

Supplementary Table S1. The information per fluorochrome from QA program.

	LAB_1	LAB_3	LAB_4
2015			
Round I			25/33 <i>CD4 PacB x3</i> <i>CD5 PerCP5-5 x2</i> <i>CD81 APCH7 x3</i>
Round II	33/ 33		30/33 <i>CD4 PacB x2</i> <i>CD81 APCH7 x1</i>
2016			
Round I	33/33	33/33	30/33 <i>IgK PE x3</i>
Round II	33/33	32/33 <i>CD3-APC</i>	28/33 <i>IgK PE x3</i> <i>CD81 APCH7 x2</i>
2017			
Round I	31/33 <i>IgK PE</i> <i>CD81 APCH7</i>	32/33 <i>CD4-PacB</i>	29/33 <i>CD4 PacB x1</i> <i>CD81 APCH7 x3</i>
Round II	33/33		25/33 <i>CD45 PacO x2</i> <i>CD56-PE x1</i> <i>IgK PE x2</i> <i>CD81 APCH7 x3</i>
2018			
Round I	32/33 <i>CD4 PacB</i>	33/33	33/33
Round II	33/33	32/33 <i>CD81-APCH7</i>	32/33 <i>CD4 PacB</i>
2019			
Round I	33/33	33/33	33/33
Round II	32/33 <i>CD4 PacB</i>		33/33

2020			
Round I			
Cyto 1	32/33 <i>CD38-APC-H7</i>	31/33 <i>CD45 PacO</i> <i>CD38 APCH7</i>	32/33 <i>CD5 PerCP5-5</i>
Cyto 2	33/33		
Round II			
Cyto 1	31/33 <i>CD3-APC</i> <i>CD4-PacB</i>	29/33 <i>CD4-PAcB x3</i> <i>CD38-APC-H7</i>	29/33 <i>CD5 PerCP5-5 x3</i> <i>CD3-APC x1</i>
Cyto 2	32/33 <i>CD3-APC</i>		

Supplementary Table S2. Designed panels to LAIP analysis

Combinations	Backbone	Different markers
1	HLADR, CD45, CD34, CD117	CD15, CD13 or CD123, CD33, CD38
3		CD15, NG2, CD33, CD14
4		CD64, CD56, CD33, CD14
5		CD7, CD13, CD33, CD38
6		CD15, CD56, CD123, CD4
7		nuTdT, CD56, CD123, CD4
8		CD64, CD56, CD300e, CD14
9		CD15, CD33 or CD13, CD19, CD38
10		CD15, CD33 or CD13, CD7, CD38
11		CD36, CD13, CD11b, CD71
12		CD15, CD56, CD33, CD38
13		nuTdT, CD13, CD33, CD38
14		CD7, CD56, CD33, CD38
15		CD16, CD13, CD33, CD10
16		CD36, CD64, CD33, CD71
17		CD15, CD13, CD22, CD38

Supplementary Table S3. Comparative analysis of MRD samples in the 4 laboratories: The table represents the MRD value determined by each laboratory.

	Lab 1	Lab 2	Lab 3	Lab 4
% MRD 1	0,54	0,55	0,39	0,54
% MRD 2	0,024	0,03	0,04	0,022
% MRD 3	0,27	0,24	0,23	0,18
% MRD 4	0,028	0,02	0,03	0,023
% MRD 5	0,002	0,003	0,005	0,002
% MRD 6	0,004	0,005	0,01	0,005

