Supplemental file

Feasibility of early tacrolimus initiation in haploidentical-PBSCT with post-transplant cyclophosphamide after melphalan-based conditioning regimen

Type of manuscript: Short Communication

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Supplementary Methods

Definitions

The hematopoietic cell transplantation-specific comorbidity index was calculated according to the previous report [1]. "Active" disease status at the time of haploidentical-peripheral blood stem cell transplantation with post-transplant cyclophosphamide (PTCy-haplo) was defined as refractory (i.e., stable or progressive disease) to treatment immediately prior to PTCy-haplo. The disease risk was determined using the refined disease risk index [2].

CRS was defined as fever (≥38°C) without clinical or microbiological evidence of infection early after infusion and graded according to the consensus grading criteria defined by the American Society of Transplantation and Cellular Therapy [3]. Neutrophil engraftment was defined as the first day of 3 consecutive days with absolute neutrophil counts $\geq 0.5 \times 10^9$/L. Platelet engraftment was defined as the first day of 7 consecutive days with absolute platelet counts $\geq 20 \times 10^9$/L without platelet transfusion. Acute and chronic graft-versus-host disease were diagnosed and graded based on the traditional criteria [4,5].

Overall survival was defined as the time from PTCy-haplo to death from any cause or until the last follow-up date for patients who were alive. Patients who remained alive were censored at the last follow-up date. Disease-free survial was defined as the time between PTCy-haplo and relapse or death in complete remission, whichever occurred first. Patients alive without evidence of disease were censored at the last follow-up date. Graft-versus-host/relapse-free survival (GRFS) was defined by the previous report [6]. Relapse was defined based on a reappearance of circulating blasts in peripheral blood, ≥5% of blasts in bone marrow, or extramedullary disease in myeloid neoplasms and acute lymphoblastic leukemia, while progressive disease by the Lugano classification in lymphoma [7].

Supplementary References

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Supplementary Table 1 Clinical outcomes according to poor baseline patient characteristics

	Previous history of allo-HSCT		Active disease at the time of PTCy-haplo	
	No (n = 11)	Yes (n = 8)	No (n = 11)	Yes (n = 8)
OS at 2 years (% [95% CI])	62.3 (27.7–84.0)	50.0 (15.2–77.5)	63.6 (29.7–84.5)	50.0 (15.2–77.5)
DFS at 2 years (% [95% CI])	53.0 (20.9–77.3)	50.0 (15.2–77.5)	54.5 (22.9–78.0)	50.0 (15.2–77.5)
GRFS at 2 years (% [95% CI])	45.5 (16.7–70.7)	37.5 (8.7–67.4)	54.5 (22.9–78.0)	25.0 (3.7–55.8)
CIR at 2 years (% [95% CI])	27.3 (5.8–55.2)	37.5 (7.0–69.6)	18.2 (2.5–45.6)	50.0 (12.6–79.3)
NRM at 2 years (% [95% CI])	19.7 (2.4–49.3)	12.5 (0.4–45.3)	27.3 (5.6–55.6)	0.0 (0.0–0.0)

Abbreviations: allo-HSCT, allogeneic hematopoietic stem cell transplantation; CIR, cumulative incidence of relapse; DFS, disease-free survival; GRFS, graft-versus-host/relapse-free survival; NRM, non-relapse mortality; OS, overall survival; PTCy-haplo, haploidentical-peripheral blood stem cell transplantation with post-transplant cyclophosphamide

