

## *Supplementary Material*

### **Haploidentical *versus* HLA-matched donor hematopoietic stem-cell transplantation for pediatric patients with acute lymphoblastic leukemia in second remission: A collaborative retrospective study of the Spanish Group for Bone Marrow Transplantation in Children (GETMON/GETH) and the Spanish Childhood Relapsed ALL Board (ReALLNet)**

Celia Moreno <sup>1</sup>, Eduardo Ramos-Elbal <sup>1</sup>, Pablo Velasco <sup>2</sup>, Yurena Aguilar <sup>3</sup>, Berta González <sup>4</sup>, Carolina Fuentes <sup>5</sup>, Águeda Molinos <sup>6</sup>, Pilar Guerra-García <sup>4, 7</sup>, Pilar Palomo <sup>8</sup>, Jaime Verdu <sup>9</sup>, Rosa María Adán <sup>10</sup>, José Manuel Vagace <sup>11</sup>, Mónica López Duarte <sup>12</sup>, Alexandra Regueiro <sup>13</sup>, María Tasso <sup>14</sup>, José Luis Dapena <sup>15, 16</sup>, José Antonio Salinas <sup>17</sup>, Samuel Navarro <sup>17</sup>, Francisco Bautista <sup>18</sup>, Álvaro Lassaletta <sup>19</sup>, Francisco Lendínez <sup>20</sup>, Susana Rives <sup>15, 16</sup>, Antonia Pascual <sup>21</sup>, Antonia Rodríguez <sup>22</sup>, José María Pérez-Hurtado <sup>6</sup>, José María Fernández <sup>5</sup>, Antonio Pérez-Martínez <sup>4</sup>, Marta González-Vicent <sup>19</sup>, Cristina Díaz de Heredia <sup>2</sup>, José Luis Fuster\* <sup>1, 23</sup>

\* **Correspondence:** José Luis Fuster, Hospital Clínico Universitario Virgen de la Arrixaca, Ctra. Madrid-Cartagena s/n, 30120, El Palmar, Murcia (Spain). Phone: (34) 968369298. Email: [josel.fuster@carm.es](mailto:josel.fuster@carm.es). ORCID: 000-0002-4881-9440

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**Table S1. Definition of relapse**

	Bone marrow <sup>1</sup>	M1 ( <b>&lt; 5% blasts</b> )	M2 ( <b>≥ 5% and &lt; 25% blasts</b> )	M3 ( <b>≥ 25% blasts</b> )
<b>Extramedullary disease <sup>2</sup></b>	<b>No</b>	No relapse	Repeat bone marrow evaluation	Isolated bone marrow relapse
	<b>Yes</b>	Isolated extramedullary relapse	Combined (bone marrow and extramedullary) relapse	

<sup>1</sup> The percentage of leukemic blasts was established by conventional cytology.

<sup>2</sup> Central nervous system relapse is defined as the identification of leukemic lymphoblasts in the cerebrospinal fluid with > 5 nucleated cells/μl or the presence of tumor lesions or evidence of meningeal infiltration by imaging or biopsy; testicular relapse is defined as a confirmatory testicular biopsy in patients with painless testicular enlargement; other extramedullary sites of relapse are diagnosed by radiological measures with confirmation by biopsy.

**Table S2. Treatment protocol before stem cell transplantation**

<b>High risk relapse</b>		
<b>Induction “HIA” (R3)</b>		
Dexamethasone	10 mg/m <sup>2</sup> / 12 h.	Days 1 to 5 of week 1 and week 3
Vincristine	1.5 mg/m <sup>2</sup>	Days 3 of weeks 1, 2, 3 and 4
Mitoxantrone	10 mg/m <sup>2</sup>	Days 1 and 2 of week 1
PEG-asparaginase	1,000 U/m <sup>2</sup>	Day 3 of week 1 and 3
TIT <sup>1</sup>		Day 1 of weeks 1 and 2
<b>Consolidation “HC1”</b>		
Dexamethasone	5 mg/m <sup>2</sup> / 12 h.	Days 1 to 5 of week 5
Vincristine	1.5 mg/m <sup>2</sup>	Days 1 and 6 of week 5
Cytarabine	2 g/m <sup>2</sup> /12 h. (2 doses)	Day 5 of week 5
Methotrexate	1 g/m <sup>2</sup> (36 h. infusion)	Day 1 of week 5
Cyclophosphamide	200 mg/m <sup>2</sup> /12 h. (5 doses)	Days 2 to 4 of week 5
PEG-asparaginase	1,000 U/m <sup>2</sup>	Day 6 of week 5
TIT <sup>1</sup>		Day 2 (day 7) of week 5
<b>Consolidation “HC2”</b>		
Dexamethasone	5 mg/m <sup>2</sup> / 12 h.	Days 1 to 6 of week 8
Cytarabine	2 g/m <sup>2</sup> /12 h. (4 doses)	Days 1 and 2 of week 8
Etoposide	100 mg/m <sup>2</sup> /12 h. (5 doses)	Days 3 to 5 of week 8
PEG-asparaginase	1,000 U/m <sup>2</sup>	Day 6 of week 8
TIT <sup>1</sup>		Day 1 of week 8
<b>Consolidation “HC3”</b>		
Dexamethasone	5 mg/m <sup>2</sup> / 12 h.	Days 1 to 6 of week 11
Vincristine	1.5 mg/m <sup>2</sup>	Days 1 and 6 of week 11
Daunorubicine	30 mg/m <sup>2</sup> (24 h. infusion)	Day 5 of week 11
Methotrexate	1 g/m <sup>2</sup> (36 h. infusion)	Day 1 of week 11
Ifosfamide	800 mg/m <sup>2</sup> /12 h. (5 doses)	Days 2 to 4 of week 11
PEG-asparaginase	1,000 U/m <sup>2</sup>	Day 6 of week 11
TIT <sup>1</sup>		Day 2 of week 11
<b>Standard risk relapse</b>		
<b>Induction “SIA”</b>		
Dexamethasone	10 mg/m <sup>2</sup> / 12 h.	Days 1 to 5 of weeks 1 and 3
Vincristine	1.5 mg/m <sup>2</sup>	Days 1 and 6 of week 1 and day 1 of week 3
Methotrexate	1 g/m <sup>2</sup> (36 h. infusion)	Day 1 of week 1
Cytarabine	3 g/m <sup>2</sup> /12 h.	Days 1 and 2 of week 3
PEG-asparaginase	1,000 U/m <sup>2</sup>	Day 4 of week 1 and 3
TIT <sup>1</sup>		Day 1 (day 6) of week 1 and day 5 of week 3

