase 1: Blinatumomab 15/30 µg/m²/Day	Phase 1: Blinatumomab 5/15 µg/m²/Day	Phase 2: Blinatumomab 5/15 µg/m²/Day
Started	6	26	44
Completed	1	0	3
Not completed	5	26	41
Disease Relapse	1	2	1
Physician decision	-	3	8
Adverse event, non-fatal	2	3	1
Other	1	6	5
Death	-	-	1
Withdrawal by Parent/Guardian	-	1	-
Hematopoietic Stem Cell Transplantation	-	5	3
Change of Chemotherapy	-	1	4
Lack of efficacy	1	5	18

Baseline characteristics

Reporting groups	
Reporting group title	Phase 1: Blinatumomab 5 µg/m²/Day
Reporting group description:	
Blinatumomab was administered as a continuous intravenous (cIV) infusion at a constant daily flow rate of 5 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.	
Reporting group title	Phase 1: Blinatumomab 15 µg/m²/Day
Reporting group description:	
Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 15 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.	
Reporting group title	Phase 1: Blinatumomab 30 µg/m²/Day
Reporting group description:	
Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 30 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.	
Reporting group title	Phase 1: Blinatumomab 15/30 µg/m²/Day
Reporting group description:	
Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 15 µg/m²/day for the first week of cycle 1 and then at 30 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 30 µg/m²/day for up to five cycles of treatment.	
Reporting group title	Phase 1: Blinatumomab 5/15 µg/m²/Day
Reporting group description:	
Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 5 µg/m²/day for the first week of cycle 1 and then at 15 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 15 µg/m²/day for up to five cycles of treatment.	
Reporting group title	Phase 2: Blinatumomab 5/15 µg/m²/Day
Reporting group description:	
Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 5 µg/m²/day for the first week of cycle 1 and then at 15 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 15 µg/m²/day for up to five cycles of treatment.	

Reporting group values	Phase 1: Blinatumomab 5 µg/m²/Day	Phase 1: Blinatumomab 15 µg/m²/Day	Phase 1: Blinatumomab 30 µg/m²/Day
Number of subjects	5	7	5
Age categorical Units: Subjects			
< 2 years	0	0	0
2 - 6 years	3	5	2
7 - 17 years	2	2	3
Gender categorical Units: Subjects			
Female	3	4	2
Male	2	3	3
Race			
Race was not recorded for any patient from France and for two further patients.			
Units: Subjects			
White	5	7	5

Asian	0	0	0
Black or African American	0	0	0
American Indian or Alaska Native	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0
Other	0	0	0
Unknown	0	0	0
Prior Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) Units: Subjects			
Yes	3	6	2
No	2	1	3

Reporting group values	Phase 1: Blinatumomab 15/30 µg/m²/Day	Phase 1: Blinatumomab 5/15 µg/m²/Day	Phase 2: Blinatumomab 5/15 µg/m²/Day
Number of subjects	6	26	44
Age categorical Units: Subjects			
< 2 years	0	8	2
2 - 6 years	4	9	11
7 - 17 years	2	9	31
Gender categorical Units: Subjects			
Female	1	11	12
Male	5	15	32
Race			
Race was not recorded for any patient from France and for two further patients.			
Units: Subjects			
White	5	22	33
Asian	0	0	0
Black or African American	0	0	0
American Indian or Alaska Native	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0
Other	1	3	5
Unknown	0	1	6
Prior Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) Units: Subjects			
Yes	4	15	25
No	2	11	19

Reporting group values	Total		
Number of subjects	93		
Age categorical Units: Subjects			
< 2 years	10		
2 - 6 years	34		
7 - 17 years	49		
Gender categorical Units: Subjects			
Female	33		

Male	60		

Race			
Race was not recorded for any patient from France and for two further patients.			
Units: Subjects			
White	77		
Asian	0		
Black or African American	0		
American Indian or Alaska Native	0		
Native Hawaiian or other Pacific Islander	0		
Other	9		
Unknown	7		
Prior Allogeneic Hematopoietic Stem Cell Transplantation (HSCT)			
Units: Subjects			
Yes	55		
No	38		

End points

End points reporting groups

Reporting group title	Phase 1: Blinatumomab 5 µg/m²/Day

Reporting group description:

Blinatumomab was administered as a continuous intravenous (cIV) infusion at a constant daily flow rate of 5 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.

Reporting group title	Phase 1: Blinatumomab 15 µg/m²/Day

Reporting group description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 15 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.

Reporting group title	Phase 1: Blinatumomab 30 µg/m²/Day

Reporting group description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 30 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.

Reporting group title	Phase 1: Blinatumomab 15/30 µg/m²/Day

Reporting group description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 15 µg/m²/day for the first week of cycle 1 and then at 30 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 30 µg/m²/day for up to five cycles of treatment.

Reporting group title	Phase 1: Blinatumomab 5/15 µg/m²/Day

Reporting group description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 5 µg/m²/day for the first week of cycle 1 and then at 15 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 15 µg/m²/day for up to five cycles of treatment.

Reporting group title	Phase 2: Blinatumomab 5/15 µg/m²/Day

Reporting group description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 5 µg/m²/day for the first week of cycle 1 and then at 15 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 15 µg/m²/day for up to five cycles of treatment.

Subject analysis set title	Phase 1: Blinatumomab 5 µg/m²/Day
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received blinatumomab administered as a continuous intravenous infusion at a constant daily flow rate of 5 µg/m²/day during the first cycle. This analysis set was used for pharmacokinetic (PK) and pharmacodynamic (PD) analyses.

