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Disease Progression, Hospital Readmissions, and Clinical Outcomes of Patients With Steroid-Refractory Acute Graft-Versus-Host Disease: A Multicenter Chart Review

Jingbo Yu, MD, PhD,[1]* Becky Hanna, MPH,[2] Dilan Paranagama, PhD,[1] Jackson Tang, MSc,[2] Ahmad Naim, MD,[1] John Galvin, MD, MPH[3]

[1]Incyte Corporation, Wilmington, DE;
[2]Asclepius Analytics, New York, NY;
[3]University of Illinois Cancer Center, Chicago, IL

*Presenting author

Background

- Acute graft-versus-host disease (aGVHD) following allogeneic hematopoietic cell transplantation (HCT) has a significant impact on morbidity and mortality[1]
- The standard first-line therapy for grade II–IV aGVHD is systemic corticosteroids (CS), which provide effective control in 40%–60% of patients[1,2]
- Patients may be unable to taper steroids due to new organ involvement or aGVHD flares[1]

Objective

- To describe the clinical course, outcomes, and hospital readmissions for patients with aGVHD who were refractory to or dependent on systemic CS

Methods

Study Design and Patients

- A multicenter retrospective chart review was conducted at 11 large US academic and community transplant centers
- Individual electronic medical records were reviewed for patients ≥12 years old who had undergone their first allogeneic HCT between Jan 1, 2014 and Jun 30, 2016, and subsequently developed grade II–IV aGVHD (defined by the International Bone Marrow Transplant Registry Severity Index)
  - Patients who participated in a trial for GVHD prophylaxis or used Janus kinase inhibitors were excluded
- This analysis evaluated patients who were refractory to or dependent on systemic CS, defined as either of the following:
  - CS refractory: use of ≥1 additional systemic anti-GVHD therapy
  - CS dependent: not able to taper high-dose CS (≥1 mg/kg) by ≥25%, or able to taper CS dose by ≥25% but not <10 mg/day

Data Collection and Variables

- Deidentified patient data were collected through an electronic form from date of allogeneic HCT to end of most recent follow-up or death
- Data collected included patient demographics, transplant-related and aGVHD characteristics, aGVHD reoccurrence, and all-cause mortality

Statistical Analyses

- Frequencies and percentages were reported for categorical variables; mean, SD, median, and interquartile range (IQR) values were calculated for continuous variables

Results

Patient Characteristics

- The analysis included 168 patients **(Table 1)**

Table 1. Patient Demographics and Baseline Clinical Characteristics

	Steroid-Refractory aGVHD (N=168)
Age, y, mean (SD)	54.8 (12.5)
Male, n (%)	107 (63.7)
White, n (%)	146 (86.9)
Insurance status at transplant,* n (%)	
Private or group health insurance	115 (68.5)
Medicare	48 (28.6)
Medicaid	11 (6.5)
Other†	11 (6.5)
Underlying malignancy, n (%)	
Acute myeloid leukemia	59 (35.1)
Myelodysplastic syndrome	32 (19.0)
Acute lymphoid leukemia	27 (16.1)
Chronic myeloid leukemia	12 (7.1)
Non-Hodgkin's lymphoma	11 (6.5)
Multiple myeloma	11 (6.5)
Other	16 (9.5)
Graft source, n (%)	
Peripheral blood	124 (73.8)
Umbilical cord blood	22 (13.1)
Bone marrow	18 (10.7)
Unknown	4 (2.4)
Duration of follow-up since transplant,‡ d, mean (SD)	502.3 (468.8)