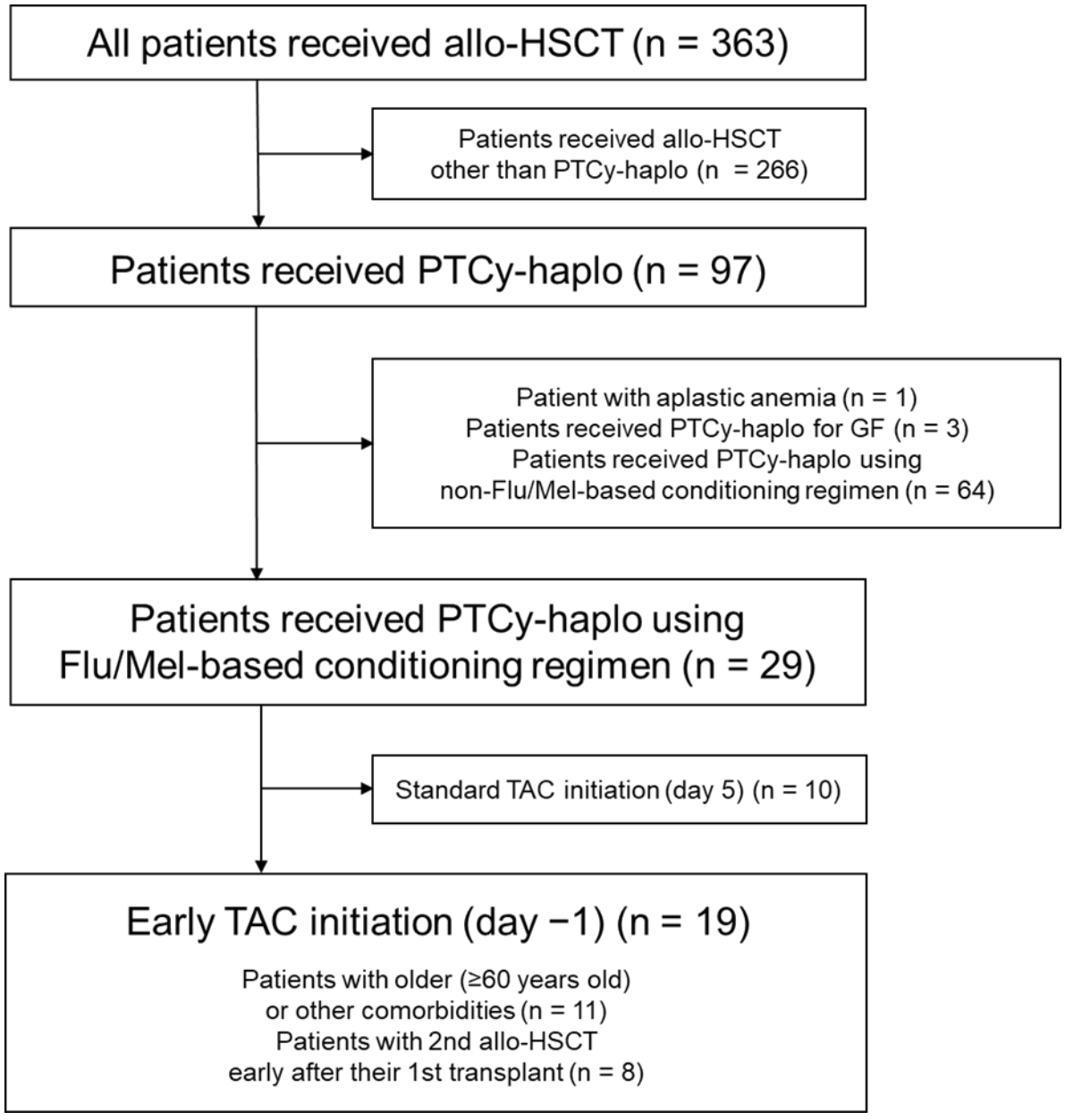
Supplementary Table 2 Infection during the first 100 days after PTCy-haplo and cause of death

	All (n = 19)	Standard-dose PTCy (n = 11)	Reduced-dose PTCy (n = 8)
Infection			
Bacterial infection	7 (36.8)	4 (36.4)	3 (37.5)
Fungal infection			
Candidemia	1 (5.3)	0 (0.0)	1 (12.5)
Aspergillus pneumonia	1 (5.3)	1 (9.1)	0 (0.0)
Viral infection			
Cytomegalovirus antigenemia	2 (10.5)	2 (18.2)	0 (0.0)
Hemorrhagic cystitis*	6 (31.6)	2 (18.2)	4 (50.0)
Cause of death			
Primary disease, n (%)	4 (21.1)	2 (18.2)	2 (25.0)
Chronic GVHD, n (%)	1 (5.3)	1 (5.3)	0 (0.0)
Infection, n (%)	1 (5.3)	0 (0.0)	1 (12.5)
Organ dysfunction, n (%)	2 (10.5)	2 (18.2)	0 (0.0)
TMA, n (%)	1 (5.3)	1 (9.1)	0 (0.0)
Unknown, n (%)	1 (5.3)	0 (0.0)	1 (12.5)

*Due to BK virus (n = 2) in the standard-dose PTCy group and adenovirus (n = 1) and BK virus (n = 3) in the reduced-dose PTCy group.

