



Sirolimus and post-transplant cyclophosphamide as graft versus host prophylaxis in patients undergoing matched allogeneic peripheral blood stem cell transplantation.

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Background

Allogeneic hematopoietic cell transplantation (HCT) is a potentially curative therapy for high-risk malignancies though graft versus host disease (GVH) limits optimal outcomes. Posttransplantation cyclophosphamide (PT-Cy) is an effective agent for the prophylaxis of GVH due to its functional inhibition of alloreactive T-lymphocytes and may enable GVH prevention while preserving graft versus tumor effect. Additional data are needed to inform the use of PT-Cy when using fully matched donors

Objective

To determine the incidence of GVH, relapse, and overall survival (OS) following allogeneic HCT from fully matched donors using sirolimus/PT-Cy as GVH prophylaxis.

Materials & Methods

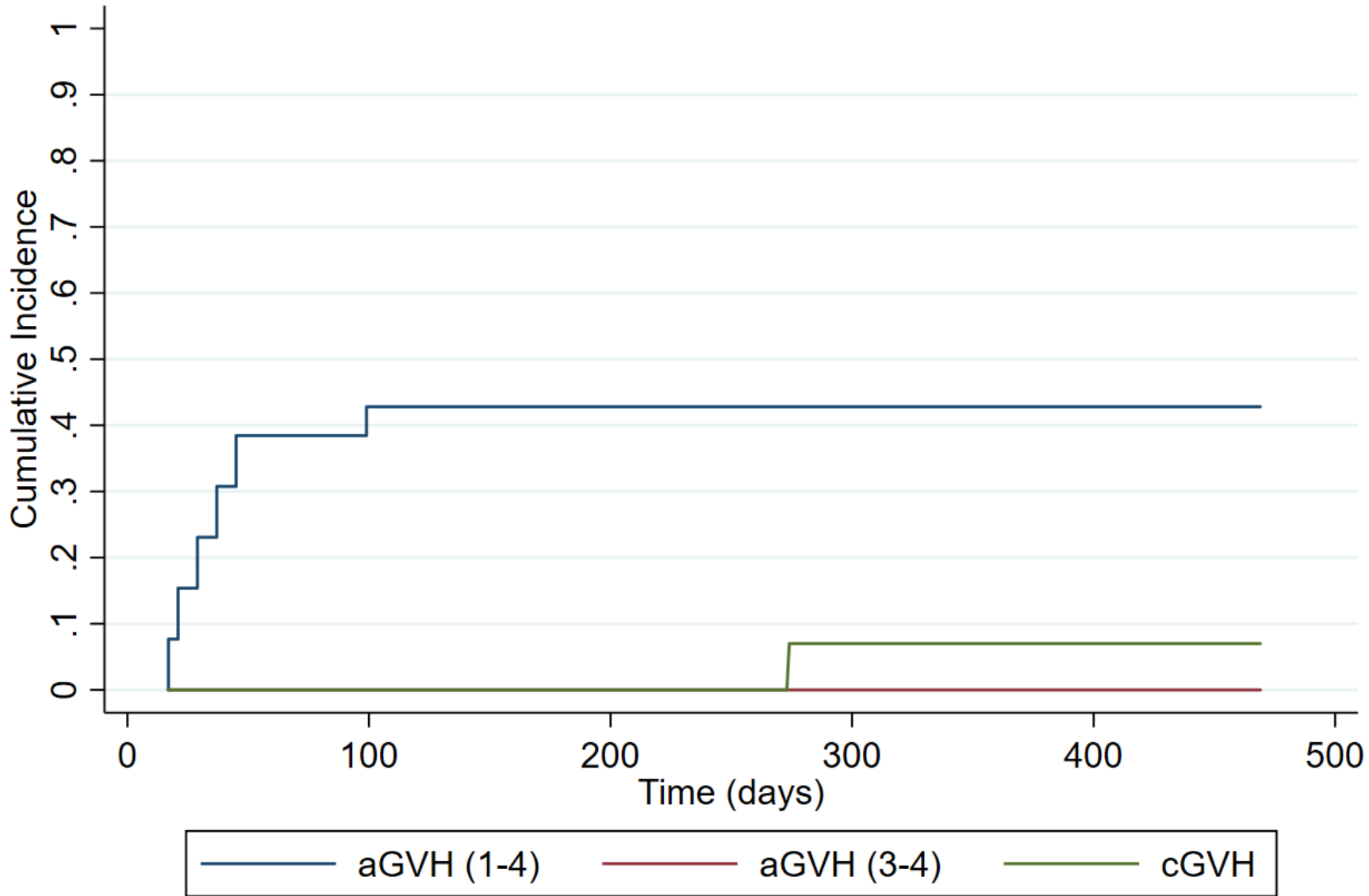
Retrospective data collected on 14 consecutive patients transplanted at BMDACC with a fully matched PBSC donor between Jan 2017 and June 2018 who received PT-Cy (day +3,4) and sirolimus (day +5) for GVH prophylaxis following reduced-intensity conditioning with thiotepa, fludarabine, and melphalan. Data collected include age, disease risk, HCT-CI, GVH incidence and grade, 1yr overall survival, median survival, and GRFS.