Subject analysis set title	Phase 1: Blinatumomab 15 µg/m²/Day
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received blinatumomab administered as a continuous intravenous infusion at a constant daily flow rate of 15 µg/m²/day during the first cycle. This analysis set was used for PK and PD analyses.

Subject analysis set title	Phase 1: Blinatumomab 30 µg/m²/Day
Subject analysis set type	Full analysis

Subject analysis set description:

Participants who received blinatumomab administered as a continuous intravenous infusion at a constant daily flow rate of 30 µg/m²/day during the first cycle. This analysis set was used for PK and PD analyses.

Subject analysis set title	Phase 1: Blinatumomab
Subject analysis set type	Full analysis

Subject analysis set description:

All participants in phase 1 who received blinatumomab administered as a continuous intravenous infusion at a constant daily flow rate ranging from 5 to 30 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.

Subject analysis set title	Phase 2: Blinatumomab 5/15 µg/m²/Day
Subject analysis set type	Full analysis

Subject analysis set description:

Participants in phase 2 who received blinatumomab administered as a continuous intravenous infusion at a constant daily flow rate of 5 µg/m²/day for the first week of cycle 1 and then at 15 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 15 µg/m²/day for up to five cycles of treatment.

Subject analysis set title	Phase 1+2: Blinatumomab 5/15 µg/m²/Day
Subject analysis set type	Full analysis

Subject analysis set description:

All participants in phase 1 and phase 2 who received blinatumomab administered as a continuous intravenous infusion at a constant daily flow rate of 5 µg/m²/day for the first week of cycle 1 and then at 15 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 15 µg/m²/day for up to five cycles of treatment.

Primary: Phase I: Number of Participants With Dose-limiting Toxicities (DLTs)

End point title	Phase I: Number of Participants With Dose-limiting Toxicities (DLTs)[1][2]

End point description:

The maximum tolerated dose (MTD) was defined as one or fewer out of 6 participants experiencing a dose limiting toxicity (DLT) or the maximum administered dose (MAD).
A dose limiting toxicity is any Grade ≥ 3 adverse event related to study drug, Grade 3 fatigue, headache, insomnia, fever, hypotension or infection were not considered dose limiting toxicities. Laboratory parameters of Grade . 3 but not considered as clinically relevant and/or responding to routine medical management, thrombocytopenia, leukopenia (including neutropenia and lymphopenia), and anemia were not considered dose limiting toxicities.
Participants in the Phase 1 dose escalation part of the study are included in the analysis.

End point type	Primary

End point timeframe:

Cycle 1, 28 days

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical testing was performed for the phase 1 part of this study.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Evaluation of dose-limiting toxicities was only performed in the phase 1 dose escalation part of the study.

End point values	Phase 1: Blinatumomab 5 µg/m²/Day	Phase 1: Blinatumomab 15 µg/m²/Day	Phase 1: Blinatumomab 30 µg/m²/Day	Phase 1: Blinatumomab 15/30 µg/m²/Day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	5	6
Units: participants	0	1	2	1

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Complete Remission in the First Two

Cycles

End point title	Percentage of Participants With Complete Remission in the First Two Cycles[3]

End point description:

Hematological assessments were performed from bone marrow biopsy samples. All hematological assessments of bone marrow were reviewed in a central laboratory. Complete remission (CR) was defined as
• M1 bone marrow (bone marrow blasts < 5%)
• No evidence of circulating blasts or extra-medullary disease
Complete remission includes participants with incomplete recovery of peripheral blood counts.

The full analysis set includes all participants who received any infusion of blinatumomab.

End point type	Primary

End point timeframe:

Cycles 1 and 2 (12 weeks)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical comparisons between treatment groups was not performed.

End point values	Phase 1: Blinatumomab 5 µg/m²/Day	Phase 1: Blinatumomab 15 µg/m²/Day	Phase 1: Blinatumomab 30 µg/m²/Day	Phase 1: Blinatumomab 15/30 µg/m²/Day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	5	6
Units: percentage of participants				
number (confidence interval 95%)	20 (0.5 to 71.6)	42.9 (9.9 to 81.6)	20 (0.5 to 71.6)	33.3 (4.3 to 77.7)

End point values	Phase 1: Blinatumomab 5/15 µg/m²/Day	Phase 2: Blinatumomab 5/15 µg/m²/Day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	44		
Units: percentage of participants				
number (confidence interval 95%)	50 (29.9 to 70.1)	31.8 (18.6 to 47.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events

End point title	Number of Participants With Adverse Events[4]

End point description:

The severity (or intensity) of adverse events (AEs) was assessed according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), v4.03 and according to the following:
Grade 1 - Mild adverse event; Grade 2 – Moderate adverse event; Grade 3 – Severe and undesirable adverse event; Grade 4 - Life-threatening or disabling adverse event; Grade 5 - Death.
The investigator used medical judgment to determine if there was a causal relationship (ie, related,

unrelated) between an adverse event and blinatumomab.

End point type	Secondary

End point timeframe:

From the start of the first infusion to 30 days after the end of the last infusion in the core study or from the start of the first retreatment cycle infusion to 30 days after the end of the last retreatment cycle, median treatment duration was 28 days.

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Safety analyses were not performed for each phase separately, hence safety results are reported combined for phase 1 and 2.

