A phase II, prospective, randomized, open-label study of defibrotide added to standard-of-care prophylaxis for the prevention of acute graft-*versus*-host disease after allogeneic hematopoietic cell transplantation

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Online Supplementary Materials

Supplementary methods

Analysis of the primary endpoint

The primary efficacy endpoint was estimated for each treatment arm by the cumulative incidence competing risk estimator as described by Marubini and Valsecchi.[1] Death prior to grade B-D acute graft-versus-host-disease (aGvHD) was considered as the competing risk. The timing variable was defined as the number of days from the date of hematopoietic cell transplantation (HCT; Day 0 post-transplant) to the first onset of grade B-D aGvHD or death. Time to death was the number of days from the date of HCT to the date of death. If a patient did not have grade B-D aGvHD or died, the patient was censored at the date of the last available evaluation of aGvHD. The timing variable was anchored at the time of HCT (Day 0 post-transplant). We anticipated that <2% of patients would not undergo HCT; for those patients, Day 0 was counted at randomization, and they were censored at Day 1.

Reference

1. Marubini E, Valsecchi MG. Analysing survival data from clinical trials and observational studies. In: Barnett V, editor. Statistics in practice. Chichester (England): John Wiley & Sons; 1995.

Supplementary figures and tables

Supplementary Table S1. SOC prophylaxis.

Therapies, n (%)[a]	Defibrotide prophylaxis (n=74)	SOC (n=70)
Use of ATG		
ATG	22 (30)	21 (30)
No ATG	52 (70)	49 (70)
MTX, with no MMF	55 (74)	52 (74)
MTX only	1 (1)	0
MTX + TAC + ATG	4 (5)	3 (4)
MTX + CSA + ATG	9 (12)	7 (10)
MTX + CSA, with no ATG	10 (14)	11 (16)
MTX + TAC, with no ATG	31 (42)	31 (44)
MMF, with no MTX	19 (26)	18 (26)
MMF + TAC + ATG	1 (1)	2 (3)
MMF + TAC, with no ATG	2 (3)	1 (1)
MMF + CSA + ATG	8 (11)	9 (13)
MMF + CSA, with no ATG	8 (11)	6 (9)

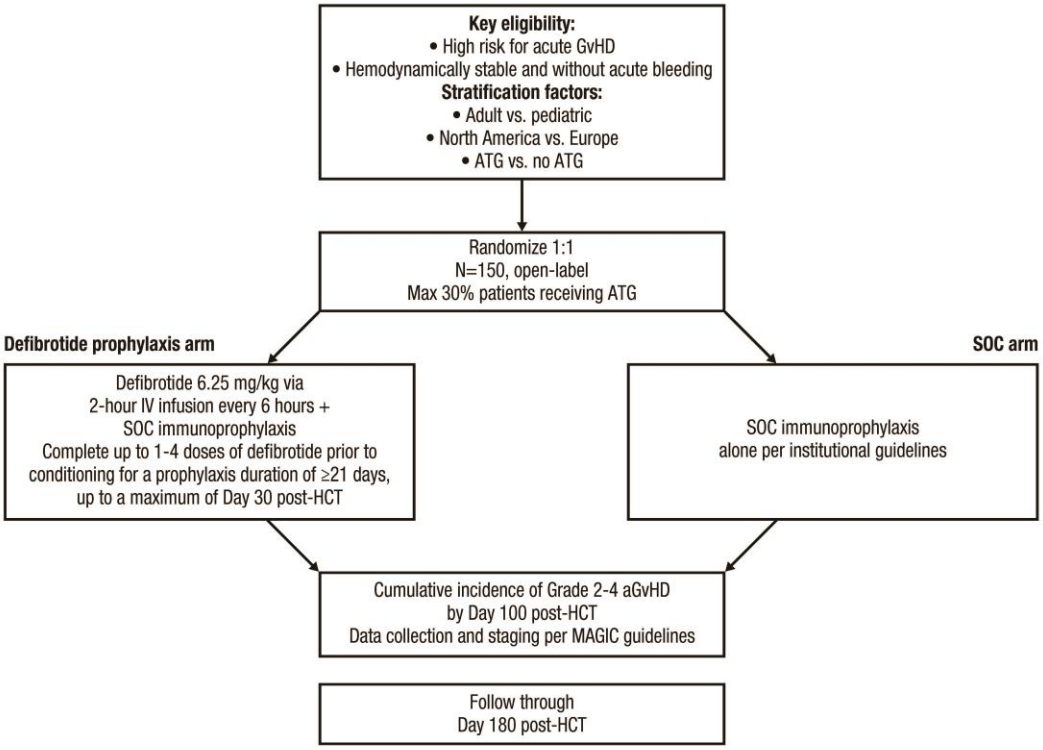
ATG: antithymocyte globulin; CSA: cyclosporine A; MMF: mycophenolate mofetil; MTX: methotrexate; SOC: standard of care; TAC: tacrolimus.

Supplementary Table S2. Treatment-related treatment-emergent adverse events.

Number of patients, n (%)[a]	Defibrotide prophylaxis (n=74)
Treatment-related treatment-emergent adverse events[b]	12 (16)
Vomiting	3 (4)
Nausea	2 (3)
Diarrhea	1 (1)
Hemorrhoidal hemorrhage	1 (1)
Anemia	1 (1)
Sinus tachycardia	1 (1)
Peripheral edema	1 (1)
Pyrexia	1 (1)
Contusion	1 (1)
Infusion-related reaction	1 (1)
Blood creatinine increased	1 (1)
Neutrophil count decreased	1 (1)
Platelet count decreased	1 (1)
Viral titer decreased	1 (1)
Hypomagnesemia	1 (1)

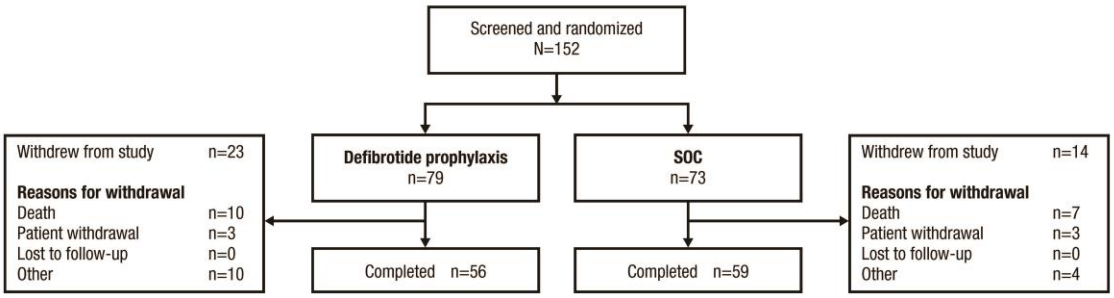
[a]Incidence was based on the number of patients, not the number of events; patients may have had >1 adverse event. [b]Coding was based on MedDRA version 21.1.

Supplementary Figure S1. Study design.



ATG: antithymocyte globulin; GvHD: graft-versus-host disease; HCT: hematopoietic cell transplantation; IV: intravenous; MAGIC: Mount Sinai Acute Graft-versus-Host Disease Consortium; SOC: standard of care.

Supplementary Figure S2. CONSORT flow diagram.



SOC: standard of care.