Safety and Efficacy of Axatilimab in Patients With Chronic Graft-Versus-Host Disease (AGAVE-201)

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Presenter Disclosures

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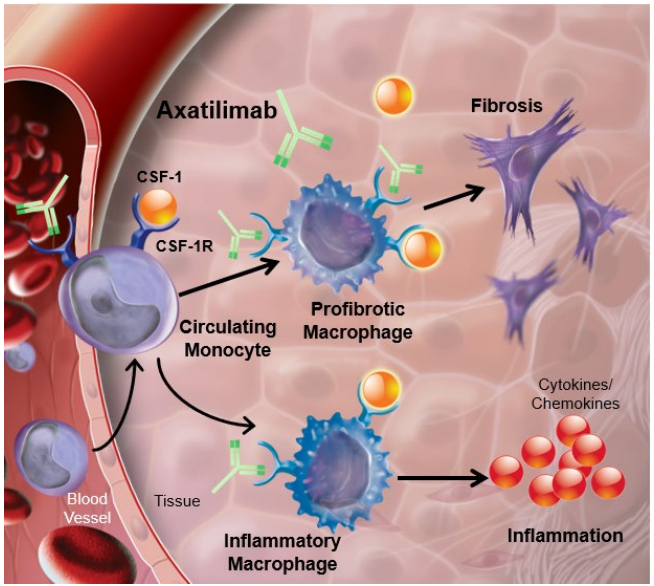
Axatilimab for cGVHD

- CSF-1R–dependent monocytes and macrophages contribute to the multiorgan inflammation and fibrosis that drives cGVHD[1]
- Axatilimab is an investigational, high-affinity anti–CSF-1R monoclonal antibody[2]
- In the AGAVE-201 study, axatilimab 0.3 mg/kg Q2W resulted in the highest response rate and most manageable safety profile compared with 2 higher doses in patients with refractory/recurrent cGVHD[3]

Axatilimab Mechanism of Action[1,2,4]



cGVHD, chronic graft-versus-host disease; CSF-1, colony-stimulating factor 1; CSF-1R, colony-stimulating factor 1 receptor; Q2W, every 2 weeks.

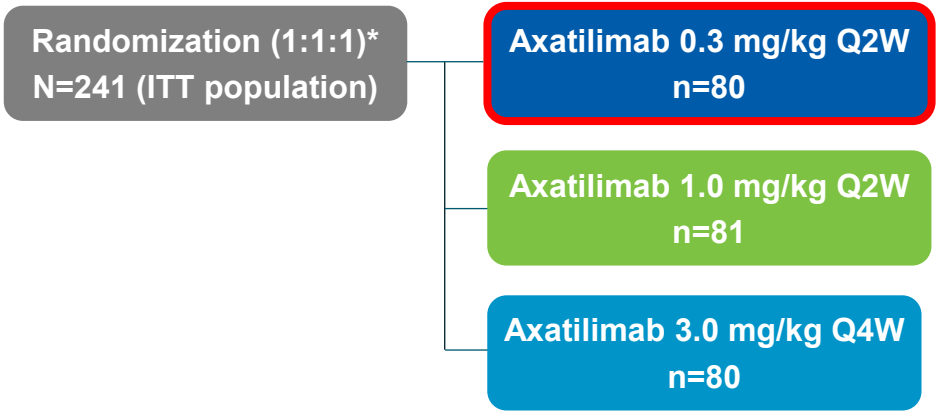
1. Alexander KA, et al. *J Clin Invest*. 2014;124(10):4266-4280. 2. Kitko CL, et al. *J Clin Oncol*. 2023;41(10):1864-1875. 3. Wolff D, et al. *Blood*. 2023;142(suppl 1):1. 4. MacDonald KPA, et al. *Blood*. 2017;129(1):13-21.

