SUPPLEMENTARY APPENDIX

Prognostic impact of day 15 blast clearance in risk-adapted remission induction chemotherapy for younger patients with acute myeloid leukemia: long-term results of the multicenter prospective LAM-2001 trial by the GOELAMS study group

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Supplementary data

Supplementary Methods

Complete response (CR) required a normocellular BM with less than 5% blasts and no Auer rods, neutrophil count $\geq 0.5x10^9$/L and platelet count $\geq 100x10^9$/L, without evidence of extramedullary disease after one or two courses of treatment. Induction failures included deaths in aplasia and resistant disease.[20] Overall survival (OS) was calculated from the date of the first day of chemotherapy until the date of death from any cause. Event-free survival (EFS) was calculated from the first day of chemotherapy until the date of treatment failure, disease relapse, or patient death from any cause. Time to relapse was evaluated as cumulative incidence of relapse (CIR) measured from CR date until date of relapse, death or last follow-up except for patients deceased without relapse where death was considered as competitive risk. Relapse-free survival (RFS) for patients who achieved CR was calculated from the date of CR until the date of relapse or death from any cause with censoring of other patients at the date of last follow-up.

Supplementary Table S1

Table S1: characteristics of the 152 AML patients of the validation cohort.

	All patients N=152	Day 15 marrow blasts <5% N=99	Day 15 marrow blasts ≥5% N=53	p
Median age (range) - years	49 (15-60)	49 (15-60)	52 (17-59)	NS
Male gender - n (%)	78 (51.3)	58 (58.6)	20 (37.7)	0.017
Performance status* - n (%)				
0-1	113 (74.3)	76 (76.8)	37 (69.8)	NS
2-4	9 (5.9)	4 (4)	5 (9.4)	
Median WBC (range) - $x10^9$/L	10.3 (0.3-356)	15 (0.3-249.7)	5.4 (1.0-356)	NS
Cytogenetics - n (%)				0.068
Favorable	18 (11.8)	16 (16.2)	2 (3.8)	
Intermediate	103 (67.8)	64 (64.7)	39 (73.6)	
Unfavorable	29 (19.1)	17 (17.2)	12 (22.6)	
Undetermined	2 (1.3)	2 (2)	0	
Day 15 marrow blasts				
Median % (range)	2 (0-88)	0 (0-4)	28 (5-88)	-
0-4-n (%)	99 (65.1)	99 (100)	0	
5-10-n (%)	16 (10.5)	0	16 (30.2)	
11-20-n (%)	9 (5.9)	0	9 (17)	
21-50-n (%)	14 (9.2)	0	14 (26.4)	
>50-n (%)	14 (9.2)	0	14 (26.4)	
2^{nd} induction at d15- n (%)	42 (27.6)	1 (1)	41 (77.4)	-
Complete Response - n (%)	128 (84.2)	89 (89.9)	39 (73.6)	0.011
Induction failure - n (%)	18 (11.8)	9 (9.1)	9 (17)	NS
Deaths in aplasia	4 (2.6)	2 (2)	2 (3.8)	
Resistant disease	14 (9.2)	7 (7.1)	7 (13.2)	
AlloSCT- n (%)	58 (38.2)	40 (40.4)	18 (34.0)	NS

Supplementary Table S2

Table S2: Multivariate Analysis of Independent Risk Factors in validation cohort

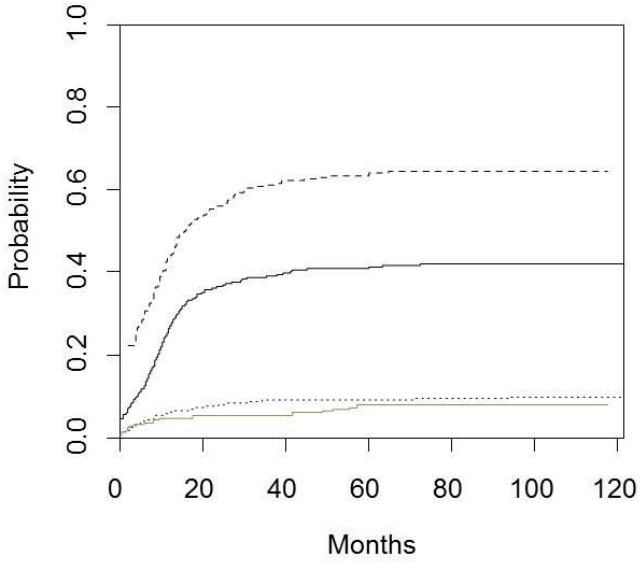
	CR		**RFS**		**EFS**		**OS**	
n	150		129		150		150	
Variable	P	OR	p	HR	p	HR	p	HR
Age	NS	-	NS	-	NS	-	NS	-
D15 blasts (< 5% vs ≥ 5%)	0.0074	0.29 [0.11-0.71]	0.034	1.79 [1.05-3.07]	0.021	1.92 [1.27-2.89]	0.004	1.93 [1.24-3.01]
WBC	NS	-	NS	-	NS	-	NS	-
Cytogenetics	NS	-	NS	-	NS	-	NS	-