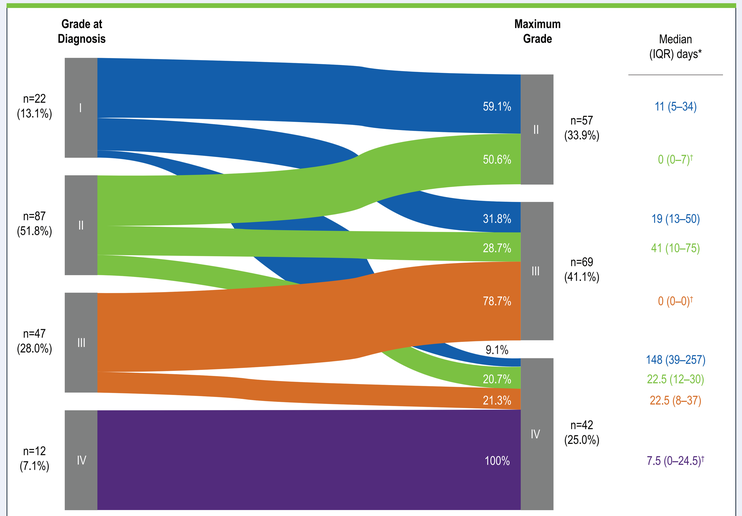
aGVHD, acute graft-versus-host disease.
*18 patients (10.7%) had multiple types of insurance coverage.
†Includes government-sponsored Veterans Affairs/military (n=3, 1.8%), employer-sponsored disability insurance (n=3, 1.8%), uninsured (n=1, 0.6%), and other (n=4, 2.4%).
‡Patients were followed for at least 2 years from transplant until death or end of observation, whichever occurred first.

- Median (IQR) time from transplant to aGVHD diagnosis was 30 (21–49) days and from aGVHD diagnosis to death/last visit was 194 (58–720) days

Disease Progression

- At aGVHD diagnosis, most patients (65%) had grade I or II disease **(Figure 1)**
  - Almost half (49%) of patients with grade II disease progressed to a higher grade
- At maximum aGVHD grade, most patients (66%) had grade III–IV disease

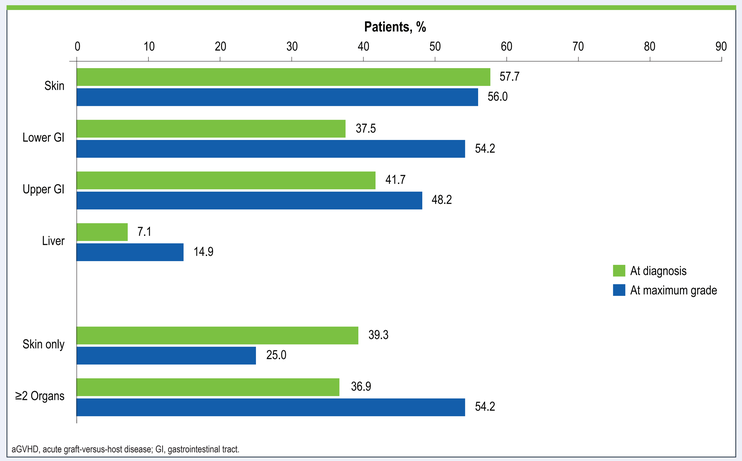
Figure 1. aGVHD Severity at Diagnosis and at Time of Maximum Grade



aGVHD, acute graft-versus-host disease; IQR, interquartile range.
*Time from aGVHD diagnosis to maximum grade.
†Patients may remain at the same grade from diagnosis to maximum grade but progressed with new organ involved.

- At aGVHD diagnosis, 39% of patients had skin involvement only, 38% had lower gastrointestinal (GI) involvement, and 37% had ≥2 organs involved **(Figure 2)**
- At maximum aGVHD grade, 25% of patients had skin involvement only, 54% had lower GI involvement, and 54% had ≥2 organs involved

Figure 2. aGVHD Organs Involved at Diagnosis and at Time of Maximum Grade



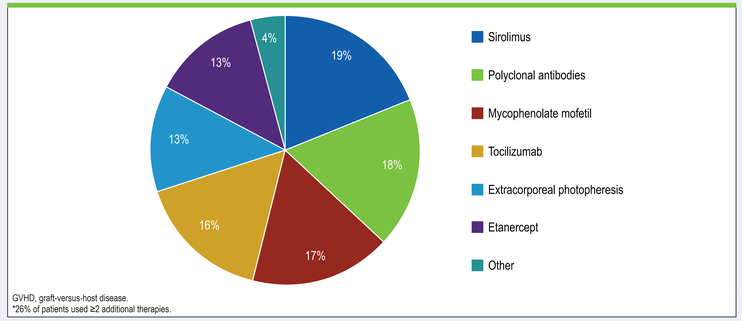
aGVHD, acute graft-versus-host disease; GI, gastrointestinal tract.

- Between diagnosis and maximum aGVHD grade, 54% of patients had new organ involvement or an increase in aGVHD grade
  - Median time from diagnosis to maximum grade was 6.0 days

Treatment Patterns

- Of 146 patients with grade II–IV aGVHD at diagnosis, 82% received systemic CS as first-line therapy
  - 49% initiated systemic CS on the day of diagnosis
  - The average starting dose for patients receiving systemic CS (n=119) was 77 mg (0.9 mg/kg) for prednisone and 166 mg (1.8 mg/kg) for methylprednisolone
- During the follow-up period, 36% of patients had an increase in steroid dose; 88% were unable to taper below 10 mg/day
- aGVHD recurred in 42% of patients and was managed by increasing the CS dose in 79%
- 53% of patients received additional systemic anti-GVHD therapy **(Figure 3)**
  - 42% of patients had an increase in CS dose before receiving additional therapy; 26% used ≥2 additional therapies
  - Median time from CS initiation to additional therapy was 21 days

Figure 3. Additional Systemic Anti-GVHD Therapy (n=89)*

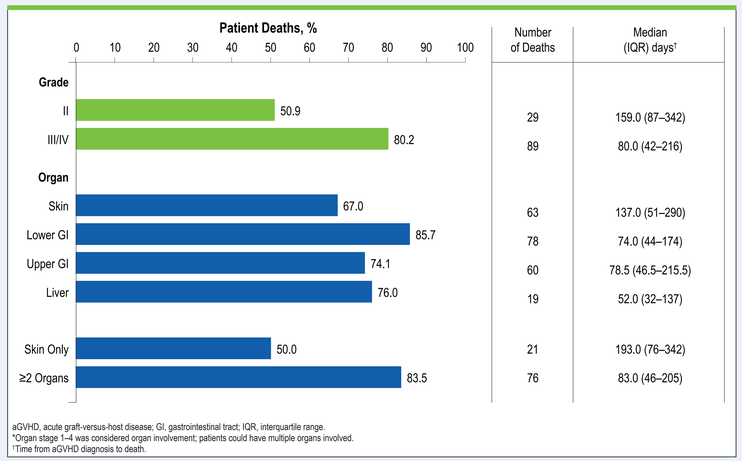


GVHD, graft-versus-host disease.
*26% of patients used ≥2 additional therapies.

Clinical Outcomes and Survival

- 57% of patients required hospital readmission(s); 24% had ≥2 readmissions within 100 days post-HCT, with a mean inpatient length of stay of 50 days
- 51% of patients had an infection within the first 100 days post-HCT
- 21% of patients had a relapse of their underlying malignancy
- 70% of patients died at a median (IQR) of 118 (62.0–234.1) days from aGVHD diagnosis **(Figure 4)**

Figure 4. Patient Deaths by aGVHD Severity and Organs* Involved at Time of Maximum Grade



aGVHD, acute graft-versus-host disease; GI, gastrointestinal tract; IQR, interquartile range.
*Organ stage 1–4 was considered organ involvement; patients could have multiple organs involved.
†Time from aGVHD diagnosis to death.

- 82% of patients with aGVHD progression died at a median (IQR) of 116.0 (49–223) days, and 80% of patients with maximum grade III–IV aGVHD died at a median (IQR) of 80 (42–216) days
- 86% of patients with lower GI aGVHD died at a median (IQR) of 74.0 (44–174) days

Conclusions

- **The majority of patients with aGVHD experienced disease progression and developed severe disease**
  - **Median time from diagnosis to maximum grade was 6.0 days**
- **Survival was poor for the majority of patients with steroid-refractory and steroid-dependent disease, with a mortality rate of 70% within 4 months of aGVHD diagnosis**
- **More than half of patients required hospital readmission with an extended length of stay**
- **The rapidly worsening clinical course and high mortality rate of aGVHD emphasize the need for effective and tolerable therapies that prevent or reverse disease progression**

Disclosures

JY, DP, and AN are employees and stockholders of Incyte Corporation. BH and JT are employees of Asclepius Analytics, who received funding for this project from Incyte Corporation. JG has received consulting fees from Incyte.

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References

1. Garnett C, et al. *Ther Adv Hematol*. 2013;4(6):366-378.

2. MacMillan ML, et al. *Biol Blood Marrow Transplant*. 2015;21(4):761-767.

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