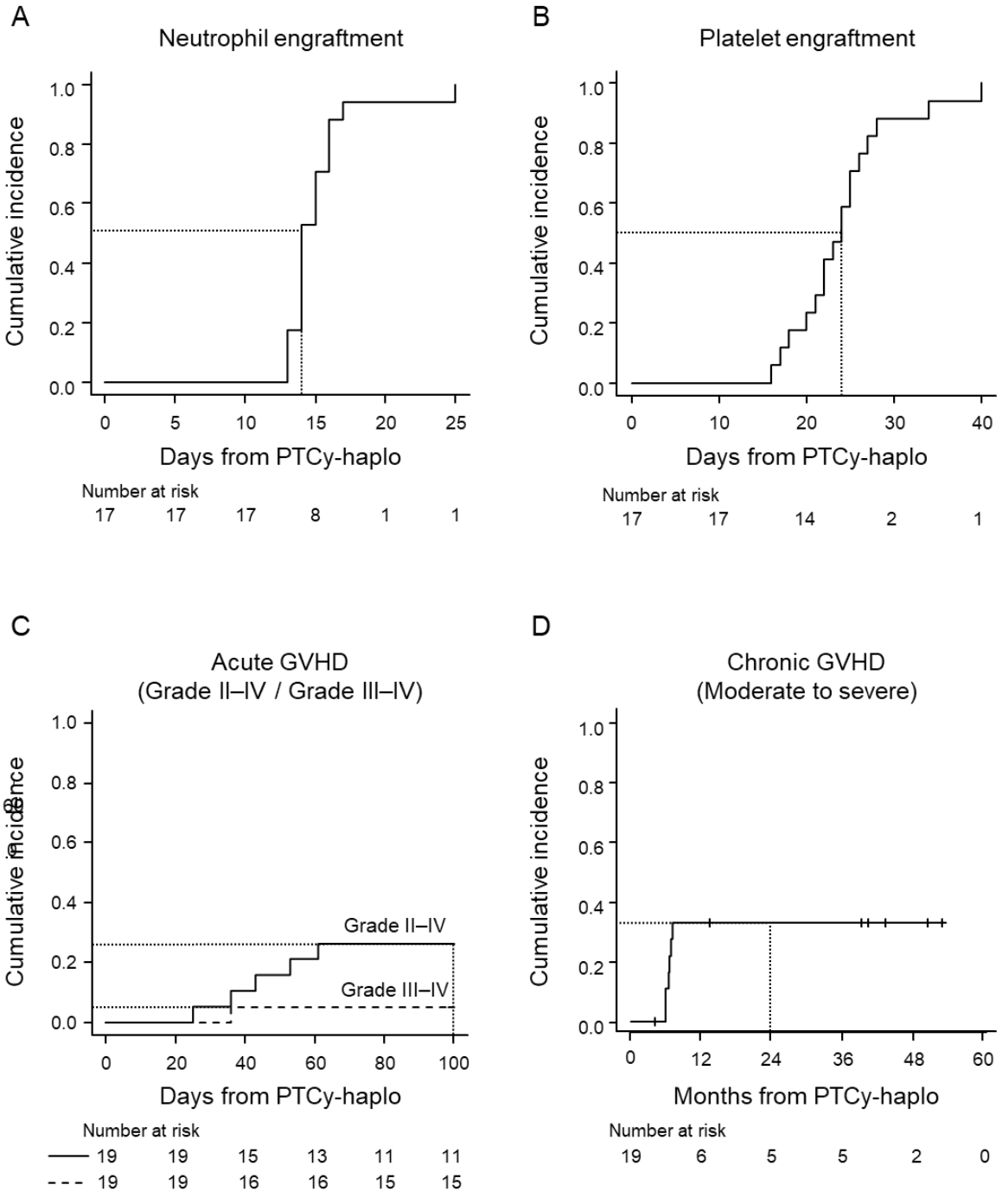
Abbreviations: GVHD, graft-versus-host disease; TAC, tacrolimus; PTCy-haplo, haploidentical-peripheral blood stem cell transplantation with post-transplant cyclophosphamide; TMA, thrombotic microangiopathy

