Outcomes of Allogeneic Haematopoietic Stem Cell Transplant (Allo-HSCT) for Acute Lymphoblastic Leukaemia/Lymphoma (ALL) in Hong Kong: A Retrospective Study

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Introduction

Acute lymphoblastic leukemia (ALL) is a haematological malignancy characterized by impairment in differentiation, proliferation and accumulation of leukaemic cells. It is associated with a high risk of disease relapse despite standard chemotherapy, and the long-term survival remains poor. In the recent decades, extensive research has been done in this field in hopes of improving disease outcome.

Recent introduction of novel therapeutic strategies including bispecific T cell engager antibodies and chimeric antigen receptor (CAR) T cells therapy have resulted in early clinical success. Studies show that blinatumomab is an effective treatment in patients with Ph chromosome negative relapsed / refractory ALL. Trials are currently in progress to establish its benefit in different patient groups.

Minimal residual disease (MRD) detection has also been shown to be promising in risk stratification of ALL. In recent years, high risk features such as age, gender and initial white cell counts are becoming less significant in determining disease prognosis. Instead, MRD status and genetic and molecular characteristics have been identified to be powerful predictors of overall survival and disease-free survival. Multiple studies have confirmed that pre-transplant MRD negativity is associated with better disease outcome.

Methodology

This was a single centre, retrospective analysis. It included all adult ALL patients receiving first allo-HSCT in Queen Mary Hospital between June 2016 and February 2020. The minimum follow-up period was 6 months.

Overall survival (OS), disease free survival (DFS), cumulative relapse rate, non-relapse or relapse mortality were the primary outcomes that were analysed. The short-term outcome of minimal residual disease (MRD) detection and haplo-identical transplantation were also included.

The data was analysed with Pearson Chi-Square test, Kaplan-Meier method, competing risk analysis and compared by the log-rank test.

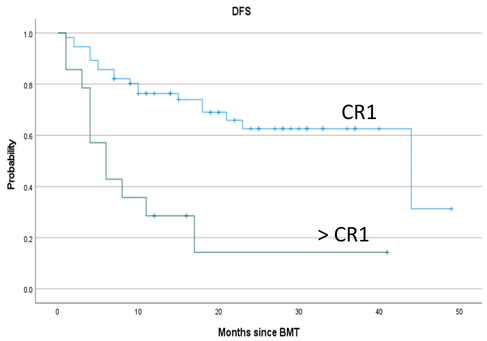
Demographics

Age – no. (%)	
Median (range) – yr	41 (19-62)
Gender – no. (%)	
Male	38 (54)
HCT-CI – no. (%)	
0-1	64 (91)
2-4	56(9)

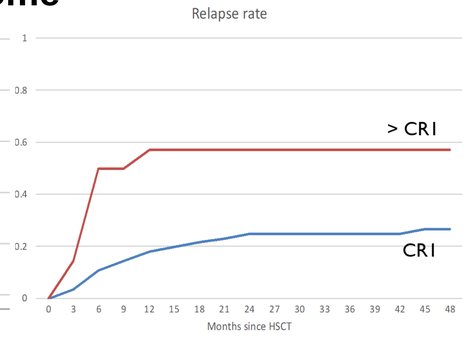
Phenotype – no. (%)	
B	56 (80)
Ph Pos	29 (50)
T	11 (15)
Bi-phenotypic	3 (4)
Disease status – no. (%)	
CR1	56 (80)
> CR1	14 (20)

Duration of disease	
Median (range) – month	9 (3-21)
Donor relationship – no. (%)	
Unrelated (≥7/8 HLA match)	32 (45)
Sibling (6/6 HLA match)	28 (40)
Haplo	10 (14)

Outcome



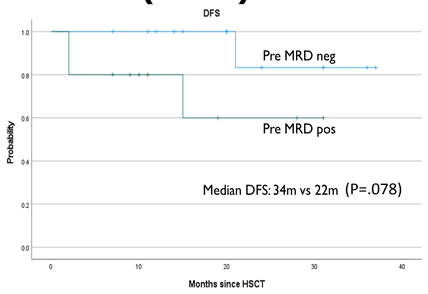
	1yr	2yr	3yr	
CR1	76%	62%	62%	P=.00
> CR1	28%	14%	14%	

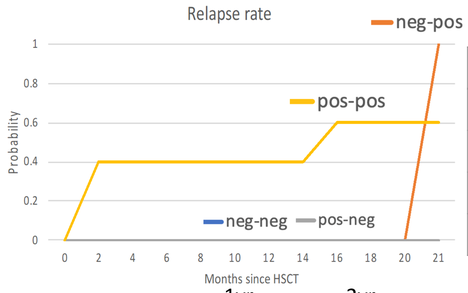


	1yr	2yr	3yr	
CR1	17%	25%	25%	P=.01
> CR1	57%	57%	57%	

Minimal residual disease (MRD)

Pretransplant MRD – no. (%)	
Tested	26 (37)
Neg	15 (57)
Pos	11 (42)
MRD Method – no. (%)	
PCR-based	22 (61)
MFC	14 (38)





	1yr	2yr	
Neg → Neg	0%	0%	P<.001
Neg → Pos	0%	100%	
Pos → Neg	0%	0%	
Pos → Pos	40%	60%	

Pre MRD	Post MRD	N=	Relapse (n=)
-	-	13	0
-	+	1	1
+	-	5	0
+	+	5	3

Discussion

The overall survival (OS) and disease-free survival (DFS) at 24 months were 75% and 53% respectively. Patients transplanted in >CR1 had worse DFS (median 44 vs 6 months, p=0.00). Our results are comparable with international data which showed OS and DFS at 24 months at 64-69% and 59-64% respectively.

Twenty-six patients had pre-transplant MRD tested: 11 positive and 15 negative. Patients who had MRD negative result had a trend towards better DFS (83% vs 60%, P=0.078). None of the pre-HSCT clinical factors determined the MRD status at transplant. Re-emergence or persistence of MRD positivity predicts relapse (P<0.001).

Blinatumomab was used in five patients pre-HSCT, two in MRD positive CR1 with one successful MRD eradication. One patient achieved MRD-negative CR2 pre-HSCT but developed morphological relapse at 5 months post-HSCT.

Conclusion

HSCT performed at CR1 with the aid of MRD detection predicts the best outcome in terms of DFS and OS. The best treatment for MRD eradication warrants further studies.

Reference

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