LETTER TO THE EDITOR

Circulating endothelial cells and the study of vascular injury in children undergoing hematopoietic stem cell transplant

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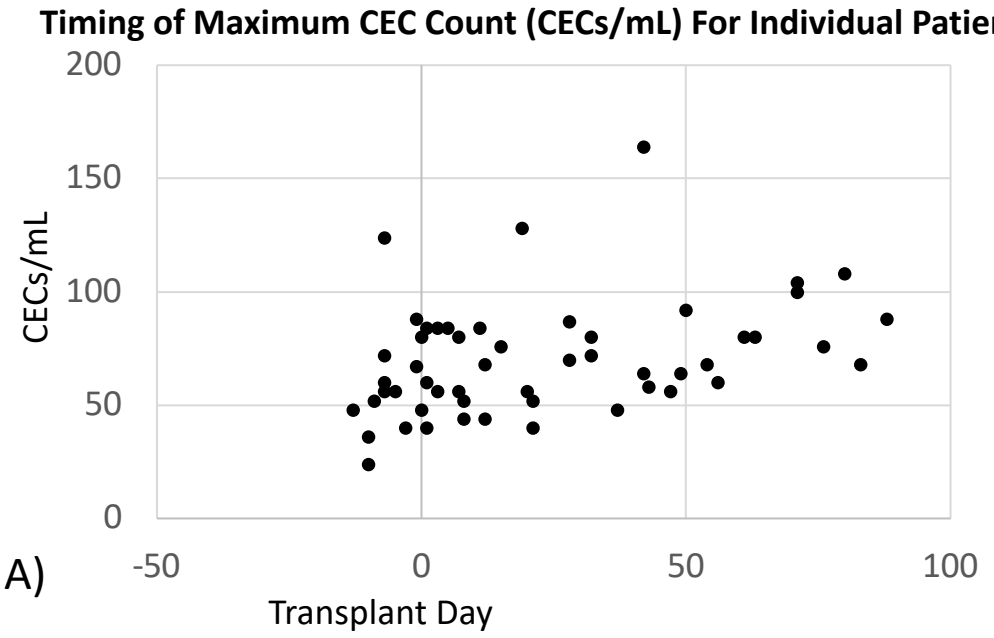
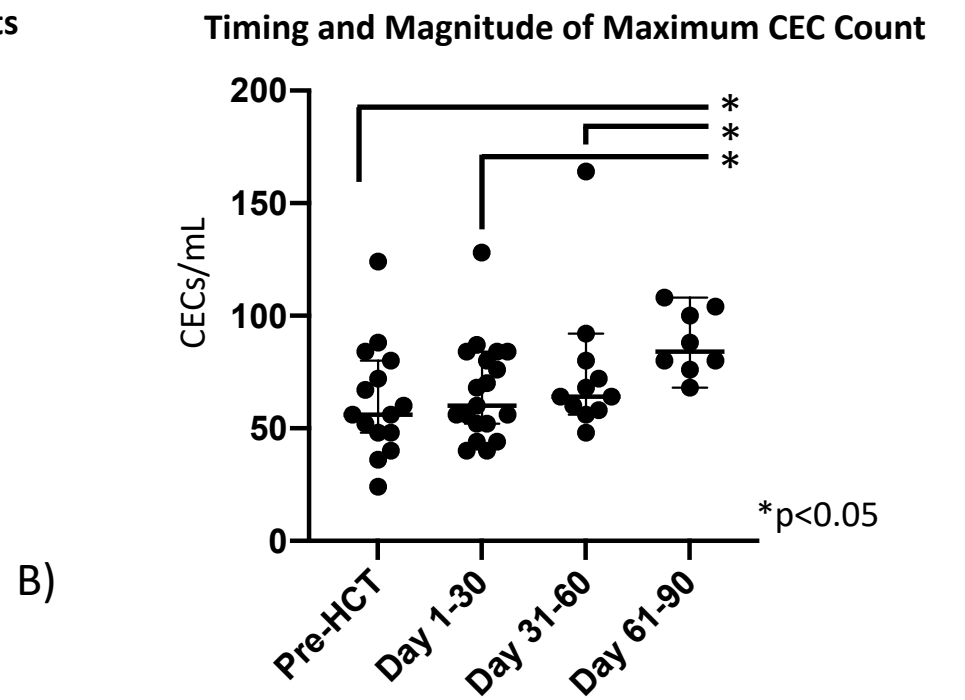
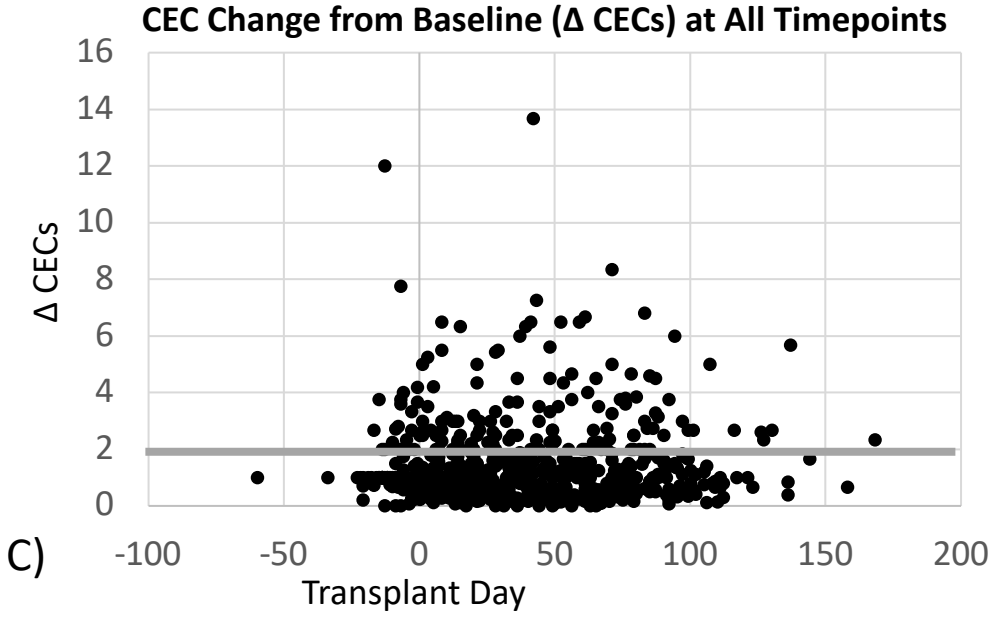
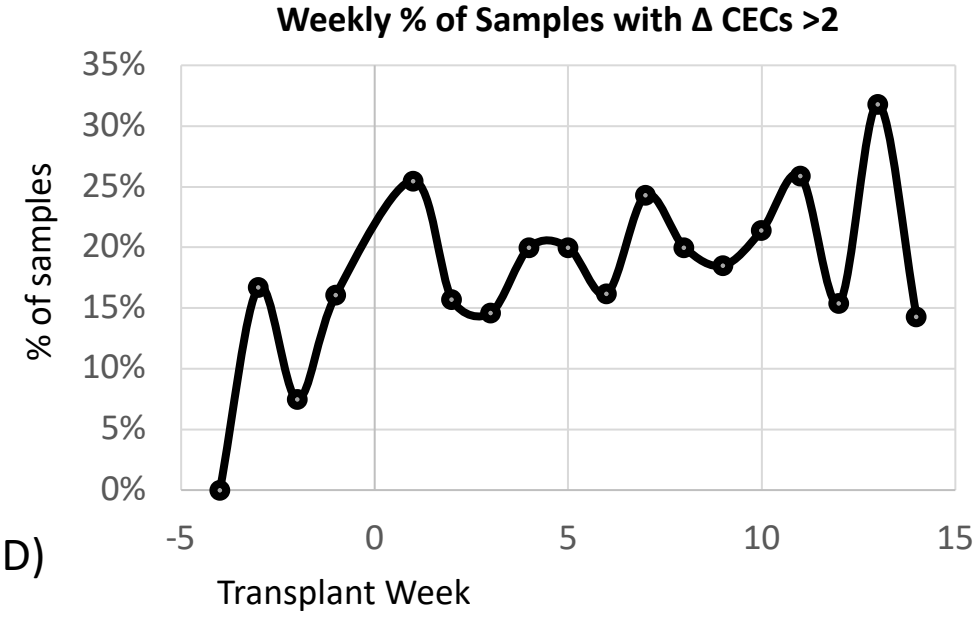
Demographics	% Patients (n = 53)
Age in years	
Median (Range)	7.3 (0.4-32.7)
Sex	
Female	39.6% (n=21)
Male	60.4% (n=32)
Diagnosis	
Leukemia/MDS	30.2% (n=16)
Bone Marrow Failure	26.4% (n=14)
Immune Deficiency	9.4% (n=5)
Neuroblastoma	7.6% (n=4)
Other	26.4% (n=14)
Conditioning Intensity	
MAC	79.2% (n=42)
RIC	20.7% (n=11)
Conditioning	
TBI-based	9.4% (n=5)
No TBI	90.6% (n=48)
Graft	
Bone Marrow	39.6% (n=21)
PBSC	54.7% (n=29)
Cord	5.6% (n=3)
GvHD Prophylaxis	
Cyclosporine-based	45.3% (n=24)
Tacrolimus-based	7.5% (n=4)
Ex vivo t-cell depletion	39.6% (n=21)
None (autologous)	7.5% (n=4)
GvHD	
No	86.8% (n=46)
Yes	13.2% (n=7)
Thrombotic Microangiopathy	
No	73.6% (n=39)
Yes	26.4% (n=14)
Received Eculizumab	11.3% (n=6)

Supplemental Table 1: Patient demographics and complications after HSCT. Bone marrow failure included Fanconi anemia (n=9), aplastic anemia (n=4) and Schwachman Diamond syndrome (n=1). Other diagnoses included: beta thalassemia (n=3), lymphoproliferative disorder (n=3), macrophage activation syndrome (n=2), sickle cell disease (n=1), Glanzmann's thrombasthenia (n=1), Hurler syndrome (n=1), hemoglobin Hammersmith (n=1), myelofibrosis (n=1) and paroxysmal nocturnal hemoglobinuria (n=1). Abbreviations: graft versus host disease (GvHD), myeloablative conditioning (MAC), myelodysplastic syndrome (MDS), peripheral blood stem cells (PBSCs), reduced intensity conditioning (RIC), total body irradiation (TBI).









Supplemental Figure 1: CEC kinetics and maximum values in HSCT recipients. A) The timing of the maximum CEC count, measured in CECs/mL, is shown for all patients. B) Maximum CEC values for each patient were grouped by those occurring before HSCT, days 1-30, days 31-60 or days 61-90. The median and 95% confidence intervals are annotated in the figure. Data were analyzed using Mann-Whitney test. Patients whose maximum value occurred between days 61-90 had significantly higher peak CEC values (median 84, IQR 77-103) than those who peaked before HSCT (median 56, IQR 48-80, p=0.009), between days 1-30 (median 60, IQR 52-84, p=0.01) and those who peaked between days 31-60 (median 64, IQR 48-80, p=0.03). C) The Δ CEC score is shown for all measured CEC values (n=642) from 53 HSCT patients. The range of sample collection days was day -60 to day 168. The solid line marks a doubling of CECs from baseline. D) The weekly percentage of samples with Δ CECs >2 is shown. Between 4 and 56 total samples were tested weekly at each of these timepoints.

Supplemental Table 2: An analysis of CEC change from baseline (Δ CECs) across multiple HSCT variables and complications. Patients with at least one Δ CEC score >2 after HSCT are compared to patients whose Δ CEC scores remained at or below 2 after HSCT. All patients with high-risk TMA, TMA requiring treatment with eculizumab and VOD requiring treatment with defibrotide had more than a two-fold elevation in CECs from baseline. A separate analysis was performed comparing patients with high-risk TMA to those without any TMA (i.e. excluding patients with moderate-risk TMA) and similarly had a P-value of 0.03. Complications that occurred outside of the CEC collection period were not included in this analysis. P-values were obtained using Chi-square or Fisher's exact tests. CSA= cyclosporine, GvHD= graft versus host disease, HSCT= hematopoietic stem cell transplant, MAC= myeloablative conditioning, MDS= myelodysplastic syndrome, PBSC= peripheral blood stem cells, RIC= reduced intensity conditioning, TBI= total body irradiation, TMA= thrombotic microangiopathy, VOD= hepatic veno-occlusive disease.

	Δ CEC score >2 after HSCT (n=31)	**No Δ CEC score >2 after HSCT (n=22)**	**p**
Diagnosis			0.58
Leukemia/MDS	29% (n=9)	31.8% (n=7)	
Marrow Failure	19.4% (n=6)	36.4% (n=8)	
Immune Deficiency	9.7% (n=3)	9.1% (n=2)	
Neuroblastoma	9.7% (n=3)	4.5% (n=1)	
Other	32.2% (n=10)	18.2% (n=4)	
Conditioning Regimen Radiation			0.64
TBI-based regimen	6.5% (n=2)	13.6% (n=3)	
Non TBI-based regimen	93.5% (n=29)	86.4% (n=19)	
Conditioning Regimen Intensity			>0.99
MAC	80.7% (n=25)	77.3% (n=17)	
RIC	19.3% (n=6)	22.7% (n=5)	
Graft Source			0.79
Autologous PBSC	9.7% (n=3)	4.5% (n=1)	
Bone Marrow	41.9% (n=13)	36.4% (n=8)	
Cord	6.5% (n=2)	4.5% (n=1)	
PBSC	41.9% (n=13)	54.5% (n=12)	
Graft Manipulation			0.57
T-cell Depleted	35.5% (n=11)	45.5% (n=10)	
None	64.5% (n=20)	54.5% (n=12)	
GvHD Prophylaxis			0.77
CSA-based	48.4% (n=15)	40.9% (n=9)	
Ex vivo T-cell depletion	35.5% (n=11)	45.5% (n=10)	
Other	16.1% (n=5)	13.6% (n=3)	
Sex			0.57
Male	64.5% (n=20)	54.5% (n=12)	
Female	35.5% (n=11)	45.5% (n=10)	
Moderate or High-Risk TMA			0.12
Yes	35.5% (N=11)	13.6% (N=3)	
No	64.5% (N=20)	86.4% (N=19)	
High-Risk TMA			**0.03**
Yes	22.6% (N=7)	0% (N=0)	
No	77.4% (N=24)	100% (N=22)	
Eculizumab Therapy for TMA			**0.04**
Yes	19.4% (N=6)	0% (N=0)	
No	80.6% (N=25)	100% (N=22)	
Defibrotide Therapy for VOD			0.26
Yes	9.7% (N=3)	0% (N=0)	
No	90.3% (N=28)	100% (N=22)	
GvHD			>0.99
Yes	12.9% (N=4)	13.6% (N=3)	
No	87.1% (N=27)	86.4% (N=19)	