**Table S2. Treatment protocol before stem cell transplantation (cont.)**

<b>Consolidation “SCA1”</b>		
Dexamethasone	3 mg/m <sup>2</sup> / 12 h.	Days 1 to 7 of weeks 5 and 6 <sup>2</sup>
Vincristine	1.5 mg/m <sup>2</sup>	Day 1 of weeks 5, 6, 7 and 8
Idarubicine	6 mg/m <sup>2</sup> (2 h. infusion)	Day 1 of weeks 5, 6, 7 and 8
PEG-asparaginase	1,000 U/m <sup>2</sup>	Day 1 of week 5 and day 4 of week 6
TIT <sup>1</sup>		Day 1 of weeks 5 (day 1 of week 6) and 7
<b>Consolidation “SCA2”</b>		
Cyclophosphamide	1 g/m <sup>2</sup>	Day 1 of week 9
Cytarabine	75 mg/m <sup>2</sup> (15 minutes)	Days 3 to 6 of weeks 9 and 10
Thioguanine	60 mg/m <sup>2</sup>	Days 1 to 7 of weeks 9 and 10
TIT <sup>1</sup>		Day 3 of weeks 9 and 10
<b>Consolidation “SCA3”</b>		
Dexamethasone	10 mg/m <sup>2</sup> / 12 hours	Days 1 to 5 of week 13 <sup>2</sup>
Mercaptopurine	100 mg/m <sup>2</sup>	Days 1 to 5 of week 13
Vincristine	1.5 mg/m <sup>2</sup>	Days 1 and 6 of week 13
Methotrexate	1 g/m <sup>2</sup> (36 h. infusion)	Day 1 of week 13
Cytarabine	2 g/m <sup>2</sup> /12 h. (2 doses)	Day 5 of week 13
PEG-asparaginase	1,000 U/m <sup>2</sup>	Day 6 of week 13
TIT <sup>1</sup>		Day 1 of weeks 13

Abbreviations; h., hours; HC1/2/3, high risk consolidation blocks 1, 2 and 3; HIA, high risk induction “A”; SCA1/2/3, standard risk consolidation blocks 1, 2 and 3; SIA, standard risk induction “A”; TIT, triple intrathecal therapy

<sup>1</sup> Age adapted doses of triple intrathecal chemotherapy: methotrexate, cytarabine and hydrocortisone 5, 16 and 10 mg, respectively for patients < 1 year old; 8, 16 and 10 mg for those ≥ 1 and < 2 year old; 10, 20 and 15 mg for those ≥ 2 and < 3 year old; 12, 30 and 20 mg for those ≥ 3 year old. Days between parentheses represent additional doses of TIT scheduled for patients with central nervous system involvement at relapse.

<sup>2</sup> Dose tapering until day 2 of week 8; 5 mg/m<sup>2</sup>/12 h. on day 6 of week 13

**Table S3. Indications of allogeneic transplantation in patients with standard risk relapse**

	Late BM isolated or combined			Early combined BM			Isolated EM	
	MRD GR <sup>1</sup>	MRD PR <sup>1</sup>	MRD ND	MRD GR <sup>1</sup>	MRD PR <sup>1</sup>	MRD ND	Late	Early
<b>MD</b>	No	Yes	Yes	Yes	Yes	Yes	No	Yes
<b>MMD</b>	No	Yes	No	No	Yes	Yes	No	No

Abbreviations; BM, bone marrow; EM, extramedullary; GR, good response; MD, matched donor; MMD, mismatched donor; MRD, minimal residual disease; ND, not done or not available; PR, poor response

<sup>1</sup> MRD GR is defined as < 0.1% (< 10<sup>-3</sup>) residual disease after re-induction by flow cytometry, and MRD PR is defined as ≥ 0.1% residual disease.