End point values	Phase 1: Blinatumomab 5 µg/m²/Day	Phase 1: Blinatumomab 15 µg/m²/Day	Phase 1: Blinatumomab 30 µg/m²/Day	Phase 1: Blinatumomab 15/30 µg/m²/Day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	5	6
Units: participants				
Any adverse event (AE)	5	7	5	6
Adverse event of at least CTC grade 3	4	7	5	6
Serious adverse event (SAEs)	4	4	3	4
SAE of at least grade 3	4	3	3	4
AE leading to interruption of study drug	0	0	2	2
AE leading to discontinuation of study drug	1	1	2	2
Adverse event leading to death	0	1	1	3
Treatment-related adverse event (TRAE)	5	6	5	5
TRAE of at least CTC grade 3	4	5	5	4
Treatment-related serious adverse event	3	2	2	1
TRAE leading to discontinuation of study drug	1	1	2	1
TRAE leading to death	0	0	0	1

End point values	Phase 1+2: Blinatumomab 5/15 µg/m²/Day			
Subject group type	Subject analysis set			
Number of subjects analysed	70			
Units: participants				
Any adverse event (AE)	70			
Adverse event of at least CTC grade 3	61			
Serious adverse event (SAEs)	39			
SAE of at least grade 3	28			
AE leading to interruption of study drug	10			
AE leading to discontinuation of study drug	4			
Adverse event leading to death	8			
Treatment-related adverse event (TRAE)	59			
TRAE of at least CTC grade 3	38			
Treatment-related serious adverse event	15			

TRAE leading to discontinuation of study drug	2			
TRAE leading to death	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Steady State Concentration of Blinatumomab

End point title	Steady State Concentration of Blinatumomab

End point description:

Blinatumomab serum concentrations were quantified in all patients at baseline (predose) and during the first 2 treatment cycles in the phase 1 part of the study only. Blinatumomab concentrations were quantified using a validated bioassay, the lower limit of quantification was 50 pg/mL.
The analysis includes Phase 1 participants with available blinatumomab concentration data.

End point type	Secondary

End point timeframe:

Cycles 1 and 2 predose, during the IV infusion on day 3 (at least 48 hours after start of infusion) and days 8, 15 and 22 (steady state) and day 29 at End of Infusion (EoI) and 2, 4, and 8 hours after EoI for ages ≥ 2 years.

End point values	Phase 1: Blinatumomab 5 µg/m²/Day	Phase 1: Blinatumomab 15 µg/m²/Day	Phase 1: Blinatumomab 30 µg/m²/Day	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	27	34	7	
Units: pg/mL				
arithmetic mean (standard deviation)				
Cycle 1 (N = 27, 34, 7)	162 (± 179)	533 (± 392)	1520 (± 1020)	
Cycle 2 (N = 3, 13, 5)	456 (± 288)	866 (± 655)	1150 (± 701)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Hematological Relapse (Duration of Response)

End point title	Time to Hematological Relapse (Duration of Response)

End point description:

Time to hematological relapse was measured only for participants in remission 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 date of death.
Hematological relapse is defined as the proportion of blasts in bone marrow > 25% following documented remission, or extramedullary relapse.
Time to hematological relapse was analyzed by Kaplan-Meier methods and the median observation time was calculated by the reverse Kaplan Meier method.

"99999" indicates data that could not be estimated due to the low number of events.

End point type	Secondary

End point timeframe:

Up to the data cut-off date of 12 January 2015; median observation time was 23.5 months for phase 1 and 11.5 months for phase 2.

End point values	Phase 1: Blinatumomab	Phase 2: Blinatumomab 5/15 µg/m²/Day	Phase 1+2: Blinatumomab 5/15 µg/m²/Day	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	21[5]	14[6]	27[7]	
Units: months				
median (confidence interval 95%)	10.3 (3.9 to 16.4)	3.4 (1.7 to 99999)	5.2 (2.3 to 16.4)	

Notes:

[5] - Full analysis set with complete remission

[6] - Full analysis set with complete remission

[7] - Full analysis set with complete remission

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse-free Survival (Primary Analysis)

End point title	Relapse-free Survival (Primary Analysis)

End point description:

Relapse-free survival (RFS) was assessed for participants who achieved a complete remission 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 and the median observation time was calculated by the reverse Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Up to the data cut-off date of 12 January 2015; median observation time was 23.5 months for phase 1 and 11.5 months for phase 2.

End point values	Phase 1: Blinatumomab	Phase 2: Blinatumomab 5/15 µg/m²/Day	Phase 1+2: Blinatumomab 5/15 µg/m²/Day	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	21[8]	14[9]	27[10]	
Units: months				
median (confidence interval 95%)	7.9 (3 to 12.4)	3.4 (1.7 to 13.9)	4.4 (2.3 to 12.1)	

Notes:

[8] - Full analysis set with complete remission

[9] - Full analysis set with complete remission

[10] - Full analysis set with complete remission

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse-free Survival (Final Analysis)

End point title	Relapse-free Survival (Final Analysis)

End point description:

Relapse-free survival (RFS) was assessed for participants who achieved a complete remission 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 and the median observation time was calculated by the reverse Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Up to the end of the follow-up period; median overall observation time was 23.1 months.

End point values	Phase 1+2: Blinatumomab 5/15 µg/m²/Day			
Subject group type	Subject analysis set			
Number of subjects analysed	27[11]			
Units: months				
median (confidence interval 95%)	4.4 (2.3 to 7.6)			

Notes:

[11] - Full analysis set with complete remission

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (Primary Analysis)

End point title	Overall Survival (Primary Analysis)

End point description:

Overall survival (OS) was measured for all participants from the first treatment of blinatumomab until death due to any cause or the date of the last follow-up. Participants who did not die were censored on the last documented visit date or the date of the last contact when the patient was last known to have been alive. For patients who withdrew their informed consent only information until the date of withdrawal was analyzed.
Overall survival was estimated using Kaplan-Meier methods. The median follow-up time with respect to overall survival was calculated by the reverse Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Up to the data cut-off date of 12 January 2015; median observation time was 23.5 months for phase 1

and 11.6 months for phase 2.