Supplementary Figure 1

Cumulative Incidence of Relapse

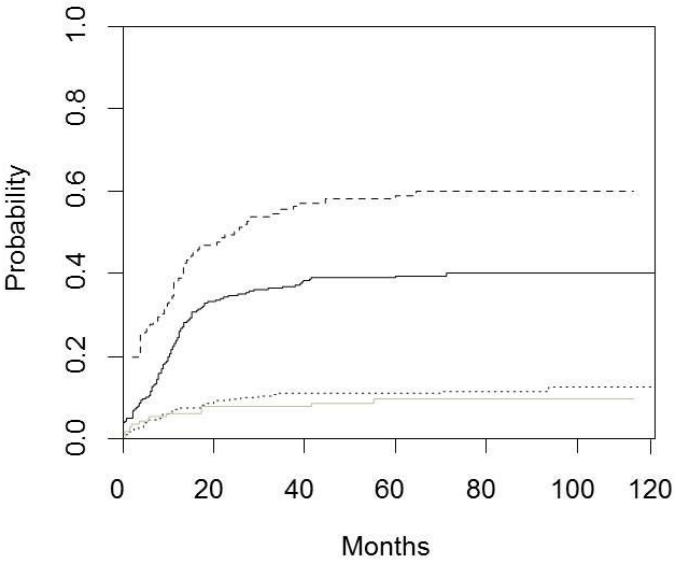
A. All patients.

5-y Cumulative Incidence of Relapse: 41% (±2.1) in patients with d15 blasts <5% vs 63.5% (± 3.2) with d15 blasts ≥5% ($p=10^{-10}$). Death w/o relapse 7.7% (± 1.2) *vs* 8.9 (±1.8) (ns).
Solid line: patients with d15 blasts <5%. Dotted line: patients with ≥5%.



