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POSTER ABSTRACTS

722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

Treatment- Sensitive, Dependent, and Refractory Chronic Gvhd: Incidence and Clinical Outcomes

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Introduction

Chronic graft-versus-host disease (cGVHD) remains a limitation to the long-term success of allogeneic hematopoietic cell transplantation (HCT). The clinical characteristics and outcomes associated with treatment-sensitive, -dependent, and -refractory cGVHD are unknown. We investigated risk factors associated with distinct cGVHD treatment response groups and analyzed the impact of treatment response on clinical outcomes of cGVHD following HCT.

Methods

The study population included 185 consecutive adult and pediatric patients who developed cGVHD after first allogeneic HCT for malignant and non-malignant disorders at the University of Minnesota between 2008 and 2016. All graft and donor sources, GVHD prophylaxis strategies, and conditioning regimens were included. Only cGVHD cases that started treatment within 30 days of diagnosis are included. We defined cGVHD diagnosis and overall severity using the 2014 NIH Consensus Criteria. We predefined treatment response categories as either treatment-sensitive (TS), -dependent (TD), or -refractory (TR) at 6, 12, and 24 months after cGVHD onset. TS requires clinical improvement after 12 months of initial therapy with discontinuation of therapy by 24 months. TR criteria include disease progression during therapy, addition of new systemic therapies, or death before 6 months of cGVHD treatment. TD patients meet TS criteria, however still require systemic therapy 24 months after initiation of cGVHD therapy.

Outcomes by response group were analyzed in a landmark analysis at the time at which treatment response was determined, excluding any with the event of interest (relapse, death) before the landmark time. To compare treatment response categories with a no-cGVHD control group, the landmark time was set to the median day of cGVHD onset (day 220) plus treatment response category ascertainment time (e.g. 12 months). Disease-free survival (DFS) was defined as survival without relapse or death. Failure-free-survival (FFS) after cGVHD was defined as survival without relapse, death, or new systemic treatment initiated more than 30 days after cGVHD onset.

Results

Patient and transplant characteristics are shown in Table 1. Among 1142 allografts, 222 (19%) developed cGVHD and of those 185 (83%) received systemic cGVHD therapy within 30 days of onset and were included in this analysis. Median time to onset of cGVHD was 216 days (range 71-945) with 7.4 years median time follow up time after cGVHD. The 3-year cumulative incidence of mild, moderate, and severe cGVHD was 3.4%, 11.5%, and 4.4%, respectively. The distribution of treatment response categories as TS, TD, or TR cGVHD are shown at 6, 12, and 24 months in the Sankey plot (Figure 1). Patients were most often TD at 6 months after diagnosis and transitioned to TS or TR by 24 months. Patients with moderate and severe cGVHD were equally likely to be either TD or TR at 6 months. By 12 months, most severe cGVHD cases were TR, while the TD group consisted mostly of moderate cGVHD cases. Patients with prior aGVHD, especially maximum grade III-IV aGVHD, were more likely to have TR cGVHD at 12 months. Patients over 18 were more likely to have TD or TR cGVHD. We noted no other significant

risk factors associated with treatment response groups. The most common second-line cGVHD therapy used in addition to systemic corticosteroids was largely sirolimus, followed by cyclosporine and tacrolimus.
We analyzed clinical outcomes by treatment response at 12 months from cGVHD diagnosis. 10-year FFS was lowest in TR followed by TD and TS groups (38%, 66%, 79%, respectively; P=0.01). Similarly, both 10-year overall survival and DFS were lowest in TR group followed by TD and TS groups. 10-year NRM was highest in TR and TD groups compared to the TS group (33%, 23%, 5%, respectively; P=0.13). In multivariate analysis, TR cGVHD was associated with worse overall survival at 12 months after cGVHD (HR 2.5 vs. no cGVHD; 95% CI, 1.7-3.7; P < .01)

Conclusions

We identified TR cGVHD as a significant risk factor for lower OS and FFS at 12 months post-diagnosis. TS and TD cGVHD groups showed similar prognoses, both better than the TR group. Our findings suggest that cGVHD treatment response states are important predictors of clinical outcomes. Additionally, we have shown that long term follow-up after cGVHD treatment is necessary to determine treatment sensitivity and therefore predict long term outcomes.

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Table 1. Patient and transplant characteristics for patients who had initial treatment for cGVHD

	Overall (N=185)
Sex: Female	64 (35%)
Age at transplant	
0-17	19 (10%)
≥ 18+	166 (90%)
Diagnosis Category	
Non-malignant	19 (10%)
Acute leukemia	114 (62%)
MDS	20 (11%)
Multiple myeloma	7 (4%)
NHL/HL	21 (11%)
Myeloproliferative disorder/other	4 (2%)
Donor type	
Haploidentical	4 (2%)
Matched Sibling	101 (55%)
Umbilical Cord Blood	55 (30%)
Unrelated Donor	25 (14%)
Conditioning intensity	
Myeloablative	89 (48%)
Reduced Intensity	96 (52%)
GVHD prophylaxis	
CSA/MTX	47 (25%)
CSA/MMF	112 (61%)
Sirolimus/MMF	8 (4%)
Other	18 (10%)
Disease Risk Index	
High/Very High risk	16 (9%)
Intermediate risk	117 (63%)
Low risk	33 (18%)
Non-malignant	19 (10%)

Figure 1. Chronic GVHD treatment response categories at 6, 12, and 24 months (N=185). Yellow, SS; green, SD; blue, SR; purple, deceased.

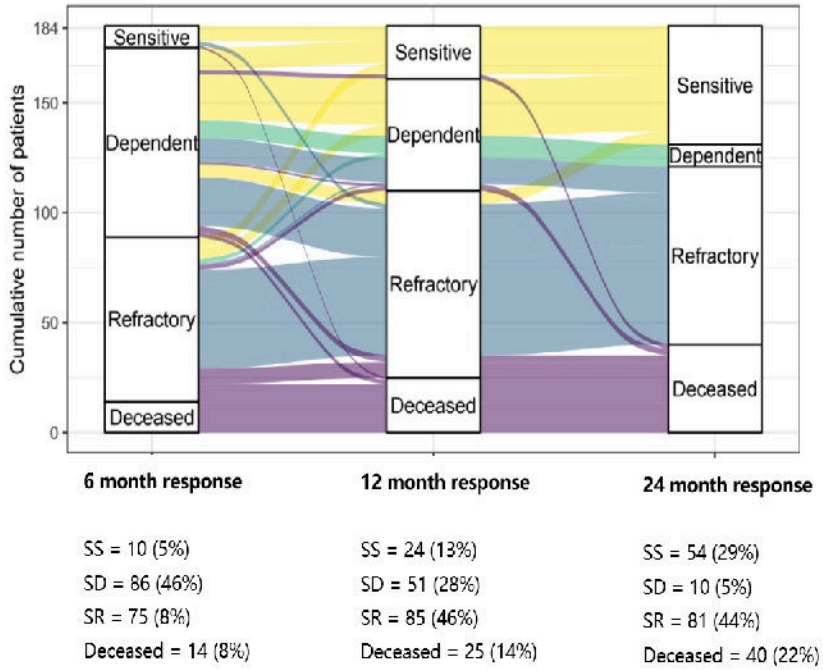

Figure 1