**Table S4. Patients undergoing stem cell transplantation without a scheduled indication**

Relapse	Genetics	Unscheduled indication for SCT <sup>1</sup>	Donor	Outcome (m) <sup>2</sup>
Late isolated EM (BCP)	<i>KMT2A</i> -r	Late isolated EM	MU	CCR (57)
Late isolated BM (BCP)	<i>TP53</i> deletion	MRD GR (< 0.01%) after re-induction	MU	CCR (5)
Late isolated BM (BCP)	High hyperdiploidy	MRD GR (< 0.01%) after re-induction	MR	CCR (59)
Late isolated BM (BCP)	B-other	MRD GR (< 0.01%) after re-induction	MU	TRD (4)
Late isolated BM (BCP)	B-other	MRD GR (0.06%) after re-induction	MU	CCR (53)
Late combined (BCP)	<i>IKZF1</i> deletion	MRD GR (0.08%) after re-induction	Haplo	TRD (8)
Early isolated EM (BCP)	No data	SCT from mismatched donor	Haplo	CCR (25)

<sup>1</sup> Deviations from scheduled indications for standard risk relapse (table S3)

<sup>2</sup> Months since transplantation.

Abbreviations; BCP, B-cell precursor; BM, bone marrow; CCR, continuous complete remission; EM, extramedullary; GR, good response; Haplo, haploidentical; *KMT2A*-r, *KMT2A* rearrangement; m, months; MR, matched related; MRD, minimal residual disease; MU, matched unrelated; SCT, allogeneic stem cell transplantation; TRD, treatment-related death.

**Table S5. Treatment and outcome of patients failing to respond to re-induction and/or with persistent minimal residual disease**

Relapse	Disease status <sup>1</sup>	Treatment	Response	Donor	Outcome (m) <sup>2</sup>
Early isolated BM (BCP) <sup>3</sup>	Refractory	Clofarabine, VP16, Cy	CR2 (MRD negative)	MR	CCR (41)
Very early isolated BM (BCP)	Refractory	Clofarabine, VP16, Cy	CR2 (MRD negative)	Haplo	TRD (2)
Early isolated BM (BCP)	Refractory	Clofarabine, VP16, Cy	CR2 (MRD negative)	MR	TRD (45)
Early isolated BM (BCP)	Refractory	TVTC	CR2 (MRD negative)	Haplo	TRD (5)
Late isolated BM (BCP)	Refractory	Inotuzumab	CR2 (MRD na)	Haplo	TRD (3)
Early isolated BM (BCP)	Persistent MRD	Blinatumomab	CR2 (MRD negative)	MU	2 <sup>nd</sup> REL (7)
Early isolated BM (BCP)	Persistent MRD	Clofarabine, VP16, Cy	CR2 (MRD negative)	MR	CCR (78)
Early combined (BCP)	Persistent MRD	Clofarabine, VP16, Cy	CR2 (MRD 1.09%)	MR	2 <sup>nd</sup> REL (6)
Late isolated BM (BCP)	Persistent MRD	Rituximab	CR2 (MRD negative)	MU	CCR (27)
Late isolated BM (BCP)	Persistent MRD	Blinatumomab	CR2 (MRD negative)	MU	CCR (20)
Late isolated BM (BCP)	Persistent MRD	Blinatumomab	CR2 (MRD negative)	Haplo	CCR (45)
Late combined (BCP)	Persistent MRD	Blinatumomab	CR2 (MRD negative)	Haplo	CCR (27)
Very early combined (T)	Persistent MRD	Daratumomab	CR2 (MRD negative)	Haplo	TRD (11)

<sup>1</sup> Disease status after re-induction and indication for salvage (rescue) treatment before SCT.

<sup>2</sup> Months since transplantation.

<sup>3</sup> Misclassified as standard risk relapse

Abbreviations; BCP, B-cell precursor; BM, bone marrow; CCR, continuous complete remission; CR2, second complete remission; Cy, cyclophosphamide; Haplo, haploidentical; m, months; MR, matched related; MRD, minimal residual disease; MU, matched unrelated; na, not available; REL, relapse; TRD, treatment-related death; T, T-cell immunophenotype; TVTC, topotecan, vinorelbine, thiotepa, clofarabine (reference number 1); VP16, etoposide.

**Table S6. Characteristics of B cell precursor ALL patients and donor-recipient HLA matching**

	Haploidentical donor		HLA-matched donor		p
	n = 23	%	n = 43	%	
<b>Age at SCT (years) <sup>1</sup></b>					
≥ mean	11	48	24	56	0.5355
< mean	12	52	19	44	
<b>Time to relapse <sup>2</sup></b>					
Very early	4	17	5	11.6	0.8267
Early	11	48	21	48.8	
Late	8	35	17	39.6	
<b>Site of relapse</b>					
Isolated BM	17	74	28	65.1	0.7654
Combined BM	5	22	11	25.6	
Isolated EM	1	4	4	9.3	
<b>Risk-group at relapse</b>					
High	14	61	17	39.5	0.1637
Standard	9	39	26	60.5	
<b>MRD before SCT <sup>3</sup></b>					
≥ 0.01%	1	4.5	7	17	0.1637
< 0.01%	21	95.5	35	83	
No data	1		1		
<b>HLA matching (matched alleles) <sup>4</sup></b>					
9/10	na	na	8	18.6	na
10/10	na	na	29 <sup>5</sup>	67.4	na
Umbilical cord blood (5 to 6/6)	na	na	6	14	na
No data	na	na	0	0	na

Abbreviations; ALL, acute lymphoblastic leukemia; BM, bone marrow; EM extramedullary; HLA, human leukocyte antigen; MRD, minimal residual disease; na, not applicable; SCT, allogeneic stem cell transplantation;

<sup>1</sup> Mean age 8 years (range: 1 to 19)

<sup>2</sup> Very early relapse: < 6 months after the end of first-line treatment and < 18 months after primary diagnosis. Early relapse: < 6 months after the end of first-line treatment but ≥ 18 months after primary diagnosis. Late relapse: ≥ 6 months after the end of first-line treatment.