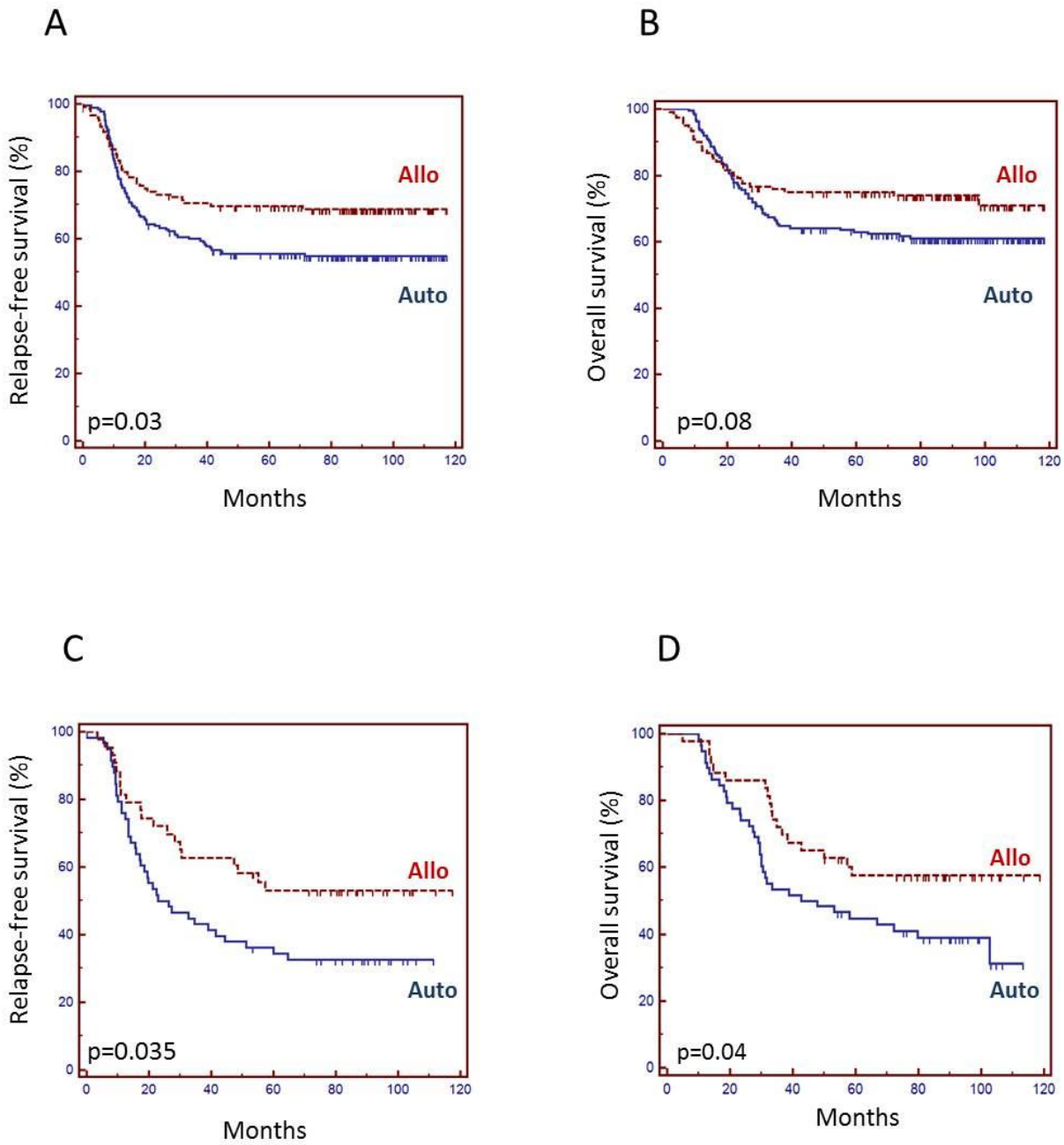
B. Intermediate cytogenetic risk.

5-y Cumulative Incidence of Relapse: 39.6% (±2.8) in patients with d15 blasts <5% vs 58.3% (±4.6) with d15 blasts ≥5% ($p=10^{-5}$). Death w/o relapse 9.6% (±2.7) *vs* 11.2 (±1.7) (ns).
Solid line: patients with d15 blasts <5%. Dotted line: patients with ≥5%



Supplementary Figure 2

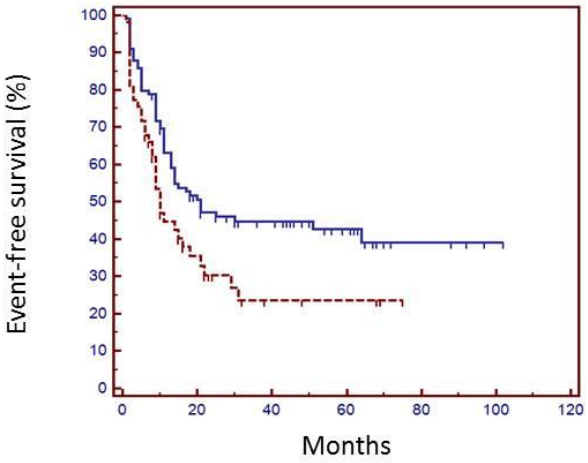
Post remission therapy



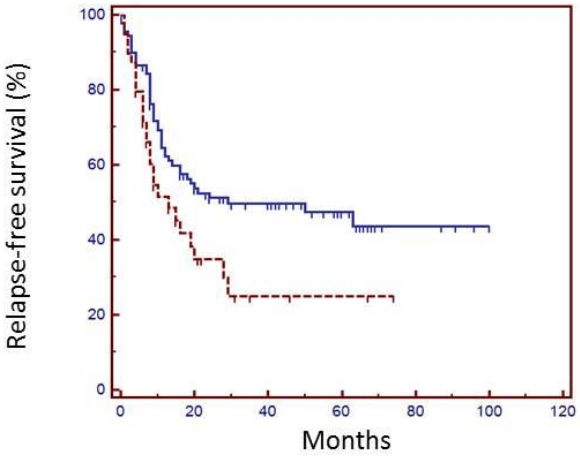
Supplementary Figure 3

Validation cohort

A



B



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