Overview of AGAVE-201 Study Design

- Phase 2, open-label, multicenter, randomized study to evaluate safety and efficacy of axatilimab in patients with recurrent/refractory cGVHD (NCT04710576)

Key eligibility criteria

- Age ≥2 years with ≥2 prior lines of systemic therapy
- Active cGVHD defined per 2014 NIH consensus criteria[1]
- Concomitant use of the following therapies was permitted but not required
  - Corticosteroids
  - Calcineurin inhibitors
  - mTOR inhibitors



Primary endpoint: ORR in the first 6 cycles[†,2]
Secondary endpoints: mLSS, organ-specific response rates, safety
Exploratory endpoint: FFS

FFS, failure-free survival; ITT, intention to treat; ORR, overall response rate; mLSS, modified Lee Symptom Scale; mTOR, mammalian target of rapamycin; NIH, National Institutes of Health; Q4W, every 4 weeks.
* Randomization was stratified by severity of cGVHD and prior use of ibrutinib, ruxolitinib, or belumosudil. † Endpoint was met if lower bound of 95% CI >30%.
1. Jagasia MH, et al. *Biol Blood Marrow Transplant*. 2015;21(3):389-401. 2. Lee SJ, et al. *Biol Blood Marrow Transplant*. 2015;21(6):984-999.

Patient Demographics and Baseline Clinical Characteristics

- Demographics and baseline characteristics were similar across cohorts

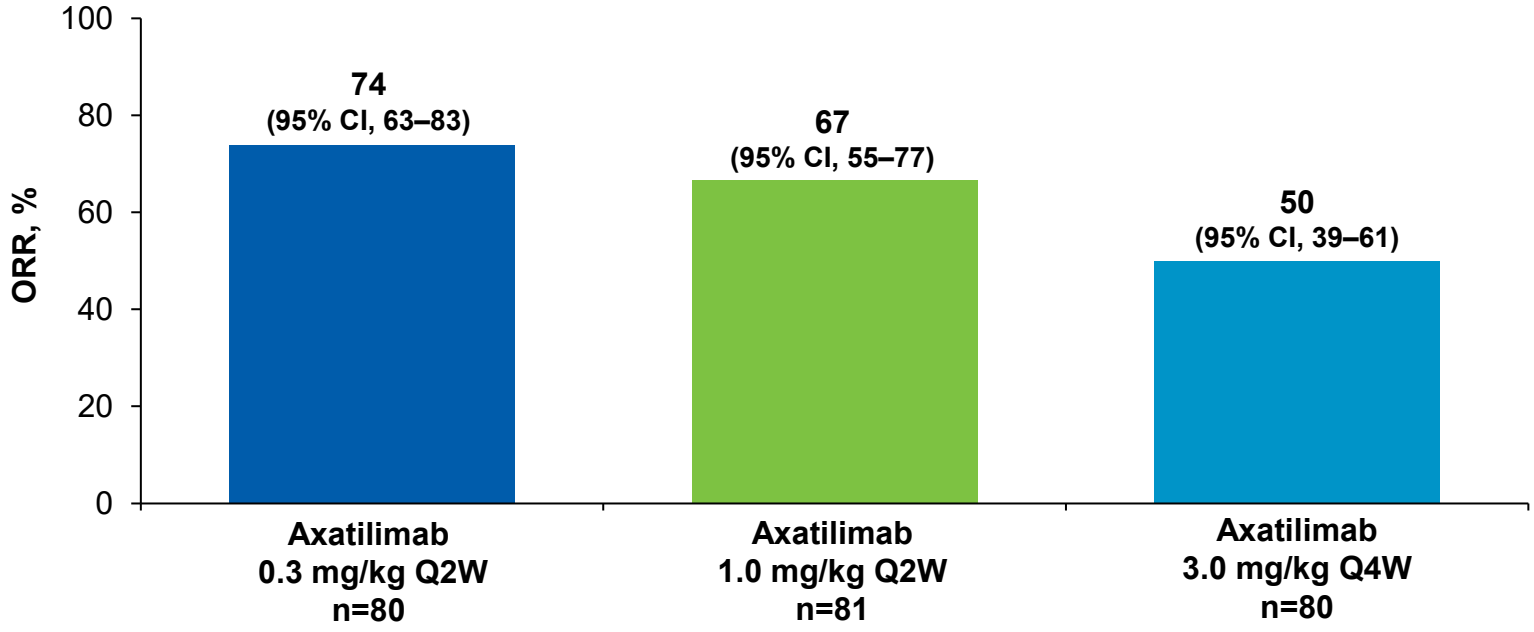
	Axatilimab 0.3 mg/kg Q2W (n=80)	Overall (N=241)
Age, median (range), y	50 (7–76)	53 (7–81)
Male, n (%)	47 (59)	151 (63)
White, n (%)	68 (85)	200 (83)
Time from cGVHD diagnosis to randomization, median (range), y	3.9 (0.4–18)	4.0 (0.4–18)
Patients with severe disease, n (%)	63 (79)	192 (80)
Number of organs involved, median (max)	4 (8)	4 (8)
≥4 organs involved, n (%)	45 (56)	130 (54)