<sup>3</sup> Five patients had MRD ≥ 0.1% (4 in the haploidentical and 1 in the HLA compatible donor group)

<sup>4</sup> Patients without available data were excluded from the analysis of the corresponding variable.

<sup>5</sup> Thirteen related and 16 unrelated donors.

**Table S7. Transplantation characteristics of B-cell precursor ALL patients**

	Haploidentical donor		HLA-matched donor		p
	n = 23	%	n = 43	%	
<b>Conditioning</b>					
TT + Bu + Flu	14	61	16	37	0.0659
Bu + Cy ± TT	0	0	4	9	0.1313
TBI + VP16	1	4	5	12	0.3269
TBI + Cy	0	0	7	16	<b>0.0407</b>
TLI + TT + Flu + L-PAM	5	22	2	5	<b>0.0317</b>
TBI + TT + Cy	0	0	4	9	0.1313
Other <sup>1</sup>	3	13	5	12	0.8667
<b>TBI-based conditioning</b>					
Yes	3	13	20	46.5	<b>0.0065</b>
No	20	87	23	53.5	
<b>Stem cell source</b>					
Peripheral blood	18	78.3	20	46.5	<b>0.027</b>
Bone marrow	5	21.7	17	39.5	
Umbilical cord blood	0		6	14	
<b>Ex vivo graft manipulation <sup>2,3</sup></b>					
No manipulation	9	40.9	39	90.7	<b>&lt;0.0001</b>
αβ T-cell and CD19+ depletion	8	36.4	0	0	<b>&lt;0.0001</b>
CD45RA+ depletion	4	18.2	4	9.3	0.3025
CD3+ and CD19+ depletion	1	4.5	0	0	0.1589
No data	1		0		
<b>CD34+ cell dose infused <sup>2,4</sup></b>					
≥ mean	11	50	19	50	1
< mean	11	50	19	50	
≥ 2 x 10 <sup>6</sup> CD34+/kg	21	81.8	34 (29 <sup>5</sup> )	89.5 (90.6 <sup>5</sup> )	0.41 (0.5)
≥ 5 x 10 <sup>6</sup> CD34+/kg	13	50	21 (18 <sup>5</sup> )	55.3 (56.2 <sup>5</sup> )	0.77 (0.83)
No data	1		5		
<b>GVHD prophylaxis <sup>2</sup></b>					
Cyclosporine + methotrexate	0	0	22	51.2	<b>&lt;0.0001</b>
Cyclosporine	8	36.4	6	14	<b>0.0376</b>
Cyclosporine + MF	5	22.7	1	2.3	<b>0.0072</b>
Tacrolimus + methotrexate	0	0	4	9.3	0.1398
Tacrolimus + MF	3	13.6	0	0	<b>0.0132</b>
Tacrolimus	1	4.5	3	7	0.6995
MF	1	4.5	2	4.6	0.9847
Cyclosporine + prednisolone	0	0	1	2.3	0.471
None <sup>6</sup>	4	18.2	4	9.3	0.3025
No data	1		0		
<b>Serotherapy <sup>2</sup></b>					
Yes	3	13.6	26	60.5	<b>0.0003</b>
No	19	86.4	17	39.5	
No data	1		0		

Abbreviations; ALL, acute lymphoblastic leukemia; Bu, busulphan; Cy, cyclophosphamide; Flu, fludarabine; GVHD, graft versus host disease; L-PAM, melphalan; na, not applicable; MF, mycophenolate mofetil; TBI, total body irradiation; TLI, total lymphoid irradiation; irradiation; TT, Thiotepa; VP16, etoposide

<sup>1</sup> Other conditioning regimens: Bu + TT; Bu + Flu; Cy + VP16; TBI + Flu ± Cy or TT; TBI + Cy + VP16; TBI + TT.

<sup>2</sup> Patients without available data were excluded from the analysis of the corresponding variable.

<sup>3</sup> Patients without graft manipulation (T-cell replete grafts) in the haploidentical donor group received post-transplant cyclophosphamide.

<sup>4</sup> Mean CD34+ cell dose infused was 5.07 x 10<sup>6</sup>/kg (range 0.35-14.6).

<sup>5</sup> Excluding 6 patients who received umbilical cord blood transplantation (n = 32)

<sup>6</sup> One and three patients in the haploidentical donor group received no pharmacologic GVHD prophylaxis after αβ T-cell depletion and CD45RA+, respectively; 4 in the HLA compatible donor group received no pharmacologic GVHD prophylaxis after CD45RA+ graft depletion.

**Table S8. CD34+ cell dose in patients with primary or secondary graft failure**

Donor	Graft manipulation	Stem cell source	CD34+ cell dose (x 10 <sup>6</sup> /kg)	Graft failure
Matched related	No	Bone marrow	1.74	Primary
Matched unrelated	CD45RA depletion	Peripheral blood	7.34	Primary
Haploidentical	CD45RA depletion	Peripheral blood	5.83	Secondary
Haploidentical	αβ depletion	Peripheral blood	4.1	Primary
Haploidentical	No data	Peripheral blood	No data	Secondary
Haploidentical	αβ depletion	Peripheral blood	10.26	Primary

