Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Farag SS, Abu Zaid M, Schwartz JE, et al. Dipeptidyl peptidase 4 inhibition for prophylaxis of acute graft-versus-host disease. N Engl J Med 2021;384:11-9. DOI: 10.1056/NEJMoa2027372

Supplementary Appendix

Supplement to: Farag SS, Abu Zaid M, Schwartz JE, et al. DPP-4 Inhibition for Prophylaxis of Graft vs Host Disease

Contents

Table S1. Modified Glucksberg criteria for scoring of acute GVHD

Organ stages

Organ	Stage	Description
Skin	0	No rash
	1	Maculopapular rash over <25% of body surface area
	2	Maculopapular rash over 25-50% of body surface area
	3	Generalized erythroderma (>50% of body surface area
	4	Generalized erythroderma with bullous formation and often with desquamation
Gut	0	Diarrhea <500 ml/day
	1	Diarrhea 500 - 1000 ml/day
	2	Diarrhea 1001 - 1500 ml/day
	3	Diarrhea 1501 - 2000 ml/day
	4	Diarrhea >2000 ml/day; or severe abdominal pain with or without ileus
Liver	0	Serum total bilirubin <2.0 mg/dl
	1	Serum total bilirubin 2.0 - 3.0 mg/dl
	2	Serum total bilirubin 3.1 - 6.0 mg/dl
	3	Serum total bilirubin 6.1 - 15.0 mg/dl
	4	Serum total bilirubin >15.0 mg/dl

Overall clinical grade*

Clinical Grade	Skin stage		Liver stage		Gut stage
I	1 to 2		0		0
II	3	and/or	1	and/or	1
III	1 to 3	and	2 to 3	and/or	2 to 4
IV	4	and/or	4		

*Overall clinical grade is based on the combination of organ stage scores as shown and reported.[1]

Table S2. National Institutes of Health global severity scoring of chronic GVHD*

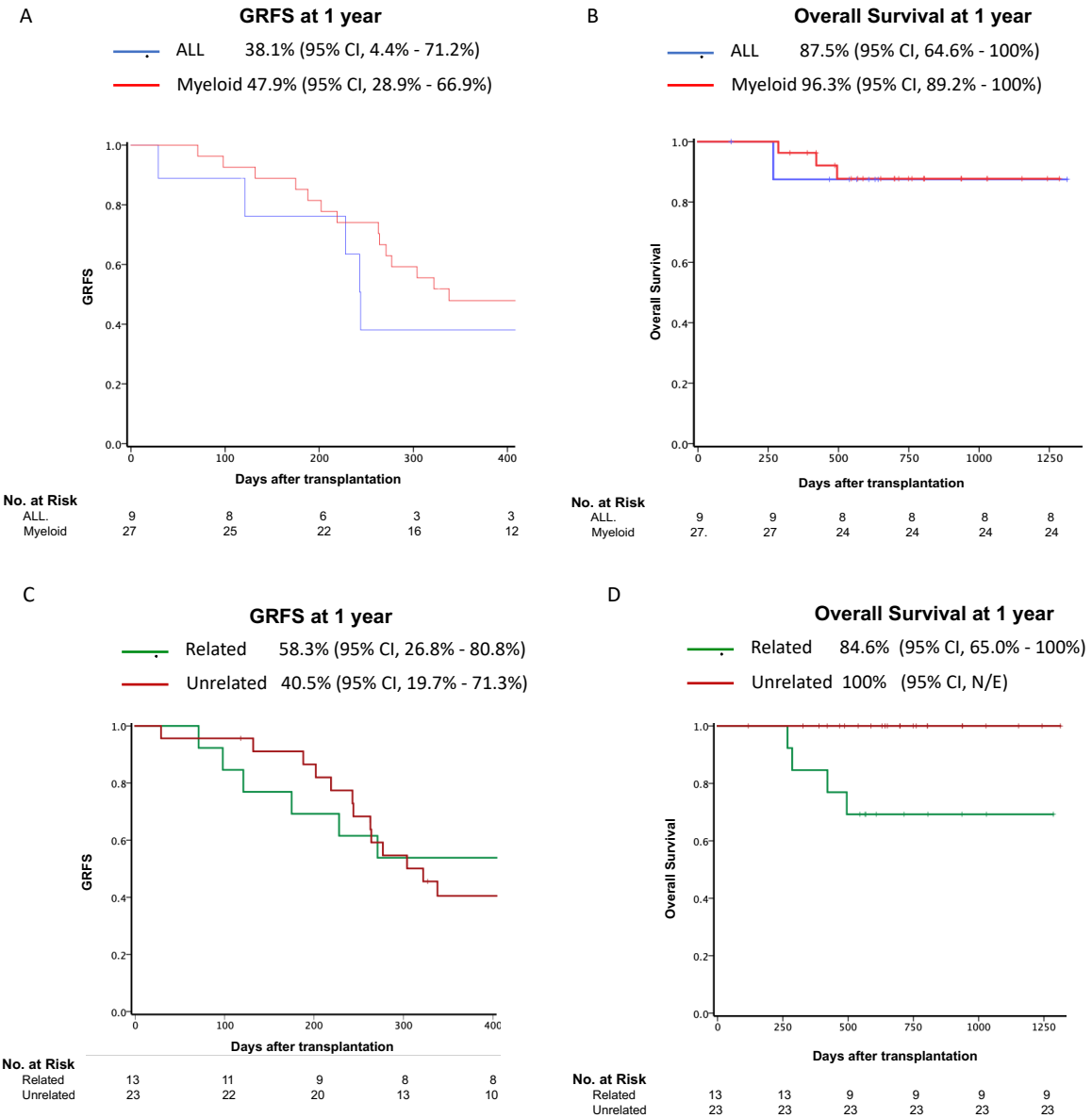
Mild	• 1 or 2 organ or site (except lung) with score 1
Moderate	• 3 or more organ or sites with score 1, or • 1 or more organs of sites with score 2, or • Lung score 1 (FEV1 60-79% or dyspnea with stairs)
Severe	• At least one organ or site with a score 3, or • Lung score 2 (FEV1 40-59% or dyspnea walking on flat ground)

