Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

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Eligibility Criteria

Inclusion Criteria

- Patients with Philadelphia chromosome negative high-risk first relapse B-cell precursor acute lymphoblastic leukemia (ALL; as defined by International BFM Study Group/IntReALL criteria) (after second consolidation after induction according to IntReALL treatment guidelines)
- Patients with M1 or M2 at the time of randomization
- Age >28 days and <18 years at the time of informed consent/assent
- Patient's legally acceptable representative has provided informed consent when the patient is legally too young to provide informed consent and the patient has provided written assent based on local regulations and/or guidelines prior to any study-specific activities/procedures being initiated
- Availability of the following material from relapse diagnosis for central analysis of minimal residual disease by polymerase chain reaction: clone-specific primers and reference DNA, as well as primer sequences and analyzed sequences of clonal rearrangements (cases with isolated extramedullary relapse or cases with technical and/or logistic hurdles to obtain and process bone marrow material are exempt from providing this material. In these cases, central minimal residual disease analysis only by flow cytometry is permitted)

Exclusion Criteria

- Clinically relevant central nervous system (CNS) pathology requiring treatment (e.g., unstable epilepsy). Evidence of current CNS (CNS 2, CNS 3) involvement by ALL. Patients with CNS relapse at the time of relapse are eligible if CNS is successfully treated prior to enrollment
- Abnormal renal or hepatic function prior to start of treatment (day 1) as defined below:

  - Serum creatinine levels above upper limit of normal, based on the normal ranges for age and gender of the local laboratories
  - Total bilirubin >3.0 mg/dL prior to start of treatment (unless related to Gilbert's or Meulengracht disease)
- Peripheral neutrophils <500/μL prior to start of treatment
- Peripheral platelets <50,000/μL prior to start of treatment
- Currently receiving treatment in another investigational device or drug study, or less than 4 weeks since ending treatment on another investigational device or drug study. Procedures required by IntReALL HR guidelines are allowed
- Chemotherapy-related toxicities that have not resolved to grade ≤ 2 (except for parameters defined above)
- Symptoms and/or clinical signs and/or radiological and/or sonographic signs that indicate an acute or uncontrolled chronic infection, any other concurrent disease or medical condition that could be exacerbated by the treatment or would seriously complicate compliance with the protocol
- Documented infection with human immunodeficiency virus
- Known hypersensitivity to immunoglobulins or any of the products or components to be administered during dosing (excluding asparaginase)
- Post-menarchal female patient who is pregnant or breastfeeding, or is planning to become pregnant or breastfeed while receiving protocol-specified therapy and for at least 6 months after the last dose of blinatumomab, or 12 months after the last dose of chemotherapy
- Post-menarchal female patient who is not willing to practice true sexual abstinence or use a highly effective form of contraception while receiving protocol-specified therapy and for at least 6 months after the last dose of blinatumomab, or 12 months after the last dose of chemotherapy

- Sexually mature male patient who is not willing to practice true sexual abstinence or use a condom with spermicide while receiving protocol-specified therapy and for at least 6 months thereafter. In countries where spermicide is not available, a condom without spermicide is acceptable
- Sexually mature male patient who is not willing to abstain from sperm donation while receiving protocol-specified therapy and for at least 6 months thereafter
- Patient likely to not be available to complete all protocol-required study visits or procedures, including follow-up visits, and/or to comply with all required study procedures to the best of the patient's and investigator's knowledge
- History or evidence of any other clinically significant disorder, condition, or disease (except for those outlined above) that, in the opinion of the investigator or Amgen physician, if consulted, would pose a risk to patient safety or interfere with the study evaluation, procedures, or completion
- Placed into an institution due to juridical or regulatory ruling