Results

Patient characteristics are listed below. Median OS was 908 days. 1yr OS was 64% and NRM at 1 year was 35% with infection (3), VOD (1), and CVA (1) as causes of death. Incidence of all-grade GVH was 42% with 2 patients having grade 1 skin, 1 patient grade 2 skin, and 3 patients with grade 2 GI GVH. There was no grade 3/4 GVH and 8% cGVH. 1 patient relapsed over 2 years post HCT. 7 of the 14 patients remain alive and disease free at the time of this abstract, with a median follow up of 3 years. There was no graft failure. Day 28 neutrophil recovery was 100% and day 100 platelet was 91%.

Patient Characteristics	
Median Age (Range)	69 (39-81)
Median HCT-CI	2 (0-5)
Sex (%)	
• Male	57
• Female	43
Diagnosis	
AML	7
MDS/MPN	5
ALL	2
Disease Risk Index	
• Intermediate	9
• High	3
• Very High	2
Donor Type	
• MRD	4
• MUD	10
• Donor/Recipient M→F	5
• Donor/Recipient F→M	1
CMV Recipient Seropositive (%)	78%
Median Days on Sirolimus	53 (5-238)
Median Relapse Free Survival (days)	861 (117-1362)
Median GVH Relapse Free Survival (days)	565 (17-1362)

