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Navigating Graft-versus-Host Disease Prophylaxis in Matched Sibling Donor Allogeneic Transplants
A Comparative Analysis of Post-Transplant Cyclophosphamide versus Diverse Regimens
Insights from a Single-Center Experience.

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INTRODUCTION

Post-transplant cyclophosphamide (PTCy) has emerged as a promising strategy to mitigate Graft-versus-Host Disease (GVHD), particularly in HLA-matched allogenic stem cell transplant (allo-SCT) settings. [1-6] This retrospective study seeks to elucidate the impact of PTCy on clinical outcomes, GVHD incidence, Graft-vs-host disease- and relapse-free survival (GRFS) and overall survival in patients undergoing HLA-matched allo-SCT. The comprehensive analysis involved a retrospective examination of patients who underwent HLA-matched allo-SCT for hematologic malignancies, comparing outcomes between those who received PTCy-based GVHD prophylaxis and other conventional prophylactic regimens. Data encompassing GVHD incidence, treatment-related complications, engraftment kinetics, and overall survival were meticulously collected and subjected to rigorous analysis.

METHOD

We analyzed transplant outcomes among 413 patients who received HLA-matched allo-SCT for hematological malignancy at Princess Margaret Hospital between January 2010 and March 2023. This study was approved by the institutional research ethics board.

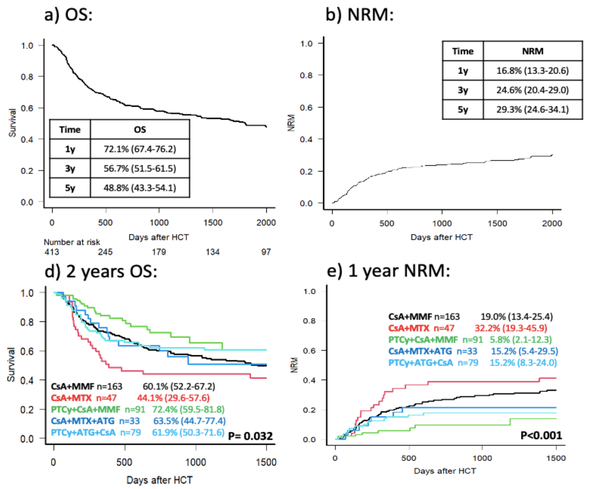
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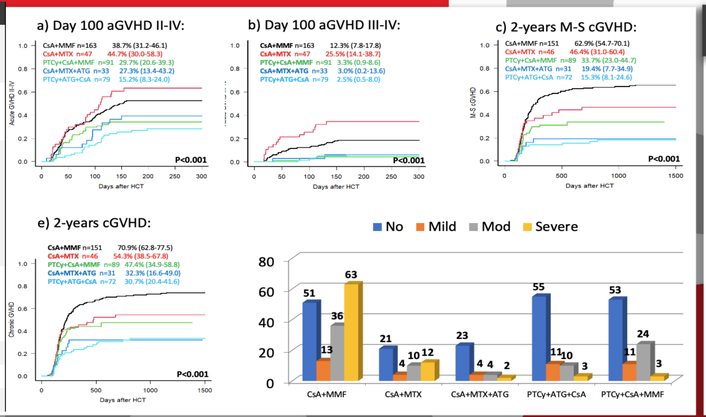
RESULTS

Patient demographic and clinical characteristics are shown in **Table 1**. Four hundred- thirteen individuals received HLA matched allo-SCT for hematological malignancy: of these 224 (54.2%) had AML, 48 (11.6%) had ALL, 63 (15.3%) had MDS, 19 (4.6%) had CML and 39 (9.4%) had Myelofibrosis. With median follow up of 53.6 (4.9-163) months, overall survival at three years was 56.7% (95% CI: 51.5-61.5), Non-relapse mortality was 16.8% (95% CI: 13.3- 20.6) at one years and 24.6% (95% CI: 20.4-29.0) at 3 years. Cumulative incidence of relapse at three years was 20.8% (95% CI: 16.9-25.0). At day-100, the incidence of grade 2-4 and grade 3-4 acute GVHD was 32.0% (95% CI: 27.5-36.5) and 9.2% (95% CI: 6.7- 12.2), respectively.

The incidence of moderate-severe cGVHD at three years was 44.1% (95% CI: 38.9- 49.1). GRFS at three years was 38.8% (95% CI: 25.0-43.7). Our findings revealed a significant reduction in both acute and chronic GVHD incidence among patients receiving PTCy-based prophylaxis compared to those managed with conventional regimens. In univariate analysis, use of PTCy had a significant impact on GVHD, with lower risk of grade 2-4 aGVHD (HR=0.52, P < 0.001), grade 3-4 aGVHD (HR=0.24, P < 0.001) and moderate-severe cGVHD (HR=0.35, P < 0.001). This reduction is of paramount importance given the considerable morbidity and mortality associated with GVHD, as patients in the PTCy group demonstrated favorable GRFS with (HR=0.37, P < 0.001).



Variable	N (%)	Variable	N (%)
Age	56 (18-73)	Graft:	
≥ 65y	71 (17.2)	Fresh graft:	212 (51.3)
Gender:		Frozen graft	201 (48.7)
Male	217	Conditioning:	
Female	196	MAC	198
Diagnosis:		RIC	215
AML	224 (54.2)	GVHD prophylaxis:	
ALL	48 (11.6)	CsA+MMF	163 (39.5)
MDS	63 (15.3)	CsA+MTX	47 (11.4)
CML	19 (4.6)	PTCy+CsA+MMF	88 (21.3)
MF	39 (9.4)	PTCy+ATG+CsA	79 (19.1)
CMML	11 (2.7)	CsA+MTX+ATG	33 (8.0)
MPAL	9 (2.2)	PTCy+CsA	3 (0.7)
Pre-transplant Status:		ATG dose:	
CR1	240 (58.1)	No ATG	301 (72.9)
CR2-3	57 (13.8)	2 mg/kg	56 (13.6)
Stable disease	108 (26.2)	4.5 mg/kg	56 (13.6)
Not in CR	7 (1.7)	KPS <90	89 (21.5)
Donor age (Median)	54 (8-74)	HCT-CI: ≥3	137 (33.2)
CD34 dose	6.8 (1.2-25.8)	Follow up (months)	53.6 (4.9-163)



CONCLUSIONS

Our study provides compelling evidence that PTCy as a GVHD prophylaxis in HLA-matched allo-SCT significantly reduces GVHD incidence without compromising overall survival. While these findings are promising, the retrospective nature of this analysis warrants cautious interpretation, and prospective studies with larger cohorts and extended follow-up periods are essential for validation. PTCy is offering improved outcomes and expanding the therapeutic horizon for patients with hematologic malignancies.