**Table S9. Early complications after stem cell transplantation and chronic GVHD of B cell precursor ALL patients**

	Haploidentical donor		HLA-matched donor		
	n = 23	%	n = 43	%	p
<b>Graft failure</b> <sup>1</sup>					
Yes	4	17.4	1	2.4	<b>0.0299</b>
No	19	82.6	41	97.6	
No data	0		1		
<b>aGVHD</b>					
Grade 1	3	13	3	7	0.7433
Grade ≥ 2	7	30.5	15	34.9	
No	13	56.5	25	58.1	
<b>Grade ≥ 3 infections</b>					
Yes	14	60.9	21	48.8	0.3507
No	9	39.1	22	51.2	
<b>SOS (any grade)</b>					
Yes	2	8.7	8	18.6	0.2847
No	21	91.3	35	81.4	
<b>Other CTCAE grade ≥ 3</b> <sup>1</sup>					
Yes	10	45.4	15	37.5	0.5413
No	12	54.6	25	62.5	
No data	1		3		
<b>cGVHD</b> <sup>1,2</sup>					
Yes	1	5.3	4	11.4	0.4554
No	18	94.7	31	88.6	
No data	1		1		

Abbreviations; aGVHD, acute graft versus host disease; cGVHD, chronic graft versus host disease; CTCAE, Common Terminology Criteria for Adverse Events version 3.0; SOS, sinusoidal obstructive syndrome (any grade)

<sup>1</sup> Patients without available data were excluded from the analysis of the corresponding variable.

<sup>2</sup> Proportions of patients with any grade cGVHD among those surviving > 100 days after transplantation (20 in the haploidentical and 36 in the HLA-matched donor group)



**Table S10. Overall results of B-cell precursor ALL patients: probability (%) and 95% CI**

	Haploidentical donor	HLA-matched donor	p
<b>OS</b>	59.4% (42-84.1)	63.9% (50.8-80.5)	0.9
<b>LFS</b>	52.2% (35.3-77.2)	38.4% (26.2-56.4)	0.6
<b>EFS</b>	43.5% (27.3-69.3)	36.1% (24.1-54)	0.9
<b>CIR</b>	26.1% (10.3-45.3)	40.5% (25.5-55.1)	0.63
<b>TRM</b>	21.7% (7.6-40.5)	21% (10.3-34.3)	0.87
<b>Cumulative incidence of cGVHD</b>	5% (0.3-21)	14.8% (4.5-30.7)	0.43
<b>GLFS</b>	47.8% (31.2-73.3)	31.2% (19.9-49)	0.5

Abbreviations; ALL, acute lymphoblastic leukemia; cGVHD, chronic graft versus host disease; GLFS, cGVHD-free and leukemia-free survival; CIR, cumulative incidence of relapse; EFS, event free survival; LFS, leukemia free survival; OS, overall survival; TRM, treatment related mortality.

**Table S11. Factors influencing leukemia-free survival in B cell precursor ALL patients: univariate analysis**

	N. of patients	Events	Probability (%)	95% CI	P value
<b>Risk group at relapse</b>					
Standard risk	35	17	50.5	36.2-70.4	0.1
High risk	31	20	31.9	21.5-56.8	
<b>MRD before SCT</b>					
< 0.01%	56	26	52.1	40.4-67.3	<b>0.006</b>
≥ 0.01%	8	9	0		
No data	2				
<b>Conditioning regimen</b>					
TBI-based	23	10	58.8	37.5-80.1	0.1
Chemotherapy-based	43	27	36.8	24.8-54.6	
No data	0				
<b>CD34+ cell dose infused</b>					
< mean	30	20	49.8	35.1-70.6	0.8
≥ mean	30	16	41.3	26.3-64.7	
No data	6				
<b>Grade 1/2 aGVHD</b>					
Yes	12	5	54.9	30.8-94.6	0.5
No	54	51	40.7	29.5-56.2	
<b>Any grade cGVHD</b>					
Yes	5	1	80	51.6-100	0.06
No	61	36	40	29.3-64.6	

Abbreviations; aGVHD, acute graft versus host disease; ALL, acute lymphoblastic leukemia; cGVHD, chronic graft versus host disease; MRD, minimal residual disease; N., numbers; SCT, stem cell transplantation; TBI, total body irradiation.

**Table S12. Factors influencing leukemia-free survival in B cell precursor ALL patients: multivariate analysis**

	Hazard ratio (95% CI)	p value
<b>MRD before SCT ≥ 0.01%</b>	2.81 (1.3056-6.088)	0.00836

Abbreviations; ALL, acute lymphoblastic leukemia; cGVHD, chronic graft versus host disease; MRD, minimal residual disease; SCT, stem cell transplantation; TBI, total body irradiation.

**Table S13. Reported results after SCT in pediatric patients with hematological malignancies undergoing allogeneic stem cell transplantation (estimated rates presented as percentages)**