MRD: measurable residual disease

Supplementary Table S4. Univariate analysis of CIR, NRM, OS and LFS

Variable	CIR HR (95% CI)	NRM HR (95% CI)	OS HR (95% CI)	LFS HR (95% CI)
Sex				
male	1.02 (0.67-1.55). p 0.927	1 (0.56-1.77) p 0.998	1.07 (0.73-1.57). p 0.728	1.02 (0.73-1.44). p 0.883
Age	1.02 (1-1.04). p 0.037	1.02 (0.99-1.05). p 0.101	1.03 (1.01-1.04). p 0.002	1.02 (1.01-1.03). p 0.008
Conditioning				
RIC	1.37 (0.9-2.1). p 0.147	1.29 (0.72-2.3). p 0.393	1.73 (1.18-2.53). p 0.005	1.43 (1.01-2.01). p 0.041
Donor				
Unrelated	0.97 (0.63-1.51). p 0.91	2.04 (1.06-3.95). p 0.033	1.31 (0.87-1.97). p 0.196	1.29 (0.89-1.85). p 0.171
Haploidentical	0.45 (0.19-1.03). p 0.06	2.73 (1.16-6.42). p 0.021	1.15 (0.63-2.13). p 0.654	0.99 (0.56-1.75). p 0.981
Depletion T				
Yes	0.86 (0.5-1.48). p 0.583	1.09 (0.53-2.27). p 0.812	0.96 (0.58-1.58). p 0.876	0.92 (0.59-1.43). p 0.707
ELN2011				
Intermediate	2.11 (0.87-5.09). p 0.095	0.97 (0.40-2.38). p 0.948	1.41 (0.71-2.8). p 0.319	1.61 (0.86-2.98). p 0.134
Adverse	4.88 (1.99-11.99). p 0.01	1.48 (0.56-3.90). p 0.429	3.26 (1.62-6.55). p 0.001	3.75 (1.98-7.09). p <0.001
MRD ≥0.1	2.29 (1.43-3.65). p 0.001	1.54 (0.78-3.06). p 0.214	2.51 (1.64-3.83). p 0.000	2.29 (1.55-3.38). p 0.000

OS: overall survival; LFS: leukemia free survival HR: Hazard ratio; CI confidence interval; Myelo: myeloablative; RIC: reduce intensity conditioning; MRD: measurable residual disease; GVHD: Graf versus Host disease.

Supplementary Table S5. OS and LFS according to multivariate time-dependent analysis (time-dependent variable GvHD):

<i>Variable</i>	<i>LFS</i>	<i>OS</i>
Age	HR 1.01 [95% CI 0.99-1.03] p 0.218	HR 1.01 [95% CI 0.99-1.03] p 0.152
Conditioning		
*Myelo/RIC	HR 1.38 [95% CI 0.91-2.09] p 0.130	HR 1.68 [95% CI 1.05-2.68] p 0.029
ELN_2011		
*Intermediate	HR 1.8 [95% CI 0.95-3.45] p 0.072	HR 1.56 [95% CI 0.76-3.19] p 0.222
*Adverse	HR 3.43 [95% CI 1.76-6.7] p< 0.001	HR 2.8 [95% CI 1.33-5.89] p 0.006
MRD ≥0.1 before transplantation	1.89 [95% CI 1.25-2.86] p 0.003	HR 1.98 [95% CI 1.26-3.11] p 0.003
GvHD	HR 0.81 [95% CI 0.52-1.27] p0.366	HR 0.88 95% CI 0.53-1.45] p 0.608

CIR: cumulative incidence of relapse; NRM: non-relapse mortality; OS: overall survival; LFS: leukemia free survival; HR: Hazard ratio; CI confidence interval; Myelo: myeloablative; RIC: reduce intensity conditioning; MRD: measurable residual disease; GvHD: Graf versus Host disease.

Supplementary Table S6. Evolution of patients who did not relapse with positive MRD prior to transplantation.

