Outcome of 421 adult patients with Philadelphia-negative acute lymphoblastic leukemia treated under an intensive program inspired by the GIMEMA LAL1913 clinical trial: a Campus ALL study

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Received: May 15, 2024.
Accepted: August 6, 2024.
Early view: August 15, 2024.

https://doi.org/10.3324/haematol.2024.285638

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SUPPLEMENTAL METHODS

Risk classification according to the GIMEMA LAL1913 clinical trial:

- Very high risk (VHR): WBC count >100 $x10^9$/L or adverse cytogenetics/molecular biology such as t(4;11)/MLL rearrangement at 11q23, +8, -7, del6q, t(8;14), low hypodiploidy with 30-39 chromosomes, near triploidy with 60-78 chromosomes, karyotype with >5 unrelated anomalies, or an early/late non-cortical immunophenotype EGIL T-I/II/IV (CD1a negative) for T-precursor ALL
- High risk (HR): complete remission after the second cycle or, for B precursor ALL, a WBC count >$30x10^9$/L or a pro-B immunophenotype.
- Standard risk (SR): for B-precursor ALL a WBC count <$30x10^9$/L, for T-precursor ALL a WBC count <$100x10^9$/L and a cortical immunophenotype EGIL T-III (CD1a+).

Response evaluation criteria: the CR was defined as the disappearance of clinical and laboratory signs of ALL/LL, including extramedullary disease if previously detected; a transfusion-free status with neutrophils >$1.0x10^9$/l and platelets >$100x10^9$/l; and a normocellular or regenerating bone marrow with blast cell content <5%. A recurrence was defined as the reappearance of >5% marrow leukemic cells and/or an extramedullary involvement. In cases of LL without marrow involvement and therefore MRD monitoring, the evaluation of response was carried out with PET scans at TP2 and TP4. Early death was defined as death not due to disease occurring before the third course of CHT.

SUPPLEMENTAL TABLE 1. Treatment protocol.

Treatment phase	Drugs	Dosing	Days
Prephase	Prednisone	20 mg/m^2 q12h	-5 to -1
	Cyclophosphamide	300 (200 if age >55) mg/m^2	-3 to -1
Course 1 (C1)	Idarubicin	12 (9 if age >55) mg/m^2	1,2
	Vincristine	1.4 mg/m^2 (max. 2 mg)	1,8,15,22
	Dexamethasone	5 mg/m^2 q12h	1-5, 15-19
	Pegaspargase	2000 (1000 if age >55) UI/ m^2	10
	IT prophylaxis		1,15
Course 2,4,6 (C2, C4, C6)	Vincristine	1.4 mg/m^2 (max. 2 mg)	1,8 (no course 2)
	Idarubicin	12 (9 if age >55) mg/m^2	1
	Cyclophosphamide	1000 mg/m^2	1
	Dexamethasone	5 mg/m^2 q12h	1-5
	Cytarabine	75 mg/m^2	2-5
	Pegaspargase	2000 (1000 if age >55) UI/ m^2	8 (no course 4)
	Mercaptopurine	60 mg/m^2	1-10
	IT prophylaxis		1 (and 15, course 2)
HD courses 3,7 (C3, C7)	Methotrexate	2500 (B), 5000 (T), 1500 (if age >55) mg/m^2 over 24 hours	1
	Cytarabine	2000 mg/m^2	3,4
HD course 5 (C5)	Methotrexate	2500 (B), 5000 (T), 1500 (if age >55) mg/m^2 over 24 hours	1
	Pegaspargase	2000 (1000 if age >55) UI/ m^2	3
	Mercaptopurine	25 mg/m^2	8-18
Course 8 (C8)	Vincristine	1.4 mg/m^2 (max. 2 mg)	1,8
	Idarubicin	10 (7.5 if age >55) mg/m^2	1,8
	Dexamethasone	5 mg/m^2 q12h	1-5
	Cyclophosphamide	300 (200 if age >55) mg/m^2	1-3
	Prednisone	20 mg/m^2 q12h	8-12
	IT prophylaxis		1,15
Maintenance courses M1,3,5,7,9,11	Cyclophosphamide	100 mg/m^2	1-4
	Mercaptopurine	75 mg/m^2	8-28
	Methotrexate	15 mg/m^2	8,15,22
	IT prophylaxis		1 (courses 3,5)
Maintenance courses M2,4,6,8,10,12	Vincristine	1 mg/m^2 (max. 2 mg)	1
	Prednisone	20 mg/m^2 q12h	1-5
	Mercaptopurine	75 mg/m^2	8-28
	Methotrexate	15 mg/m^2	8,15,22
	IT prophylaxis		1 (courses 2,4)
Maintenance courses M13-24	Mercaptopurine	75 mg/m^2	1-28
	Methotrexate	15 mg/m^2	1,8,15,22

Abbreviations: IT, intrathecal

SUPPLEMENTAL TABLE 2. Characteristics of the patients in the propensity score matching

Characteristic	**Overall**, N = 602	**RL-LAL1913**, N = 419	**LAL1913**, N = 183	**p-value**
Age, median (range)	42 (18 - 80)	42 (18 - 80)	41 (18 - 65)	0.5
Sex, n (%)				0.6
Male	349 (58%)	246 (59%)	103 (56%)	
Female	253 (42%)	173 (41%)	80 (44%)	
WBC, median (range)	9 (0 - 627)	10 (0 - 627)	6 (0 - 347)	**0.001**
Unknown	1	1	0	
Lineage, n (%)				**<0.001**
B	359 (60%)	221 (53%)	138 (75%)	
T	243 (40%)	198 (47%)	45 (25%)	
Risk, n (%)				0.6
SR	302 (50%)	207 (49%)	95 (52%)	
HR	63 (10%)	42 (10%)	21 (11%)	
VHR	237 (39%)	170 (41%)	67 (37%)	
Cytogenetics, n (%)				**0.026**
Normal	219 (48%)	173 (51%)	46 (39%)	
Non adverse	148 (32%)	108 (32%)	40 (34%)	
Adverse	93 (20%)	60 (18%)	33 (28%)	
Unknown	142	78	64	
CR, n (%)				0.2
CR	556 (92%)	391 (93%)	165 (90%)	
no CR	46 (7.6%)	28 (6.7%)	18 (9.8%)	
Transplant, n (%)	200 (33%)	144 (34%)	56 (31%)	0.4
Time to transplant, median (range)	6.12 (2.93 - 28.88)	6.04 (2.93 - 28.88)	6.41 (3.72 - 12.20)	0.2
Unknown	402	275	127	