Clinical trial results:
An Open Label, Multicenter, Exploratory Phase 2 Study to Evaluate the Efficacy and Safety of the Bispecific T-Cell Engager (BiTE®) Blinatumomab in Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma (DLBCL)

Summary

EudraCT number	2011-005781-38
Trial protocol	DE
Global end of trial date	09 September 2015

Results information

Result version number	v1 (current)
This version publication date	25 September 2016
First version publication date	25 September 2016

Trial information

Trial identification

Sponsor protocol code	MT103-208

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01741792
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)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 September 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to confirm whether the bispecific T-cell engager blinatumomab is effective and safe in the treatment of patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL).

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines, and other regulations, as applicable.
All subjects 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	25 July 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
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	Germany: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	12
From 65 to 84 years	12
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Adults with a diagnosis of diffuse large B-cell lymphoma (DLBCL) which was refractory to first or subsequent treatment or who had a first or later relapse and were not eligible for autologous hematopoietic stem cell transplant (HSCT), or relapsed after autologous HSCT were eligible to enrol. The primary analysis cut-off date was 10 July 2014.

Pre-assignment

Screening details:

The study was conducted sequentially in 2 stages and 3 cohorts: In Stage 1, Cohort 1 received an escalating dose of 9/28/112 µg/day blinatumomab and Cohort 2 received a constant dose of 112 µg/day for 8 weeks. In Stage 2, the Cohort 3 dose regimen was determined from the outcome of Cohorts 1 and 2.

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	Cohort 1: Blinatumomab 9/28/112 µg/d

Arm description:

Participants received blinatumomab administered via a continuous intravenous infusion (CIV) 9 µg/day for the first week, followed by 28 µg/day for the second week, then 112 µg/day for the remaining 6 weeks of treatment during Cycle 1. Participants who achieved a complete response (CR) or partial response (PR), or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.

Arm type	Experimental
Investigational medicinal product name	Blinatumomab
Investigational medicinal product code	MT103
Other name	AMG103, BLINCYTO®
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by continuous intravenous infusion over 8 weeks in the first cycle and 4 weeks in the second cycle.

Arm title	Cohort 2: Blinatumomab 112 µg/d

Arm description:

Participants received blinatumomab administered CIV at a constant dose of 112 µg/day for 8 weeks of treatment during Cycle 1. Participants who achieved a CR or PR, or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.

Arm type	Experimental
Investigational medicinal product name	Blinatumomab
Investigational medicinal product code	MT103
Other name	AMG103, BLINCYTO®
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by continuous intravenous infusion over 8 weeks in the first cycle and 4 weeks in the second cycle.

Arm title	Cohort 3: Blinatumomab 9/28/112 µg/d

Arm description:

Participants received blinatumomab administered CIV 9 µg/day for the first week, followed by 28 µg/day for the second week, then 112 µg/day for the remaining 6 weeks of treatment during Cycle 1. Participants who achieved CR or PR, or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.

Arm type	Experimental
Investigational medicinal product name	Blinatumomab
Investigational medicinal product code	MT103
Other name	AMG103, BLINCYTO®
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by continuous intravenous infusion over 8 weeks in the first cycle and 4 weeks in the second cycle.

Number of subjects in period 1	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d
Started	9	2	14
Efficacy Set	7	1	13
Completed	3	1	2
Not completed	6	1	12
Death	6	1	12

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: Blinatumomab 9/28/112 µg/d
Reporting group description:	
Participants received blinatumomab administered via a continuous intravenous infusion (CIV) 9 µg/day for the first week, followed by 28 µg/day for the second week, then 112 µg/day for the remaining 6 weeks of treatment during Cycle 1. Participants who achieved a complete response (CR) or partial response (PR), or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.	
Reporting group title	Cohort 2: Blinatumomab 112 µg/d
Reporting group description:	
Participants received blinatumomab administered CIV at a constant dose of 112 µg/day for 8 weeks of treatment during Cycle 1. Participants who achieved a CR or PR, or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.	
Reporting group title	Cohort 3: Blinatumomab 9/28/112 µg/d
Reporting group description:	
Participants received blinatumomab administered CIV 9 µg/day for the first week, followed by 28 µg/day for the second week, then 112 µg/day for the remaining 6 weeks of treatment during Cycle 1. Participants who achieved CR or PR, or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.	

Reporting group values	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d
Number of subjects	9	2	14
Age categorical Units: Subjects			
18 - 64 years	2	1	9
65 - 84 years	6	1	5
85 years and over	1	0	0
Age Continuous Units: years			
arithmetic mean	71.7	64.5	57.1
standard deviation	± 7.8	± 13.4	± 13.6
Gender, Male/Female Units: participants			
Female	7	0	4
Male	2	2	10
Race/Ethnicity, Customized Units: Subjects			
White	9	2	14
Relapsed/refractory Status to Last Prior Treatment Units: Subjects			
Relapsed	4	1	4
Refractory	5	1	10
Number of Previous Autologous Hematopoietic Stem Cell Transplants (HSCT) Units: Subjects			
None	7	1	10

≥ 1	2	1	4

Reporting group values	Total		
Number of subjects	25		
Age categorical Units: Subjects			
18 - 64 years	12		
65 - 84 years	12		
85 years and over	1		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender, Male/Female Units: participants			
Female	11		
Male	14		
Race/Ethnicity, Customized Units: Subjects			
White	25		
Relapsed/refractory Status to Last Prior Treatment Units: Subjects			
Relapsed	9		
Refractory	16		
Number of Previous Autologous Hematopoietic Stem Cell Transplants (HSCT) Units: Subjects			
None	18		
≥ 1	7		

End points

End points reporting groups

Reporting group title	Cohort 1: Blinatumomab 9/28/112 µg/d

Reporting group description:

Participants received blinatumomab administered via a continuous intravenous infusion (CIV) 9 µg/day for the first week, followed by 28 µg/day for the second week, then 112 µg/day for the remaining 6 weeks of treatment during Cycle 1. Participants who achieved a complete response (CR) or partial response (PR), or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.

Reporting group title	Cohort 2: Blinatumomab 112 µg/d

Reporting group description:

Participants received blinatumomab administered CIV at a constant dose of 112 µg/day for 8 weeks of treatment during Cycle 1. Participants who achieved a CR or PR, or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.

Reporting group title	Cohort 3: Blinatumomab 9/28/112 µg/d

Reporting group description:

Participants received blinatumomab administered CIV 9 µg/day for the first week, followed by 28 µg/day for the second week, then 112 µg/day for the remaining 6 weeks of treatment during Cycle 1. Participants who achieved CR or PR, or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.

Subject analysis set title	Blinatumomab 9 µg/d
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received blinatumomab administered via a continuous intravenous infusion (CIV) 9 µg/day.

Subject analysis set title	Blinatumomab 28 µg/d
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received blinatumomab CIV 28 µg/day.

Subject analysis set title	Blinatumomab 112 µg/d
Subject analysis set type	Full analysis

Subject analysis set description:

Participants received blinatumomab administered CIV 112 µg/day.

Subject analysis set title	Blinatumomab
Subject analysis set type	Full analysis

Subject analysis set description:

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

Primary: Overall objective response rate during treatment cycle 1

End point title	Overall objective response rate during treatment cycle 1[1]

End point description:

Overall response within the first treatment cycle was assessed according to Cheson criteria by a central reader. Response was evaluated using computerized tomography (CT) scans and positron emission tomography (PET) (to assess nodal disease/organ enlargement due to nodal/diffuse infiltration), and bone marrow biopsy (to assess bone marrow infiltration). Overall objective response rate (ORR) is the percentage of participants with a best overall response of complete response (CR) or partial response (PR).
Complete response is defined as the disappearance of all evidence of disease and partial response is defined as regression of measureable disease and no new sites.
Objective response was analyzed in the Efficacy Set which includes all participants who completed at least 7 days of infusion on the highest intended dose level.

End point type	Primary

End point timeframe:

During the first 8 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Since all subjects received blinatumomab, no statistical comparisons between arms was performed. The null hypothesis was that the response rate for participants with DLBCL treated with blinatumomab was less than 15%; if the lower bound of the 95% CI around the ORR rate was ≥ 15% the null hypothesis was rejected.

End point values	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	1	13	
Units: percentage of participants				
number (confidence interval 95%)	57.1 (18.4 to 90.1)	100 (2.5 to 100)	30.8 (9.1 to 61.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a best overall response of Complete response

End point title	Percentage of participants with a best overall response of Complete response

End point description:

Response within the first treatment cycle was assessed according to Cheson criteria by a central reader. Response was evaluated using computerized tomography (CT) scans and positron emission tomography (PET) (to assess nodal disease/organ enlargement due to nodal/diffuse infiltration), and bone marrow biopsy (to assess bone marrow infiltration). Complete response is defined as the disappearance of all evidence of disease.

End point type	Secondary

End point timeframe:

During the first 8 weeks

End point values	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	1	13	
Units: percentage of participants				
number (confidence interval 95%)	28.6 (3.7 to 71)	0 (0 to 97.5)	15.4 (1.9 to 45.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with a Best overall Response of Partial

response	
End point title	Percentage of participants with a Best overall Response of Partial response

End point description:

Response within the first treatment cycle was assessed according to Cheson criteria by a central reader. Response was evaluated using computerized tomography (CT) scans and positron emission tomography (PET) (to assess nodal disease/organ enlargement due to nodal/diffuse infiltration), and bone marrow biopsy (to assess bone marrow infiltration). Partial response is defined as regression (<50% decrease in size of masses) of measureable disease and no new sites.

End point type	Secondary

End point timeframe:

During the first 8 weeks

End point values	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	1	13	
Units: percentage of participants				
number (confidence interval 95%)	28.6 (3.7 to 71)	100 (2.5 to 100)	15.4 (1.9 to 45.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of objective response	
End point title	Duration of objective response

End point description:

The time from documentation of the first assessment of either partial or complete response until the start of new anti-tumor treatment (excluding any stem cell transplantation), progression of disease, or death, whichever is the earliest event. A patient who did not have new anti-tumor treatment (excluding any stem cell transplantation), progression of disease, or death was censored at last tumor assessment date. Disease progression is defined as any new lesion or increase by ≥ 50% of previously involved sites from nadir.
"99999" indicates data that could not be estimated due to the low number of events.

End point type	Secondary

End point timeframe:

From first infusion of blinatumomab until the end of study; median follow-up time for duration of response was 23.7 months.

End point values	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	1	4	
Units: months				
median (confidence interval 95%)	8.7 (0.9 to	99999 (99999	4 (1.9 to	

99999)	to 99999)	99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of complete response

End point title	Duration of complete response

End point description:

The time from documentation of the first assessment of complete response until the start of new anti-tumor treatment (excluding any stem cell transplantation), progression of disease, or death, whichever is the earliest event. A patient who did not have new anti-tumor treatment (excluding any stem cell transplantation), progression of disease, or death was censored at last tumor assessment date. Disease progression is defined as any new lesion or increase by ≥ 50% of previously involved sites from nadir. "99999" indicates values that could not be estimated due to the low number of events.

End point type	Secondary

End point timeframe:

From first infusion of blinatumomab until the end of study; median follow-up time for duration of response was 23.7 months.

End point values	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	0[2]	2	
Units: months				
median (confidence interval 95%)	99999 (11.6 to 99999)	(to)	99999 (5.9 to 99999)	

Notes:

[2] - No subjects had a complete response

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of partial response

End point title	Duration of partial response

End point description:

The time from documentation of the first assessment of partial response until the start of new anti-tumor treatment (excluding any stem cell transplantation), progression of disease, or death, whichever is the earliest event. A patient who did not have new anti-tumor treatment (excluding any stem cell transplantation), progression of disease, or death was censored at last tumor assessment date. Disease progression is defined as any new lesion or increase by ≥ 50% of previously involved sites from nadir. "99999" indicates values that could not be estimated due to the low number of events.

End point type	Secondary

End point timeframe:

From first infusion of blinatumomab until the end of study; median follow-up time for duration of response was 23.7 months.

End point values	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	2	1	2	
Units: months				
median (confidence interval 95%)	3.3 (0.9 to 5.8)	99999 (99999 to 99999)	2 (1.9 to 2.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)

End point description:

The time from the date of first blinatumomab infusion until the date of diagnosis of progression of lymphoma, the start date of new anti-tumor treatment (excluding any stem cell transplantation) or date of death, whichever is the earliest. Patients alive who did not have progression or new anti-tumor treatment (excluding any stem cell transplantation) were censored at last date of tumor assessment. "99999" indicates values that could not be estimated due to the low number of events.

End point type	Secondary

End point timeframe:

From first infusion of blinatumomab until the end of study; median time on follow-up for PFS was 27.0 months.

End point values	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	1	13	
Units: months				
median (confidence interval 95%)	3.7 (0.7 to 14.1)	99999 (99999 to 99999)	1.6 (0.6 to 4.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

The time from the date of first blinatumomab infusion until death as a result of any cause. Patients still alive were censored on the last documented visit date or the date of the last phone 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.
"99999" indicates values that could not be estimated due to the low number of events.

End point type	Secondary

End point timeframe:

From the first infusion of blinatumomab until the end of study; median time on follow-up for overall survival was 26.6 months.

End point values	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	1	13	
Units: months				
median (confidence interval 95%)	20.1 (2.3 to 99999)	99999 (99999 to 99999)	3.6 (1.5 to 14.8)	

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

End point description:

Adverse events were evaluated for severity according to the grading scale provided in the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 4.0.
An adverse event or suspected adverse drug reaction was considered "serious" if it resulted in one of the following outcomes:
- Resulted in death;
- Was life-threatening;
- Required inpatient hospitalization or prolongation of existing hospitalization;
- Resulted in persistent or significant incapacity or substantial disruption to conduct normal life functions;
- Was a congenital anomaly or birth defect;
- Was a medically important condition.

The Investigator used medical judgment to determine whether there was a causal relationship (ie, related [reasonably possible] or unrelated [not reasonably possible]) between an adverse event and blinatumomab.

End point type	Secondary

End point timeframe:

From the first dose of blinatumomab until up to 30 days after the last dose or until the data cut-off date of 10 July 2014, whichever occurred first; the overall median duration of treatment exposure was 46.8 days.

End point values	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	2	14	
Units: participants				
number (not applicable)				
Any adverse event (AE)	9	2	14	
AE of Grade ≥ 3	9	2	13	
AE of Grade ≥ 4	0	2	6	
Serious adverse event (SAE)	9	2	12	
Fatal adverse events	0	0	2	
Led to discontinuation of study drug	3	1	2	
Led to interruption of study drug	4	1	6	
Related adverse events	9	2	11	
Related AE Grade ≥ 3	5	2	5	
Related AE Grade ≥ 4	0	1	2	
Serious related adverse events	5	2	3	
Related AE led to discontinuation of study drug	2	1	2	
Related AE led to interruption of study drug	3	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Blinatumomab steady state serum concentration

End point title	Blinatumomab steady state serum concentration

End point description:

Blinatumomab serum levels were analyzed using a validated cluster of differentiation (CD)69 activation bioassay with a lower limit of quantification (LLOQ) of 50 pg/mL. Steady-state concentration (Css) was based on actual dose received, rather than based on cohort or time or day.
Analyses were performed n the Pharmacokinetic (PK) data set which includes all participants who received any infusion of blinatumomab and had at least one PK sample collected.

End point type	Secondary

End point timeframe:

Cycle 1: predose; Day 3 and Day 8 (Css for 9 ug/day); Day 15 (Css for 28 ug/day); and Day 29, Day 43 and Day 57 (Css for 112 ug/day)

End point values	Blinatumomab 9 µg/d	Blinatumomab 28 µg/d	Blinatumomab 112 µg/d	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	20	16	12	
Units: pg/mL				
arithmetic mean (standard deviation)	277 (± 210)	565 (± 208)	2800 (± 1150)	

Statistical analyses

No statistical analyses for this end point

Secondary: Leukocyte Counts

End point title	Leukocyte Counts

End point description:

Leukocyte (white blood cells) counts were analyzed by differential blood count analysis.
The analysis Population for all pharmacodynamic endpoints includes enrolled participants with available data at each time point. All participants are included in pre-infusion and follow-up data points, only those participants in Cohorts 1 and 3 who had the same treatment schedule of 9/28/112 µg/day step dosing are included in the infusion time points (day 8 through end of infusion).

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	6.376 (± 3.284)			
Day 1 Prior (N = 24)	5.729 (± 2.891)			
Day 8 (N = 21)	6.819 (± 3.201)			
Day 15 (N = 16)	6.4 (± 2.486)			
Day 29 (N = 11)	3.764 (± 2.16)			
Day 43 (N = 8)	4.95 (± 3.819)			
End of Infusion (N = 9)	4.611 (± 2.114)			
End of Core Study (N = 6)	6.85 (± 2.818)			
3-Month Follow-up (N = 5)	4.82 (± 1.616)			
6-Month Follow-up (N = 6)	5.183 (± 1.38)			
9-Month Follow-up (N = 4)	4.425 (± 0.854)			
12-Month Follow-up (N = 4)	5.7 (± 1.424)			
15-Month Follow-up (N = 3)	4.767 (± 0.874)			
18-Month Follow-up (N = 3)	6.467 (± 1.779)			
21-Month Follow-up (N = 21)	5.45 (± 0.495)			
24-Month Follow-up (N = 3)	4.533 (± 1.069)			

Statistical analyses

No statistical analyses for this end point

Secondary: Lymphocyte Counts

End point title	Lymphocyte Counts

End point description:

Lymphocyte counts were analyzed by differential blood count analysis.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.779 (± 0.425)			
Day 1 Prior (N = 24)	0.491 (± 0.259)			
Day 8 (N = 21)	0.382 (± 0.215)			
Day 15 (N = 16)	0.277 (± 0.165)			
Day 29 (N = 11)	0.472 (± 0.273)			
Day 43 (N = 8)	0.847 (± 0.511)			
End of Infusion (N = 9)	0.767 (± 0.505)			
End of Core Study (N = 6)	1.06 (± 0.489)			
3-Month Follow-up (N = 5)	1.053 (± 0.421)			
6-Month Follow-up (N = 6)	1.12 (± 0.621)			
9-Month Follow-up (N = 4)	1.048 (± 0.381)			
12-Month Follow-up (N = 4)	1.12 (± 0.449)			
15-Month Follow-up (N = 3)	0.998 (± 0.527)			
18-Month Follow-up (N = 3)	0.565 (± 0.18)			
21-Month Follow-up (N = 21)	1.205 (± 0.839)			
24-Month Follow-up (N = 3)	0.737 (± 0.478)			

Statistical analyses

No statistical analyses for this end point

Secondary: Monocyte Counts

End point title	Monocyte Counts

End point description:

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.638 (± 0.415)			
Day 1 Prior (N = 24)	0.3 (± 0.565)			
Day 8 (N = 21)	0.202 (± 0.386)			
Day 15 (N = 16)	0.188 (± 0.317)			
Day 29 (N = 11)	0.318 (± 0.185)			
Day 43 (N = 8)	0.646 (± 0.375)			
End of Infusion (N = 9)	0.473 (± 0.241)			
End of Core Study (N = 6)	0.711 (± 0.569)			
3-Month Follow-up (N = 5)	0.585 (± 0.28)			
6-Month Follow-up (N = 6)	0.487 (± 0.239)			
9-Month Follow-up (N = 4)	0.452 (± 0.112)			
12-Month Follow-up (N = 4)	0.469 (± 0.061)			
15-Month Follow-up (N = 3)	0.511 (± 0.053)			
18-Month Follow-up (N = 3)	0.29 (± 0.123)			
21-Month Follow-up (N = 21)	0.516 (± 0.008)			
24-Month Follow-up (N = 3)	0.234 (± 0.176)			

Statistical analyses

No statistical analyses for this end point

Secondary: Granulocyte Count

End point title	Granulocyte Count

End point description:

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	4.968 (± 3.187)			
Day 1 Prior (N = 24)	4.91 (± 2.425)			
Day 8 (N = 21)	6.235 (± 2.881)			
Day 15 (N = 16)	5.935 (± 2.387)			
Day 29 (N = 11)	2.974 (± 2.019)			
Day 43 (N = 8)	3.457 (± 3.395)			
End of Infusion (N = 9)	3.353 (± 2.134)			
End of Core Study (N = 6)	5.08 (± 3.012)			
3-Month Follow-up (N = 5)	3.182 (± 1.117)			
6-Month Follow-up (N = 6)	3.594 (± 0.95)			
9-Month Follow-up (N = 4)	2.925 (± 0.675)			
12-Month Follow-up (N = 4)	4.111 (± 1.382)			
15-Month Follow-up (N = 3)	3.258 (± 0.745)			
18-Month Follow-up (N = 3)	5.612 (± 1.713)			
21-Month Follow-up (N = 21)	3.729 (± 0.352)			
24-Month Follow-up (N = 3)	3.563 (± 0.711)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD19+ B-Cell Count

End point title	CD19+ B-Cell Count

End point description:

CD19+ B-cell counts were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.026 (± 0.072)			
Day 1 Prior (N = 24)	0.029 (± 0.085)			
Day 8 (N = 21)	0.001 (± 0.002)			
Day 15 (N = 16)	0 (± 0.001)			
Day 29 (N = 11)	0 (± 0)			
Day 43 (N = 8)	0 (± 0.001)			
End of Infusion (N = 9)	0.001 (± 0.001)			
End of Core Study (N = 6)	0.001 (± 0.002)			
3-Month Follow-up (N = 5)	0.025 (± 0.026)			
6-Month Follow-up (N = 6)	0.029 (± 0.043)			
9-Month Follow-up (N = 4)	0.054 (± 0.066)			
12-Month Follow-up (N = 4)	0.082 (± 0.113)			
15-Month Follow-up (N = 3)	0.094 (± 0.118)			
18-Month Follow-up (N = 3)	0.071 (± 0.075)			
21-Month Follow-up (N = 21)	0.131 (± 0.17)			
24-Month Follow-up (N = 3)	0.108 (± 0.12)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD19+ B-Cells as a Percentage of All Lymphocytes

End point title	CD19+ B-Cells as a Percentage of All Lymphocytes

End point description:

CD19+ B-cell counts were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of

core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: percentage of lymphocytes				
arithmetic mean (standard deviation)				
Screening (N = 25)	2 (± 7)			
Day 1 Prior (N = 24)	4 (± 9)			
Day 8 (N = 21)	0 (± 0)			
Day 15 (N = 16)	0 (± 0)			
Day 29 (N = 11)	0 (± 0)			
Day 43 (N = 8)	0 (± 0)			
End of Infusion (N = 9)	0 (± 0)			
End of Core Study (N = 6)	0 (± 0)			
3-Month Follow-up (N = 5)	2 (± 2)			
6-Month Follow-up (N = 6)	2 (± 3)			
9-Month Follow-up (N = 4)	5 (± 5)			
12-Month Follow-up (N = 4)	7 (± 9)			
15-Month Follow-up (N = 3)	7 (± 7)			
18-Month Follow-up (N = 3)	11 (± 9)			
21-Month Follow-up (N = 21)	8 (± 8)			
24-Month Follow-up (N = 3)	12 (± 7)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD3+ T-Cell Count

End point title	CD3+ T-Cell Count

End point description:

CD3+ T-cell counts were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.578 (± 0.355)			
Day 1 Prior (N = 24)	0.349 (± 0.233)			
Day 8 (N = 21)	0.282 (± 0.194)			
Day 15 (N = 16)	0.199 (± 0.159)			
Day 29 (N = 11)	0.348 (± 0.231)			
Day 43 (N = 8)	0.613 (± 0.426)			
End of Infusion (N = 9)	0.543 (± 0.421)			
End of Core Study (N = 6)	0.825 (± 0.431)			
3-Month Follow-up (N = 5)	0.773 (± 0.443)			
6-Month Follow-up (N = 6)	0.782 (± 0.345)			
9-Month Follow-up (N = 4)	0.671 (± 0.184)			
12-Month Follow-up (N = 4)	0.703 (± 0.203)			
15-Month Follow-up (N = 3)	0.594 (± 0.227)			
18-Month Follow-up (N = 3)	0.298 (± 0.049)			
21-Month Follow-up (N = 21)	0.623 (± 0.266)			
24-Month Follow-up (N = 3)	0.456 (± 0.257)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD3+ T-Cells as a Percentage of All Lymphocytes

End point title	CD3+ T-Cells as a Percentage of All Lymphocytes

End point description:

CD3+ T-cell counts were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: percentage of lymphocytes				
arithmetic mean (standard deviation)				
Screening (N = 25)	72 (± 14)			
Day 1 Prior (N = 24)	68 (± 18)			
Day 8 (N = 21)	70 (± 19)			
Day 15 (N = 16)	67 (± 19)			
Day 29 (N = 11)	73 (± 15)			
Day 43 (N = 8)	71 (± 13)			
End of Infusion (N = 9)	66 (± 14)			
End of Core Study (N = 6)	76 (± 16)			
3-Month Follow-up (N = 5)	73 (± 11)			
6-Month Follow-up (N = 6)	66 (± 21)			
9-Month Follow-up (N = 4)	66 (± 6)			
12-Month Follow-up (N = 4)	65 (± 9)			
15-Month Follow-up (N = 3)	61 (± 7)			
18-Month Follow-up (N = 3)	57 (± 20)			
21-Month Follow-up (N = 21)	58 (± 16)			
24-Month Follow-up (N = 3)	63 (± 8)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD4+ T-Cell Count

End point title	CD4+ T-Cell Count

End point description:

CD4+ T-cell counts were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.254 (± 0.16)			
Day 1 Prior (N = 24)	0.152 (± 0.128)			
Day 8 (N = 21)	0.131 (± 0.128)			

Day 15 (N = 16)	0.085 (± 0.084)			
Day 29 (N = 11)	0.17 (± 0.172)			
Day 43 (N = 8)	0.261 (± 0.219)			
End of Infusion (N = 9)	0.241 (± 0.254)			
End of Core Study (N = 6)	0.375 (± 0.251)			
3-Month Follow-up (N = 5)	0.371 (± 0.216)			
6-Month Follow-up (N = 6)	0.371 (± 0.237)			
9-Month Follow-up (N = 4)	0.309 (± 0.184)			
12-Month Follow-up (N = 4)	0.399 (± 0.193)			
15-Month Follow-up (N = 3)	0.326 (± 0.22)			
18-Month Follow-up (N = 3)	0.178 (± 0.042)			
21-Month Follow-up (N = 21)	0.373 (± 0.279)			
24-Month Follow-up (N = 3)	0.258 (± 0.248)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD4+ T-Cells as a Percentage of All Lymphocytes

End point title	CD4+ T-Cells as a Percentage of All Lymphocytes

End point description:

CD4+ T-cell counts were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: percentage of lymphocytes				
arithmetic mean (standard deviation)				
Screening (N = 25)	33 (± 11)			
Day 1 Prior (N = 24)	28 (± 14)			
Day 8 (N = 21)	32 (± 17)			
Day 15 (N = 16)	29 (± 13)			
Day 29 (N = 11)	34 (± 18)			
Day 43 (N = 8)	30 (± 12)			

End of Infusion (N = 9)	28 (± 13)			
End of Core Study (N = 6)	32 (± 15)			
3-Month Follow-up (N = 5)	33 (± 9)			
6-Month Follow-up (N = 6)	30 (± 10)			
9-Month Follow-up (N = 4)	31 (± 13)			
12-Month Follow-up (N = 4)	35 (± 7)			
15-Month Follow-up (N = 3)	31 (± 7)			
18-Month Follow-up (N = 3)	32 (± 6)			
21-Month Follow-up (N = 21)	29 (± 4)			
24-Month Follow-up (N = 3)	34 (± 8)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD8+ T-Cell Count

End point title	CD8+ T-Cell Count

End point description:

CD8+ T-cell counts were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.298 (± 0.256)			
Day 1 Prior (N = 24)	0.186 (± 0.136)			
Day 8 (N = 21)	0.134 (± 0.099)			
Day 15 (N = 16)	0.102 (± 0.095)			
Day 29 (N = 11)	0.14 (± 0.076)			
Day 43 (N = 8)	0.299 (± 0.237)			
End of Infusion (N = 9)	0.284 (± 0.195)			
End of Core Study (N = 6)	0.438 (± 0.284)			
3-Month Follow-up (N = 5)	0.381 (± 0.254)			
6-Month Follow-up (N = 6)	0.403 (± 0.304)			

9-Month Follow-up (N = 4)	0.225 (± 0.039)			
12-Month Follow-up (N = 4)	0.31 (± 0.2)			
15-Month Follow-up (N = 3)	0.214 (± 0.023)			
18-Month Follow-up (N = 3)	0.105 (± 0.057)			
21-Month Follow-up (N = 21)	0.185 (± 0.026)			
24-Month Follow-up (N = 3)	0.187 (± 0.068)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD8+ T-Cells as a Percentage of All Lymphocytes

End point title	CD8+ T-Cells as a Percentage of All Lymphocytes

End point description:

CD8+ T-cell counts were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: percentage of lymphocytes				
arithmetic mean (standard deviation)				
Screening (N = 25)	37 (± 18)			
Day 1 Prior (N = 24)	37 (± 19)			
Day 8 (N = 21)	35 (± 19)			
Day 15 (N = 16)	35 (± 17)			
Day 29 (N = 11)	33 (± 17)			
Day 43 (N = 8)	37 (± 15)			
End of Infusion (N = 9)	36 (± 16)			
End of Core Study (N = 6)	43 (± 23)			
3-Month Follow-up (N = 5)	36 (± 19)			
6-Month Follow-up (N = 6)	34 (± 16)			
9-Month Follow-up (N = 4)	25 (± 11)			
12-Month Follow-up (N = 4)	28 (± 13)			
15-Month Follow-up (N = 3)	24 (± 9)			
18-Month Follow-up (N = 3)	21 (± 13)			
21-Month Follow-up (N = 21)	20 (± 12)			
24-Month Follow-up (N = 3)	27 (± 16)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD19+ B-Cell to CD3+ T-Cell Ratio

End point title	CD19+ B-Cell to CD3+ T-Cell Ratio

End point description:

CD19+ B-cells and CD3+ T-cell counts were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: ratio				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.04 (± 0.15)			
Day 1 Prior (N = 24)	0.07 (± 0.24)			
Day 8 (N = 21)	0 (± 0.01)			
Day 15 (N = 16)	0 (± 0)			
Day 29 (N = 11)	0 (± 0)			
Day 43 (N = 8)	0 (± 0)			
End of Infusion (N = 9)	0 (± 0.01)			
End of Core Study (N = 6)	0 (± 0)			
3-Month Follow-up (N = 5)	0.03 (± 0.03)			
6-Month Follow-up (N = 6)	0.04 (± 0.05)			
9-Month Follow-up (N = 4)	0.08 (± 0.08)			
12-Month Follow-up (N = 4)	0.12 (± 0.15)			
15-Month Follow-up (N = 3)	0.13 (± 0.13)			
18-Month Follow-up (N = 3)	0.25 (± 0.3)			
21-Month Follow-up (N = 21)	0.17 (± 0.2)			
24-Month Follow-up (N = 3)	0.19 (± 0.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD4+ T-Cell to CD8+ T-Cell Ratio

End point title	CD4+ T-Cell to CD8+ T-Cell Ratio

End point description:

CD4+ T-cells and CD8+ T-cell counts were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: ratio				
arithmetic mean (standard deviation)				
Screening (N = 25)	1.32 (± 1.19)			
Day 1 Prior (N = 24)	1.16 (± 1.45)			
Day 8 (N = 21)	1.2 (± 0.96)			
Day 15 (N = 16)	1.03 (± 0.71)			
Day 29 (N = 11)	1.43 (± 1.08)			
Day 43 (N = 8)	0.96 (± 0.53)			
End of Infusion (N = 9)	1.09 (± 1)			
End of Core Study (N = 6)	1.03 (± 0.8)			
3-Month Follow-up (N = 5)	1.18 (± 0.79)			
6-Month Follow-up (N = 6)	1.1 (± 0.7)			
9-Month Follow-up (N = 4)	1.53 (± 1.25)			
12-Month Follow-up (N = 4)	1.7 (± 1.47)			
15-Month Follow-up (N = 3)	1.47 (± 0.81)			
18-Month Follow-up (N = 3)	2.23 (± 1.7)			
21-Month Follow-up (N = 21)	1.85 (± 1.34)			
24-Month Follow-up (N = 3)	1.73 (± 1.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD4+ Naive T Cell Count

End point title	CD4+ Naive T Cell Count

End point description:

CD4+ naive T-cell counts are native T-cells characterized by the cell-surface expression of CD197 and CD45RA and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.028 (± 0.056)			
Day 1 Prior (N = 24)	0.013 (± 0.022)			
Day 8 (N = 21)	0.014 (± 0.033)			
Day 15 (N = 16)	0.012 (± 0.024)			
Day 29 (N = 11)	0.032 (± 0.071)			
Day 43 (N = 8)	0.036 (± 0.06)			
End of Infusion (N = 9)	0.037 (± 0.088)			
End of Core Study (N = 6)	0.05 (± 0.083)			
3-Month Follow-up (N = 5)	0.015 (± 0.019)			
6-Month Follow-up (N = 6)	0.023 (± 0.044)			
9-Month Follow-up (N = 4)	0.053 (± 0.09)			
12-Month Follow-up (N = 4)	0.053 (± 0.084)			
15-Month Follow-up (N = 3)	0.044 (± 0.059)			
18-Month Follow-up (N = 3)	0.035 (± 0.041)			
21-Month Follow-up (N = 21)	0.098 (± 0.103)			
24-Month Follow-up (N = 3)	0.016 (± 0.013)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD4+ Naive T Cells as a Percentage of All CD4+ T-Cells

End point title	CD4+ Naive T Cells as a Percentage of All CD4+ T-Cells

End point description:

CD4+ naive T-cell counts are native T-cells characterized by the cell-surface expression of CD197 and CD45RA and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: percentage of CD4+ T-cells				
arithmetic mean (standard deviation)				
Screening (N = 25)	8 (± 9)			
Day 1 Prior (N = 24)	7 (± 7)			
Day 8 (N = 21)	7 (± 7)			
Day 15 (N = 16)	10 (± 9)			
Day 29 (N = 11)	9 (± 11)			
Day 43 (N = 8)	10 (± 10)			
End of Infusion (N = 9)	8 (± 9)			
End of Core Study (N = 6)	9 (± 13)			
3-Month Follow-up (N = 5)	4 (± 3)			
6-Month Follow-up (N = 6)	4 (± 7)			
9-Month Follow-up (N = 4)	11 (± 15)			
12-Month Follow-up (N = 4)	12 (± 14)			
15-Month Follow-up (N = 3)	10 (± 9)			
18-Month Follow-up (N = 3)	19 (± 19)			
21-Month Follow-up (N = 21)	23 (± 9)			
24-Month Follow-up (N = 3)	8 (± 10)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD4+ Central Memory T-Cell (TCM) Count

End point title	CD4+ Central Memory T-Cell (TCM) Count

End point description:

Central memory T cells are characterized by the cell-surface expression of CD197 but not CD45RA and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.048 (± 0.053)			
Day 1 Prior (N = 24)	0.029 (± 0.034)			
Day 8 (N = 21)	0.027 (± 0.042)			
Day 15 (N = 16)	0.014 (± 0.025)			
Day 29 (N = 11)	0.032 (± 0.065)			
Day 43 (N = 8)	0.032 (± 0.035)			
End of Infusion (N = 9)	0.049 (± 0.103)			
End of Core Study (N = 6)	0.062 (± 0.075)			
3-Month Follow-up (N = 5)	0.019 (± 0.009)			
6-Month Follow-up (N = 6)	0.027 (± 0.02)			
9-Month Follow-up (N = 4)	0.043 (± 0.056)			
12-Month Follow-up (N = 4)	0.065 (± 0.073)			
15-Month Follow-up (N = 3)	0.039 (± 0.02)			
18-Month Follow-up (N = 3)	0.033 (± 0.031)			
21-Month Follow-up (N = 21)	0.056 (± 0.054)			
24-Month Follow-up (N = 3)	0.021 (± 0.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD4+ TCM Cells as a Percentage of All CD4+ T-Cells

End point title	CD4+ TCM Cells as a Percentage of All CD4+ T-Cells

End point description:

Central memory T cells are characterized by the cell-surface expression of CD197 but not CD45RA and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: percentage of CD4+ T-cells				
arithmetic mean (standard deviation)				
Screening (N = 25)	18 (± 12)			
Day 1 Prior (N = 24)	20 (± 15)			
Day 8 (N = 21)	19 (± 15)			
Day 15 (N = 16)	14 (± 12)			
Day 29 (N = 11)	13 (± 10)			
Day 43 (N = 8)	13 (± 9)			
End of Infusion (N = 9)	15 (± 11)			
End of Core Study (N = 6)	14 (± 11)			
3-Month Follow-up (N = 5)	6 (± 3)			
6-Month Follow-up (N = 6)	9 (± 4)			
9-Month Follow-up (N = 4)	11 (± 9)			
12-Month Follow-up (N = 4)	18 (± 16)			
15-Month Follow-up (N = 3)	13 (± 6)			
18-Month Follow-up (N = 3)	18 (± 14)			
21-Month Follow-up (N = 21)	14 (± 4)			
24-Month Follow-up (N = 3)	12 (± 11)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD4+ Effector Memory T-Cell (TEM) Count

End point title	CD4+ Effector Memory T-Cell (TEM) Count

End point description:

Effector memory T cells are characterized by the lack of expression of CD197 and CD45RA and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.161 (± 0.089)			
Day 1 Prior (N = 24)	0.099 (± 0.096)			

Day 8 (N = 21)	0.083 (± 0.076)			
Day 15 (N = 16)	0.051 (± 0.044)			
Day 29 (N = 11)	0.097 (± 0.059)			
Day 43 (N = 8)	0.169 (± 0.117)			
End of Infusion (N = 9)	0.14 (± 0.091)			
End of Core Study (N = 6)	0.22 (± 0.142)			
3-Month Follow-up (N = 5)	0.279 (± 0.153)			
6-Month Follow-up (N = 6)	0.267 (± 0.158)			
9-Month Follow-up (N = 4)	0.191 (± 0.037)			
12-Month Follow-up (N = 4)	0.226 (± 0.1)			
15-Month Follow-up (N = 3)	0.199 (± 0.087)			
18-Month Follow-up (N = 3)	0.106 (± 0.066)			
21-Month Follow-up (N = 21)	0.181 (± 0.107)			
24-Month Follow-up (N = 3)	0.175 (± 0.133)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD4+ TEM Cells as a Percentage of All CD4+ T-Cells

End point title	CD4+ TEM Cells as a Percentage of All CD4+ T-Cells

End point description:

Effector memory T cells are characterized by the lack of expression of CD197 and CD45RA and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: percentage of CD4+ T-cells				
arithmetic mean (standard deviation)				
Screening (N = 25)	41 (± 19)			
Day 1 Prior (N = 24)	39 (± 19)			
Day 8 (N = 21)	36 (± 19)			
Day 15 (N = 16)	46 (± 17)			
Day 29 (N = 11)	34 (± 20)			

Day 43 (N = 8)	39 (± 26)			
End of Infusion (N = 9)	41 (± 24)			
End of Core Study (N = 6)	41 (± 24)			
3-Month Follow-up (N = 5)	46 (± 26)			
6-Month Follow-up (N = 6)	41 (± 21)			
9-Month Follow-up (N = 4)	42 (± 18)			
12-Month Follow-up (N = 4)	40 (± 15)			
15-Month Follow-up (N = 3)	46 (± 17)			
18-Month Follow-up (N = 3)	43 (± 12)			
21-Month Follow-up (N = 21)	45 (± 3)			
24-Month Follow-up (N = 3)	51 (± 22)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD8+ Naive T-Cell Count

End point title	CD8+ Naive T-Cell Count

End point description:

CD8+ naive T-cell counts are native T-cells characterized by the cell-surface expression of CD197 and CD45RA and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.029 (± 0.043)			
Day 1 Prior (N = 24)	0.024 (± 0.05)			
Day 8 (N = 21)	0.01 (± 0.012)			
Day 15 (N = 16)	0.006 (± 0.005)			
Day 29 (N = 11)	0.012 (± 0.014)			
Day 43 (N = 8)	0.019 (± 0.036)			
End of Infusion (N = 9)	0.011 (± 0.015)			
End of Core Study (N = 6)	0.023 (± 0.018)			
3-Month Follow-up (N = 5)	0.011 (± 0.007)			
6-Month Follow-up (N = 6)	0.02 (± 0.022)			

9-Month Follow-up (N = 4)	0.011 (± 0.012)			
12-Month Follow-up (N = 4)	0.011 (± 0.009)			
15-Month Follow-up (N = 3)	0.014 (± 0.011)			
18-Month Follow-up (N = 3)	0.007 (± 0.008)			
21-Month Follow-up (N = 21)	0.015 (± 0.006)			
24-Month Follow-up (N = 3)	0.01 (± 0.009)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD8+ Naive T-Cells as a Percentage of All CD8+ T-Cells

End point title	CD8+ Naive T-Cells as a Percentage of All CD8+ T-Cells

End point description:

CD8+ naive T-cell counts are native T-cells characterized by the cell-surface expression of CD197 and CD45RA and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: percentage of CD8+ T-cells				
arithmetic mean (standard deviation)				
Screening (N = 25)	10 (± 10)			
Day 1 Prior (N = 24)	12 (± 13)			
Day 8 (N = 21)	9 (± 8)			
Day 15 (N = 16)	8 (± 7)			
Day 29 (N = 11)	8 (± 7)			
Day 43 (N = 8)	6 (± 7)			
End of Infusion (N = 9)	3 (± 3)			
End of Core Study (N = 6)	6 (± 6)			
3-Month Follow-up (N = 5)	4 (± 4)			
6-Month Follow-up (N = 6)	5 (± 5)			
9-Month Follow-up (N = 4)	6 (± 7)			
12-Month Follow-up (N = 4)	6 (± 6)			
15-Month Follow-up (N = 3)	6 (± 5)			
18-Month Follow-up (N = 3)	10 (± 8)			
21-Month Follow-up (N = 21)	8 (± 4)			
24-Month Follow-up (N = 3)	10 (± 12)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD8+ TCM Cell Counts

End point title	CD8+ TCM Cell Counts

End point description:

Central memory T cells are characterized by the cell-surface expression of CD197 but not CD45RA and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 100 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.02 (± 0.027)			
Day 1 Prior (N = 24)	0.014 (± 0.021)			
Day 8 (N = 21)	0.01 (± 0.013)			
Day 15 (N = 16)	0.004 (± 0.005)			
Day 29 (N = 11)	0.007 (± 0.007)			
Day 43 (N = 8)	0.012 (± 0.015)			
End of Infusion (N = 9)	0.009 (± 0.009)			
End of Core Study (N = 6)	0.016 (± 0.023)			
3-Month Follow-up (N = 5)	0.008 (± 0.003)			
6-Month Follow-up (N = 6)	0.016 (± 0.014)			
9-Month Follow-up (N = 4)	0.006 (± 0.004)			
12-Month Follow-up (N = 4)	0.01 (± 0.01)			
15-Month Follow-up (N = 3)	0.004 (± 0.002)			
18-Month Follow-up (N = 3)	0.002 (± 0.001)			
21-Month Follow-up (N = 21)	0.002 (± 0.001)			

24-Month Follow-up (N = 3)	0.006 (± 0.004)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD8+ TCM Cells as a Percentage of All CD8+ T-Cells

End point title	CD8+ TCM Cells as a Percentage of All CD8+ T-Cells

End point description:

Central memory T cells are characterized by the cell-surface expression of CD197 but not CD45RA and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: percentage of CD8+ T-cells				
arithmetic mean (standard deviation)				
Screening (N = 25)	7 (± 7)			
Day 1 Prior (N = 24)	8 (± 11)			
Day 8 (N = 21)	10 (± 13)			
Day 15 (N = 16)	4 (± 5)			
Day 29 (N = 11)	7 (± 10)			
Day 43 (N = 8)	9 (± 18)			
End of Infusion (N = 9)	5 (± 6)			
End of Core Study (N = 6)	5 (± 8)			
3-Month Follow-up (N = 5)	3 (± 2)			
6-Month Follow-up (N = 6)	4 (± 3)			
9-Month Follow-up (N = 4)	3 (± 2)			
12-Month Follow-up (N = 4)	3 (± 3)			
15-Month Follow-up (N = 3)	2 (± 1)			
18-Month Follow-up (N = 3)	2 (± 1)			
21-Month Follow-up (N = 21)	1 (± 0)			
24-Month Follow-up (N = 3)	6 (± 8)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD8+ Effector Memory T-Cell (TEM) Count

End point title	CD8+ Effector Memory T-Cell (TEM) Count

End point description:

Effector memory T cells are characterized by the lack of expression of CD197 and CD45RA and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.127 (± 0.162)			
Day 1 Prior (N = 24)	0.075 (± 0.066)			
Day 8 (N = 21)	0.065 (± 0.058)			
Day 15 (N = 16)	0.045 (± 0.053)			
Day 29 (N = 11)	0.067 (± 0.039)			
Day 43 (N = 8)	0.135 (± 0.108)			
End of Infusion (N = 9)	0.128 (± 0.077)			
End of Core Study (N = 6)	0.18 (± 0.089)			
3-Month Follow-up (N = 5)	0.146 (± 0.071)			
6-Month Follow-up (N = 6)	0.179 (± 0.158)			
9-Month Follow-up (N = 4)	0.116 (± 0.061)			
12-Month Follow-up (N = 4)	0.174 (± 0.162)			
15-Month Follow-up (N = 3)	0.095 (± 0.025)			
18-Month Follow-up (N = 3)	0.049 (± 0.027)			
21-Month Follow-up (N = 21)	0.085 (± 0.013)			
24-Month Follow-up (N = 3)	0.054 (± 0.027)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD8+ TEM Cells as a Percentage of All CD8+ T-Cells

End point title	CD8+ TEM Cells as a Percentage of All CD8+ T-Cells

End point description:

Effector memory T cells are characterized by the lack of expression of CD197 and CD45RA and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: percentage of CD8+ T-cells				
arithmetic mean (standard deviation)				
Screening (N = 25)	42 (± 19)			
Day 1 Prior (N = 24)	42 (± 17)			
Day 8 (N = 21)	46 (± 18)			
Day 15 (N = 16)	43 (± 13)			
Day 29 (N = 11)	51 (± 19)			
Day 43 (N = 8)	46 (± 23)			
End of Infusion (N = 9)	51 (± 21)			
End of Core Study (N = 6)	49 (± 22)			
3-Month Follow-up (N = 5)	47 (± 23)			
6-Month Follow-up (N = 6)	50 (± 24)			
9-Month Follow-up (N = 4)	50 (± 21)			
12-Month Follow-up (N = 4)	51 (± 13)			
15-Month Follow-up (N = 3)	46 (± 15)			
18-Month Follow-up (N = 3)	46 (± 7)			
21-Month Follow-up (N = 21)	46 (± 1)			
24-Month Follow-up (N = 3)	33 (± 9)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD8+ Terminally Differentiated Effector Memory T-cells (TEMRA) Count

End point title	CD8+ Terminally Differentiated Effector Memory T-cells (TEMRA) Count

End point description:

Terminally differentiated effector memory T cells are characterized by the cell-surface expression of CD45RA but not CD197 and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: 1000 cells/µL				
arithmetic mean (standard deviation)				
Screening (N = 25)	0.123 (± 0.099)			
Day 1 Prior (N = 24)	0.072 (± 0.069)			
Day 8 (N = 21)	0.051 (± 0.042)			
Day 15 (N = 16)	0.047 (± 0.048)			
Day 29 (N = 11)	0.058 (± 0.05)			
Day 43 (N = 8)	0.132 (± 0.126)			
End of Infusion (N = 9)	0.135 (± 0.131)			
End of Core Study (N = 6)	0.226 (± 0.249)			
3-Month Follow-up (N = 5)	0.214 (± 0.22)			
6-Month Follow-up (N = 6)	0.187 (± 0.182)			
9-Month Follow-up (N = 4)	0.094 (± 0.046)			
12-Month Follow-up (N = 4)	0.117 (± 0.065)			
15-Month Follow-up (N = 3)	0.099 (± 0.041)			
18-Month Follow-up (N = 3)	0.047 (± 0.035)			
21-Month Follow-up (N = 21)	0.086 (± 0.016)			
24-Month Follow-up (N = 3)	0.1 (± 0.084)			

Statistical analyses

No statistical analyses for this end point

Secondary: CD8+ TEMRA Cells as a Percentage of All CD8+ T-Cells

End point title	CD8+ TEMRA Cells as a Percentage of All CD8+ T-Cells

End point description:

Terminally differentiated effector memory T cells are characterized by the cell-surface expression of CD45RA but not CD197 and were analyzed by flow cytometry.

End point type	Secondary

End point timeframe:

Screening (Day -20 to Day 0), Day 1 pre-infusion, Days 8, 15, 29, 43, end of infusion (day 53), end of core study (day 87), and follow-up at 3, 6, 9, 12, 15, 18, 21 and 24 months after the first response assessment

End point values	Blinatumomab			
Subject group type	Subject analysis set			
Number of subjects analysed	25			
Units: percentage of CD8+ T-cells				
arithmetic mean (standard deviation)				
Screening (N = 25)	41 (± 19)			
Day 1 Prior (N = 24)	39 (± 19)			
Day 8 (N = 21)	36 (± 19)			
Day 15 (N = 16)	46 (± 17)			
Day 29 (N = 11)	34 (± 20)			
Day 43 (N = 8)	39 (± 26)			
End of Infusion (N = 9)	41 (± 24)			
End of Core Study (N = 6)	41 (± 24)			
3-Month Follow-up (N = 5)	46 (± 26)			
6-Month Follow-up (N = 6)	41 (± 21)			
9-Month Follow-up (N = 4)	42 (± 18)			
12-Month Follow-up (N = 4)	40 (± 15)			
15-Month Follow-up (N = 3)	46 (± 17)			
18-Month Follow-up (N = 3)	43 (± 12)			
21-Month Follow-up (N = 21)	45 (± 3)			
24-Month Follow-up (N = 3)	51 (± 22)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of blinatumomab until up to 30 days after the last dose, until the data cut-off date of 10 July 2014; the overall median duration of treatment exposure was 46.8 days.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Cohort 1: Blinatumomab 9/28/112 µg/d

Reporting group description:

Participants received blinatumomab administered CIV 9 µg/day for the first week, followed by 28 µg/day for the second week, then 112 µg/day for the remaining 6 weeks of treatment during Cycle 1. Participants who achieved a CR or PR, or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.

Reporting group title	Cohort 2: Blinatumomab 112 µg/d

Reporting group description:

Participants received blinatumomab administered CIV at a constant dose of 112 µg/day for 8 weeks of treatment during Cycle 1. Participants who achieved CR or PR, or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.

Reporting group title	Cohort 3: Blinatumomab 9/28/112 µg/d

Reporting group description:

Participants received blinatumomab administered CIV 9 µg/day for the first week, followed by 28 µg/day for the second week, then 112 µg/day for the remaining 6 weeks of treatment during Cycle 1. Participants who achieved CR or PR, or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.

Reporting group title	Cohort 1 + 3: Blinatumomab 9/28/112 µg/d

Reporting group description:

Participants received blinatumomab administered CIV 9 µg/day for the first week, followed by 28 µg/day for the second week, then 112 µg/day for the remaining 6 weeks of treatment during Cycle 1. Participants who achieved CR or PR, or had stable disease after the first treatment cycle were eligible to receive a second (consolidation) cycle of treatment over 4 weeks, following a 4-week treatment-free interval.

Serious adverse events	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)	2 / 2 (100.00%)	12 / 14 (85.71%)
number of deaths (all causes)	5	1	9
number of deaths resulting from adverse events			
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	2 / 9 (22.22%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 2 (50.00%)	2 / 14 (14.29%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleurisy			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (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
Pulmonary embolism			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (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
Respiratory failure			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	0 / 14 (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
Investigations			
Pancreatic enzymes increased			

subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug administration error			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Aphasia			
subjects affected / exposed	2 / 9 (22.22%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Encephalopathy			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurological symptom			
subjects affected / exposed	1 / 9 (11.11%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Speech disorder			
subjects affected / exposed	1 / 9 (11.11%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tremor			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow toxicity			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			

subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Oesophagitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Catheter site infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	5 / 14 (35.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes virus infection			

subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (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
Lung infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 9 (33.33%)	1 / 2 (50.00%)	2 / 14 (14.29%)
occurrences causally related to treatment / all	0 / 3	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Viral infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 1 + 3: Blinatumomab 9/28/112 µg/d		
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 23 (91.30%)		
number of deaths (all causes)	14		
number of deaths resulting from adverse events			
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	2 / 23 (8.70%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleurisy			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Pancreatic enzymes increased			

subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Drug administration error			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Aphasia			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Convulsion			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Encephalopathy				
subjects affected / exposed	2 / 23 (8.70%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neurological symptom				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Speech disorder				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Tremor				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Agranulocytosis				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone marrow toxicity				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenia				

subjects affected / exposed	0 / 23 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Oesophagitis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Catheter site infection			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	5 / 23 (21.74%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Herpes virus infection			

subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lobar pneumonia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	5 / 23 (21.74%)		
occurrences causally related to treatment / all	2 / 6		
deaths causally related to treatment / all	0 / 1		
Viral infection			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Cohort 1: Blinatumomab 9/28/112 µg/d	Cohort 2: Blinatumomab 112 µg/d	Cohort 3: Blinatumomab 9/28/112 µg/d
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)	2 / 2 (100.00%)	14 / 14 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			

subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Oncologic complication			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Tumour pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Catheter site erythema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Catheter site rash			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Chills			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	1	0	2
Disease progression			

subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	3 / 14 (21.43%)
occurrences (all)	0	0	4
Facial pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	3 / 9 (33.33%)	1 / 2 (50.00%)	3 / 14 (21.43%)
occurrences (all)	4	1	7
General physical health deterioration			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Oedema			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	5 / 14 (35.71%)
occurrences (all)	1	0	5
Oedema peripheral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	4 / 9 (44.44%)	1 / 2 (50.00%)	5 / 14 (35.71%)
occurrences (all)	9	2	5
Ulcer			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 9 (11.11%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	1	1	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	3 / 9 (33.33%)	1 / 2 (50.00%)	1 / 14 (7.14%)
occurrences (all)	3	1	1
Dysphonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Nasal disorder			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Pulmonary congestion			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Tachypnoea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Disorientation			
subjects affected / exposed	2 / 9 (22.22%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	2	1	0
Encopresis			

subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Fear			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Nervousness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Investigations			
Antithrombin III decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Blood fibrinogen increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Blood glucose increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	4 / 14 (28.57%)
occurrences (all)	0	0	5
Blood immunoglobulin G decreased			
subjects affected / exposed	2 / 9 (22.22%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Blood magnesium decreased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Blood potassium decreased			

subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	2
Blood sodium decreased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	3 / 14 (21.43%)
occurrences (all)	1	0	4
Corneal reflex decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Fibrin D dimer increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Fibrinolysis increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Neutrophil count decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
PO2 decreased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Platelet count decreased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	1 / 14 (7.14%)
occurrences (all)	0	1	1

Weight increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	3 / 14 (21.43%)
occurrences (all)	0	0	3
White blood cell count decreased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Injury, poisoning and procedural complications			
Spinal compression fracture			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Cardiac failure			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Cardiovascular insufficiency			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Burning sensation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Coordination abnormal			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1

Dyscalculia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Encephalopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Epilepsy			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Facial paresis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Hyporeflexia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Memory impairment			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Radiculopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Sensory disturbance			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	2 / 9 (22.22%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0

Speech disorder			
subjects affected / exposed	3 / 9 (33.33%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	3	1	0
Tremor			
subjects affected / exposed	6 / 9 (66.67%)	2 / 2 (100.00%)	4 / 14 (28.57%)
occurrences (all)	7	2	6
Vocal cord paralysis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	1 / 14 (7.14%)
occurrences (all)	0	1	1
Leukopenia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	3 / 14 (21.43%)
occurrences (all)	1	0	8
Neutropenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	2
Thrombocytopenia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	4 / 14 (28.57%)
occurrences (all)	1	0	5
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	2 / 9 (22.22%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Keratitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Visual acuity reduced			

subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Aphthous stomatitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	4 / 9 (44.44%)	1 / 2 (50.00%)	1 / 14 (7.14%)
occurrences (all)	7	1	1
Dyspepsia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Flatulence			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	0	0	2
Gastrointestinal motility disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Odynophagia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

Vomiting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Drug eruption			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Eczema asteatotic			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	1	0	3
Night sweats			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	2	0	2
Rash			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Skin ulcer			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Enuresis			
subjects affected / exposed	2 / 9 (22.22%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Haematuria			
subjects affected / exposed	2 / 9 (22.22%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Renal failure			

subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Ureteric obstruction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Urinary retention			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	2 / 14 (14.29%)
occurrences (all)	1	0	2
Bone pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Intervertebral disc protrusion			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	2 / 9 (22.22%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Myopathy			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Infections and infestations			

Bronchitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Candida infection			
subjects affected / exposed	2 / 9 (22.22%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Candiduria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Diverticulitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Fungal infection			
subjects affected / exposed	1 / 9 (11.11%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	3	1	0
Herpes simplex			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	3 / 14 (21.43%)
occurrences (all)	0	0	3
Otitis media			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	1	0	1
Respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

Rhinitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 2 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	0	1
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	2 / 9 (22.22%)	1 / 2 (50.00%)	2 / 14 (14.29%)
occurrences (all)	3	1	2
Hypocalcaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 2 (50.00%)	0 / 14 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	3 / 14 (21.43%)
occurrences (all)	2	0	3
Vitamin K deficiency			
subjects affected / exposed	1 / 9 (11.11%)	0 / 2 (0.00%)	0 / 14 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Cohort 1 + 3: Blinatumomab 9/28/112 µg/d		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 23 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Oncologic complication			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		

Tumour pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Haematoma			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Thrombosis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Catheter site erythema			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Catheter site rash			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Chills			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Disease progression			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	4		
Facial pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Fatigue			

subjects affected / exposed	6 / 23 (26.09%)		
occurrences (all)	11		
General physical health deterioration			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Mucosal inflammation			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Oedema			
subjects affected / exposed	6 / 23 (26.09%)		
occurrences (all)	6		
Oedema peripheral			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	9 / 23 (39.13%)		
occurrences (all)	14		
Ulcer			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	4		
Dysphonia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Dyspnoea			

subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Nasal disorder			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Pleural effusion			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Pulmonary congestion			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Pulmonary embolism			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	2		
Tachypnoea			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Disorientation			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Encopresis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Fear			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		

Nervousness			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Sleep disorder			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Investigations			
Antithrombin III decreased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Blood fibrinogen increased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Blood glucose increased			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	5		
Blood immunoglobulin G decreased			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Blood magnesium decreased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Blood potassium decreased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	2		
Blood sodium decreased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Blood uric acid increased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
C-reactive protein increased			

subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	5		
Corneal reflex decreased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Fibrin D dimer increased			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Fibrinolysis increased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Hepatic enzyme increased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Neutrophil count decreased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
PO2 decreased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
White blood cell count decreased			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Spinal compression fracture			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	2		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Cardiac failure			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Cardiovascular insufficiency			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Burning sensation			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Coordination abnormal			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Dyscalculia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Encephalopathy			

subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Epilepsy				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Facial paresis				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Headache				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	2			
Hyporeflexia				
subjects affected / exposed	0 / 23 (0.00%)			
occurrences (all)	0			
Memory impairment				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Paraesthesia				
subjects affected / exposed	2 / 23 (8.70%)			
occurrences (all)	2			
Radiculopathy				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Sensory disturbance				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Somnolence				
subjects affected / exposed	2 / 23 (8.70%)			
occurrences (all)	2			
Speech disorder				
subjects affected / exposed	3 / 23 (13.04%)			
occurrences (all)	3			
Tremor				
subjects affected / exposed	10 / 23 (43.48%)			
occurrences (all)	13			
Vocal cord paralysis				

subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	9		
Neutropenia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	2		
Thrombocytopenia			
subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	6		
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Eye disorders			
Blepharospasm			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Keratitis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Visual acuity reduced			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Abdominal pain			

subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Aphthous stomatitis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	5 / 23 (21.74%)		
occurrences (all)	8		
Dyspepsia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	2		
Flatulence			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Gastrointestinal motility disorder			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Mouth ulceration			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Odynophagia			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		

Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Drug eruption			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Eczema asteatotic			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Hyperhidrosis			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	4		
Night sweats			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	4		
Rash			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Skin ulcer			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Renal and urinary disorders			
Enuresis			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Haematuria			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Renal failure			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Ureteric obstruction			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Urinary retention			

subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 23 (13.04%)		
occurrences (all)	3		
Bone pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Musculoskeletal pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Myopathy			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	2		
Candida infection			
subjects affected / exposed	2 / 23 (8.70%)		
occurrences (all)	2		
Candiduria			

subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Conjunctivitis				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Diverticulitis				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Fungal infection				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	3			
Herpes simplex				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Infection				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	3 / 23 (13.04%)			
occurrences (all)	3			
Otitis media				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Pneumonia				
subjects affected / exposed	2 / 23 (8.70%)			
occurrences (all)	2			
Respiratory tract infection				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Rhinitis				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	2			
Urinary tract infection				
subjects affected / exposed	1 / 23 (4.35%)			
occurrences (all)	1			
Vulvovaginal candidiasis				

subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		
Hyperglycaemia			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	5		
Hypocalcaemia			
subjects affected / exposed	0 / 23 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	4 / 23 (17.39%)		
occurrences (all)	5		
Vitamin K deficiency			
subjects affected / exposed	1 / 23 (4.35%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported