To evaluate HCT outcomes in patients undergoing mismatched (related and unrelated) donor transplantation with FTBI/ fludarabine based regimen with posttransplant cyclophosphamide (PTCy).

Amrita Desai MD MPH[1], Dongyun Yang PhD[2], Amanda Blackmon DO MS[1], Anthony Stein MD[1], Guido Marcucci MD[1], Stephen J Forman MD[1], Ryotaro Nakamura MD[1], Monzr M. Al-Malki MD[1]

1. Department of Hematology and HCT, City of Hope, Duarte, CA 2. Department of Computational and Quantitative Medicine, City of Hope, Duarte, CA

Background

- Allogeneic Hematopoietic cell transplantation (HCT) remains the only curable treatment option for malignant hematological disorders.
- Conditioning regimen and GVL are both important in preventing graft rejection, relapses and GVHD.
- Choice of regimen depends on the diagnosis, patient characteristic, donor type, disease status and graft source.
- We present the outcome of patients undergoing FTBI/Fludarabine myeloablative conditioning for mismatched (related or unrelated) donor HCT and PTCy as GvHD prophylaxis. We plan to assess toxicity, outcomes and feasibility of this regimen

Materials & Methods

- All consecutive patients who underwent myeloablative conditioning for hematologic malignancy at City of Hope from January 2015 to 31st December 2021.
- All patients received PBSC as the stem cell source.
- The study was conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

Conditioning regimen and GVHD prophylaxis:

- Conditioning regimen was Fractionated Total Body Irradiation (FTBI)-based with fludarabine. The dose of radiation was greater than or equal to1200 cGy
- All patients received GVHD prophylaxis with PTCy 50 mg/kg on days +3 and +4, with mycophenolate mofetil (MMF) on days +5 to +35 and tacrolimus or sirolimus started on day +5.

Objective

To evaluate HCT outcomes in patients undergoing mismatched (related and unrelated) donor transplantation with FTBI/ fludarabine based regimen with posttransplant cyclophosphamide (PTCy).

	Total (N=155)
Age at HSCT, years	
Median	38
Interquartile range	28, 47
Range	(9-60)
Recipient sex	
Male	88 (56.8%)
Female	67 (43.2%)
Karnofsky performance status %	
≥80	151(97.5%)
<80	4 (2.5%)
HCT Comorbidity Index	
0	37 (23.9%)
1-2	61 (39.4%)
>=3	56 (36.1%)
Unknown	1 (0.6%)
Primary diagnosis	
AML	56 (36.1%)
ALL	72 (46.5%)
MDS/MPN	10 (6.5%)
BPDCN	2 (1.3%)
CML/CMMoL	15 (9.7%)
DRI	
Low	25 (16.1%)
Intermediate	85 (54.8%)
High	42 (27.0%)
Very High	3 (1.9%)
Female donor to male recipient	
Yes	28 (18.1%)
No	127 (81.9%)

	Total (N=155)
Donor age	
Median	31
Interquartile range	23, 42
Range	(12-57)
Donor Type	
MMUD	51 (32.9%)
Haplo-identical	104 (67.1%)
ABO blood group compatibility	
ABO compatible	103 (66.5%)
Minor mismatch (donor is O)	22 (14.2%)
Major mismatch (Recipient is O)	18 (11.6%)
Bidirectional (None are O)	12 (7.7%)
Donor/Recipient CMV serostatus	
D-/R-	14 (9%)
D-/R+	33 (21.3%)
D+/R-	21 (13.5%)
D+/R+	87 (56.1%)
Year of HCT	
2015	11 (7.1%)
2016	9 (5.8%)
2017	9 (5.8%)
2018	26 (16.8%)
2019	26 (16.8%)
2020	48 (31%)
2021	26 (16.8%)
Conditioning regimen	
FTBI/FLUDARABINE	153 (98.7%)
FTBI/FLUDARABINE/CTX	2 (1.3%)
GVHD prophylaxis	
CTX/TACROLIMUS/CELLCEPT	154 (99.4%)
CTX/TACROLIMUS/SIROLIMUS	1 (0.6%)

