

**Long-term relapse-free survival in a phase 2 study of blinatumomab for the treatment of patients with minimal residual disease in B-lineage acute lymphoblastic leukemia**

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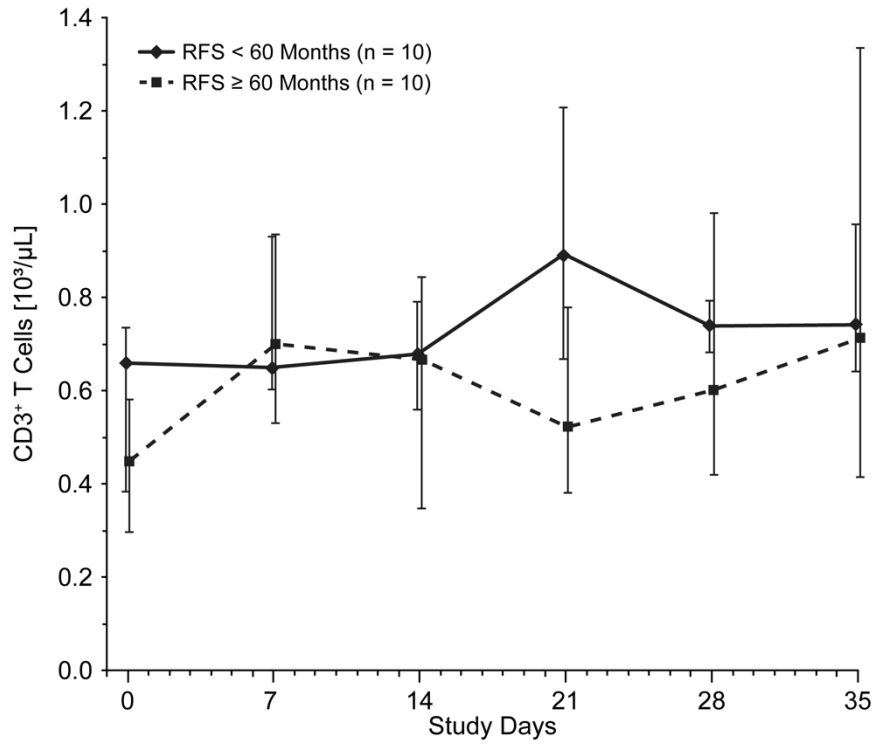
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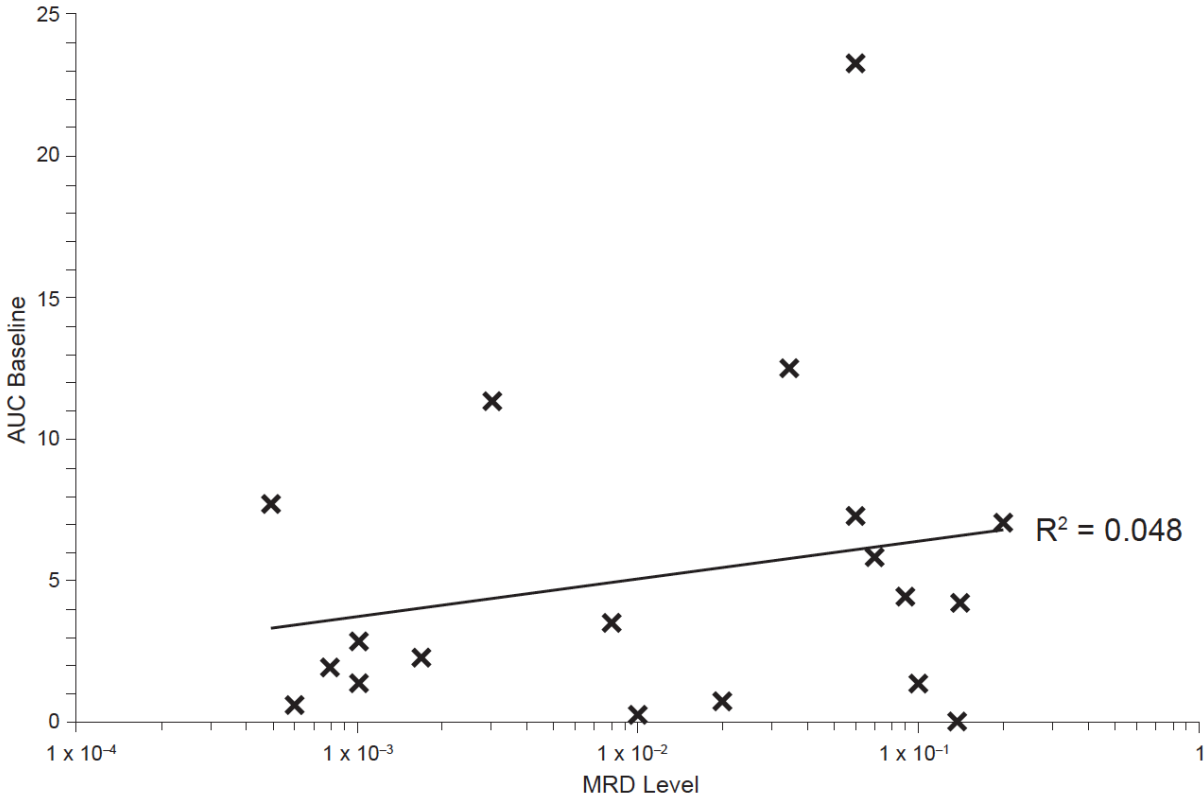
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**SUPPLEMENTAL DATA**

**Online Supplementary Figure S1. CD3<sup>+</sup> T-cell expansion during cycle 1 of blinatumomab treatment (study day 0 to 28) and during the subsequent 2-week treatment-free interval (study day 35). Evaluable patients (N=20) were grouped according to duration of relapse-free survival (RFS) (<5 versus ≥5 years; n=10 each). Data shown are median (interquartile range) cell values. For clarity, initial T-cell redistribution during the first week of cycle 1 is not shown.**

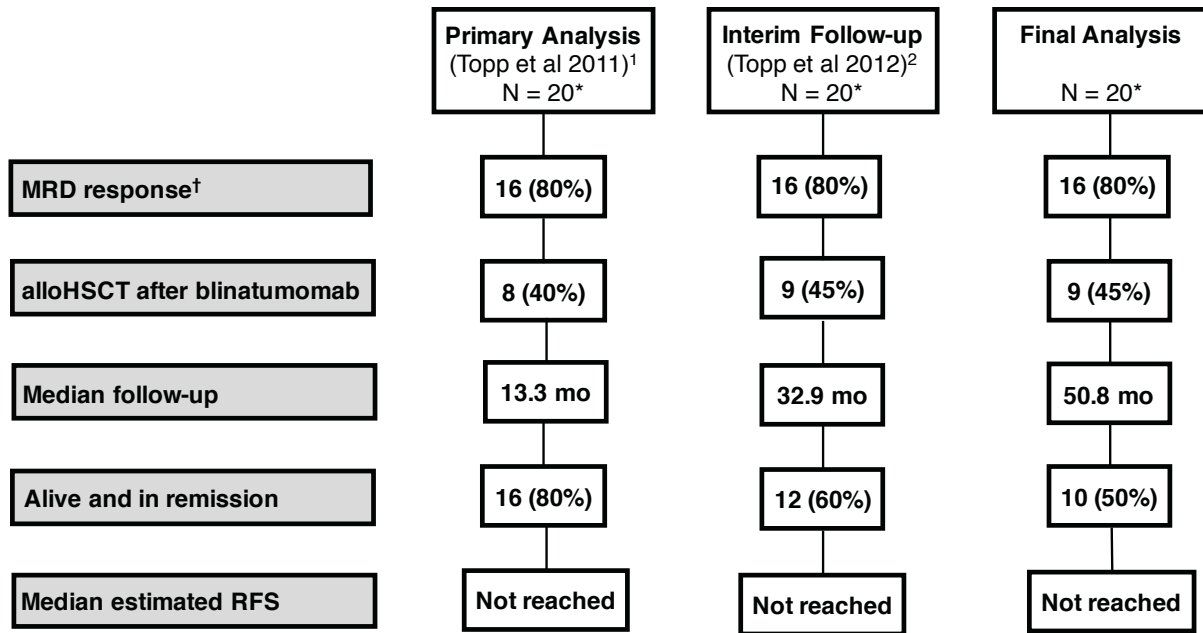


Online Supplementary Figure S2. CD3<sup>+</sup> T-cell expansion as baseline-adjusted area under the T-cell curve (AUC baseline) versus initial minimal residual disease (MRD) level.



**Online Supplementary Figure S3. Key outcomes from each study analysis.**

alloHSCT: allogeneic hematopoietic stem cell transplantation; MRD: minimal residual disease; mo: months; RFS: relapse-free survival. \*Number of evaluable patients. †MRD response within the first 4 cycles was defined as *BCR-ABL* or *MLL-AF4* below the detection limit or individual rearrangements of immunoglobulin or T-cell receptor genes  $<10^{-4}$ ; all MRD responses occurred in the first cycle of blinatumomab treatment.



**Online Supplementary Table S1. Baseline characteristics and treatment outcome by alloHSCT after blinatumomab**

	alloHSCT (n=9)	No alloHSCT (n=11)
Sex, n (%)		
Male	5 (56)	3 (27)
Female	4 (44)	8 (73)
Age, years, median (range)	31 (20-47)	65 (42-77)
Prior consolidation II, n (%)	3 (33)	8 (73)
Disease status, n (%)		
Molecular relapse in CR1	1 (11)	3 (27)
Molecular relapse in CR2+	1 (11)	0 (0)
Molecular failure in CR1	7 (78)	8 (73)
Molecular failure in CR2+	0 (0)	0 (0)
MRD status, n (%)		
MRD <10 <sup>-3</sup>	2 (22)	2 (18)
MRD ≥10 <sup>-3</sup>	7 (78)	9 (82)
Method for MRD evaluation, n (%)*		
Ig/TCR rearrangements	7 (78)	9 (82)
<i>BCR-ABL</i> PCR translocations	1 (11)	4 (36)
<i>MLL-AF4</i> PCR translocations	1 (11)	1 (9)
Number of blinatumomab cycles, median	2.0	4.0
Complete MRD response after 1 cycle, n (%)	7 (78)	9 (82)
RFS, months, median (range)	59.5 (12.4-65.8)	44.3 (1.4-70.1)

\*Patients could have both rearrangements and translocations.

alloHSCT: allogeneic hematopoietic stem cell transplantation; CR1: first hematologic complete remission; CR2+: second or greater hematologic CR; Ig: immunoglobulin; MRD: minimal residual disease; PCR: polymerase chain reaction; RFS: relapse-free survival; TCR: T-cell receptor.

**Online Supplementary Table S2. Serum immunoglobulin levels of individual long-term survivors at screening and last follow-up (modified from Zugmaier et al, 2014)<sup>3</sup>**

Patient	Ph		IgA	IgG	IgM	TKI After
	Status	Statistic				Blinatumomab
13	Ph–	Screening, mg/dL	217	629	66	None
		Last follow-up, mg/dL	13	250	49	
		% Change*	–94%	–60%	–26%	
15	Ph–	Screening, mg/dL	58	457	111	None
		Last follow-up, mg/dL	37	320	72	
		% Change*	–36%	–30%	–35%	
16	Ph–	Screening, mg/dL	132	830	103	None
		Last follow-up, mg/dL	58	801	100	
		% Change*	–56%	–3%	–3%	
18	Ph–	Screening, mg/dL	64	700	58	None
		Last follow-up, mg/dL	30	789	137	
		% Change*	–53%	+13%	+136%	
20	Ph +	Screening, mg/dL	54	330	31	Imatinib, dasatinib
		Last follow-up, mg/dL	26	333	14	
		% Change*	–52%	+1%	–55%	
9	Ph+	Screening, mg/dL	178	696	38	Imatinib
		Last follow-up, mg/dL	63	487	36	
		% Change*	–65%	–30%	–5%	
		Reference range	(70–400)	(700–1600)	(40–230)	

\* The original publication<sup>3</sup> reported final percentages relative to the value at screening; the percent change shown here represents the change from screening to last follow-up. “Screening” refers to baseline.

TKI: tyrosine kinase inhibitor.

## REFERENCES

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