Axatilimab for Chronic Graft-Versus-Host Disease: Responses in Fibrosis-Dominant Organs in AGAVE-201

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Presenter Disclosures

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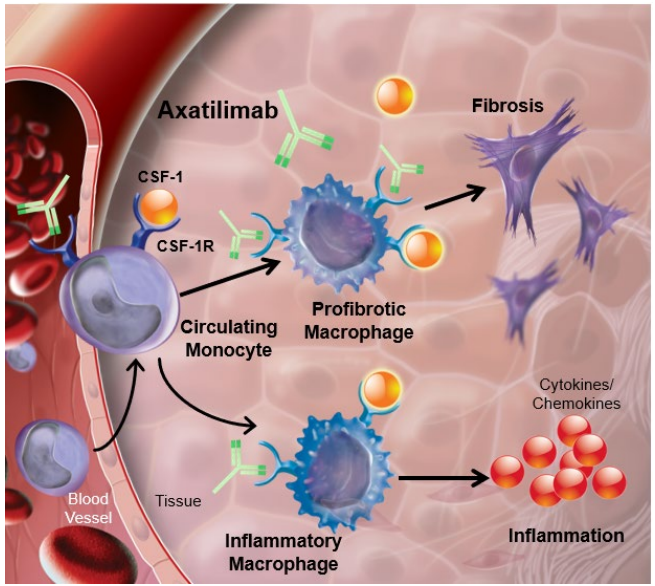
Axatilimab for cGVHD

- 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[3]
- In this subanalysis, we evaluated
  - Fibrosis-dominant organ-specific responses and changes in patient-reported symptom burden
  - Safety, with an emphasis on infections

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.

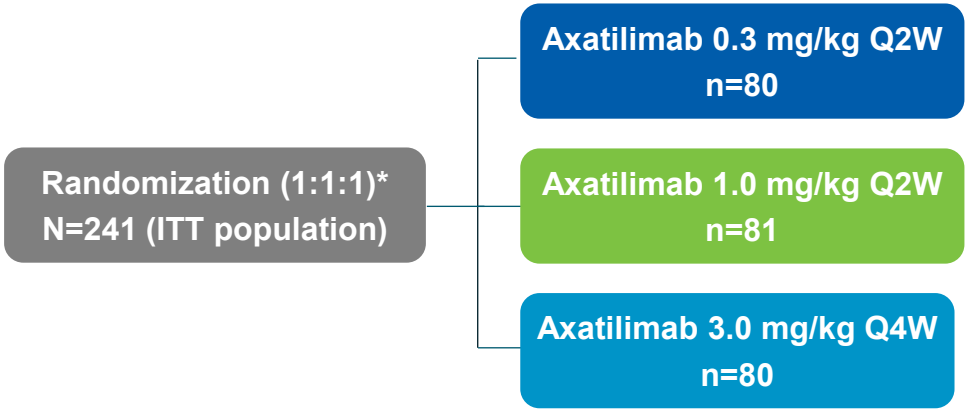
1. Alexander KA, et al. *J Clin Invest*. 2014;124(10):4266-4280. 2. Kitko CL, et al. *J Clin Oncol*. 2023;41(10):1864-1875. 3. Wolff D, et al. *Blood*. 2023;142(suppl 1):1. 4. MacDonald KPA, et al. *Blood*. 2017;129(1):13-21.

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

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 endpoints: Physician and patient-reported symptom changes‡

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. ClinicalTrials.gov: NCT04710576. * 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%. ‡ mLSS items are not validated as single measures.

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
- A high proportion of patients had severe disease with multiorgan involvement