End point values	Phase 1: Blinatumomab	Phase 2: Blinatumomab 5/15 µg/m²/Day	Phase 1+2: Blinatumomab 5/15 µg/m²/Day	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	49	44	70	
Units: months				
median (confidence interval 95%)	6.5 (3.6 to 10.6)	8.2 (4 to 14.6)	7.5 (4 to 11.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (Final Analysis)

End point title	Overall Survival (Final Analysis)

End point description:

Overall survival (OS) was measured for all participants from the first treatment of blinatumomab until death due to any cause or the date of the last follow-up. Participants who did not die were censored on the last documented visit date or the date of the last contact when the patient was last known to have been alive. For patients who withdrew their informed consent only information until the date of withdrawal was analyzed.
Overall survival was estimated using Kaplan-Meier methods. The median follow-up time with respect to overall survival was calculated by the reverse Kaplan-Meier method.

End point type	Secondary

End point timeframe:

Up to the end of the follow-up period; median overall observation time was 23.8 months.

End point values	Phase 1+2: Blinatumomab 5/15 µg/m²/Day			
Subject group type	Subject analysis set			
Number of subjects analysed	70			
Units: months				
median (confidence interval 95%)	7.5 (4 to 11.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Received an Allogeneic Hematopoietic Stem Cell Transplant During Blinatumomab Induced Remission

End point title	Percentage of Participants Who Received an Allogeneic Hematopoietic Stem Cell Transplant During Blinatumomab Induced Remission

End point description:

The percentage of participants who received allogeneic hematopoietic stem cell transplantation (HSCT) while in remission due to treatment with blinatumomab during the first two cycles, and received no further anti-leukemic medication before HSCT.

End point type	Secondary

End point timeframe:

Up to the data cut-off date of 12 January 2015; Maximum duration on study was 24 months in phase 1 and 15 months for phase 2.

End point values	Phase 1: Blinatumomab 5 µg/m²/Day	Phase 1: Blinatumomab 15 µg/m²/Day	Phase 1: Blinatumomab 30 µg/m²/Day	Phase 1: Blinatumomab 15/30 µg/m²/Day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	5	6
Units: percentage of participants				
number (confidence interval 95%)	20 (0.5 to 71.6)	28.6 (3.7 to 71)	20 (0.5 to 71.6)	16.7 (0.4 to 64.1)

End point values	Phase 1: Blinatumomab 5/15 µg/m²/Day	Phase 2: Blinatumomab 5/15 µg/m²/Day	Phase 1+2: Blinatumomab 5/15 µg/m²/Day	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	26	44	70	
Units: percentage of participants				
number (confidence interval 95%)	30.8 (14.3 to 51.8)	11.4 (3.8 to 24.6)	18.6 (10.3 to 29.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Developed Anti-blinatumomab Antibodies

End point title	Number of Participants Who Developed Anti-blinatumomab Antibodies

End point description:

Antibodies to blinatumomab were detected using an electrochemiluminescence (ECL)-based assay.

End point type	Secondary

End point timeframe:

Predose up until 30 days after last dose of study medication; median treatment duration was 28 days.

End point values	Phase 1: Blinatumomab 5 µg/m²/Day	Phase 1: Blinatumomab 15 µg/m²/Day	Phase 1: Blinatumomab 30 µg/m²/Day	Phase 1: Blinatumomab 15/30 µg/m²/Day
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	7	5	6
Units: participants				
number (not applicable)	0	0	0	0

End point values	Phase 1: Blinatumomab 5/15 µg/m²/Day	Phase 2: Blinatumomab 5/15 µg/m²/Day		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	44		
Units: participants				
number (not applicable)	0	0		

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-4, IL-6, IL-10, tumor necrosis factor-alpha (TNF-α) and interferon gamma (IFN-γ) using cytometric bead assays. The limit of detection of the assay (LOD) was 20 pg/mL and the lower limit of quantification (LLOQ) was 125 pg/mL. Data below LOD were set to 10 pg/mL while data < LOQ and > LOD were reported as measured.
Serum IL-4 levels were below detection limit (< 20 pg/mL) at all time points in all participants studied.

End point type	Secondary

End point timeframe:

Cycle 1 and 2 day 1 (prior to infusion, 2 and 6 hours after infusion start), day 2 and day 3.

End point values	Phase 1: Blinatumomab 5 µg/m²/Day	Phase 1: Blinatumomab 15 µg/m²/Day	Phase 1: Blinatumomab 30 µg/m²/Day	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	31[12]	14[13]	5[14]	
Units: pg/mL				
arithmetic mean (standard deviation)				
IL-6: Cycle 1 Week 1 (N=31, 13, 5)	4970 (± 17000)	1780 (± 2620)	23400 (± 24100)	
IL-6: Cycle 2 Week 1 (N=4, 14, 5)	526 (± 844)	892 (± 2370)	40.4 (± 68)	
IL-10: Cycle 1 Week 1 (N=31, 13, 5)	562 (± 710)	1400 (± 2030)	3170 (± 1720)	
IL-10: Cycle 2 Week 1 (N=4, 14, 5)	519 (± 497)	432 (± 692)	277 (± 308)	
IFN-: Cycle 1 Week 1 (N=31, 13, 5)	207 (± 516)	539 (± 1240)	2260 (± 1540)	