	Axatilimab 0.3 mg/kg Q2W (n=80)	Overall (N=241)
Number of prior systemic cGVHD therapies, median (range)	4 (2–12)	4 (2–15)
Refractory to last prior cGVHD treatment,* n (%)	38 (48)	132 (55)
Prior ibrutinib, ruxolitinib, and/or belumosudil, n (%)	67 (84)	204 (85)
Ruxolitinib	57 (71)	179 (74)
Ibrutinib	27 (34)	75 (31)
Belumosudil	16 (20)	56 (23)

Intention-to-treat population. * Defined as patients with a best response to last prior treatment of no change or progressive disease reported at baseline.

ORR in the First 6 Cycles* (Primary Endpoint)

- Approximately 3/4 of patients assigned to axatilimab 0.3 mg/kg Q2W had a response
- Median time to first response in the 0.3 mg/kg Q2W cohort was 1.5 (range, 0.9–5.1) months

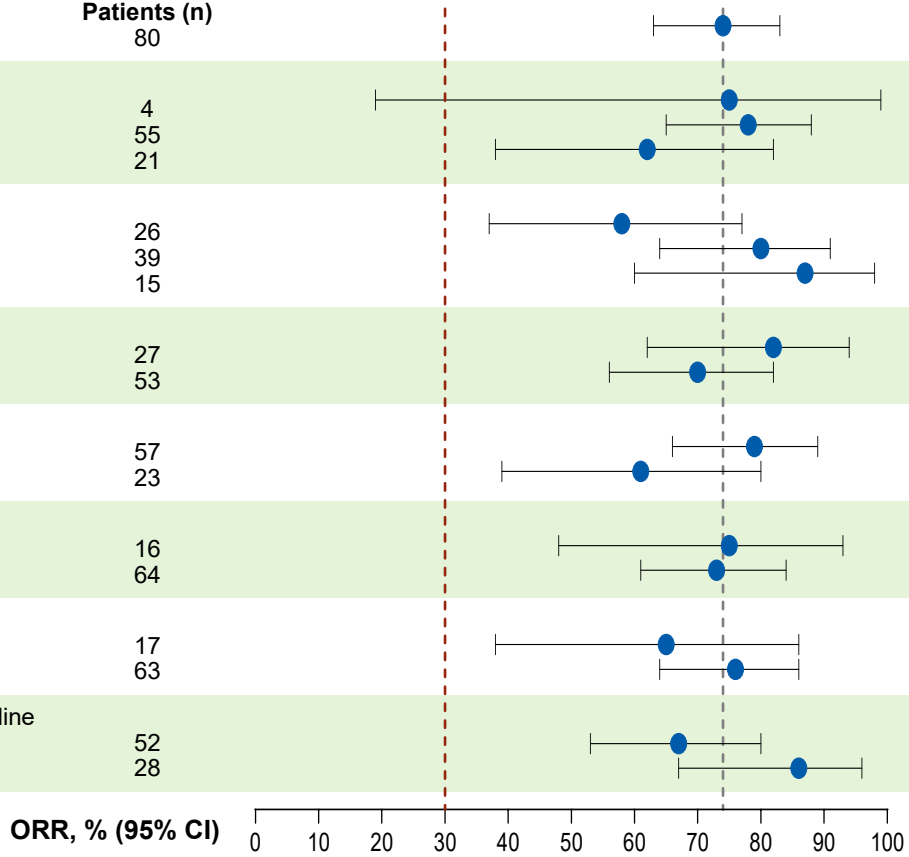


* Defined by NIH 2014 consensus criteria.[1]