Study / study group	Year of publication	OS	LFS/ PFS	EFS	CIR	TRM/ NRM	cGVHD	GLFS	FU (y)	Ref.
EBMT Registry <sup>1</sup>	2010	39	34	-	36	30	-	-	5	2
Peking University <sup>2</sup>	2013	60.2	56.6	-	34.3	19.5	40.1	-	5	3
BFM <sup>3</sup>	2015	73-79	-	67-71	22-24	3-10	-	-	4	4
AIEOP-GITMO <sup>4</sup>	2016	72	61	-	24	9	0-7	-	1	5
China <sup>5</sup>	2016	82	71	-	16.1	12.8	64	-	2	6
China <sup>6</sup>	2016	69.6	57.2	-	24.1	18.8	6.3	-	2	6
Madrid (Spain) <sup>7</sup>	2016	-	52	-	32	23	46	-	2	7
Montevideo <sup>4</sup>	2016	48	-	-	23	26	53	-	-	8
Montevideo <sup>7</sup>	2016	47	-	-	31	24	9	-	-	8
Monterrey <sup>4</sup>	2016	50	-	33	40	36	-	-	1	9
NCT0181010 <sup>8</sup>	2017	72	71	69.5	24	5	5	71	5	10
BFM <sup>9</sup>	2018	56	-	52	31	19	15	-	4	11
Texas Children's Hospital <sup>10</sup>	2018	40		35	47	15	-	-	3	12
JSHCT <sup>11</sup>	2019	75.8		69.3	20.1	9.1	29.5	-	3	13
Multinational <sup>12</sup>	2019	63	-	57	30	14	21	-	4	14
BFM ALL SCT 2007 <sup>3</sup>	2019	68-72	-	61-65	24-25	10-14	25-37	-	4	15
EBMT <sup>13</sup> (TBI)	2020	58.8	53.7	-	30.6	15.7	21.2	-	5	16
EBMT <sup>13</sup> (CC)	2020	35.9	29.4	-	49.3	21.3	26	-	5	16
SJCRH <sup>14</sup>	2020	88.1	-	77.7	11.5	5.6 (1 y)	25.9	-	3	17
Arizona <sup>4</sup>	2020	84	74.3	-	17.6	9.5	18.1	-	2	18
NCT01949129 <sup>3</sup> (TBI)	2021	91	-	75	22	4	-	72	2	19
NCT01949129 <sup>3</sup> (CC)	2021	74	-	46	44	9	-	51	2	19
ALLR3 & ALL-REZ BFM 2002 <sup>15</sup>	2021	52.7	46.4	-	31.6	14.9	-	-	-	20
ALL-SCT-(I)BFM 2013 & 2007 <sup>12</sup>	2021	65	-	53	36	9	11-17	-	4	21
HIUNJ <sup>8</sup>	2022	58	45	-	34	21	23	-	-	22
HIUNJ <sup>16</sup>	2022	53	45		32	23	32	-	-	22

Abbreviations; ALL, acute lymphoblastic leukemia; AML, acute myeloblastic leukemia; BFM, Berlin-Frankfurt, Muenster; CC, chemotherapy-based conditioning; cGVHD, cumulative incidence of chronic graft versus host disease; CIR, cumulative incidence of relapse; CR1, first complete remission; CR2 second, complete remission; EBMT, European Bone Marrow Transplantation; EFS, event free survival; FU, follow up; GLFS, graft versus host disease and leukemia free survival; HIUNJ, Hospital Infantil Universitario Niño Jesús; JSHCT, Japan Society for Hematopoietic Cell Transplantation; LFS, leukemia free survival; MMD, mismatched donor; MRD, matched related donor; MUR, matched unrelated donor; NRM, nonrelapse mortality; OS, overall survival; PFS, progression free survival; Ref., reference; SCT, allogeneic stem cell transplantation; SJCRH, Saint Jude Children's Research Hospital; TBI, total body irradiation; TRM, treatment related mortality; y, years

<sup>1</sup> Data from patients with ALL who received haploidentical transplantation in CR2

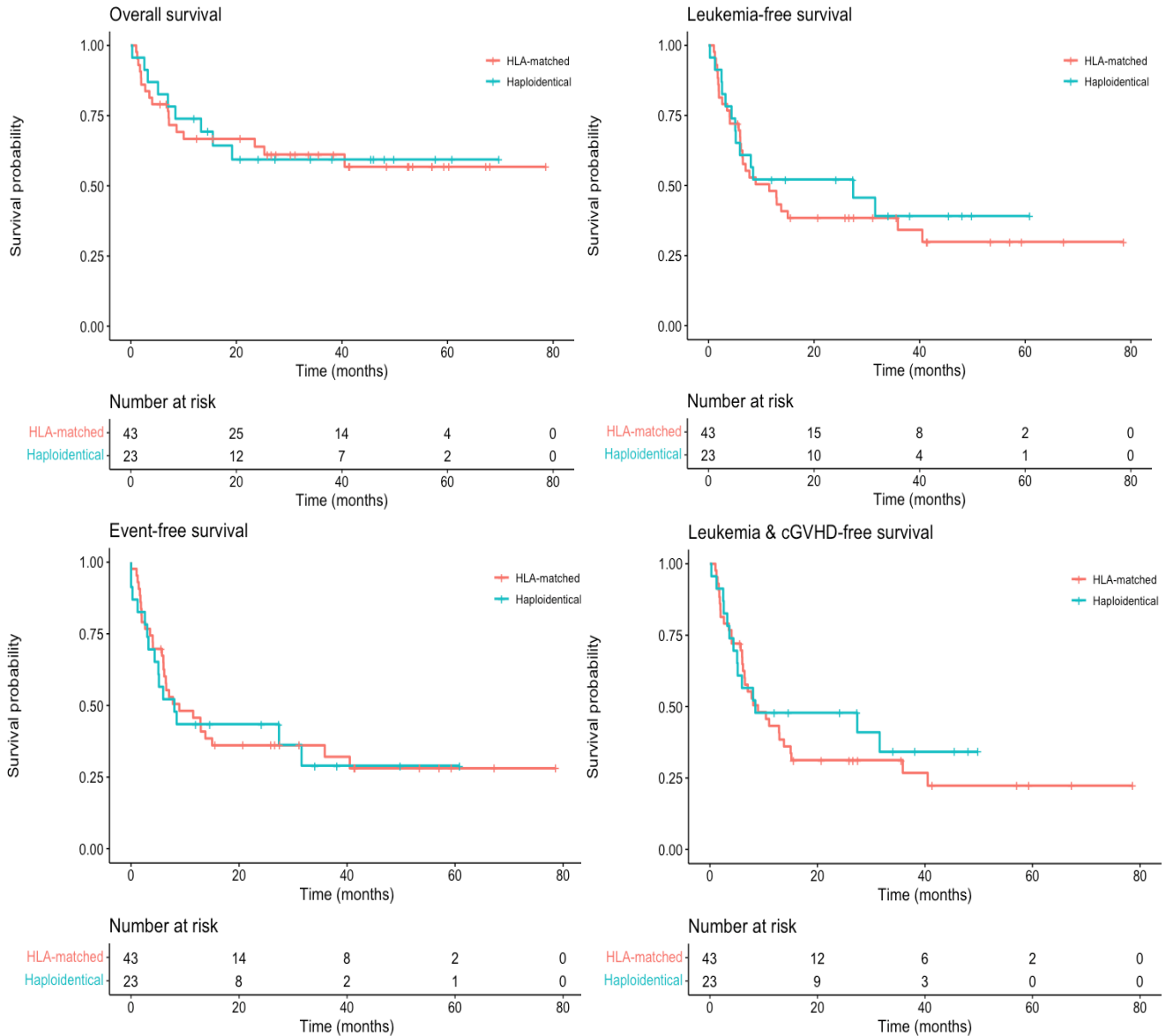
<sup>2</sup> OS, LFS, CIR and TRM data from 59 patients with ALL in CR2 undergoing unmanipulated haploidentical transplantation without post-transplant high-dose cyclophosphamide ("Beijing protocol"), cGVHD data from 193 patients with ALL and other hematological malignancies in different remission status

<sup>3</sup> Include patients with ALL in CR1 and  $\geq$  CR2 undergoing SCT from MRD and MUD

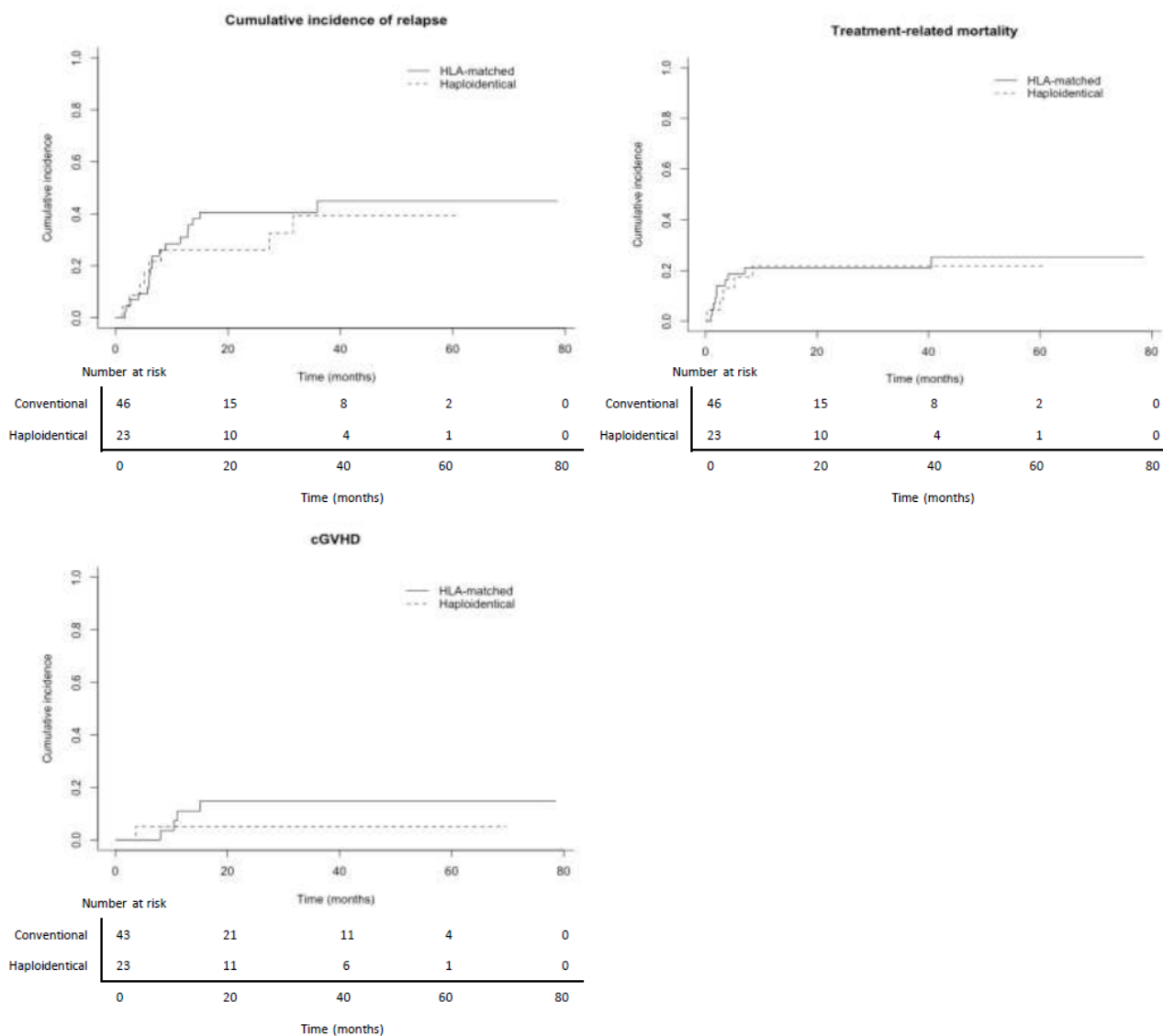
<sup>4</sup> Include patients with ALL, AML and other hematological malignancies in CR1 and  $\geq$  CR2 undergoing haploidentical transplantation with post-transplant high-dose cyclophosphamide

<sup>5</sup> Data from patients with ALL, including CR1, CR2 and  $\geq$  CR3, undergoing unmanipulated haploidentical transplantation without post-transplant high-dose cyclophosphamide ("Beijing protocol")

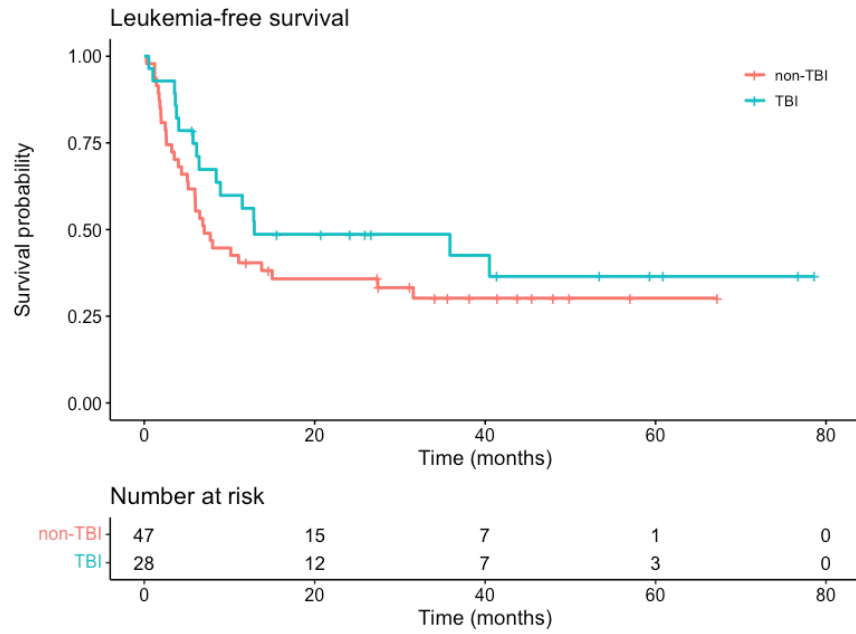
- <sup>6</sup> Data from patients with ALL, including CR1, CR2 and  $\geq$  CR3, undergoing umbilical cord blood transplantation
- <sup>7</sup> Include patients with ALL, AML and other hematological malignancies in CR1 and  $\geq$  CR2 undergoing haploidentical transplantation using CD3/CD19-depleted grafts
- <sup>8</sup> Include patients with ALL and AML in CR1 and  $\geq$  CR2 undergoing haploidentical transplantation after  $\alpha\beta$  T-cell depletion
- <sup>9</sup> Data from patients with ALL in CR1 and  $\geq$  CR2 undergoing transplantation from MMD (CIR of patients undergoing SCT in CR2).
- <sup>10</sup> Data from patients with ALL in different remission status (including CR1) undergoing haploidentical transplantation using CD34+ selected grafts
- <sup>11</sup> Data from patients with ALL and AML in CR1 and CR2 undergoing SCT from MRD, MUD and MMD
- <sup>12</sup> Data from patients with ALL in CR1 and  $\geq$  CR2 undergoing SCT from MRD, MUD and MMD
- <sup>13</sup> Data from patients with ALL in CR2 undergoing SCT from MRD and MUD after TBI-based and CC
- <sup>14</sup> Include patients with ALL, AML and other hematological malignancies in CR1 and  $\geq$  CR2 undergoing haploidentical transplantation using CD45RA-depleted grafts
- <sup>15</sup> Data from patients with ALL in CR2 undergoing SCT from MRD, MUD and MMD
- <sup>16</sup> Include patients with ALL and AML in different remission status undergoing haploidentical transplantation using CD3/CD19-depleted grafts



**Supplementary Figure S1.** Two year overall survival (59.4% versus 63.9%;  $p = 0.9$ ), leukemia free survival (52.2% versus 38.4%;  $p = 0.6$ ), event-free survival (43.5% versus 36.1%;  $p = 0.9$ ), and chronic graft versus host disease free and leukemia free survival (47.8% versus 31.2%;  $p = 0.5$ ) among patients with B-cell precursor acute lymphoblastic leukemia undergoing transplantation from haploidentical (blue lines) and HLA-matched (red lines) donors.



**Supplementary Figure S2.** Two year cumulative incidence of second relapse (26.1% *versus* 40.5%;  $p = 0.63$ ), treatment related mortality (21.7% *versus* 21%;  $p = 0.87$ ), and chronic graft versus host disease (5% *versus* 14.8%;  $p = 0.43$ ) among patients with B-cell precursor acute lymphoblastic leukemia undergoing transplantation from haploidentical (dashed lines) and HLA-matched donors (solid lines).



**Supplementary Figure S3.** Two year leukemia free survival (48.6% *versus* 35.8%;  $p = 0.2$ ), among patients undergoing transplantation after TBI-conditioning (blue lines) and non-TBI conditioning (red lines) regimens.

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