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Real-world outcomes and age-related analysis of adult acute lymphoblastic leukemia patients treated with a pediatric-inspired regimen

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INTRODUCTION

Pediatric-inspired chemotherapies which utilize asparaginase and central nervous system (CNS) prophylaxis have dramatically improved outcomes for pediatric and young adult patients with acute lymphoblastic leukemia (ALL). While its use is not widespread for older adults, we have implemented this approach with excellent outcomes for ALL patients in a wide range of ages.

AIMS

- Describe clinical characteristics and treatment outcomes in patients treated with pediatric-inspired protocol
- Compare survival across diverse age groups

METHODS

- Retrospective study of 373 patients diagnosed with Ph- or Ph+ B-ALL, T-ALL or mixed phenotype acute leukemia (MPAL) between January 2002-2022
- Ph+ patients received tyrosine kinase inhibitors (TKIs) while Ph- patients received asparaginase
- Patients were grouped by age to receive multiagent-multiphase treatment (PM-DFCI)

Group	Age range	Size (N)	
1	30 to <40 years	50	PM-DFCI, <60
2	40 to <50 years	89	
3	50 to <60 years	94	
4	60 to <70	88	PM-DFCI, ≥60
5	>70	52	

- Dose adjustments made for patients aged 60 and older compared to patients under 60, notably methotrexate 40mg/m^2 (vs 4g/m^2) during induction and PEG-ASP 1000IU for 7 cycles (vs 10 cycles) during intensification
- Overall survival calculated by measuring time from initial diagnosis to death and leukemia free survival determined for patients achieving CR1, measuring time from CR1 to either relapse or death
- Statistical analyses performed using Stata 13 (StataCorp LP, College Station, TX, USA)

RESULTS

Out of 373 overall patients, 196 (53%) were male, 171 (46%) patients were diagnosed with Ph- B-ALL, the Ph+ mutation was present in 135 (36%) patients, 83 (22%) patients had extramedullary disease, and 49 (13%) patients had prior malignancies. Clinical characteristics across age groups are found in **Table 1**.

Table 1. Clinical characteristics and a comparative analysis among different age groups. Numbers in brackets represent number of patients possessing given characteristic.

	Age group 1 (50) <40	Age group 2 (89) 40-49	Age group 3 (94) 50-59	Age group 4 (88) 60-69	Age group 5 (55) >70	p
Sex, male	58% (29)	56% (50)	50% (47)	51% (45)	48% (25)	0.773
Phenotype						
Ph+ALL	28% (14)	39% (35)	36% (34)	39% (34)	35% (18)	0.186
Ph-ALL	42% (21)	37% (33)	50% (47)	48% (42)	54% (28)	
MPAL	2% (1)	4% (4)	3% (3)	4% (3)	4% (2)	
T-ALL	28% (14)	19% (17)	11% (10)	10% (9)	7% (4)	
Ploidy						
Diploid	76% (38)	69% (61)	35% (33)	40% (35)	40% (21)	0.05
Hyperdiploid	0%	3% (3)	5% (5)	3% (3)	10% (5)	
Hypodiploid	12% (4)	2% (2)	6% (6)	3% (3)	8% (4)	
Ph+, mut	28% (14)	40% (35)	36% (34)	39% (34)	35% (18)	0.715
MLL, mut	6% (3)	7% (5)	27% (4)	3% (2)	4% (2)	0.016
Extramedullary disease	34% (17)	21% (19)	18% (17)	22% (19)	24% (11)	0.284
Prior malignancy	8% (4)	9% (8)	11% (10)	16% (14)	25% (13)	0.040
WBC, median (IQR) 10*9/L	11.7 (7.2 - 40)	12 (4.2 - 27)	9.9 (3.4 - 29.7)	5.5 (2.3 - 14.3)	12.45 (2.6 - 40.16)	0.284

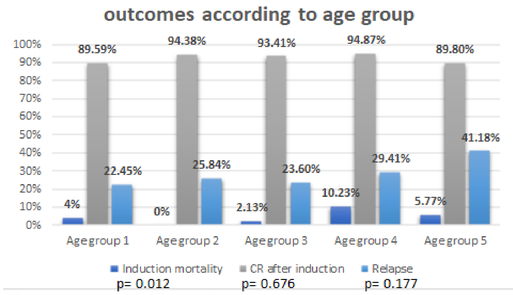


Fig 1. Frequencies of different clinical outcomes according to age groups

A significant proportion, 330 patients (92.96%), achieved complete remission (CR) after induction. Group 5 had the highest incidence of relapse while induction-related mortality was greatest in group 4 (**Fig 1**).

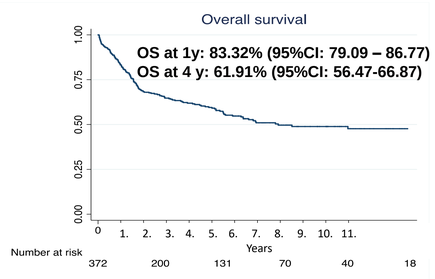


Fig 2. Overall survival outcome of all patients

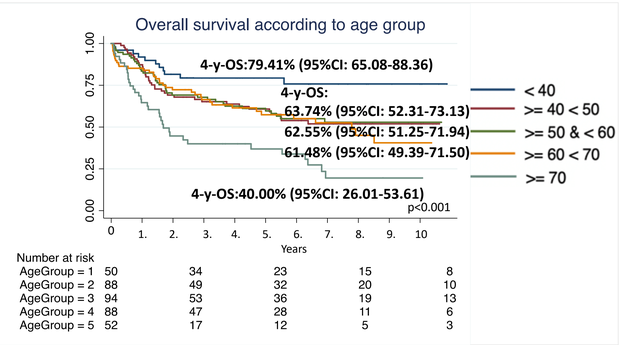


Fig 3. Overall survival outcomes based on age groups

Regarding survival outcomes, overall survival (OS) at 1 and 4 years was 83.32% (95%CI: 79.09 – 86.77) and 61.91% (95%CI: 56.47-66.87), respectively (**Fig 2**). Patients in age group 1 had greater OS than any other age group (**Fig 3**).

Leukemia free survival (LFS) at 1 and 4 years was 83.07% (95%CI: 78.43- 86.79) and 58.18% (95%CI: 52.27-63.63) respectively. Hematopoietic stem cell transplantation (HSCT) in CR1 was performed in 17.58% of the patients. After censoring patients who underwent HSCT in CR1, there were no significant differences in OS between Ph-positive and Ph-negative patients.

Uni- and multivariable analysis identified older age group, absence of CR after induction, and history of previous malignancy as independent significant prognostic factors for worse OS (HR 1.28, *P*=0.002; HR 2.27, *P*=0.026; HR 1.75, *P*=0.015, respectively).

CONCLUSIONS

Our study demonstrates the feasibility and effectiveness of a pediatric-inspired treatment protocol for adult patients diagnosed with ALL across a wide age range. We observed excellent outcomes in terms of OS and LFS across different age groups, underscoring the adaptability of this protocol for diverse patient populations. These findings contribute to a broader understanding of ALL treatment in the adult population and support the continued use of this treatment approach across different age groups.

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