Patient-reported treatment response in chronic graft-*versus*-host disease

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Supplemental data:

Table S1 – Baseline patient demographic variables

Characteristic	Total (N=382)	GVHD not improved (N=112)	GVHD improved (N=270)	P-value*
Sex				0.40
Female	148 (38.7%)	47 (42.0%)	101 (37.4%)	
Male	234 (61.3%)	65 (58.0%)	169 (62.6%)	
Acute GVHD grade II-IV				0.47
No	203 (53.8%)	56 (50.9%)	147 (55.1%)	
Yes	174 (46.2%)	54 (49.1%)	120 (44.9%)	
Missing	(N=5)	(N=2)	(N=3)	
Age at transplant (years)				
Median (IQR)	54.0 (41.4-61.2)	53.5 (40.0-61.0)	54.0 (42.0-61.6)	0.576
Age at cGVHD (years)				
Median (IQR)	55.0 (42.0-62.0)	54.5 (42.0-61.7)	55.0 (43.0-62.0)	0.62
Months from HCT to cGVHD				
Median (IQR)	8.1 (5.2-12.1)	9.0 (5.6-14.4)	7.6 (5.1-11.8)	0.03
Months from cGVHD to enroll				
Median (IQR)	0.5 (0.0-8.6)	2.6 (0.1-22.7)	0.4 (0.0-4.9)	<.001
KPS at onset				
Median (IQR)	80.0 (80.0-90.0)	90.0 (80.0-90.0)	80.0 (80.0-90.0)	0.85

Table S2. Univariate analysis of NIH organ response by patient perception

Variables	Categories	Total (N=382)	GVHD Not Improved (N=112)	GVHD Improved (N=270)	P-value
Skin response	Not involved	81 (21.3%)	20 (17.9%)	61 (22.7%)	0.003
	CR	92 (24.1%)	17 (15.2%)	75 (27.9%)	
	PR	51 (13.4%)	12 (10.7%)	39 (14.5%)	
	Stable	126 (33.1%)	51 (45.5%)	75 (27.9%)	
	Prog	31 (8.1%)	12 (10.7%)	19 (7.1%)	
	Missing	(N=1)	(N=0)	(N=1)	
Eye response	Not involved	122 (32.0%)	25 (22.5%)	97 (35.9%)	<.001
	CR	38 (10.0%)	6 (5.4%)	32 (11.9%)	
	PR	21 (5.5%)	9 (8.1%)	12 (4.4%)	
	Stable	147 (38.6%)	44 (39.6%)	103 (38.1%)	
	Prog	53 (13.9%)	27 (24.3%)	26 (9.6%)	
	Missing	(N=1)	(N=1)	(N=0)	
Mouth response	Not involved	95 (24.9%)	25 (22.3%)	70 (25.9%)	0.004
	CR	78 (20.4%)	17 (15.2%)	61 (22.6%)	
	PR	66 (17.3%)	12 (10.7%)	54 (20.0%)	
	Stable	118 (30.9%)	49 (43.8%)	69 (25.6%)	
	Prog	25 (6.5%)	9 (8.0%)	16 (5.9%)	
Esophagus response	Not involved	299 (78.3%)	88 (78.6%)	211 (78.1%)	0.939
	CR	39 (10.2%)	11 (9.8%)	28 (10.4%)	
	PR	4 (1.0%)	1 (0.9%)	3 (1.1%)	
	Stable	36 (9.4%)	10 (8.9%)	26 (9.6%)	

Variables	Categories	Total (N=382)	GVHD Not Improved (N=112)	GVHD Improved (N=270)	P-value
	Prog	4 (1.0%)	2 (1.8%)	2 (0.7%)	
Upper GI response	Not involved	298 (78.0%)	86 (76.8%)	212 (78.5%)	0.18
	CR	53 (13.9%)	12 (10.7%)	41 (15.2%)	
	PR	5 (1.3%)	3 (2.7%)	2 (0.7%)	
	Stable	23 (6.0%)	10 (8.9%)	13 (4.8%)	
	Prog	3 (0.8%)	1 (0.9%)	2 (0.7%)	
Lower GI response	Not involved	311 (81.8%)	88 (78.6%)	223 (83.2%)	0.16
	CR	40 (10.5%)	10 (8.9%)	30 (11.2%)	
	PR	3 (0.8%)	1 (0.9%)	2 (0.7%)	
	Stable	17 (4.5%)	8 (7.1%)	9 (3.4%)	
	Prog	9 (2.4%)	5 (4.5%)	4 (1.5%)	
	Missing	(N=2)	(N=0)	(N=2)	
Liver response	Not involved	165 (45.0%)	41 (38.7%)	124 (47.5%)	0.14
	CR	78 (21.3%)	20 (18.9%)	58 (22.2%)	
	PR	56 (15.3%)	18 (17.0%)	38 (14.6%)	
	Stable	63 (17.2%)	24 (22.6%)	39 (14.9%)	
	Prog	5 (1.4%)	3 (2.8%)	2 (0.8%)	
	Missing	(N=15)	(N=6)	(N=9)	
Lung response	Not involved	227 (59.4%)	51 (45.5%)	176 (65.2%)	<.001
	CR	37 (9.7%)	7 (6.3%)	30 (11.1%)	
	PR	10 (2.6%)	5 (4.5%)	5 (1.9%)	
	Stable	76 (19.9%)	31 (27.7%)	45 (16.7%)	
	Prog	32 (8.4%)	18 (16.1%)	14 (5.2%)	
Joint response	Not involved	159 (41.6%)	46 (41.1%)	113 (41.9%)	0.20
	CR	40 (10.5%)	6 (5.4%)	34 (12.6%)	

Variables	Categories	Total (N=382)	GVHD Not Improved (N=112)	GVHD Improved (N=270)	P-value
	PR	44 (11.5%)	12 (10.7%)	32 (11.9%)	
	Stable	31 (8.1%)	10 (8.9%)	21 (7.8%)	
	Prog	108 (28.3%)	38 (33.9%)	70 (25.9%)	

Abbreviations: GVHD, graft-versus-host disease; CR, complete response; PR, partial response; Prog, progression

Table S3 – Patient characteristics grouped by those with vs. without 6 month patient-reported response data

Characteristic	Total (N=605)	No 6mo Pt response (N=223)	Had 6mo Pt response (N=382)	P-value*
Sex				0.948
Female	235 (38.8%)	87 (39.0%)	148 (38.7%)	
Male	370 (61.2%)	136 (61.0%)	234 (61.3%)	
Diagnosis at transplant				0.112
AML	219 (36.2%)	91 (40.8%)	128 (33.5%)	
ALL	69 (11.4%)	24 (10.8%)	45 (11.8%)	
CML	27 (4.5%)	16 (7.2%)	11 (2.9%)	
CLL	33 (5.5%)	11 (4.9%)	22 (5.8%)	
MDS	88 (14.5%)	32 (14.3%)	56 (14.7%)	
NHL	82 (13.6%)	26 (11.7%)	56 (14.7%)	
HD	13 (2.1%)	4 (1.8%)	9 (2.4%)	
MPD	14 (2.3%)	3 (1.3%)	11 (2.9%)	
MM	21 (3.5%)	3 (1.3%)	18 (4.7%)	
AA	9 (1.5%)	3 (1.3%)	6 (1.6%)	
Other	30 (5.0%)	10 (4.5%)	20 (5.2%)	
Disease status				0.580
Early	259 (42.8%)	100 (44.8%)	159 (41.6%)	
Intermediate	248 (41.0%)	91 (40.8%)	157 (41.1%)	
Advanced	98 (16.2%)	32 (14.3%)	66 (17.3%)	
Myeloablative				0.017
No	306 (50.7%)	99 (44.4%)	207 (54.5%)	
Yes	297 (49.3%)	124 (55.6%)	173 (45.5%)	
Missing	(N=2)	(N=0)	(N=2)	
Donor type				0.799
HLA-identical sibling	197 (32.7%)	71 (32.0%)	126 (33.2%)	
HLA-matched other relative	20 (3.3%)	9 (4.1%)	11 (2.9%)	

Characteristic	Total (N=605)	No 6mo Pt response (N=223)	Had 6mo Pt response (N=382)	P-value*
HLA-mismatched relative	10 (1.7%)	5 (2.3%)	5 (1.3%)	
Haploidentical relative	5 (0.8%)	1 (0.5%)	4 (1.1%)	
Matched unrelated donor	298 (49.5%)	112 (50.5%)	186 (48.9%)	
Mismatched unrelated donor	72 (12.0%)	24 (10.8%)	48 (12.6%)	
Missing	(N=3)	(N=1)	(N=2)	
Transplant source				0.289
Peripheral blood	544 (90.2%)	195 (87.8%)	349 (91.6%)	
Bone marrow	39 (6.5%)	17 (7.7%)	22 (5.8%)	
Cord blood	20 (3.3%)	10 (4.5%)	10 (2.6%)	
Missing	(N=2)	(N=1)	(N=1)	
Female donor, male recipient				0.115
No	433 (72.4%)	151 (68.6%)	282 (74.6%)	
Yes	165 (27.6%)	69 (31.4%)	96 (25.4%)	
Missing	(N=7)	(N=3)	(N=4)	
Donor-recipient CMV match				0.412
-/-	213 (35.8%)	84 (38.4%)	129 (34.3%)	
+/-	78 (13.1%)	31 (14.2%)	47 (12.5%)	
-/+	153 (25.7%)	48 (21.9%)	105 (27.9%)	
+/+	151 (25.4%)	56 (25.6%)	95 (25.3%)	
Missing	(N=10)	(N=4)	(N=6)	
AGVH grade II-IV				0.337
No	312 (52.3%)	109 (49.8%)	203 (53.8%)	
Yes	284 (47.7%)	110 (50.2%)	174 (46.2%)	
Missing	(N=9)	(N=4)	(N=5)	
Site				<.001
Fred Hutchinson Cancer Research Center	265 (43.8%)	97 (43.5%)	168 (44.0%)	
University of Minnesota	52 (8.6%)	19 (8.5%)	33 (8.6%)	
Dana-Farber Cancer Institute	51 (8.4%)	26 (11.7%)	25 (6.5%)	
Stanford University	39 (6.4%)	14 (6.3%)	25 (6.5%)	

Characteristic	Total (N=605)	No 6mo Pt response (N=223)	Had 6mo Pt response (N=382)	P-value*
Vanderbilt University	55 (9.1%)	18 (8.1%)	37 (9.7%)	
H. Lee Moffitt Cancer Center	30 (5.0%)	17 (7.6%)	13 (3.4%)	
Roswell Park Cancer Institute	27 (4.5%)	7 (3.1%)	20 (5.2%)	
Cleveland Clinic	30 (5.0%)	10 (4.5%)	20 (5.2%)	
Ohio State University	2 (0.3%)	1 (0.4%)	1 (0.3%)	
University of British Columbia	23 (3.8%)	7 (3.1%)	16 (4.2%)	
Duke University	7 (1.2%)	1 (0.4%)	6 (1.6%)	
MD Anderson	11 (1.8%)	3 (1.3%)	8 (2.1%)	
NW Children's	3 (0.5%)	2 (0.9%)	1 (0.3%)	
Medical College of Wisconsin	10 (1.7%)	1 (0.4%)	9 (2.4%)	
Age at transplant (years)				
Median (Range)	52.0 (0.2-78.0)	49.4 (7.5-75.0)	54.0 (0.2-78.0)	0.020
Median (IQR)	52.0 (39.9-61.0)	49.4 (38.7-58.7)	54.0 (41.4-61.2)	0.020
Mean (STD)	49.8 (14.0)	48.3 (14.0)	50.6 (13.9)	0.048
N	605	223	382	
Age at cGVHD (years)				
Median (Range)	53.0 (2.0-79.0)	50.2 (8.0-76.3)	55.0 (2.0-79.0)	0.023
Median (IQR)	53.0 (41.0-61.9)	50.2 (40.0-60.0)	55.0 (42.0-62.0)	0.023
Mean (STD)	50.6 (14.0)	49.1 (14.0)	51.4 (13.9)	0.048
N	605	223	382	
Donor age (years)				
Median (Range)	37.0 (0.0-76.0)	34.0 (0.1-70.4)	38.0 (0.0-76.0)	0.108
Median (IQR)	37.0 (26.1-50.6)	34.0 (25.0-48.0)	38.0 (26.6-51.9)	0.108
Mean (STD)	38.6 (14.1)	37.2 (13.8)	39.4 (14.3)	0.094
N	544	196	348	
Months from HCT to cGVHD				
Median (Range)	7.8 (1.0-140.8)	7.6 (1.0-140.8)	8.1 (1.9-74.9)	0.706
Median (IQR)	7.8 (5.4-12.1)	7.6 (5.5-11.9)	8.1 (5.2-12.1)	0.706
Mean (STD)	10.5 (9.9)	10.4 (11.4)	10.6 (8.9)	0.856

Characteristic	Total (N=605)	No 6mo Pt response (N=223)	Had 6mo Pt response (N=382)	P-value*
N	605	223	382	
Months from cGVHD to enroll				
Median (Range)	0.6 (-0.1-329.1)	0.6 (0.0-329.1)	0.5 (-0.1-142.8)	0.370
Median (IQR)	0.6 (0.0-11.2)	0.6 (0.0-14.8)	0.5 (0.0-8.6)	0.370
Mean (STD)	10.6 (25.4)	12.5 (33.0)	9.4 (19.7)	0.211
N	605	223	382	
KPS at onset				
Median (Range)	80.0 (30.0-100.0)	80.0 (30.0-100.0)	80.0 (40.0-100.0)	0.139
Median (IQR)	80.0 (80.0-90.0)	80.0 (80.0-90.0)	80.0 (80.0-90.0)	0.139
Mean (STD)	82.8 (11.4)	81.7 (11.8)	83.4 (11.0)	0.101
N	506	185	321	
Platelet at onset				
Median (Range)	170.0 (13.0-912.0)	169.0 (16.0-545.0)	171.0 (13.0-912.0)	0.351
Median (IQR)	170.0 (116.0-228.0)	169.0 (109.0-220.5)	171.0 (119.0-233.0)	0.351
Mean (STD)	181.8 (95.5)	175.1 (90.3)	185.7 (98.3)	0.196
N	583	216	367	
Bilirubin at onset				
Median (Range)	0.5 (0.1-17.9)	0.6 (0.1-10.5)	0.5 (0.1-17.9)	0.156
Median (IQR)	0.5 (0.4-0.8)	0.6 (0.4-0.9)	0.5 (0.4-0.8)	0.156
Mean (STD)	0.9 (1.5)	0.9 (1.1)	0.9 (1.7)	0.670
N	578	216	362	

Table S4 – NIH and clinician-reported 6 month response categories grouped according to 6 month patient-reported response of improved vs. not improved

	Not Improved (N=112)	Improved (N=270)
NIH response		
CR	0	10 (3.7%)
PR	33 (29.5%)	130 (48.1%)
Stable	4 (3.6%)	13 (4.8%)
Progressive	75 (67.0%)	117 (43.3%)
Md GVHD status		
CR	4 (3.6%)	31 (11.7%)
PR	28 (25.0%)	161 (60.5%)
Stable	22 (19.6%)	32 (12.0%)
Progressive	58 (51.8%)	42 (15.8%)

Table S5 – Skin sclerosis and fascial involvement per patient-reported 6 month treatment response

	Patient perception of cGVHD at 6 months		
	All	**Not Improved**	**Improved**
Sclerosis at enrollment			
Yes	197 (52.2%)	59 (52.7%)	138 (52.1%)
No	180 (47.8%)	53 (47.3%)	127 (47.9%)
[missing]	[n=5]	[n=0]	[n=5]
Sclerosis at 6 months			
Yes	147 (38.8%)	54 (49.1%)	93 (34.6%)
No	232 (61.2%)	56 (50.9%)	176 (65.4%)
[missing]	[n=3]	[n=2]	[n=1]

*Sclerosis was defined per the original provider surveys completed in the parent cohort studies, and included for the both cohort studies indication of sclerotic features, superficial or deep sclerosis, or indication of any tightness from fascial involvement using NIH criteria-based organ severity scales for skin and joint; the second cohort study included these features as well as skin thickening per the Hopkins sclerosis scale.

Figure S1 – Cumulative incidence of new systemic immune suppressive therapy stratified by 6 month patient-reported response