Supplementary Figure. 1



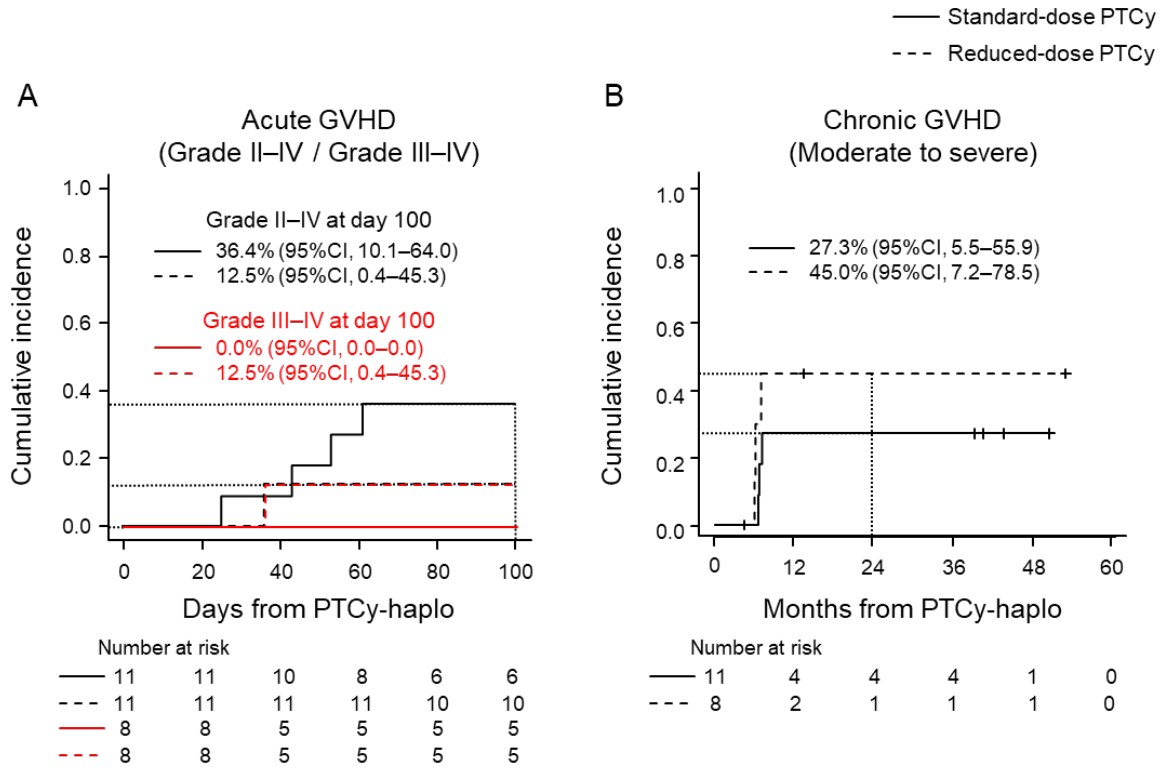
Supplementary Figure. 1 A flowchart of patient selection. Abbreviations: allo-HSCT, allogeneic hematopoietic stem cell transplantation; PTCy-haplo, haploidentical-peripheral blood stem cell transplantation with post-transplant cyclophosphamide, Flu, fludarabine; GF, graft failure; Mel, melphalan; TAC, tacrolimus

Supplementary Figure. 2



Supplementary Figure. 2 The cumulative incidence of (A) neutrophil engraftment, (B) platelet engraftment, (C) grade II–IV and III–IV acute GVHD, and (D) moderate to severe chronic GVHD. Abbreviations: GVHD, graft-versus-host disease; PTCy-haplo, haploidentical-peripheral blood stem cell transplantation with post-transplant cyclophosphamide

Supplementary Figure. 3



Supplementary Figure. 3 The cumulative incidence of (A) grade II–IV and III–IV acute GVHD and (B) moderate to severe chronic GVHD in the standard- and reduced-dose PTCy groups. Abbreviations: GVHD, graft-versus-host disease; PTCy-haplo, haploidentical-peripheral blood stem cell transplantation with post-transplant cyclophosphamide