Supplemental Materials

RIALTO Expanded Access Study Final Analysis: Blinatumomab In Pediatric Relapsed/Refractory B-cell Precursor Acute Lymphoblastic Leukemia

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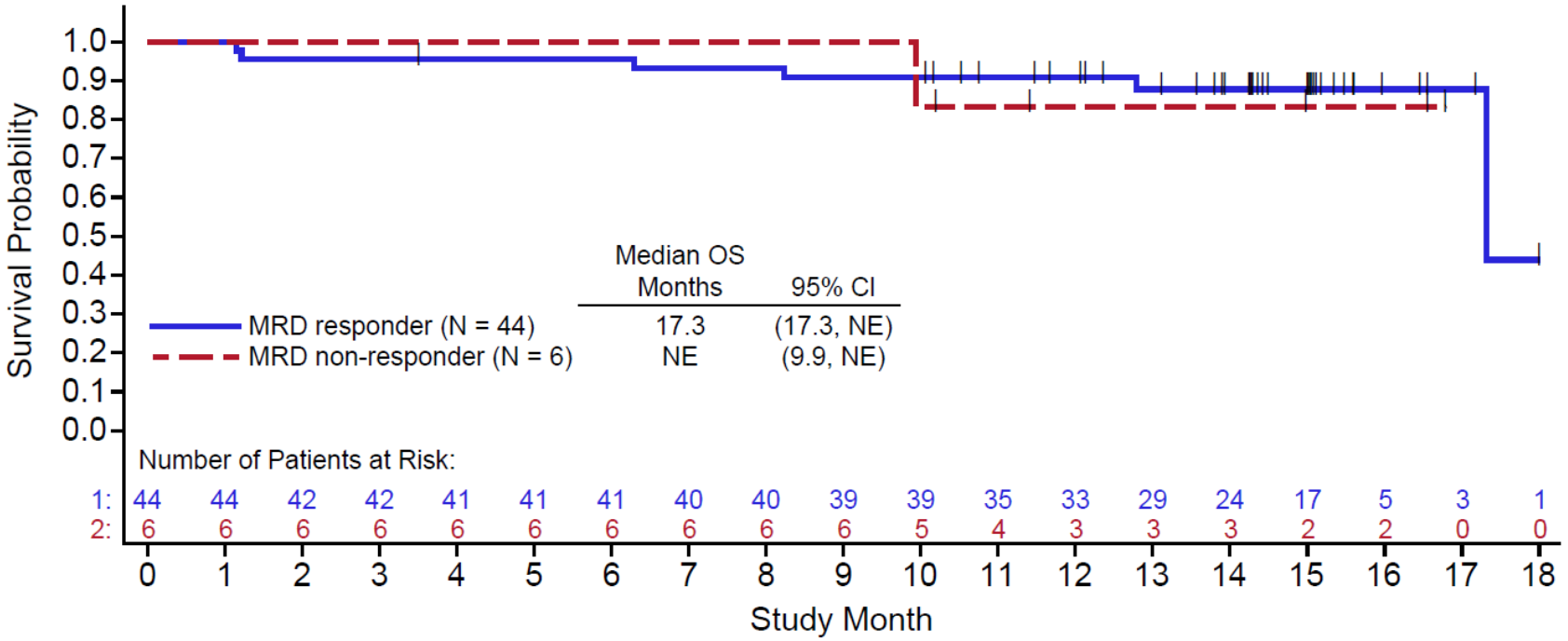
Figure S1: Overall survival after alloHSCT by MRD response. Vertical bars indicate censoring. Overall survival was defined from the start of blinatumomab infusion until death. Overall survival after alloHSCT was analyzed according to MRD response using the Kaplan-Meier method.

Figure S1



Censor indicated by vertical bar |
Months = Days/30.5
Figure includes retreatment data (treated as cycle 2) for one subject

Supplemental Table 1: Principal Investigators by Country

Country	Principal Investigator
Austria	Christina Peters
France	Benoit Brethon Gérard Michel
Germany	Peter Bader Christiane Chen-Santel Rupert Handgretinger Claudia Rössig Paul Gerhardt Schlegel Martin Schrappe
Italy	Giuseppe Basso Franco Locatelli
Switzerland	Jean-Pierre Bourquin
United Kingdom	Katharine Patrick
United States	Phillip Barnette Sima Jeha Maureen O'Brien

Supplemental Table 2: Subject Incidence of Treatment-Emergent Adverse Events, Any Grade with > 5% Incidence

	Patients treated with blinatumomab (N = 110) n (%)
Patients reporting TEAEs	71 (64.5)
Pyrexia	92 (83.6)
Vomiting	30 (27.3)
Headache	27 (24.5)
Cytokine release syndrome	22 (20.0)
Anemia	20 (18.2)
Nausea	20 (18.2)
Cough	19 (17.3)
Pain	18 (16.4)
Hypotension	14 (12.7)
Pain in extremity	14 (12.7)
Abdominal pain	12 (10.9)
Hypokalemia	12 (10.9)
Platelet count decreased	12 (10.9)
Rash	12 (10.9)
Alanine aminotransferase increased	11 (10.0)
Constipation	11 (10.0)
Febrile neutropenia	11 (10.0)
Fluid balance positive	11 (10.0)
Neutropenia	11 (10.0)
Back pain	10 (9.1)
Diarrhea	10 (9.1)
Thrombocytopenia	10 (9.1)
Hypertension	9 (8.2)
Rhinitis	8 (7.3)
Stomatitis	8 (7.3)
Tremor	8 (7.3)
Aspartate aminotransferase increased	7 (6.4)
C-reactive protein increased	7 (6.4)
Chills	7 (6.4)
Fatigue	7 (6.4)
Fluid retention	7 (6.4)
Pruritus	7 (6.4)
Abdominal pain upper	6 (5.5)
Bone pain	6 (5.5)

Dry skin	6 (5.5)
Epistaxis	6 (5.5)
Fluid overload	6 (5.5)
Gamma-glutamyltransferase increased	6 (5.5)
Hypocalcaemia	6 (5.5)
Sepsis	6 (5.5)
Tachycardia	6 (5.5)

Retreatment data (treated as cycle 2) for one patient is included.
Adverse events coded using MedDRA version 22.1.
Severity graded using CTCAE v4.03.

Supplemental Table 3: Subject Incidence of Treatment-Related Adverse Events, Any Grade with > 2% Incidence

	Patients treated with blinatumomab (N = 110) n (%)
Patients reporting TRAEs, any grade	81 (73.6)
Pyrexia	63 (57.3)
Cytokine release syndrome	18 (16.4)
Headache	11 (10.0)
Vomiting	11 (10.0)
Nausea	8 (7.3)
Tremor	6 (5.5)
Chills	5 (4.5)
Hypotension	5 (4.5)
Rash	5 (4.5)
C-reactive protein increased	4 (3.6)
Hypertension	4 (3.6)
Hypokalemia	4 (3.6)
Pain	4 (3.6)
Pain in extremity	4 (3.6)
Seizure	4 (3.6)
Tachycardia	4 (3.6)
Tumor lysis syndrome	4 (3.6)
Abdominal pain	3 (2.7)
Anemia	3 (2.7)
Dry skin	3 (2.7)
Febrile neutropenia	3 (2.7)
Hypocalcemia	3 (2.7)
Edema	3 (2.7)

Retreatment data (treated as cycle 2) for one patient is included.
Adverse events coded using MedDRA version 22.1.
Severity graded using CTCAE v4.03.

Supplemental Table 4: Subject Incidence of Grade ≥ 3 Treatment-Emergent Adverse Events

	Patients treated with blinatumomab (N = 110) n (%)
Patients reporting grade ≥ 3 TEAEs	71 (64.5)
Pyrexia	15 (13.6)
Platelet count decreased	11 (10.0)
Febrile neutropenia	10 (9.1)
Hypokalemia	8 (7.3)
Neutropenia	8 (7.3)
Alanine aminotransferase increased	7 (6.4)
Acute lymphocytic leukemia	5 (4.5)
Anemia	5 (4.5)
Thrombocytopenia	5 (4.5)
White blood cell count decreased	5 (4.5)
Aspartate aminotransferase increased	4 (3.6)
Device related infection	4 (3.6)
Gamma-glutamyltransferase increased	4 (3.6)
Sepsis	4 (3.6)
C-reactive protein increased	3 (2.7)
Hepatic enzyme increased	3 (2.7)
Hypertransaminasemia	3 (2.7)
Tumor lysis syndrome	3 (2.7)
Bacteremia	2 (1.8)
Cytokine release syndrome	2 (1.8)
Cytopenia	2 (1.8)
Device related sepsis	2 (1.8)
Headache	2 (1.8)
Hypertension	2 (1.8)
Hypoalbuminemia	2 (1.8)
Hyponatremia	2 (1.8)
Hypotension	2 (1.8)
Infection	2 (1.8)
Leukemia recurrent	2 (1.8)
Neutrophil count decreased	2 (1.8)
Pain	2 (1.8)
Stomatitis	2 (1.8)
Acute kidney injury	1 (0.9)

Acute lymphocytic leukemia	1 (0.9)
Acute myeloid leukemia	1 (0.9)
Agitation	1 (0.9)
Bacterial infection	1 (0.9)
Bacterial sepsis	1 (0.9)
Bacterial test positive	1 (0.9)
Bile duct stone	1 (0.9)
Blood bilirubin increased	1 (0.9)
Blood creatine increased	1 (0.9)
Blood fibrinogen increased	1 (0.9)
Blood lactate dehydrogenase increased	1 (0.9)
Blood phosphorus decreased	1 (0.9)
Blood uric acid increased	1 (0.9)
Bronchopulmonary aspergillosis	1 (0.9)
Candida infection	1 (0.9)
Cardiac failure	1 (0.9)
Chest pain	1 (0.9)
Colitis	1 (0.9)
Depressed level of consciousness	1 (0.9)
Device defective	1 (0.9)
Device dislocation	1 (0.9)
Diarrhea	1 (0.9)
Diarrhea infectious	1 (0.9)
Disseminated intravascular coagulation	1 (0.9)
Dyspnea	1 (0.9)
Fungal infection	1 (0.9)
Gastroenteritis viral	1 (0.9)
Hemoglobin decreased	1 (0.9)
Hepatic failure	1 (0.9)
Hyperbilirubinemia	1 (0.9)
Hypercalcemia	1 (0.9)
Hypophosphatemia	1 (0.9)
Inappropriate schedule of product administration	1 (0.9)
Leukemic infiltration extramedullary	1 (0.9)
Leukopenia	1 (0.9)
Lymph gland infection	1 (0.9)
Lymphocytic leukemia	1 (0.9)
Platelet disorder	1 (0.9)
Pruritus	1 (0.9)

Pseudomonas infection	1 (0.9)
Seizure	1 (0.9)
Soft tissue infection	1 (0.9)
Trigeminal nerve disorder	1 (0.9)
Urticaria	1 (0.9)
Vomiting	1 (0.9)
Weight decreased	1 (0.9)
White blood count increased	1 (0.9)

Retreatment data (treated as cycle 2) for one patient is included.
Adverse events coded using MedDRA version 22.1.
Severity graded using CTCAE v4.03.

Supplemental Table 5: Subject Incidence of Grade ≥ 3 Treatment-Related Adverse Events

	Patients treated with blinatumomab (N = 110) n (%)
Patients reporting grade ≥ 3 TRAEs	29 (26.4)
Pyrexia	11 (10.0)
Febrile neutropenia	3 (2.7)
Hypokalaemia	3 (2.7)
Cytokine release syndrome	2 (1.8)
Headache	2 (1.8)
Hypotension	2 (1.8)
Tumor lysis syndrome	2 (1.8)
Acute kidney injury	1 (0.9)
Acute myeloid leukemia	1 (0.9)
Alanine aminotransferase increased	1 (0.9)
Aspartate aminotransferase increased	1 (0.9)
Bacterial infection	1 (0.9)
Blood bilirubin increased	1 (0.9)
Blood creatine increased	1 (0.9)
Blood uric acid increased	1 (0.9)
Depressed level of consciousness	1 (0.9)
Device related infection	1 (0.9)
Device related sepsis	1 (0.9)
Gamma-glutamyltransferase increased	1 (0.9)
Hyperbilirubinaemia	1 (0.9)
Hypertension	1 (0.9)
Leukemia recurrent	1 (0.9)
Lymph gland infection	1 (0.9)
Neutropenia	1 (0.9)
Neutrophil count decreased	1 (0.9)
Pain	1 (0.9)
Platelet count decreased	1 (0.9)
Seizure	1 (0.9)
Sepsis	1 (0.9)

Soft tissue infection	1 (0.9)
White blood cell count decreased	1 (0.9)

Retreatment data (treated as cycle 2) for one patient is included.
Adverse events coded using MedDRA version 22.1.
Severity graded using CTCAE v4.03.

Supplemental Table 6: Subject Incidence of Treatment-Related Neurologic Events

	Patients treated with blinatumomab (N = 110) n (%)
Patients reporting treatment-related neurologic events	22 (20.0)
Nervous system disorders	20 (18.2)
Headache	11 (10.0)
Tremor	6 (5.5)
Seizure	4 (3.6)
Ataxia	2 (1.8)
Depressed level of consciousness	2 (1.8)
Dizziness	2 (1.8)
Amnesia	1 (0.9)
Aphasia	1 (0.9)
Dysarthria	1 (0.9)
Generalized tonic-clonic seizure	1 (0.9)
Meningism	1 (0.9)
Paraesthesia	1 (0.9)
VIth nerve paralysis	1 (0.9)
Psychiatric disorders	4 (3.6)
Agitation	1 (0.9)
Insomnia	1 (0.9)
Irritability	1 (0.9)
Sleep disorders	1 (0.9)

Retreatment data (treated as cycle 2) for one patient is included.
Table incudes only 'Nervous system disorders' or 'Psychiatric disorders' in adverse event body system organ class search criteria.
Adverse events coded using MedDRA version 22.1.
Severity graded using CTCAE v4.03.

Supplemental Table 7: HSCT Following Treatment with Blinatumomab

	Blinatumomab(N = 58) n (%)
Type of last HSCT	
Autologous	0 (0.0)
Allogeneic	58 (100.0)
Stem cell source of last HSCT	
Peripheral blood	20 (34.5)
Bone marrow	36 (62.1)
Cord blood	1 (1.7)
Unknown	1 (1.7)
Donor type of last alloHSCT	
Sibling	5 (8.6)
Haploidentical (mother)	19 (32.8)
Haploidentical (father)	13 (22.4)
Unrelated	21 (36.2)

N includes all patients who received HSCT any time after the first blinatumomab infusion.
Only the information from the most recent HSCT per patient is included.
Table includes retreatment data (treated as cycle 2) for one patient.
HSCT, hematopoietic stem cell transplant.