1. Lee SJ, et al. *Biol Blood Marrow Transplant*. 2015;21(6):984-999.

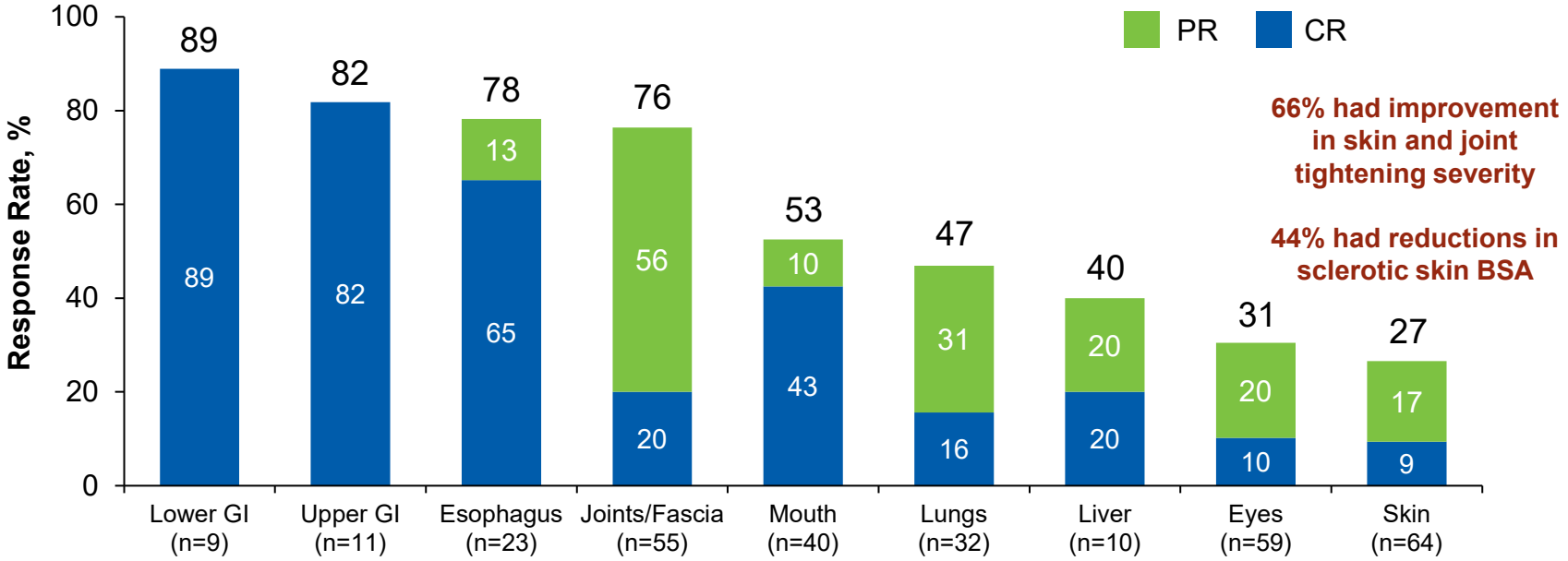
Subgroup Responses (0.3 mg/kg Q2W)

Subgroup	Patients (n)	ORR (95% CI)
Overall	80	74 (63–83)
Age group		
<17 years	4	75 (19–99)
≥17 years and <65 years	55	78 (65–88)
≥65 years	21	62 (38–82)
Number of lines of prior therapy		
<4	26	58 (37–77)
4–6	39	80 (64–91)
>6	15	87 (60–98)
Prior ibrutinib		
Yes	27	82 (62–94)
No	53	70 (56–82)
Prior ruxolitinib		
Yes	57	79 (66–89)
No	23	61 (39–80)
Prior belumosudil		
Yes	16	75 (48–93)
No	64	73 (61–84)
cGVHD severity at screening		
Mild/moderate	17	65 (38–86)
Severe	63	76 (64–86)
Number of organs involved at baseline		
≤4	52	67 (53–80)
>4	28	86 (67–96)