IFN-: Cycle 2 Week 1 (N=4, 14, 5)	51.8 (± 65.6)	47.6 (± 51.5)	22.8 (± 28.6)	
IL-2: Cycle 1 Week 1 (N=31, 13, 5)	22.7 (± 23)	93.9 (± 150)	900 (± 1390)	
IL-2: Cycle 2 Week 1 (N=4, 14, 5)	10 (± 0)	14.3 (± 8.84)	10 (± 0)	
TNF-α: Cycle 1 Week 1 (N=31, 13, 5)	87.3 (± 241)	60.2 (± 127)	285 (± 306)	
TNF-α: Cycle 2 Week 1 (N=4, 14, 5)	10 (± 0)	10 (± 0)	10 (± 0)	

Notes:

[12] - Phase 1 full analysis set participants with available data

[13] - Phase 1 full analysis set participants with available data

[14] - Phase 1 full analysis set participants with available data

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of the first infusion to 30 days after the end of the last infusion in the core study or from the start of the first retreatment cycle infusion to 30 days after the end of the last retreatment cycle, median treatment duration was 28 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Phase 1: Blinatumomab 5 µg/m²/Day

Reporting group description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 5 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.

Reporting group title	Phase 1: Blinatumomab 15 µg/m²/Day

Reporting group description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 15 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.

Reporting group title	Phase 1+2: Blinatumomab 5/15 µg/m²/Day

Reporting group description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 5 µg/m²/day for the first week of cycle 1 and then at 15 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 15 µg/m²/day for up to five cycles of treatment.

Reporting group title	Phase 1: Blinatumomab 15/30 µg/m²/Day

Reporting group description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 15 µg/m²/day for the first week of cycle 1 and then at 30 µg/m²/day for 3 weeks followed by a treatment-free interval of 2 weeks. Participants received subsequent cycles at 30 µg/m²/day for up to five cycles of treatment.

Reporting group title	Phase 1: Blinatumomab 30 µg/m²/Day

Reporting group description:

Blinatumomab was administered as a continuous intravenous infusion at a constant daily flow rate of 30 µg/m²/day over 4 weeks followed by a treatment-free interval of 2 weeks for up to five cycles of treatment.

Serious adverse events	Phase 1: Blinatumomab 5 µg/m²/Day	Phase 1: Blinatumomab 15 µg/m²/Day	Phase 1+2: Blinatumomab 5/15 µg/m²/Day
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	4 / 7 (57.14%)	39 / 70 (55.71%)
number of deaths (all causes)	2	6	43
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Leukaemia recurrent			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (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
Haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (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
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Device malfunction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Disease progression			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Influenza like illness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (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
Multi-organ failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Pyrexia			
subjects affected / exposed	2 / 5 (40.00%)	1 / 7 (14.29%)	8 / 70 (11.43%)
occurrences causally related to treatment / all	2 / 3	1 / 1	4 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	4 / 70 (5.71%)
occurrences causally related to treatment / all	0 / 0	1 / 1	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Acquired phimosis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (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
Epistaxis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (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
Hypoxia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (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
Pneumonitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 5 (0.00%)	2 / 7 (28.57%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Psychiatric disorders			
Confusional state			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Enterococcus test positive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia test positive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcus test positive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stenotrophomonas test positive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	3 / 70 (4.29%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access complication			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Atonic seizures			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	8 / 70 (11.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Histiocytosis haematophagic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	3 / 70 (4.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastroenteritis viral			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (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
Infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	3 / 70 (4.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1: Blinatumomab 15/30 µg/m²/Day	Phase 1: Blinatumomab 30 µg/m²/Day	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	3 / 5 (60.00%)	
number of deaths (all causes)	4	4	
number of deaths resulting from			

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Leukaemia recurrent			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device malfunction			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Acquired phimosis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	

Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Enterococcus test positive			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia test positive			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcus test positive			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stenotrophomonas test positive			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Overdose			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access complication			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Atonic seizures			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotonia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Histiocytosis haematophagic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mouth haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			

subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour lysis syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Phase 1: Blinatumomab 5 µg/m²/Day	Phase 1: Blinatumomab 15 µg/m²/Day	Phase 1+2: Blinatumomab 5/15 µg/m²/Day
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	7 / 7 (100.00%)	70 / 70 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Flushing			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	3 / 70 (4.29%)
occurrences (all)	0	0	3
Haematoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Hyperaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	5 / 7 (71.43%)	18 / 70 (25.71%)
occurrences (all)	0	9	26
Hypotension			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	10 / 70 (14.29%)
occurrences (all)	0	1	10
Surgical and medical procedures			
Infusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Oxygen supplementation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences (all)	0	1	1

Parenteral nutrition			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Application site scab			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Catheter site haematoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	1	0	4
Chills			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	3 / 70 (4.29%)
occurrences (all)	0	0	4
Face oedema			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	2	0	1
Facial pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 5 (40.00%)	2 / 7 (28.57%)	5 / 70 (7.14%)
occurrences (all)	2	2	7
Injection site erythema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	2	0
Injection site haematoma			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Localised oedema			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	4 / 70 (5.71%)
occurrences (all)	0	0	5
Oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	3 / 70 (4.29%)
occurrences (all)	0	0	3
Oedema peripheral			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	5 / 70 (7.14%)
occurrences (all)	1	0	6
Pain			
subjects affected / exposed	1 / 5 (20.00%)	2 / 7 (28.57%)	6 / 70 (8.57%)
occurrences (all)	1	2	7
Pyrexia			
subjects affected / exposed	4 / 5 (80.00%)	7 / 7 (100.00%)	54 / 70 (77.14%)
occurrences (all)	12	27	154
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	4 / 70 (5.71%)
occurrences (all)	1	0	4
Drug hypersensitivity			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	3 / 70 (4.29%)
occurrences (all)	0	0	3
Cough			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	13 / 70 (18.57%)
occurrences (all)	2	0	16
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Epistaxis			

subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	10 / 70 (14.29%)
occurrences (all)	0	1	14
Hypoxia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	3
Laryngeal oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Lung disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Pleural effusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Pneumonia aspiration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Pulmonary oedema			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	3 / 70 (4.29%)
occurrences (all)	0	1	4
Anxiety			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	4 / 70 (5.71%)
occurrences (all)	1	0	5