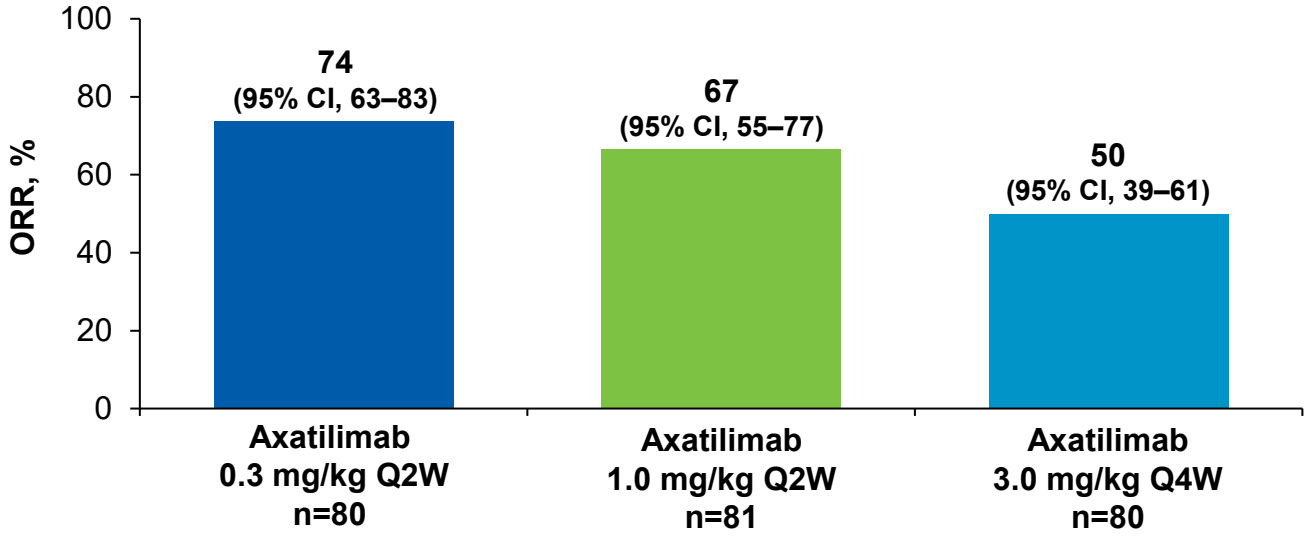
	Axatilimab 0.3 mg/kg Q2W n=80	Axatilimab 1.0 mg/kg Q2W n=81	Axatilimab 3.0 mg/kg Q4W n=80	Overall (N=241)
Age, median (range), y	50 (7–76)	56 (26–81)	53 (7–79)	53 (7–81)
Patients with severe disease, n (%)	63 (79)	64 (79)	65 (81)	192 (80)
Number of organs involved, median (max)	4 (8)	4 (7)	3 (7)	4 (8)
Organs involved at baseline, n (%)				
Skin	64 (80)	63 (78)	66 (83)	193 (80)
Sclerotic skin*	60 (94)	60 (95)	60 (91)	180 (93)
Skin features score of 3†	46 (77)	48 (80)	55 (92)	149 (83)
Joints/fascia	55 (69)	56 (69)	51 (64)	162 (67)
Lung	32 (40)	41 (51)	35 (44)	108 (45)
NIH cGVHD lung score of 3‡	8 (25)	10 (26)	8 (23)	26 (25)
FEV1 ≤39%§	14 (47)	15 (42)	7 (26)	36 (39)
Esophagus	23 (29)	18 (22)	20 (25)	61 (25)

FEV1, forced expiratory volume in first second.
Intention-to-treat population. * Denominator includes the patients with skin involvement. † Denominator includes the patients with sclerotic skin. ‡ Denominator includes the patients with baseline evaluation of NIH lung score. § Denominator includes the patients with baseline evaluation of FEV1.

Responses Observed With All Doses

ORR in the First 6 Cycles (Primary Endpoint)

- Substantial clinical responses were observed in the 0.3 mg/kg cohort



Response maintained for ≥12 months,* % (95% CI)	60 (43–74)	60 (43–74)	53 (30–71)

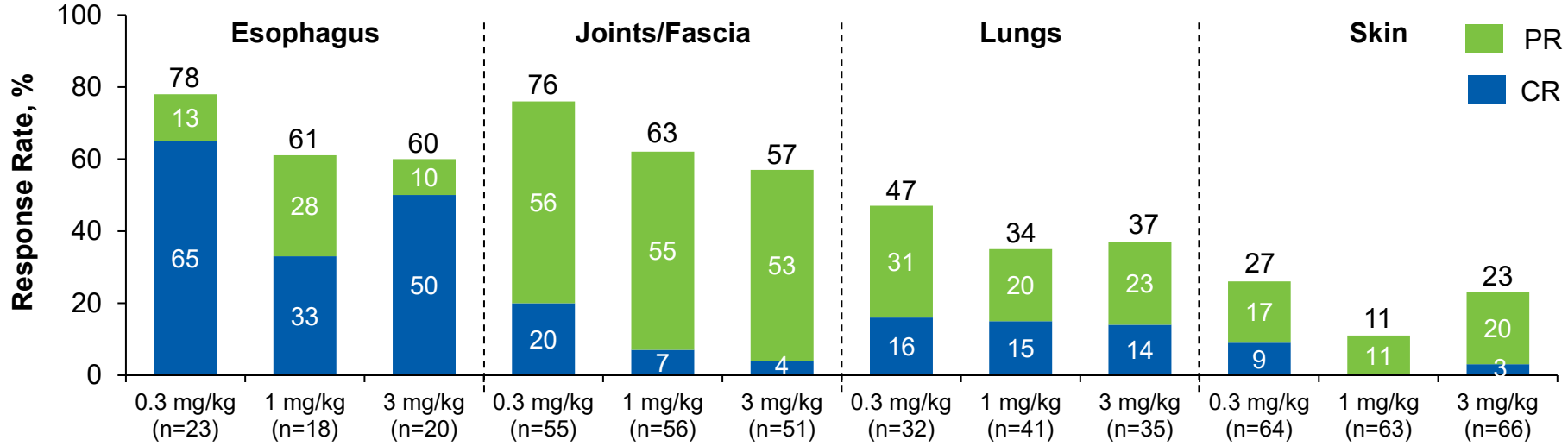
ORR was defined by NIH 2014 consensus criteria. The primary endpoint was met if lower bound of 95% CI >30%.
* Based on Kaplan–Meier estimate of 12-month event-free probability.