Dose Modifications

Infusion Interruption/Dose Modification of Blinatumomab Due to Adverse Events

Treatment with blinatumomab was interrupted for clinically relevant neurologic events of grade ≥ 2 related to blinatumomab (grade 3 and grade 4 resulted in permanent discontinuation of blinatumomab), cytokine release syndrome grade ≥ 2 related to blinatumomab, and any clinically relevant adverse event grade ≥ 3 related to blinatumomab. If an adverse event resolved to grade ≤ 1 within 1 week after the end of the infusion, the infusion could be resumed to complete the 28-day infusion (not counting the duration of treatment interruption) at a reduced dose of 5 $\mu g/m^2$/day. The reduced dose could be administered for at least 7 days before it could be increased (except for clinically relevant neurologic events). The maximum

administered dose was not higher than 15 µg/m^2/day (maximum daily dose of 28 µg/day). The restart of the infusion was performed in a hospital under supervision of the investigator.

Infusion Interruption/Dose Modification of Blinatumomab Due to Neurologic Events

In the event of clinically relevant neurologic events, dexamethasone was administered at a total daily dose of at least 0.2–0.4 mg/kg/day**,** preferably intravenously (maximum of 24 mg/day), divided into three doses per day for up to 3 days. The dose was then reduced step-wise by at least 25% per day for up to 4 days. If a neurologic event resolved to grade ≤1 within 1 week after the end of the infusion, the treatment cycle could be resumed at the reduced dose of 5 µg/m^2/day with no further dose escalations.

If the neurologic event was a seizure, appropriate prophylactic anti-epileptic treatment (a therapeutic dose of, for example, phenytoin or levetiracetam) was administered before resumption of the treatment cycle.

Criteria for Discontinuation of Blinatumomab

Blinatumomab was discontinued for the following reasons:

- Relapse
- Adverse event(s) requiring dose interruption at the 5 µg/m^2/day dose
- Clinically relevant toxicities that the investigator viewed as an unacceptable safety risk to the patient
- Clinically relevant neurologic events related to blinatumomab that required more than 1 week to resolve to grade ≤1, that were grade 3 or 4, or that occurred after restart of treatment
- Adverse event that did not resolve to grade ≤1 within 1 week or more than two interruptions per cycle due to an adverse event
- Medical condition that, in the opinion of the investigator, precluded further treatment

- Withdrawal of patient's consent to further study treatment

Chemotherapy

Dosage Adjustments, Delays, Rules for Withholding or Restarting, and Permanent Discontinuation of Chemotherapy

Dose reductions in chemotherapy were allowed in the event of unacceptable toxicity or substantial treatment delays due to intolerance of treatment. For severe methotrexate-associated toxicity, high-dose methotrexate was given at a shorter infusion duration of 24 hours, at a lower dose of 500 mg/m^2, and/or with earlier leucovorin rescue. For corticosteroid-associated diabetes, the dexamethasone dose was reduced, and a glucose-free infusion was administered. For asparaginase-associated complications, the asparaginase administration was postponed or cancelled. For prolonged treatment delays, dose reductions were made according to published guidelines.

Criteria for Discontinuation of Standard of Care

Treatment with chemotherapy was discontinued for the following reasons:

- Relapse
- Investigator's opinion/local treatment standards
- Adverse event, which makes discontinuation from treatment necessary due to protocol-specified safety criteria or desirable in the opinion of the investigator and/or the patient
- Investigator's decision that a change of therapy (including immediate hematopoietic stem cell transplantation) is in the patient's best interest
- Investigator's decision that a patient would no longer benefit from treatment
- Intercurrent medical condition that, in the opinion of the investigator or the patient, precludes further treatment of the patient

- Withdrawal of a patient’s consent to study treatment

Data Sharing Statement

Qualified researchers may request data from Amgen clinical studies. Complete details are available at http://www.amgen.com/datasharing.

eTable 1. Enrollment by Region and Country

	Blinatumomab (N = 54)	Consolidation Chemotherapy (N = 54)	Total (N = 108)
Europe — no. (%)	49 (90.7)	52 (96.3)	101 (93.5)
Belgium	1 (1.9)	1 (1.9)	2 (1.9)
Czech Republic	0 (0.0)	2 (3.7)	2 (1.9)
Denmark	0 (0.0)	2 (3.7)	2 (1.9)
France	7 (13.0)	3 (5.6)	10 (9.3)
Germany	9 (16.7)	12 (22.2)	21 (19.4)
Italy	23 (42.6)	18 (33.3)	41 (38.0)
Netherlands	2 (3.7)	0 (0.0)	2 (1.9)
Poland	1 (1.9)	1 (1.9)	2 (1.9)
Portugal	1 (1.9)	3 (5.6)	4 (3.7)
Spain	1 (1.9)	7 (13.0)	8 (7.4)
United Kingdom	4 (7.4)	3 (5.6)	7 (6.5)
Rest of world — no. (%)	5 (9.3)	2 (3.7)	7 (6.5)
Australia	3 (5.6)	1 (1.9)	4 (3.7)
Israel	2 (3.7)	1 (1.9)	3 (2.8)

eTable 2. Risk Stratification by Time From Diagnosis to Relapse and Site of Relapse According to IntReALL Risk Classification

Time Point	Isolated Extramedullary Relapse	Combined Bone Marrow/Extramedullary Relapse[a]	Isolated Bone Marrow Relapse[b]
Very early	High risk	High risk	High risk
Early	Standard risk	Standard risk	High risk
Late	Standard risk	Standard risk	Standard risk

Very early relapse occurs <18 months after primary diagnosis; early relapse occurs ≥18 months after primary diagnosis and <6 months after completion of primary therapy; and late relapse occurs ≥6 months after completion of primary therapy.

Isolated extramedullary relapse involves M1 (bone marrow blasts < 5%) with extramedullary involvement; combined bone marrow and extramedullary relapse involves M2 (≥5% and <25% blasts) or M3 (≥25% blasts) bone marrow relapse with extramedullary involvement; isolated bone marrow relapse involves M3 bone marrow relapse with no extramedullary involvement.

[a]Patients with early combined bone marrow/extramedullary relapse were considered high risk if they were treated with a high-risk regimen.

[b]Patients with M1 or M2 bone marrow were considered high risk if blasts were confirmed to be relapse and not early regenerating normal cells (by flow cytometry or polymerase chain reaction), and they were treated with a high-risk regimen.

eTable 3. Components of High-Risk Consolidation Therapy

Chemotherapy Components		First Block of Consolidation Chemotherapy[a]	Second Block of Consolidation Chemotherapy[a]	Third Block of Consolidation Chemotherapy[a]
Agent	Dosage			
Dexamethasone	10 mg/m^2/day	2 doses on days 1–6	2 doses on days 1–6	2 doses on days 1–6
Vincristine	1.5 mg/m^2/day	Days 1 and 6		Days 1 and 6
ARA-C	2 g/m^2/dose	2 doses on day 5 of week 5	Days 1–3	
Methotrexate	1 g/m^2/dose	Over 36 hours, starting on day 1		36 hours starting on day 1
Cyclophosphamide	200 mg/m^2/dose	Every 12 hours on days 2–4 (5 doses total)		
PEG-asparaginase	1000 U/m^2	Day 6	Day 6	Day 6
Etoposide	100 mg/m^2/dose		Every 12 hours on days 3–5 (5 doses total)	
Daunorubicin	30 mg/m^2			24-hour continuous infusion starting on day 5

Chemotherapy Components		First Block of Consolidation Chemotherapy[a]	Second Block of Consolidation Chemotherapy[a]	Third Block of Consolidation Chemotherapy[a]
Agent	Dosage			
Ifosfamide	800 mg/m^2/dose			Every 12 hours on days 2–4 (5 doses total)
Methotrexate[b]	Age-adapted intrathecal chemotherapy	Day 2	Day 1	Day 2
Cytarabine[b]	Age-adapted intrathecal chemotherapy	Day 2	Day 1	Day 2
Prednisolone[b]	Age-adapted intrathecal chemotherapy	Day 2	Day 1	Day 2

[a]Two weeks is the minimum interval between consolidation chemotherapy blocks. In some cases, this interval may be longer because patients must recover from peripheral cytopenia before staring the next treatment.
[b]See eTable 5 for details regarding age-adapted intrathecal chemotherapy.

eTable 4. Age-Adapted Doses of Intrathecal Chemotherapy

Age (years)	Methotrexate (mg)	Cytarabine (mg)	Prednisolone[a] (mg)	0.9% NaCl (mL)
<1	6	16	4	1.5
1	8	20	6	2.0
2	10	26	8	2.5
≥3	12	30	10	3.0

[a]Or equivalent dose of hydrocortisone.

eTable 5. Subgroup Analysis of Event-Free Survival

	Blinatumomab Events (N = 54) Events/no. Patients (%)	Consolidation Chemotherapy Events (N = 54) Events/no. Patients (%)	Hazard Ratio (95% CI)	p-value
All patients	17/54 (31.5)	31/54 (57.4)	0.37 (0.20–0.66)	
Strata				0.35
Age 1–9 years + M1[a] with minimal residual disease level[b] $\geq 10^{-3}$	3/12 (25.0)	7/12 (58.3)	0.27 (0.07–1.08)	
Age 1–9 years + M1[a] with minimal residual disease level[b] $< 10^{-3}$	8/25 (32.0)	14/24 (58.3)	0.45 (0.19–1.07)	
Age 1–9 years + M2[a]	1/2 (50.0)	2/2 (100.0)	NE	
Age <1 year and >9 years + M1[a] with minimal residual disease level[b] $\geq 10^{-3}$	0/3 (0.0)	2/4 (50.0)	NE	
Age <1 year and >9 years + M1[a] with minimal residual disease level[b] $< 10^{-3}$	4/10 (40.0)	5/10 (50.0)	0.43 (0.11–1.66)	
Age <1 year and >9 years + M2[a]	1/2 (50.0)	1/2 (50.0)	NE	
Sex				0.08
Male	9/30 (30.0)	14/22 (63.6)	0.20 (0.08–0.47)	
Female	8/24 (33.3)	17/32 (53.1)	0.54 (0.23–1.26)	
Time from initial diagnosis to relapse				0.51
<18 months	6/19 (31.6)	14/22 (63.6)	0.21 (0.07–0.59)	

	Blinatumomab Events (N = 54) Events/no. Patients (%)	Consolidation Chemotherapy Events (N = 54) Events/no. Patients (%)	Hazard Ratio (95% CI)	p-value
≥18 months and ≤30 months	10/32 (31.3)	17/28 (60.7)	0.43 (0.20–0.95)	
>30 months[c]	1/3 (33.3)	0/4 (0.0)	NE	
Minimal Residual Disease remission at baseline[d]				0.59
Yes	6/25 (24.0)	13/26 (50.0)	0.42 (0.16–1.11)	
No	11/29 (37.9)	18/28 (64.3)	0.32 (0.15–0.68)	

Event-free survival was calculated from the time of randomization until the date of relapse or M2 marrow after having achieved a complete remission, failure to achieve a complete remission at the end of treatment, second malignancy, or death due to any cause, whichever occurred first. The hazard ratio estimate for all patients was obtained from an unstratified Cox proportional hazard model.

[a]M1 and M2 cytomorphology was determined at screening.

[b]Minimal Residual Disease level was measured at the end of induction/before first consolidation.

[c]Treated per investigator's discretion. Patients were high risk, had isolated bone marrow relapse, and were being treated with high-risk therapy.

[d]Measured at screening.

Abbreviations: CI, confidence interval; NE, not estimable.

eTable 6. Overall Survival

	Blinatumomab (N = 54)	Consolidation Chemotherapy (N = 54)	Treatment Difference
Events — no. (%)	8 (14.8)	16 (29.6)	
Death from any cause[a]	8 (14.8)	16 (29.6)	
Censored	46 (85.2)	38 (70.4)	
Stratified hazard ratio[b,c] (95% CI)			0.43 (0.18–1.01)
Unstratified hazard ratio[†] (95% CI)			0.42 (0.18–0.99)
Kaplan-Meier estimate — % (95% CI)			
6 months	93.9 (82.3–98.0)	91.4 (78.6–96.7)	
12 months	86.7 (72.6–93.9)	70.6 (53.7–82.3)	
24 months	81.1 (65.5–90.2)	55.8 (36.9–71.0)	
36 months	81.1 (65.5–90.2)	55.8 (36.9–71.0)	

Overall survival time is calculated from time of randomization until death due to any cause.

[a]Deaths prior to hematopoietic stem cell transplantation: blinatumomab = 0; consolidation chemotherapy = 2, due to refractory disease

[b]Stratification factors are: age (1–9 years vs. other [<1 year and >9 years]), and marrow/Minimal Residual Disease status (M1 with Minimal Residual Disease level $<10^{-3}$ vs. M1 with Minimal Residual Disease level $\geq 10^{-3}$ vs. M2).

[c]The hazard ratio estimates are obtained from the Cox proportional hazard model.

Abbreviations: CI, confidence interval

eTable 7. Estimated Latent Treatment Effect on Overall Survival Without Subsequent Blinatumomab Drop-in by Consolidation Chemotherapy Group

	n-subjects/n-events[a]	Hazard ratio[b]	95% CI
n-subjects/events	108/24		
Blinatumomab vs. Consolidation Chemotherapy		0.35	0.12, 1.01

Overall survival time is calculated from time of randomization until death due to any cause. The table is based on the method assuming a Weibull accelerated failure time model and a time-invariant treatment benefit at time of subsequent therapy that is the same as the blinatumomab treatment effect at randomization (Branson M, Whitehead J. Estimating a treatment effect in survival studies in which patients switch treatment. Stat Med. 2002;21:2449-2463.).

[a] Number of subjects and events in the parametric model.

[b] A hazard ratio < 1.0 indicates a lower average event rate and a longer survival for Blinatumomab relative to Consolidation Chemotherapy.

eTable 8. Subgroup Analysis of Overall Survival

	Blinatumomab Events (N = 54) Events/no. Patients (%)	Consolidation Chemotherapy Events (N = 54) Events/no. Patients (%)	Hazard Ratio (95% CI)
All patients	8/54 (14.8)	16/54 (29.6)	0.42 (0.18–0.99)
Strata			
Age 1–9 years + M1[a] with Minimal Residual Disease level[b] $\geq 10^{-3}$	0/12 (0.0)	6/12 (50.0)	not estimable
Age 1–9 years + M1[a] with Minimal Residual Disease level[b] $< 10^{-3}$	4/25 (16.0)	8/24 (33.3)	0.46 (0.14–1.53)
Age 1–9 years + M2[a]	1/2 (50.0)	0/2 (0.0)	not estimable
Age <1 year and >9 years + M1[a] with Minimal Residual Disease level[b] $\geq 10^{-3}$	0/3 (0.0)	0/4 (0.0)	not estimable
Age <1 year and >9 years + M1[a] with Minimal Residual Disease level[b] $< 10^{-3}$	2/10 (20.0)	2/10 (20.0)	0.83 (0.12–5.92)
Age <1 year and >9 years + M2[a]	1/2 (50.0)	0/2 (0.0)	not estimable
Sex			
Male	4/30 (13.3)	7/22 (31.8)	0.29 (0.09–1.01)
Female	4/24 (16.7)	9/32 (28.1)	0.61 (0.19–1.97)
Time from initial diagnosis to relapse			
<18 months	2/19 (10.5)	7/22 (31.8)	0.23 (0.05–1.13)

	Blinatumomab Events (N = 54) Events/no. Patients (%)	Consolidation Chemotherapy Events (N = 54) Events/no. Patients (%)	Hazard Ratio (95% CI)
≥18 months and ≤30 months	5/32 (15.6)	9/28 (32.1)	0.51 (0.17–1.53)
>30 months[c]	1/3 (33.3)	0/4 (0.0)	not estimable

Overall survival time was calculated from time of randomization until death due to any cause.

The hazard ratio estimate for all patients was obtained from an unstratified Cox proportional hazard model.

[a]M1 and M2 cytomorphology was determined at screening.

[b]Minimal residual disease level was measured at the end of induction/before first consolidation.

[c]Treated per investigator's discretion. Patients were high risk, had isolated bone marrow relapse, and were being treated with high-risk therapy.

Abbreviations: CI, confidence interval

eTable 9: Adverse Events Reported for >5% of Patients in the Blinatumomab Group

	Blinatumomab (N = 54) no. (%)	Consolidation Chemotherapy (N = 51) no. (%)
Pyrexia	44 (81.5)	10 (19.6)
Nausea	22 (40.7)	9 (17.6)
Headache	19 (35.2)	9 (17.6)
Stomatitis[a]	19 (35.2)	31 (57.4)
Vomiting	16 (29.6)	11 (21.6)
Anemia	12 (22.2)	23 (45.1)
Erythema/rash[b]	12 (22.2)	5 (9.8)
Thrombocytopenia[c]	11 (20.4)	20 (39.2)
Diarrhea	11 (20.4)	9 (17.6)
Neutropenia[d]	10 (18.5)	18 (35.3)
Abdominal pain	7 (13.0)	11 (21.6)
Hypertension	7 (13.0)	4 (7.8)
Hypokalemia	7 (13.0)	5 (9.8)
Hypotension	7 (13.0)	4 (7.8)
Hypogammaglobulinemia	6 (11.1)	2 (3.9)
Pruritus	6 (11.1)	5 (9.8)
Constipation	5 (9.3)	7 (13.7)
Epistaxis	5 (9.3)	7 (13.7)
Tremor	5 (9.3)	0 (0.0)
Elevated liver enzymes[e]	5 (9.3)	12 (23.5)
Abdominal pain upper	4 (7.4)	3 (5.9)

Agitation	4 (7.4)	1 (2.0)
Cough	4 (7.4)	1 (2.0)
Fluid overload	4 (7.4)	0 (0.0)
Immunodeficiency[f]	4 (7.4)	0 (0.0)
Febrile neutropenia	3 (5.6)	13 (25.5)

[a]Adverse events for combined preferred terms stomatitis and mucosal inflammation

[b]Adverse events for combined preferred terms erythema, rash, and rash maculo-papular

[c]Adverse events for combined preferred terms thrombocytopenia and platelet count decreased

[d]Adverse events for combined preferred terms neutropenia and neutrophil count decreased

[e]Alanine aminotransferase increased, alanine aminotransferase, aspartate aminotransferase increased, aspartate aminotransferase, gamma-glutamyltransferase increased, and/or hypertransaminasemia.

[f]Low immunoglobulin.

eTable 10. Serious Adverse Events

System Organ Class Preferred Term	Blinatumomab (N = 54) no. (%)	Consolidation Chemotherapy (N = 51) no. (%)
Any serious treatment-emergent adverse event	13 (24.1)	22 (43.1)
Nervous system disorders	5 (9.3)	1 (2.0)
Neurological symptom	2 (3.7)	0 (0.0)
Seizure	2 (3.7)	0 (0.0)
Nervous system disorder	1 (1.9)	0 (0.0)
Headache	0 (0.0)	1 (2.0)
Infections and infestations	3 (5.6)	4 (7.8)
Herpes virus infection	1 (1.9)	0 (0.0)
Klebsiella infection	1 (1.9)	0 (0.0)
Perineal cellulitis	1 (1.9)	0 (0.0)
Bronchitis	0 (0.0)	1 (2.0)
Clostridium difficile colitis	0 (0.0)	1 (2.0)
Device-related infection	0 (0.0)	1 (2.0)
Escherichia bacteremia	0 (0.0)	1 (2.0)
Septic shock	0 (0.0)	1 (2.0)
Investigations	2 (3.7)	1 (2.0)
Blood immunoglobulin G decreased	1 (1.9)	0 (0.0)
Body temperature increased	1 (1.9)	0 (0.0)
Neurological examination abnormal	1 (1.9)	0 (0.0)
Lipase increased	0 (0.0)	1 (2.0)
Gastrointestinal disorders	1 (1.9)	3 (5.9)

System Organ Class Preferred Term	Blinatumomab (N = 54) no. (%)	Consolidation Chemotherapy (N = 51) no. (%)
Stomatitis	1 (1.9)	2 (3.9)
Acute pancreatitis	0 (0.0)	1 (2.0)
General disorders and administration-site conditions	1 (1.9)	0 (0.0)
Pyrexia	1 (1.9)	0 (0.0)
Injury, poisoning, and procedural complications	1 (1.9)	1 (2.0)
Accidental overdose	1 (1.9)	0 (0.0)
Pneumothorax	0 (0.0)	1 (2.0)
Metabolism and nutrition disorders	1 (1.9)	0 (0.0)
Hypokalemia	1 (1.9)	0 (0.0)
Surgical and medical procedures	1 (1.9)	0 (0.0)
Vascular disorders	1 (1.9)	1 (2.0)
Hypotension	1 (1.9)	0 (0.0)
Capillary leak syndrome	0 (0.0)	1 (2.0)
Blood and lymphatic system disorders	0 (0.0)	13 (25.5)
Febrile neutropenia	0 (0.0)	9 (17.6)
Leukopenia	0 (0.0)	1 (2.0)
Neutropenia	0 (0.0)	3 (5.9)
Thrombocytopenia	0 (0.0)	2 (3.9)
Hepatobiliary disorders	0 (0.0)	2 (3.9)
Hepatotoxicity	0 (0.0)	1 (2.0)
Hypertransaminasemia	0 (0.0)	1 (2.0)
Musculoskeletal and connective tissue disorders	0 (0.0)	1 (2.0)

System Organ Class Preferred Term	Blinatumomab (N = 54) no. (%)	Consolidation Chemotherapy (N = 51) no. (%)
Back pain	0 (0.0)	1 (2.0)
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	0 (0.0)	1 (2.0)

eTable 11. Neurologic Events and Cytokine Release Syndrome

Preferred Term Grade	Blinatumomab (N = 54) no. (%)	Consolidation Chemotherapy (N = 51) no. (%)
Neurologic events		
Any	26 (48.1)	15 (29.4)
Grade 3	2 (3.7)	1 (2.0)
Grade 4	1 (1.9)	0 (0.0)
Headache	19 (35.2)	9 (17.6)
Tremor	5 (9.3)	0 (0.0)
Agitation	4 (7.4)	1 (2.0)
Anxiety	2 (3.7)	2 (3.9)
Depression	2 (3.7)	1 (2.0)
Nervous system disorder	2 (3.7)	0 (0.0)
Grade 3	1 (1.9)	0 (0.0)
Neurological symptom	2 (3.7)	0 (0.0)
Seizure	2 (3.7)	0 (0.0)
Grade 4	1 (1.9)	0 (0.0)
Depressed mood	1 (1.9)	1 (2.0)
Dizziness	1 (1.9)	1 (2.0)
Encephalopathy	1 (1.9)	0 (0.0)
Irritability	1 (1.9)	1 (2.0)
Neuralgia	1 (1.9)	1 (2.0)
Grade 3	1 (1.9)	0 (0.0)
Confusional state	0 (0.0)	1 (2.0)

Preferred Term Grade	Blinatumomab (N = 54) no. (%)	Consolidation Chemotherapy (N = 51) no. (%)
Grade 3	0 (0.0)	1 (2.0)
Insomnia	0 (0.0)	1 (2.0)
Petit mal epilepsy	0 (0.0)	1 (2.0)
Cytokine release syndrome		
Any	2 (3.7)	1 (2.0)

Adverse events were coded using MedDRA version 22.1 and graded using CTCAE version 4.03.

Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events; MedDRA, Medical Dictionary for Regulatory Activities.