Confusional state			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Personality change			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	4 / 70 (5.71%)
occurrences (all)	0	1	5
Alanine aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	13 / 70 (18.57%)
occurrences (all)	1	0	22
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	10 / 70 (14.29%)
occurrences (all)	1	1	18
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	4 / 70 (5.71%)
occurrences (all)	0	1	4
Blood creatinine increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	3
Blood fibrinogen decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Blood fibrinogen increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Blood immunoglobulin A decreased			

subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Blood immunoglobulin G decreased			
subjects affected / exposed	0 / 5 (0.00%)	4 / 7 (57.14%)	1 / 70 (1.43%)
occurrences (all)	0	7	1
Blood immunoglobulin M decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	7 / 70 (10.00%)
occurrences (all)	0	1	7
C-reactive protein increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Cytomegalovirus test positive			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Electroencephalogram abnormal			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Fibrin D dimer increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 7 (28.57%)	6 / 70 (8.57%)
occurrences (all)	0	2	8
Haemoglobin decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	1 / 5 (20.00%)	2 / 7 (28.57%)	3 / 70 (4.29%)
occurrences (all)	1	2	4
Lymphocyte count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	3 / 70 (4.29%)
occurrences (all)	0	0	6
Neutrophil count decreased			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	9 / 70 (12.86%)
occurrences (all)	0	0	13
Platelet count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	10 / 70 (14.29%)
occurrences (all)	0	0	19
Protein total decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	3
Roseolovirus test positive			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	2	0
Weight decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	4 / 70 (5.71%)
occurrences (all)	0	0	4
Weight increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	12 / 70 (17.14%)
occurrences (all)	0	1	17
White blood cell count decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	8 / 70 (11.43%)
occurrences (all)	0	0	10
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Ear abrasion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			

subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Skin abrasion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Sinus bradycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	3 / 70 (4.29%)
occurrences (all)	0	0	3
Sinus tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	5 / 70 (7.14%)
occurrences (all)	0	0	9
Tachycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	3 / 70 (4.29%)
occurrences (all)	0	0	6
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	3 / 70 (4.29%)
occurrences (all)	2	1	3
Dysaesthesia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Dyskinesia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Encephalopathy			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Epilepsy			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Essential tremor			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	5 / 5 (100.00%)	4 / 7 (57.14%)	20 / 70 (28.57%)
occurrences (all)	16	6	36
Lethargy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	4 / 70 (5.71%)
occurrences (all)	0	1	5
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 5 (60.00%)	2 / 7 (28.57%)	29 / 70 (41.43%)
occurrences (all)	8	5	54
Bone marrow failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Coagulopathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Disseminated intravascular coagulation			

subjects affected / exposed	1 / 5 (20.00%)	2 / 7 (28.57%)	3 / 70 (4.29%)
occurrences (all)	1	2	6
Febrile neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	8 / 70 (11.43%)
occurrences (all)	0	0	8
Hypoglobulinaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	1	0	1
Leukopenia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 7 (28.57%)	9 / 70 (12.86%)
occurrences (all)	0	2	12
Lymphopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	3
Neutropenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	12 / 70 (17.14%)
occurrences (all)	0	2	26
Thrombocytopenia			
subjects affected / exposed	2 / 5 (40.00%)	2 / 7 (28.57%)	14 / 70 (20.00%)
occurrences (all)	13	7	41
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	2
Eye disorders			
Eyelid haematoma			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Eyelid oedema			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	2 / 70 (2.86%)
occurrences (all)	0	1	2
Ocular icterus			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Photophobia			

subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	2 / 70 (2.86%)
occurrences (all)	0	1	4
Vision blurred			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Abdominal pain			
subjects affected / exposed	3 / 5 (60.00%)	3 / 7 (42.86%)	13 / 70 (18.57%)
occurrences (all)	7	3	18
Abdominal pain upper			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Ascites			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	6 / 70 (8.57%)
occurrences (all)	0	0	6
Diarrhoea			
subjects affected / exposed	2 / 5 (40.00%)	2 / 7 (28.57%)	9 / 70 (12.86%)
occurrences (all)	3	5	10
Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Glossodynia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Ileus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Mouth haemorrhage			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0

Nausea			
subjects affected / exposed	2 / 5 (40.00%)	1 / 7 (14.29%)	23 / 70 (32.86%)
occurrences (all)	3	1	31
Stomatitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	5 / 70 (7.14%)
occurrences (all)	0	0	7
Vomiting			
subjects affected / exposed	2 / 5 (40.00%)	2 / 7 (28.57%)	17 / 70 (24.29%)
occurrences (all)	7	4	29
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Hepatic failure			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Hepatosplenomegaly			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Hepatotoxicity			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Dermatitis diaper			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences (all)	0	1	2
Drug eruption			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Erythema			

subjects affected / exposed	2 / 5 (40.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	2	0	2
Erythema nodosum			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Hair growth abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	1	0	2
Rash			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences (all)	1	2	1
Rash maculo-papular			
subjects affected / exposed	0 / 5 (0.00%)	2 / 7 (28.57%)	3 / 70 (4.29%)
occurrences (all)	0	2	4
Skin discolouration			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Trichorrhexis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences (all)	1	1	2
Haematuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Oliguria			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0

Proteinuria			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	3
Renal failure chronic			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	2	0
Renal tubular disorder			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Urinary retention			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Cushingoid			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	4 / 70 (5.71%)
occurrences (all)	0	0	4
Back pain			
subjects affected / exposed	2 / 5 (40.00%)	2 / 7 (28.57%)	14 / 70 (20.00%)
occurrences (all)	4	3	17
Bone pain			
subjects affected / exposed	1 / 5 (20.00%)	1 / 7 (14.29%)	7 / 70 (10.00%)
occurrences (all)	2	1	10
Muscular weakness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	4 / 70 (5.71%)
occurrences (all)	0	0	4
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	2 / 70 (2.86%)
occurrences (all)	0	0	2
Myalgia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Myopathy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	3 / 70 (4.29%)
occurrences (all)	0	1	3
Pain in extremity			
subjects affected / exposed	3 / 5 (60.00%)	2 / 7 (28.57%)	8 / 70 (11.43%)
occurrences (all)	7	8	12
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
BK virus infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	2 / 70 (2.86%)
occurrences (all)	0	1	2
Device related infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Enterocolitis infectious			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Legionella infection			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0
Lung infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	1	0	0

Oral herpes			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences (all)	0	1	1
Polyomavirus-associated nephropathy			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	7 / 70 (10.00%)
occurrences (all)	0	0	9
Rhinovirus infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Staphylococcal infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Staphylococcal sepsis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Viral myositis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	1 / 70 (1.43%)
occurrences (all)	0	4	1
Decreased appetite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	3 / 70 (4.29%)
occurrences (all)	0	0	3
Dehydration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	6 / 70 (8.57%)
occurrences (all)	0	0	8
Hyperkalaemia			

subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0
Hypernatraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	0 / 70 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 7 (28.57%)	0 / 70 (0.00%)
occurrences (all)	0	2	0
Hyperuricaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	2 / 70 (2.86%)
occurrences (all)	0	1	2
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 7 (28.57%)	4 / 70 (5.71%)
occurrences (all)	0	3	5
Hypocalcaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	8 / 70 (11.43%)
occurrences (all)	0	1	10
Hypokalaemia			
subjects affected / exposed	0 / 5 (0.00%)	4 / 7 (57.14%)	15 / 70 (21.43%)
occurrences (all)	0	5	35
Hypomagnesaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	6 / 70 (8.57%)
occurrences (all)	0	0	7
Hyponatraemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	5 / 70 (7.14%)
occurrences (all)	0	0	9
Hypophosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 7 (0.00%)	10 / 70 (14.29%)
occurrences (all)	0	0	15
Tumour lysis syndrome			
subjects affected / exposed	0 / 5 (0.00%)	1 / 7 (14.29%)	0 / 70 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Phase 1: Blinatumomab 15/30 µg/m²/Day	Phase 1: Blinatumomab 30 µg/m²/Day	
Total subjects affected by non-serious adverse events			

subjects affected / exposed	6 / 6 (100.00%)	5 / 5 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Capillary leak syndrome			
subjects affected / exposed	2 / 6 (33.33%)	0 / 5 (0.00%)	
occurrences (all)	4	0	
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hyperaemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	2 / 6 (33.33%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Hypotension			
subjects affected / exposed	2 / 6 (33.33%)	1 / 5 (20.00%)	
occurrences (all)	2	2	
Surgical and medical procedures			
Infusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Oxygen supplementation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Parenteral nutrition			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			

Adverse drug reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Application site scab			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Catheter site haematoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Facial pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	0	2	
Injection site erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Injection site haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Localised oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	

Oedema			
subjects affected / exposed	2 / 6 (33.33%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Oedema peripheral			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Pain			
subjects affected / exposed	3 / 6 (50.00%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Pyrexia			
subjects affected / exposed	4 / 6 (66.67%)	5 / 5 (100.00%)	
occurrences (all)	18	8	
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	2 / 6 (33.33%)	2 / 5 (40.00%)	
occurrences (all)	2	2	
Drug hypersensitivity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	0	2	
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hypoxia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Laryngeal oedema			

subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Lung disorder			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Pneumonia aspiration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Pulmonary oedema			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	3	
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	2	
Confusional state			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Irritability			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	

Personality change			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 6 (33.33%)	2 / 5 (40.00%)	
occurrences (all)	3	2	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 6 (33.33%)	2 / 5 (40.00%)	
occurrences (all)	4	2	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Blood bilirubin increased			
subjects affected / exposed	1 / 6 (16.67%)	3 / 5 (60.00%)	
occurrences (all)	1	3	
Blood creatinine increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	0	2	
Blood fibrinogen decreased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Blood fibrinogen increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Blood immunoglobulin A decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Blood immunoglobulin G decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Blood immunoglobulin M decreased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)		
occurrences (all)	0	0		
Blood lactate dehydrogenase increased				
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)		
occurrences (all)	0	3		
C-reactive protein increased				
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)		
occurrences (all)	0	0		
Cytomegalovirus test positive				
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)		
occurrences (all)	0	0		
Electroencephalogram abnormal				
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)		
occurrences (all)	0	0		
Fibrin D dimer increased				
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)		
occurrences (all)	1	1		
Haemoglobin decreased				
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)		
occurrences (all)	1	0		
International normalised ratio increased				
subjects affected / exposed	2 / 6 (33.33%)	0 / 5 (0.00%)		
occurrences (all)	3	0		
Lymphocyte count decreased				
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)		
occurrences (all)	1	1		
Neutrophil count decreased				
subjects affected / exposed	3 / 6 (50.00%)	2 / 5 (40.00%)		
occurrences (all)	7	4		
Platelet count decreased				
subjects affected / exposed	2 / 6 (33.33%)	1 / 5 (20.00%)		
occurrences (all)	3	1		
Protein total decreased				

subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Roseolovirus test positive			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Urine output decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Weight increased			
subjects affected / exposed	2 / 6 (33.33%)	1 / 5 (20.00%)	
occurrences (all)	2	1	
White blood cell count decreased			
subjects affected / exposed	3 / 6 (50.00%)	2 / 5 (40.00%)	
occurrences (all)	3	2	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Ear abrasion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	2	
Infusion related reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Skin abrasion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Cardiac disorders			

Pericardial effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Sinus bradycardia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 5 (40.00%)	
occurrences (all)	1	2	
Sinus tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Cognitive disorder			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	4	
Dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dysaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dyskinesia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Encephalopathy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Epilepsy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Essential tremor			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	0	10	
Lethargy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Neuralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	2 / 6 (33.33%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 6 (33.33%)	4 / 5 (80.00%)	
occurrences (all)	9	4	
Bone marrow failure			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Coagulopathy			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Febrile neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Hypoglobulinaemia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Leukopenia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 5 (40.00%)	
occurrences (all)	1	4	
Lymphopenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Thrombocytopenia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 5 (40.00%)	
occurrences (all)	2	3	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Eye disorders			
Eyelid haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Eyelid oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Ocular icterus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Photophobia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			

Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Glossodynia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Ileus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Mouth haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	2	
Stomatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	

Vomiting			
subjects affected / exposed	2 / 6 (33.33%)	2 / 5 (40.00%)	
occurrences (all)	5	3	
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hepatic failure			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hepatosplenomegaly			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hepatotoxicity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Dermatitis diaper			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Drug eruption			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Erythema nodosum			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hair growth abnormal			

subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Petechiae			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Rash maculo-papular			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	3	
Skin discolouration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Trichorrhexis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Haematuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Oliguria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Proteinuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Renal failure chronic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	

Renal tubular disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Urinary retention			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	1	2	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Cushingoid			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	0	2	
Bone pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Myopathy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Neck pain			

subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	2 / 6 (33.33%)	2 / 5 (40.00%)	
occurrences (all)	2	4	
Infections and infestations			
Adenovirus infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
BK virus infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Device related infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Enterocolitis infectious			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Legionella infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Lung infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Polyomavirus-associated nephropathy			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Rhinitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Rhinovirus infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Staphylococcal infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Viral myositis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hypernatraemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	

Hyperphosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hyperuricaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hypoalbuminaemia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 5 (0.00%)	
occurrences (all)	4	0	
Hypocalcaemia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Hypokalaemia			
subjects affected / exposed	3 / 6 (50.00%)	0 / 5 (0.00%)	
occurrences (all)	6	0	
Hypomagnesaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hyponatraemia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Hypophosphataemia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Tumour lysis syndrome			
subjects affected / exposed	0 / 6 (0.00%)	2 / 5 (40.00%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 February 2012	•To implement an urgent safety measure because of a case of death due to an invasive fungal infection with fungal thrombus of the basilar artery (in study MT103-206) •To change treatment discontinuation criteria for DLTs and for CNS events not meeting DLT criteria •To remove grade 3 hypotension from definition of DLT •To update safety sections in patient information and ICF in accordance with IB version 13.0
11 July 2012	•To change inclusion/exclusion criteria re upper age limit, previous blinatumomab treatment, subjects in institutions due to juridical or regulatory ruling, treatment-free interval between radiotherapy and blinatumomab •To clarify the impact of laboratory abnormalities in the definition of the DLT •To delete the possibility of intra-subject dose escalation and expansion of dose cohort •To strengthen measures for the prevention of cytokine release syndrome; to clarify that DLTs lead to treatment discontinuation •To add blast-free but hypoplastic or aplastic bone marrow to the hematological response criteria •To implement a lower starting dose during the first week of treatment if DLTs caused by tumor load occurred during the first week. •To allow the possibility of retreatment for subjects suffering hematological relapse of B-precursor ALL during the follow-up period. •To clarify sample size consideration for the phase 2 part of the study •To mention requirements for qualifications of investigators who inform the subjects and their parents, to add information for the inclusion of foreign patients and handling of screening failures •To reflect different conditions for storage and handling of IMP in US and in Europe •To revise timing of assessment of immunogenicity •To update PK/PD information •To implement the possibility of 10% inaccuracy for dosing •To clarify/adapt some protocol mandated assessments/procedures based on current experiences •To implement country-specific requests •To update Appendix 3: DSMB procedures.
03 June 2013	•To implement changes for inclusion/exclusion criteria regarding evidence of ALL, organ functions, and severe infections •To revise early stopping criteria due to adverse events, criteria for subsequent treatment cycles, permanent treatment discontinuation •To revise recommended, mandatory, prohibited pre- and concomitant medications •To clarify definitions of treatment response (term M1 bone marrow) •To update exclusion criteria for retreatment •To update Appendix 3: DSMB procedures. •To extend the flexibility for delay of day 29 until day 42 for the complete visit. •To clarify/adapt some protocol mandated assessments/procedures based on current experiences
23 September 2013	•To modify language regarding recommendations for pre-and concomitant medication •To clarify/adapt some protocol mandated assessments/procedures based on current experiences

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported