Blinatumomab in induction therapy improves molecular response in untreated adults with Ph- B-cell precursor acute lymphoblastic leukemia

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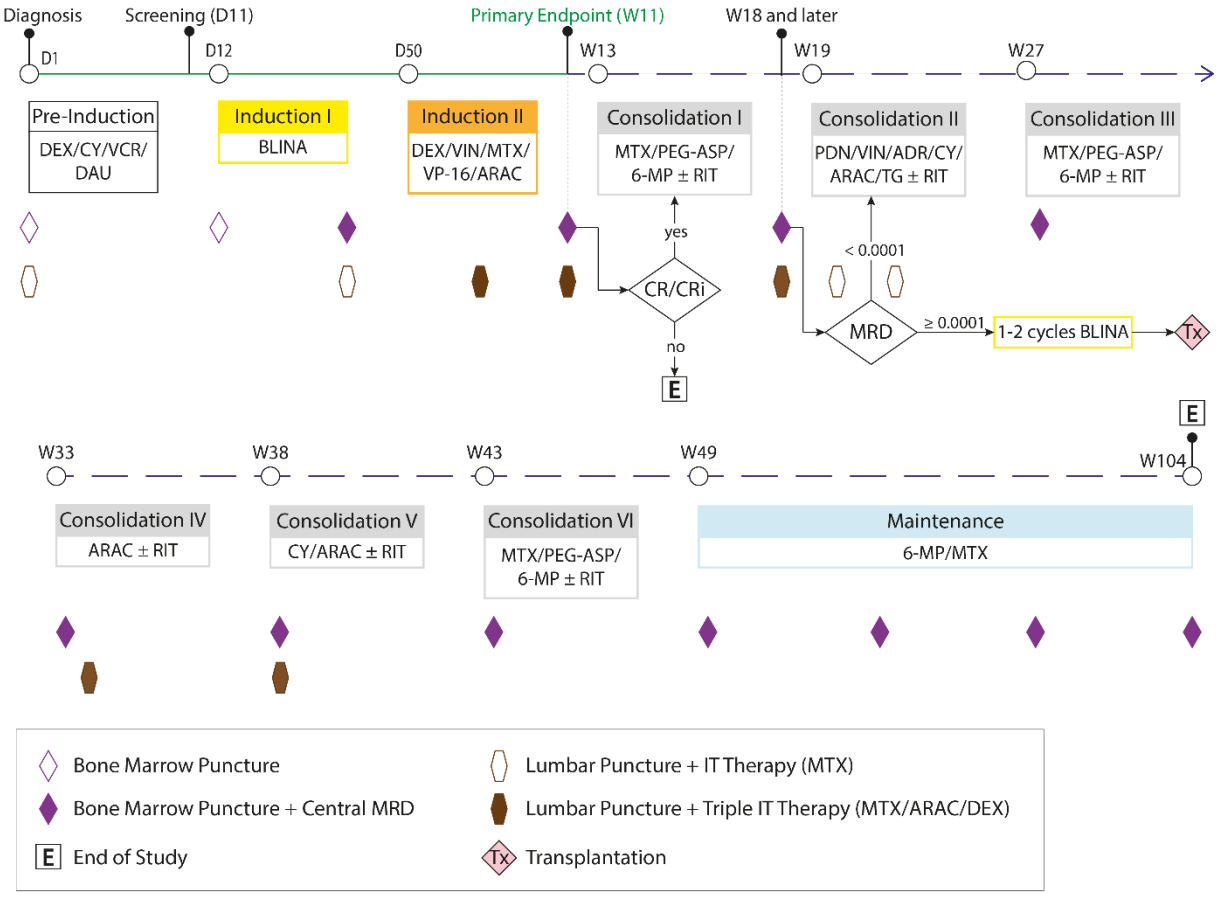
Supplementary Figure 1. Treatment schedule of the Blina-CELL trial.

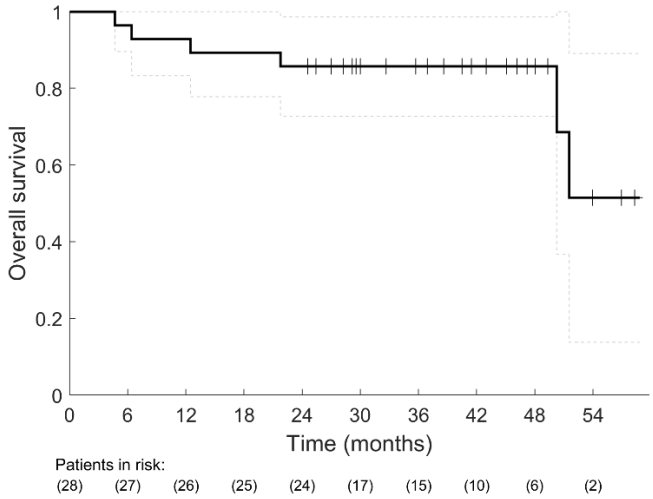


Composition of treatment blocks: Pre-Induction: DEX 10 mg/m² PO D1–7, CY 200 mg/m² IV D3–5, VCR 2 mg IV D6, DAU 45 mg/m² IV D6–7. **Induction I:** BLINA 9 µg/day CIV D12–19, BLINA 28 µg/day CIV D19–40, DEX 20 mg IV D12+19. **Induction II:** DEX 10 mg/m² PO D50–54, VIN 3 mg/m² IV D50, MTX 1.5 g/m² IV D50, VP-16 250 mg/m² IV day 53-54, ARAC 2x 2 g/m² IV D54. **Consolidation I, III and VI:** MTX 1.5 g/m² IV D1+15, PEG-ASP 2000 U/m² IV D2+16, 6-MP 60 mg/m² PO D 1–7 and D15–21, TG 60 mg/m² PO D15–28. **Consolidation II:** PDN 3x 20 mg/m² PO D1–14, VIN 3 mg/m² IV D1+7, ADR 50 mg/m² IV D1+7, CY 1000 mg/m² IV D15, ARAC 75 mg/m² IV D17–20 and D24–27. **Consolidation IV:** ARAC 1000 mg/m² IV D1+3+5. **Consolidation V:** CY 1000 mg/m² IV D1, ARAC 500 mg/m² IV D1. **Rituximab** 375 mg/m² IV D0 of all consolidation cycles if CD20+ at diagnosis (any positivity). **Maintenance:** 6-MP 60 mg/m² PO daily, MTX 20 mg/m² PO weekly. **IT therapy (arrows):** ARAC 40 mg IT, DEX 4 mg IT, MTX 15 mg IT.

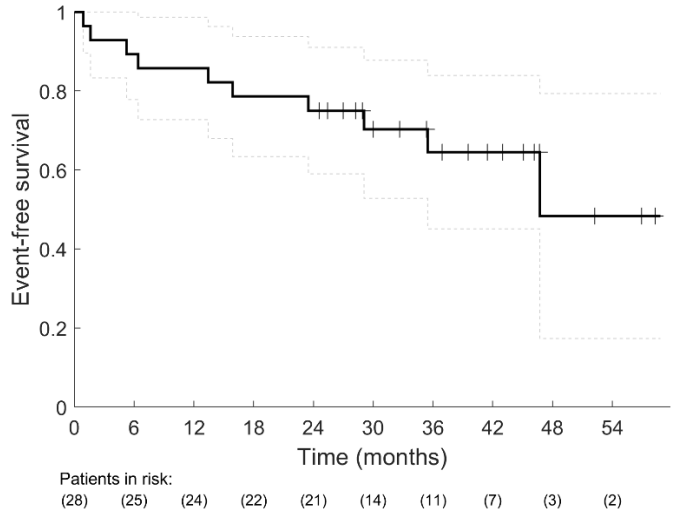
Abbreviations: 6-MP, mercaptopurine; ADR, adriamycine; ARAC, cytarabine; BLINA, blinatumomab; CIV, continuous intravenous infusion; CR, complete remission; CRi, complete remission with incomplete blood count recovery; CY, cyclophosphamide; D, day; DAU, daunorubicin; DEX, dexamethasone; IT, intrathecally; IV, intravenously; MRD; measurable residual disease; MTX, methotrexate; PDN, prednisone; PEG-ASP, pegylated asparaginase; RIT, rituximab; TG, thioguanine; Tx, transplantation; VCR, vincristine; VIN, vindesine; VP-16, etoposide, W, week.

Supplementary Figure 2. Overall survival (A), event-free survival (B), and cumulative incidence of relapse in CR1 (C).

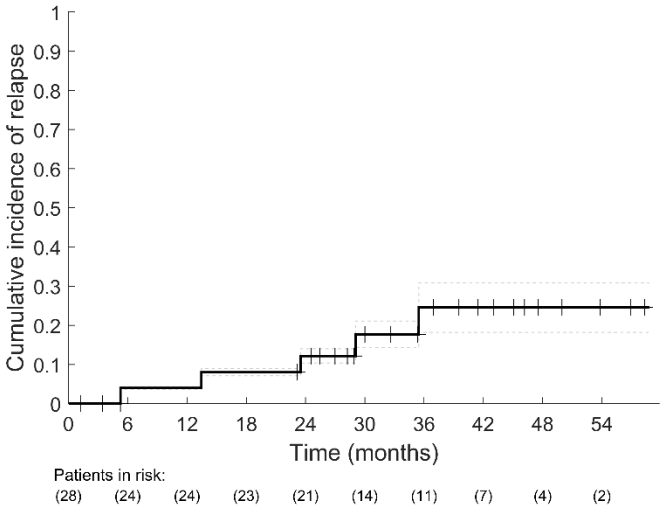
A.



B.



C.



Supplementary Table 1. Clinical and laboratory characteristics of relapsed and refractory patients.

Patient Number	Age [yrs]	WBC at Dg [× 10^9/L]	Pheno-type	Karyotype	Mutations	Fusion Gene	Subtype	MRD D40	MRD W11	MRD W18	Time To Relapse [months]	Previous Malignancy
Refractory												
1-02	65	11.5	B-II	complex	FLT3 D835Y	–	B-other; IKZF1plus	–	–	–	–	no
5-01	52	23.3	B-III	low hyperdiploid	wt	–	B-other; IKZF1plus	–	–	–	–	no
Molecular Response												
2-05	38	16.1	B-II	low hyperdiploid	JAK2 R683G; NF1 I2412Pfs	CRLF2::IGH	Ph-like	nq	neg	neg	24	no
2-06	45	4.6	B-I	normal	SETD2 Q1219X; KMT2D I5497del; KMT2D T4271Afs; KMT2D K3573X; PAX5 S55C, KRAS G13D	DUX4::IGH	DUX4r; IKZF1plus	nq	nq	nq	36	no
2-12	39	6.2	B-II	normal	NRAS G12V; IDH1 R132C	–	B-other; IKZF1plus	neg	neg	neg	14	no
Hematological Relapse												
5-04	22	25.2	B-I	47,XY,t(7,11;12),+19	wt	KMT2A::TNRC18	KMT2Ar	10e-2	10e-3	10e-3	5	no
CNS Relapse												
2-16	23	2.4	B-III	normal	wt	–	B-other	nq	nq	nq	29	no
Secondary MDS												
1-02	65	11.5	B-II	N/A	TP53 H193R, EZH2 G743D	–	Low hypodiploid	neg	neg	neg	47	no
5-01	52	23.3	B-III	near triploid	TP53 P278S; DNMT3A K766Rfs; DNMT3A I670delinsHfs	–	Low hypodiploid; IKZF1plus	nq	neg	neg	16	breast carcinoma