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

Responses in Fibrosis-Dominant Organs

*Best Responses at Any Time**

- Responses were seen in all organs, including organs that can have fibrotic manifestations
- Lungs and skin had slightly prolonged time to first response



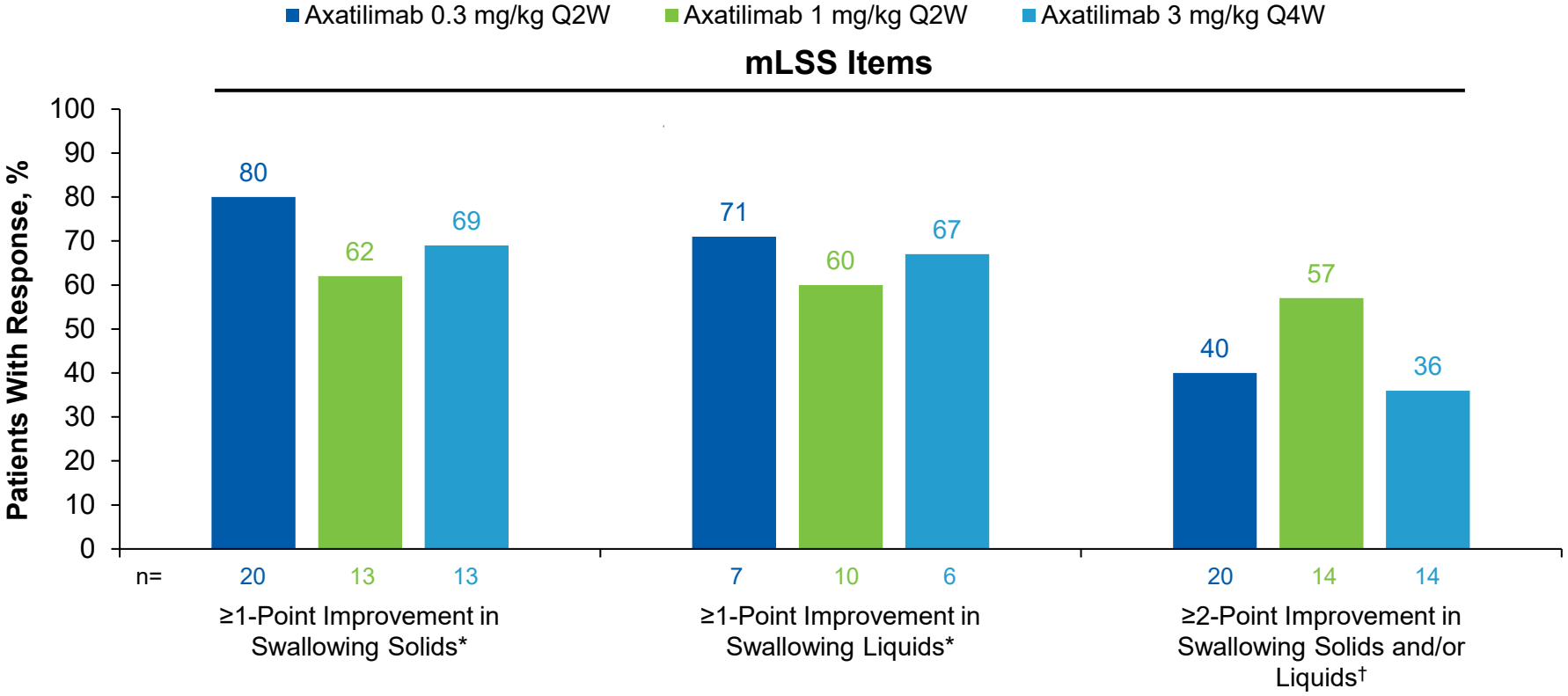
Time to first response, mo

	0.3 mg/kg (n=23)	1 mg/kg (n=18)	3 mg/kg (n=20)	0.3 mg/kg (n=55)	1 mg/kg (n=56)	3 mg/kg (n=51)	0.3 mg/kg (n=32)	1 mg/kg (n=41)	3 mg/kg (n=35)	0.3 mg/kg (n=64)	1 mg/kg (n=63)	3 mg/kg (n=66)
Median	1.9	1.1	1.2	1.9	1.9	1.9	2.9	2.8	2.6	3.7	2.9	3.3