Table 1. Baseline Demographics and Characteristics

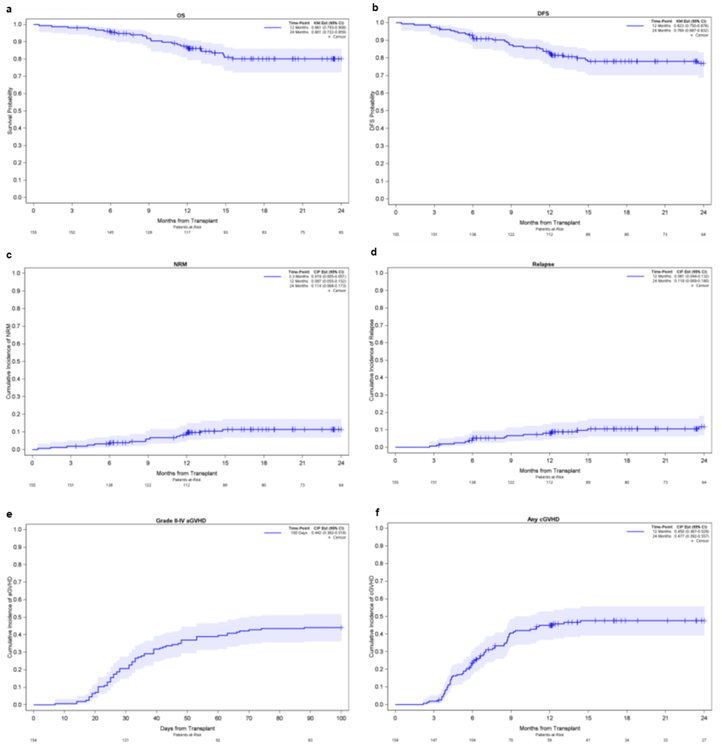


Figure1: (a) 2-year OS.(b) 2-year Disease Free Survival. (c)2- year Non-relapse Mortality. (d) Cumulative Incidence of Relapse. (e) Rate of Grade II-IV acute GVHD. (f) Rate of chronic GVHD

Summary

- 155 patients with median age of 38 (range 9-60) received FTBI/Fludarabine based conditioning with PTCy.
- 56.8% of patients were male and 97.5% pd a Karnofsky performance status ≥ 80 with a HCT comorbidity index ≥ 3 in 36.1% cases.
- The main reason for transplantation was ALL (46.5% cases) and AML (36.1%cases). The median donor age was 31 with 67.1% haplo donors & 32.9% mismatched unrelated.
- With a median follow-up of 24 months (range: 3 to 81), 100-day NRM was 1.9% and 9.7% at 1-year, while 1- year & 2-year relapse rates were 8.1% & 11.8% respectively
- 1 & 2-year DFS were 82.3% & 76.9% respectively while the 2-year OS was 80.1%.
- Grade II-IV acute GVHD at D100 was 44.2% (95% CI 0.36- 0.51) and grade III-IV acute GVHD at D100 was 5.8% (95% CI 0.029 - 0.103). Any chronic GVHD at 2-years was 47.7% (95% CI 0.39- 0.55) while extensive chronic GVHD at 2-years was 35.6% (95% CI 0.27-0.43).

Discussion

- FTBI/ fludarabine is well tolerated MAC regimen in mismatched donors with leukemia and MDS with low transplant related mortality and good outcomes.
- The study shows FTBI/fludarabine based conditioning regimen as a promising regimen which needs to be studied in future prospective randomized trials.

References

1. Solomon SR, et al. Total Body Irradiation-Based Myeloablative Haploidentical Stem Cell Transplantation Is a Safe and Effective Alternative to Unrelated Donor Transplantation in Patients Without Matched Sibling Donors. Biol Blood Marrow Transplant. 2015 Jul;21(7):1299-307.
2. Gagelmann N et al. Haploidentical Stem Cell Transplantation With Posttransplant Cyclophosphamide Therapy vs Other Donor Transplantations in Adults With Hematologic Cancers: A Systematic Review and Meta-analysis. JAMA Oncol. 2019 Dec 1;5(12):1739-1748.