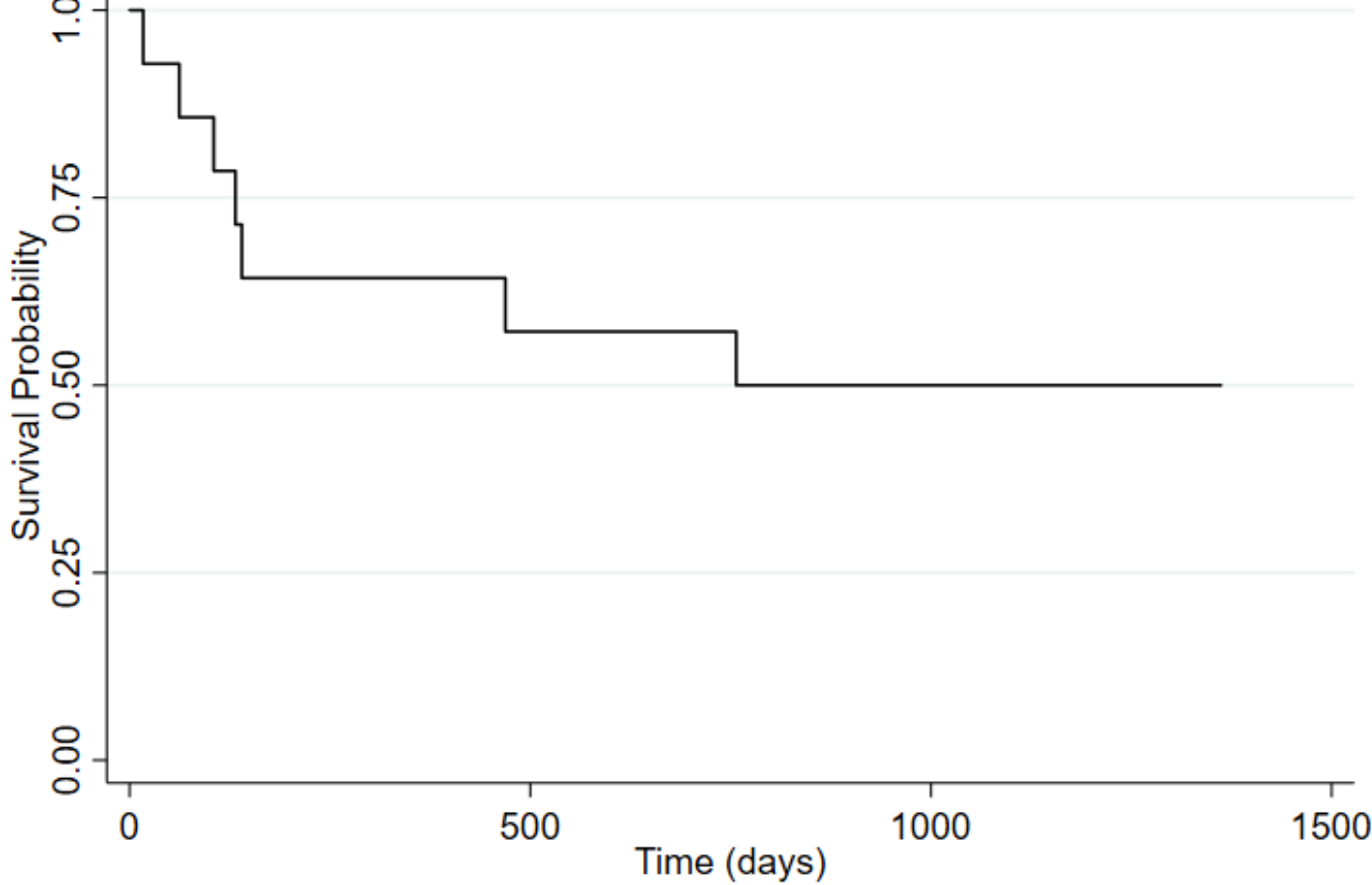
Cumulative Incidence of GVH



Summary

GVH prophylaxis with PT-Cy and sirolimus led to a low rate of grade 3/4 GVH and cGVH within this population. Relapse risk remained low suggesting preserved graft versus tumor effect. Infectious deaths may be related to timing of immune reconstitution following PT-Cy. Additional data are needed to inform the use of PT-Cy in the setting of fully matched donors.

Overall Survival



Discussion

Using PTCy and sirolimus alone in a RIC HCT setting, the incidence of GVH was 42% with comparable rates of NRM and relapse and very low cGVH and grade III/IV GVH. Sample size represents a major limitation of our data. Since these data were submitted, a larger retrospective study by Dr. Gooptu and colleagues was published comparing haploidentical and MUD RIC HCT using PTCy/CNI/MMF GVH prophylaxis which found lower rates of graft failure, GVH, and NRM with MUD compared to haploidentical transplants. Incidence of GVH in the MUD cohort was 27% with 4% Grade III/IV and 28% cGVH. These data and ours continue to add support for the use of PTCy for matched donor transplants while awaiting the results of the randomized BMT CTN 1703.

References

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