*The global severity score (mild, moderate, severe) is calculated from the individual organ or site scores according to the number and severity of organ or sites reported.[2] The scoring of individual organ or site scores is based on the 2014 National Institutes of Health Consensus Criteria for scoring.[3] Briefly, a clinical scoring system (0-3) is used for individual organs that describes the severity for each affected organ taking functional impact into account. Eight organs (skin, mouth, eyes, gastrointestinal tract, liver, lungs, joints, and female genital tract) are assessed. In general, a score of 0 means no manifestations or symptoms, a score of 1 indicates no significant impairment of function or activities of daily living, a score of 2 reflects significant impairment of activities of daily living but no major disability, and a score of 3 indicates significant impairment of activities of daily living with major disability. The scoring is clinical and the only mandated laboratory tests for its completion are liver function tests, although pulmonary function tests are performed only when indicated by symptoms.

Supplementary Figure S1

Figure S1. GRFS and overall survival by disease and donor types

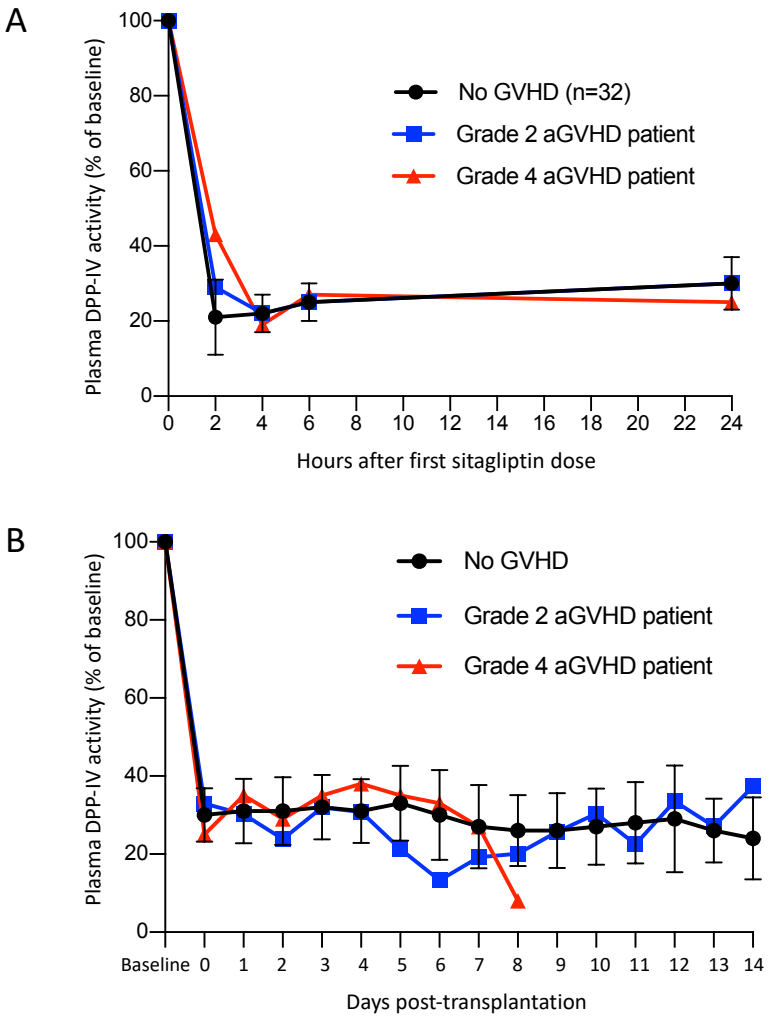
The outcomes of GRFS and overall survival curves for patients with acute lymphoblastic leukemia (ALL) and those with myeloid malignancies are shown in panels A and B, respectively. Panels C and D show the GRFS and overall survival curves, respectively, for patients receiving stem cells from related and unrelated donors. Survival point estimates at 1 year with 95% confidence intervals (CI) are shown. N/E, not estimable.



Supplementary Figure S2

Figure S2. Plasma DPP-4 activity

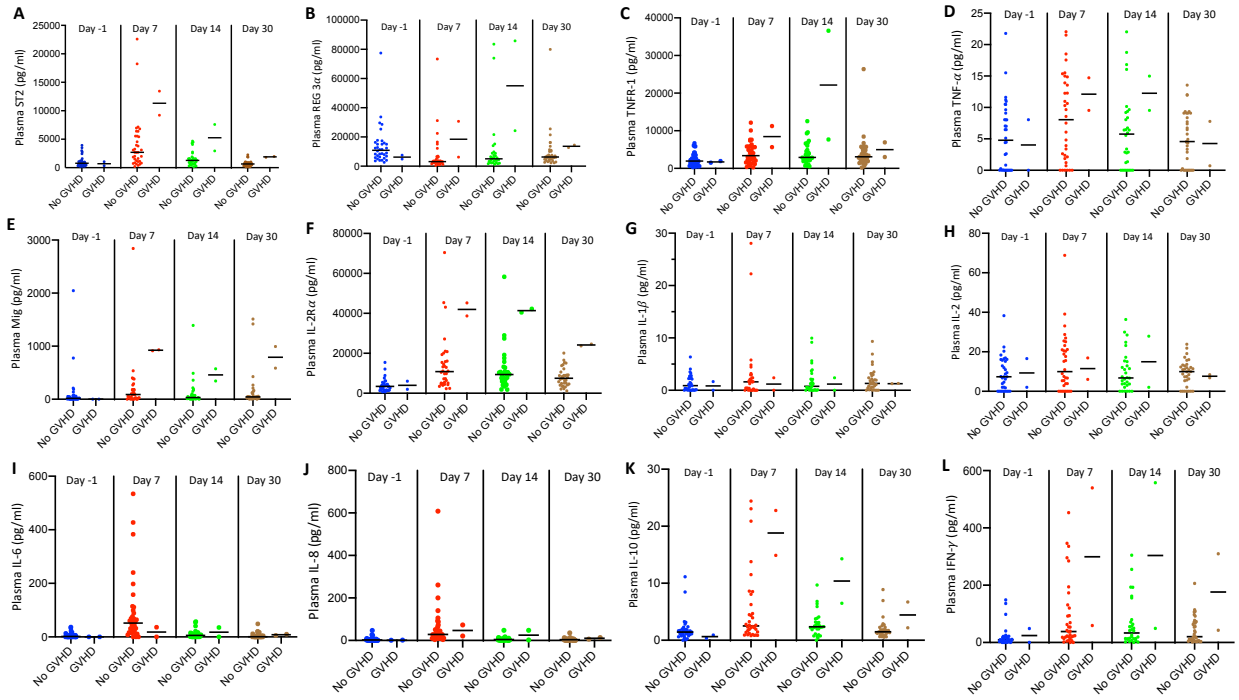
Panel A shows the DPP-4 activity after the first dose of sitagliptin on day -1. Baseline activity was set at 100% and residual activity expressed as a percentage of baseline at 2, 4, 6 and 24 hours after the first dose. Panel B shows the trough residual DPP-4 levels before each morning sitagliptin dose through day 14 post-transplantation. In both panels, the mean DPP-IV activity and standard deviation bars for patients who did not develop aGVHD by day 100 are shown by the black curve. The DPP-IV activity levels at the corresponding times are also shown individually in blue and red for the two patients who developed grade II and grade IV aGVHD by day 100, respectively.



Supplementary Figure S3

Figure S3. Plasma cytokine and aGVHD biomarker levels.

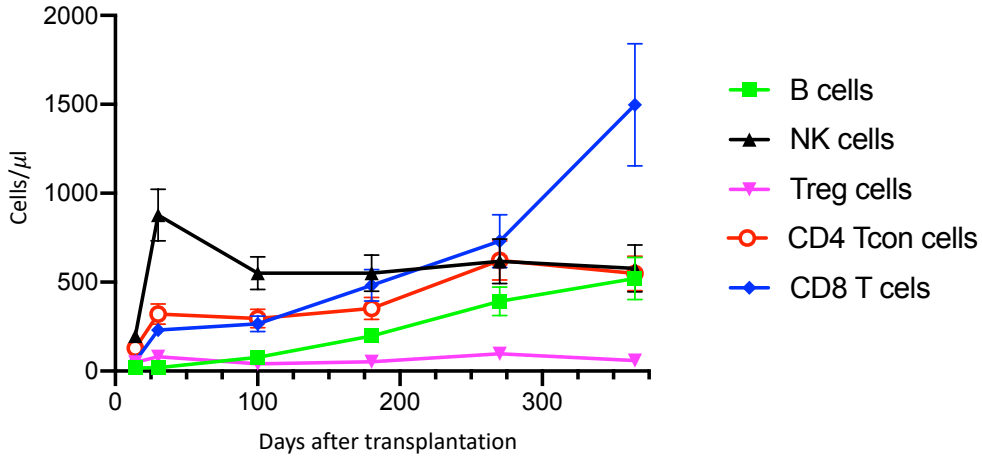
Panels A-L show plasma cytokine and aGVHD biomarker levels at day -1 and days 7, 14 and 30 post-transplantation for patients who did not develop aGVHD by day 100 and the two patients who did. Horizontal bars represent medians.



Supplementary Figure S4

Figure S4. Immune cell reconstitution post-transplantation

Blood levels of B cells, natural killer (NK) cells, T regulatory (Treg) cells, CD4 conventional T (CD4 Tcon) cells, and CD8 T cells are shown on days 7, 14, 30, 100, 180, 270 and 365 post-transplantation. Point estimates are means with standard errors bars.



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3. Jagasia MH, Greinix HT, Arora M, et al. National Insitutes of Health Consensus Development Project on criteria for clinical trials in chronic graft-versus-host disease: I. The 2014 Diagnosis and Staging Working Group Report. Biol Blood Marrow Transplant 2015; 21:389-401.