	Type	Status disease at transplantation	aGvHD	cGVHD	MRD after	Last follow-up	Cause
1	AML NPM1	1 st CR MRD 0.66%	Grade 2	NO	0,02%	DEATH (6 m)	VOD
2	AML NOS	Aplasia 2.4% blasts	Grade 4	Severe	NO	DEATH (3 y 1 m)	Unknown
3	AML CEBPA	1 st CR MRD 0.12%	NO	mild	NO	ALIVE (4 y 2 m)	
4	AML NPM1	1 st CR MRD 0.51%	Grade 1	mild	NO	ALIVE (3y 10m)	
5	AML NOS (IDH2)	1 st CR MRD 0.15%	Grade 2	-	-	DEATH (3m)	Pneumonia
6	AML NOS WT1	1 st CR MRD 0.01%	Grade 2	mild	NO	ALIVE (2y 9 m)	
7	AML NOS ASXL1	1 st CR MRD 0.21%	Grade 4	-	0.26%	DEATH (2m)	aGVHD
8	TRML	1 st CR MRD 0.3%	Grade 1	NO	NO	ALIVE (2 y y 6 m)	
9	AML KMT2	1 st CR MRD (4.27%)	Grade 2	NO	NO	ALIVE (2 y y 9 m)	
10	AML -7	Aplasia (3.1% blasts)	Grade 1	Mild	NO	ALIVE (2 y y 1 mes)	
11	AML MCR (FLT3 0,13%)	1 st CR MRD (0.2%)			NO	ALIVE (1 año y 7 m)	
12	AML NOS	1 st CR MRD (0.2%)	Grade 1		NO	DEATH (6 m)	Pneumonia
13	AML t(6;9)	1 st CR con MRD (1.04%)	Grade 1	Mild	NO	ALIVE (1 año y 3 m)	
14	AML NOS WT1	1 st CR con MRD (0.11%)	Grade 2		NO	ALIVE (1 año y 3 m)	
15	AML MCR FLT3	Active disease (10% blasts)			NO	ALIVE (1 año y 2 m)	
16	AML NOS +7	1 st CR con MRD (0.08%)	Grade 1	-	NO	DEATH (7 m)	Acute abdomen
17	AML NPM1	1 st CR con MRD (0.1%)	Grade 2		NO	ALIVE (10 m)	
18	AML MCR KMT2A	1 st CR con MRD (0.02%)	Grade 2		NO	ALIVE (10 m)	
19	AML CEBPA	1 st CR con MRD (0.7%)	Grade 2	-	NO	ALIVE (3 m)	
20	AML t(9;11)	2 nd CR con MRD (0.5%)			-	ALIVE (2.6 m)	
21	AML CRMD	1 st CR con MRD (2.2%)	Grade 1	Moderate	NO	DEATH (8 m)	Infection
22	AML NPM/FLT3	2 nd CR (0.2%)			NO	ALIVE (5 y y 8 m)	
23	AML inv16	2 nd CR (0.08%)	Grade 2		NO	ALIVE (5 y y 6 m)	
24	AML NOS	1 st CR (0.01%)	Grade 1	Mild	NO	ALIVE (5 y)	

25	AML del(20)(q12)	1 st CR MRD (0.4%)		Mild	NO	ALIVE (5y 6 m)	
26	AML MCR (-7)	1 st CR MRD (0.6%)			3% IS withdrawal	DEATH (6 m)	Infection MRD elevated
27	AML MCR RUNX1	1 st CR MRD (0.4%)	Grade 4			DEATH (2 m)	Infection
28	AML IDH2	1 st CR MRD (0.01%)	Grade 1	Severe	5% IS withdrawal	ALIVE (2 y)	
29	AML MCR t(16;17)	1 st CR MRD (0.03%)	-	-	-	DEATH (<1m)	Infection
30	AML IDH2	1 st CR MRD (0.01%)				ALIVE (2y 7 m)	
31	AML FLT3/NPM	1 st CR MRD (0.02%)	Grade 2	Moderate		ALIVE (1y 3m)	
32	AML IDH	2 nd CR MRD (2.1%)				ALIVE (9 m)	
33	AML RUNX1/RUNX1T(KIT mutation)	1 st CR MRD (0.69%)	Grade 2			DEATH (3 m)	Infection
34	AML CBFB/MYH11	1 st CR MRD (0.04%)		Severe	NO	ALIVE (4y 3 m)	
35	AML CBFB/MYH11	1 st CR MRD (0.3%)	yes	Severe (after ILD)	NO	DEATH (1y 11m)	GVHD
36	AML 47XX	1 st CR MRD 0.05%	Grade 2	-	NO	DEATH (8 m)	Septic shock
37	AML MCR	1 st CR MRD (0.22%)		Mild		DEATH (2y 5 m)	Ureteral neoplasm
38	AML del(7q)	1 st CR MRD (1%)	Grade 2			ALIVE (2 y 5 m)	
39	AML CBFB/MYH11	1 st CR MRD (0.3%)			NO	ALIVE (2 y 4 m)	
40	AML NPM1	2 nd CR MRD (0.2%)	Grade 4	Severe	0.2%	ALIVE (2y 2 m)	
41	AML NPM1	2 nd CR MRD (0.01%)			Yes	ALIVE (4y 5m)	
42	AML t(7;13)	CR MRD (0.04%)	Grade 2	Extensive	-	ALIVE (1y 2 m)	
43	AML NOS	CR MRD (0.01%)	Grade 1	Extensive	-	ALIVE (2 y)	
44	AML NOS	CR MRD (0.16%)		Extensive	-	ALIVE (4 y)	
45	AML 47,XX, del(9)	CR MRD (0.13%)	Grade 2		-	ALIVE (4 y)	
46	AML 46XX	CR MRD (0.12%)		Extensive	-	ALIVE (5y 2 m)	

AML: acute myeloid leukemia; NOS: Not otherwise specified; CR: complete remission; MRD: measurable residual disease; GvHD: Graf versus Host disease.