Organ-Specific Responses (0.3 mg/kg Q2W)

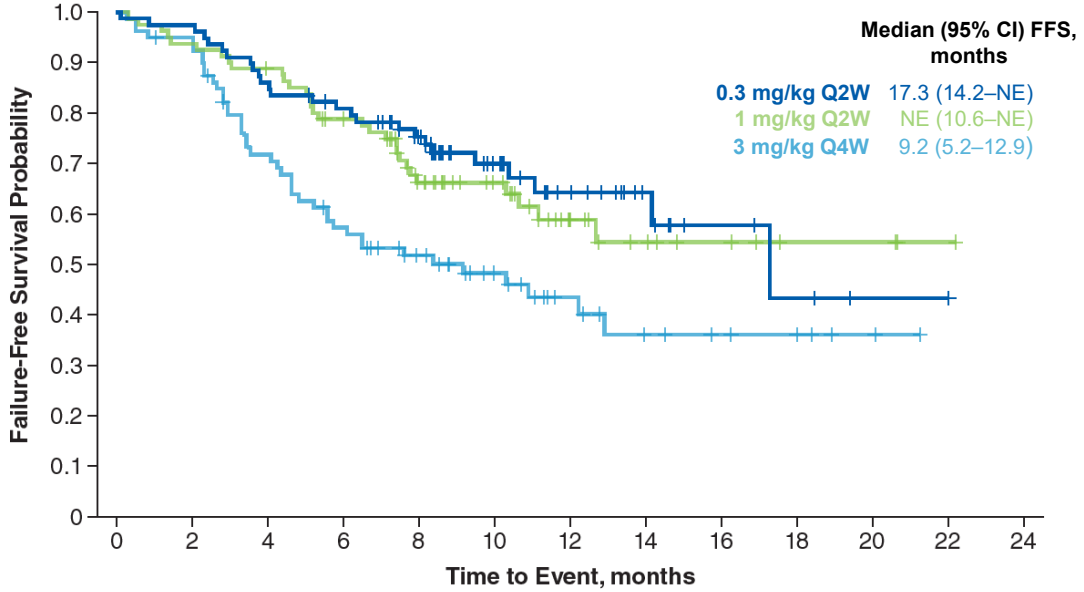
- Responses were observed in fibrosis-dominated organs, including joints and fascia (76%), lung (47%), and skin (27%)



BSA, body surface area; CR, complete response; GI, gastrointestinal; PR, partial response.
Differences in percentage totals are due to rounding.

Failure-Free Survival*

- Median FFS was 17.3 (95% CI, 14.2–NE) months in the 0.3 mg/kg Q2W cohort



Number of patients at risk

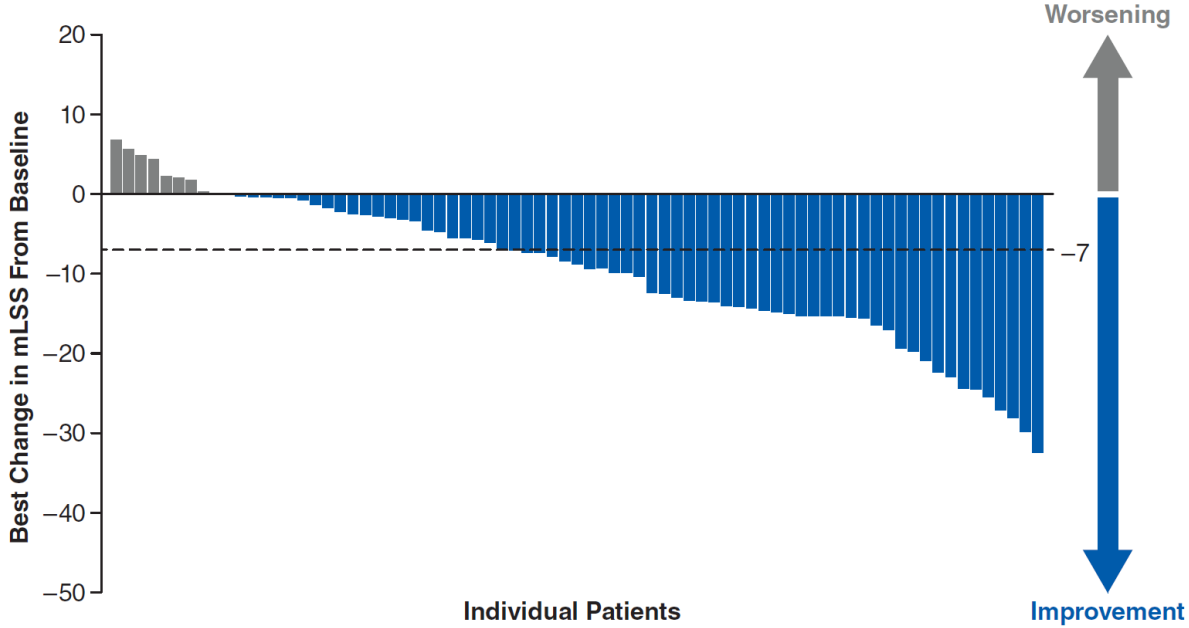
0.3 mg/kg Q2W	80	77	68	62	49	28	18	10	5	3	1	1	0
1 mg/kg Q2W	81	76	71	61	43	31	17	10	7	3	3	1	0
3 mg/kg Q4W	80	75	55	43	32	22	13	8	6	5	2	0	

NE, not estimable.

* Defined as time from randomization to new systemic cGVHD therapy (excluding dose increases of axatilimab), relapse of underlying malignancy, or death.

Patient-Reported Symptom Burden Changes (0.3 mg/kg Q2W)

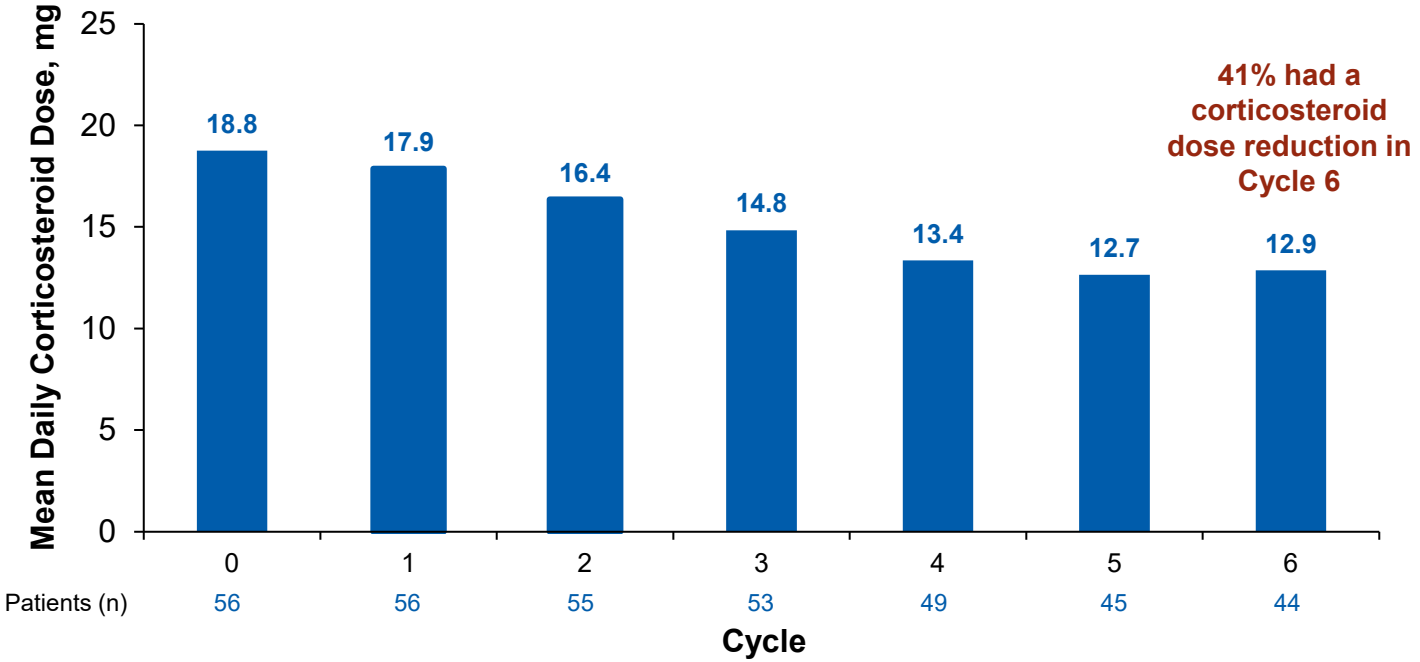
- 55% of patients reported clinically meaningful change of ≥7-point improvement in mLSS
- Median time to ≥7-point mLSS improvement was 1.5 (range, 1.0–7.2) months



mLSS, modified Lee Symptom Scale.

Corticosteroid Dose Reductions (0.3 mg/kg Q2W)

- Among 56 patients who received concomitant corticosteroids, 11% discontinued corticosteroids in the first 6 cycles



Safety Profile (0.3 mg/kg Q2W)

- A manageable safety profile was observed with the 0.3 mg/kg Q2W dose
- Discontinuations, grade ≥3 TEAEs, and TRAEs (all grade) were more frequent in the higher dose groups
- TRAEs with the 0.3 mg/kg Q2W dose were mostly low grade and reversible; grade ≥3 treatment-related infections were infrequent (n=6; 8%)

n (%)	Axatilimab 0.3 mg/kg Q2W* (n=79)
TEAE (all grade)	76 (96)
Most frequent TEAEs†	
Fatigue	18 (23)
Headache	15 (19)
COVID-19	13 (16)
Diarrhea	13 (16)
Nausea	13 (16)
URTI	13 (16)
Grade ≥3 TEAEs	39 (49)

n (%)	Axatilimab 0.3 mg/kg Q2W* (n=79)
Discontinuation due to TEAE	5 (6)
Fatal TEAE‡	1 (1)
TRAE (all grade)	56 (71)
Grade ≥3 TRAE	14 (18)
Most frequent grade ≥3 TRAEs§	
Pneumonia	3 (4)
Colitis	2 (3)
Hypertension	2 (3)

TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; URTI, upper respiratory tract infection.
* 1 patient in the 0.3 mg/kg Q2W cohort did not receive ≥1 dose of axatilimab and was not included in safety analyses. † Occurring in ≥15% of patients. ‡ Dyspnea; event was assessed as not related to treatment by the investigator. § Occurring in ≥2 patients.

Conclusions

- Axatilimab at 0.3 mg/kg Q2W is highly effective and has a manageable safety profile in recurrent/refractory cGVHD
- Rapid and durable responses were documented in all organs and patient subgroups
- Significant reduction of symptom burden was reported by most patients, including those with fibrotic cGVHD manifestations
- Treatment-related AEs were mostly low grade and reversible with no new safety concerns
- Unique mechanism of action of axatilimab may provide a new therapeutic approach in cGVHD

Strengths/Limitations and Future Directions

Strengths/Limitations

- This study included a high proportion of patients with severe disease and multiorgan involvement, which remains a therapeutic challenge to treat
- No comparator arm was included
- Although the study was powered to evaluate responses across doses, subgroup sizes were small

Future Directions

- Preclinical studies are ongoing to further understand the mechanism of action and biological rationale for higher response rates in the lower dose cohorts
- Further analyses of axatilimab responses in fibrosis-dominant organs are planned
- Additional studies are warranted to evaluate axatilimab in combination with other therapies and for earlier treatment of cGVHD

Acknowledgments

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