PF1041

Correlations of Clinician-Reported Responses With Other Response Measures in Patients With Chronic Graft-Versus-Host Disease: An Analysis From the AGAVE-201 Trial

Presented at the
European Hematology Association (EHA) 2025 Congress
Milan, Italy • 12–15 June 2025

Joseph Pidala, MD, PhD,[1] Gizelle Popradi, MDCM,[2] María Sola Soto, MD,[3] Britnie Thomas, PhD,[4] Valkal Bhatt, PharmD,[4] Zhenyi Xue, PhD,[4] Vedran Radojcic, MD,[5] Annie Im, MD, FASCO[6]

[1]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [2]McGill University Health Center – Research Institute, Montreal, QC, Canada; [3]Hospital Universitario Vall d'Hebron, Barcelona, Spain; [4]Incyte Corporation, Wilmington, DE, USA; [5]Syndax Pharmaceuticals, Inc, New York, NY, USA; [6]University of Pittsburgh, Pittsburgh, PA, USA

Introduction

- National Institutes of Health overall response rate (NIH-ORR, including complete and partial responses) per the 2014 chronic graft-versus-host disease (cGVHD) consensus criteria may not completely assess the clinical or symptom benefit of cGVHD therapies[1]
- Alternative measures include the clinician-reported graft-versus-host disease (GVHD) global activity assessment of patient symptoms and the modified Lee Symptom Scale (mLSS), a patient-reported assessment of symptom burden[2]
- In the pivotal AGAVE-201 trial (NCT04710576), axatilimab 0.3 mg/kg once every 2 weeks (Q2W) demonstrated promising NIH-ORR in patients with cGVHD and was generally well tolerated[3]

Objective

- In this post hoc analysis, we evaluated positive/negative percent agreement (PPA/NPA) and response correlations among NIH-ORR, clinician-reported symptom improvement, and mLSS improvement at Cycle (C)7 Day (D)1

Methods

- In AGAVE-201, patients were randomized 1:1:1 to receive axatilimab 0.3 mg/kg Q2W, 1 mg/kg Q2W, or 3 mg/kg once every 4 weeks (Q4W)
- Clinician-reported GVHD global activity assessment of patient symptoms (scale, 0–10) and response determination per NIH consensus criteria was performed on D1 of each cycle
  - For clinician-reported GVHD symptoms, a ≥2-point decrease and a ≥2-point increase in symptom severity were considered improvement and worsening, respectively
- Patients reported symptom improvements using the mLSS; a ≥7-point improvement from baseline was considered clinically meaningful
- Kappa (κ) and PPA/NPA were used to assess response agreement
  - κ values range from −1 to +1, with higher values indicating greater agreement; values ≥0.6 indicate at least moderate agreement, while those ranging between 0.4 and 0.59 indicate weak agreement and 0.21 and 0.39 indicate minimal agreement[4]
  - PPA and NPA, which range from 0 to 1, are probability estimates that 2 items will demonstrate the same outcome[5]
- Tetrachoric correlations were used to assess response correlations between NIH-ORR and the clinician-/patient-reported symptom measures for binary data
  - Values range from −1 to +1, in which −1 and +1 indicate strong negative and positive correlations, respectively, and 0 indicates no correlation[6]; in general, values ≥0.7 are considered to be strong
- The Kaplan-Meier method was used to estimate failure-free survival (FFS), defined as the time from the landmark of C7D1 to addition of another systemic immunosuppressive therapy for cGVHD, relapse of underlying malignancy, or death, whichever is earlier

Results

Patient Characteristics

- In total, 241 patients received axatilimab, 80 of whom received 0.3 mg/kg Q2W
- Among the 141 patients across all doses and the 57 patients with 0.3 mg/kg Q2W who had clinician-reported symptom assessments, 58 (41.1%) and 31 (54.4%) had symptom improvements
- Baseline demographics and disease characteristics were generally similar between patients with and without clinician-reported symptom improvement (**Table 1**)

Table 1. Patient Demographics and Baseline Characteristics by Clinician-Reported Symptom Improvement†

	Axatilimab 0.3 mg/kg Q2W		Axatilimab all doses	
	Improvement (n=31)	No improvement (n=26)	Improvement (n=58)	No improvement (n=83)
Age, median (range), y	48.0 (20–75)	58.0 (7–76)	50.5 (7–75)	52.0 (7–81)
Male, n (%)	19 (61.3)	17 (65.4)	37 (63.8)	52 (62.7)
Time from transplant to cGVHD diagnosis, median (range), mo	7.6 (0.4–33.6)	9.7 (2.3–37.1)	7.8 (0.4–55.0)	8.1 (1.0–73.3)
Type of transplant, n (%)				
Myeloablative	24 (77.4)	17 (65.4)	41 (70.7)	54 (65.1)
Nonmyeloablative	6 (19.4)	9 (34.6)	15 (25.9)	29 (34.9)
Other	1 (3.2)	0	2 (3.4)	0
Time from initial cGVHD diagnosis to randomization, median (range), y	4.3 (1.4–17.6)	5.9 (0.8–14.4)	4.3 (0.4–17.6)	4.6 (0.8–14.4)
Severe disease, n (%)	23 (74.2)	23 (88.5)	45 (77.6)	70 (84.3)
Prior cGVHD therapy, n (%)	28 (90.3)	21 (80.8)	51 (87.9)	70 (84.3)
Ruxolitinib	22 (71.0)	20 (76.9)	42 (72.4)	66 (79.5)
Ibrutinib	12 (38.7)	9 (34.6)	20 (34.5)	26 (31.3)
Belumosudil	7 (22.6)	4 (15.4)	13 (22.4)	18 (21.7)

cGVHD; chronic graft-versus-host disease; Q2W, once every 2 weeks.
† Improvement by ≥2 points at Cycle 7 Day 1.

NIH-ORR/Clinician-Reported Correlation

- A total of 129 and 47 patients across all axatilimab doses and with 0.3 mg/kg Q2W had available NIH-ORR and clinician-reported symptom assessments
- Among the 80 patients across all doses and the 33 patients with 0.3 mg/kg Q2W who achieved an NIH-ORR, 45 (56.3%) and 25 (75.8%), respectively, had clinician-reported symptom improvements
  - Among the 49 and 14 patients with no NIH-ORR, 9 (18.4%) and 4 (28.6%) had clinician-reported symptom improvement
- κ indicated fair agreement between NIH-ORR and clinician-reported symptom improvement; moderate positive associations were observed with tetrachoric correlations (**Table 2**)

NIH-ORR/mLSS (Patient-Reported) Correlation

- A total of 131 and 48 patients across axatilimab doses and with 0.3 mg/kg Q2W had available NIH-ORR and mLSS data
- Among the 81 and 33 patients who achieved an overall response across all doses and with 0.3 mg/kg Q2W, respectively, 57 (70.4%) and 25 (75.8%) reported mLSS improvement
  - Among the 50 and 15 patients with no overall response, 25 (50.0%) and 6 (40.0%) reported mLSS improvement
- κ indicated fair agreement between overall response and mLSS; minimal to weak positive associations were observed with tetrachoric correlations (**Table 2**)

Clinician-Reported/mLSS (Patient-Reported) Correlation

- A total of 135 and 52 patients across axatilimab doses and with 0.3 mg/kg Q2W had available clinician-reported symptom and mLSS data
- Among the 54 and 28 patients who had clinician-reported symptom improvement across all doses and with 0.3 mg/kg Q2W, respectively, 23 (42.6%) and 13 (46.4%) had mLSS improvement
  - Among the 81 and 24 patients with no clinician-reported symptom improvement, 30 (37.0%) and 6 (25.0%) had mLSS improvement
- κ indicated minimal to fair agreement between clinician-/patient-reported symptom improvement; weak/mild associations were observed with tetrachoric correlations (**Table 2**)

Table 2. Correlations of NIH-ORR and Clinician-Reported and Patient-Reported Symptom Improvements

	Axatilimab 0.3 mg/kg Q2W	Axatilimab all doses*
Clinician-reported symptom assessment vs NIH-ORR		
Tetrachoric correlation	0.66	0.58
κ	0.44	0.34
PPA†	0.76	0.56
NPA†	0.71	0.82
mLSS vs NIH-ORR		
Tetrachoric correlation	0.53	0.32
κ	0.35	0.20
PPA‡	0.76	0.70
NPA‡	0.60	0.50
Clinician-reported symptom assessment vs mLSS		
Tetrachoric correlation	0.35	0.09
κ	0.21	0.06
PPA§	0.68	0.43
NPA§	0.55	0.62

κ, kappa; mLSS, modified Lee Symptom Scale; NIH-ORR, National Institutes of Health overall response rate; NPA, negative percent agreement; PPA, positive percent agreement; Q2W, once every 2 weeks; Q4W, once every 4 weeks.
* Includes patients who received axatilimab 0.3 mg/kg Q2W, 1 mg/kg Q2W, or 3 mg/kg Q4W.
† PPA is defined as the proportion of patients who are responders by clinician-reported symptom assessment among those who are responders by NIH-ORR; NPA is defined as the proportion of patients who are nonresponders by clinician-reported symptom assessment among those who are nonresponders by NIH-ORR.
‡ PPA is defined as the proportion of patients who are responders by mLSS among those who are responders by NIH-ORR; NPA is defined as the proportion of patients who are nonresponders by mLSS among those who are nonresponders by NIH-ORR.
§ PPA is defined as the proportion of patients who are responders by clinician-reported symptom assessment among those who are responders by mLSS; NPA is defined as the proportion of patients who are nonresponders by clinician-reported symptom assessment among those who are nonresponders by mLSS.

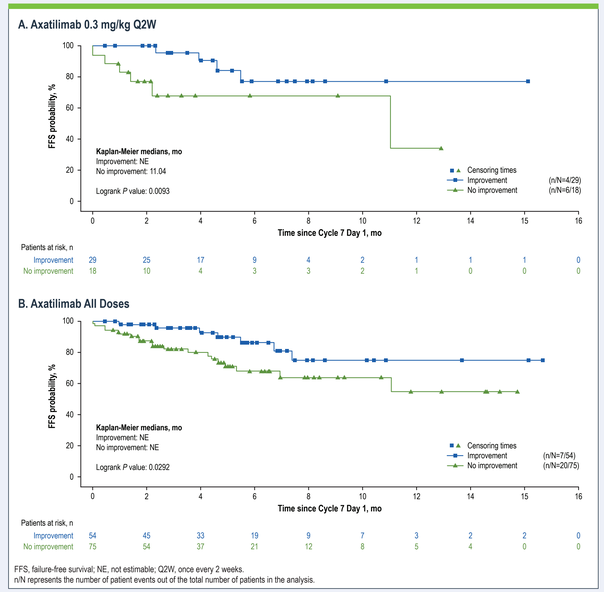
FFS

- Landmark analyses of FFS from C7D1 indicate significantly better survival for patients with clinician-reported improvement than for those with no improvement with 0.3 mg/kg Q2W (P=0.0093; **Figure 1A**) and across all doses (P=0.0292; **Figure 1B**), although the findings were not statistically significant with the 2 higher doses when assessed separately

Safety

- Treatment-emergent adverse events (TEAEs) of any grade occurred in 96.2% of patients with 0.3 mg/kg Q2W and 97.9% across all doses; grade ≥3 TEAEs occurred in 49.4% and 60.3% of patients, respectively
- The most frequent TEAEs in AGAVE-201 were elevations in aspartate aminotransferase (13.9% with 0.3 mg/kg Q2W and 35.6% across all doses), creatine phosphatase (11.4% and 35.1%), lipase (11.4% and 28.9%), lactate dehydrogenase (13.9% and 27.2%), and alanine aminotransferase (12.7% and 24.7%)
- With 0.3 mg/kg Q2W and across all doses, 6.3% and 15.5% of patients, respectively, had TEAEs that led to discontinuation of treatment

Figure 1. Kaplan-Meier Estimates of FFS by Clinician-Reported Symptom Improvement With (A) Axatilimab 0.3 mg/kg Q2W and (B) Axatilimab All Doses



FFS, failure-free survival; NE, not estimable; Q2W, once every 2 weeks.
n/N represents the number of patient events out of the total number of patients in the analysis.

Conclusions

- **These results suggest there is limited agreement between NIH-ORR as a clinical trial endpoint and symptom-based clinical improvement or worsening perceived by clinicians and patients**
- **In the 0.3 mg/kg Q2W group, median FFS after C7D1 was prolonged among patients with clinician-reported symptom improvements vs those without improvements**
- **These data provide insights into the clinical benefit achieved with axatilimab and suggest that additional exploration of secondary endpoints is warranted for cGVHD therapies**

Disclosures

JP served as a consultant and advisory board member for Amgen, CTI Biopharma, Incyte Corporation, Regeneron, Sanofi, and Syndax Pharmaceuticals and received clinical trial support from AbbVie, Amgen, Bristol Myers Squibb, CTI Biopharma, Janssen, Johnson and Johnson, Novartis, Pharmacyclics, and Takeda. GP served as a consultant for or received honoraria from AbbVie, Amgen, Bristol Myers Squibb, Daiichi Sankyo, Gilead, Jazz, Kyowa Kirin, Mallinckrodt, Medexus, Merck, Novartis, Paladin, Pfizer, Seagen, Sanofi, Servier, Sobi, and Takeda. MSS has received honoraria from Sanofi. BT, VB, and ZX are employees and shareholders of Incyte Corporation. VR was an employee and shareholder of Syndax Pharmaceuticals at the time the work was completed. AI served as a consultant for Incyte Corporation and Sanofi and received research funding from Incyte Corporation.

Acknowledgments

This study was funded by Incyte Corporation (Wilmington, DE) and Syndax Pharmaceuticals (New York, NY). Medical writing support was provided by Rob M. Camp, PhD, from Citrus Health Group (Chicago, IL), and was funded by Incyte Corporation and Syndax Pharmaceuticals.

References

1. Im A, et al. *Haematologica*. 2024;109(1):143-150. **2.** Teh C, et al. *Biol Blood Marrow Transplant*. 2020;26(3):562-567. **3.** Wolff D, et al. *N Engl J Med*. 2024;391(11):1002-1014. **4.** McHugh ML. *Biochemia Medica (Zagreb)*. 2012;22(3):276-282. **5.** Bock D, et al. *BMC Urol*. 2019;19(1):35. **6.** Drasgow F. Polychoric and polyserial correlations. In: Kotz S, et al, eds. *Encyclopedia of Statistical Sciences*. John Wiley & Sons; 1986.

Originally presented at EBMT 2025.