Range	0.9–10.5	1.0–4.5	0.9–2.8	1.0–9.5	0.9–8.1	0.9–8.3	1.0–7.2	1.0–14.8	1.0–4.1	1.0–8.4	1.0–8.0	1.0–14.4

CR, complete response; PR, partial response.
Differences in percentage totals are due to rounding. Denominator is the number of patients with baseline organ involvement.
* Assessed by NIH 2014 criteria.

Patient-Reported Improvements in Swallowing

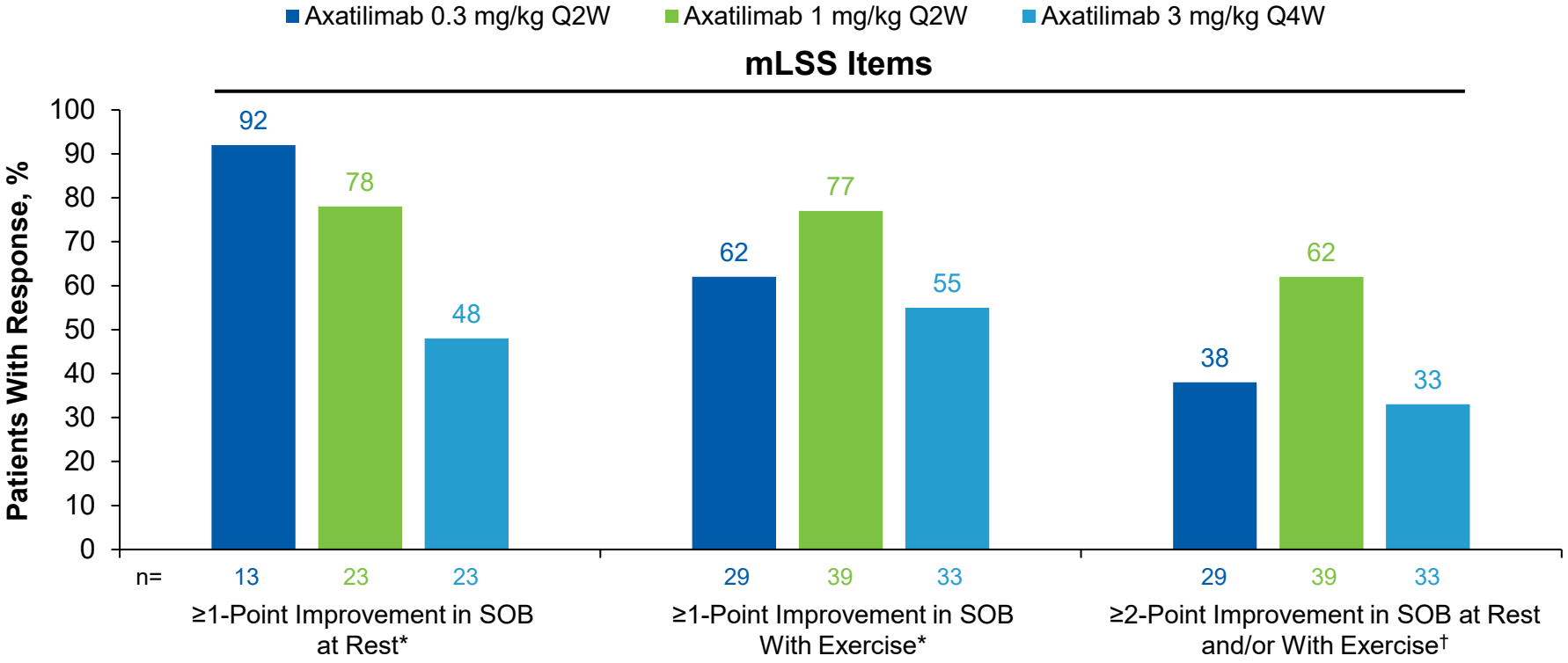
Best Responses at Any Time



Denominator is the number of patients with corresponding organ involvement and assessment at baseline.
* mLSS item with score range of 0–4. † Combined mLSS items with a score range of 0–8.

Patient-Reported Improvements in Shortness of Breath

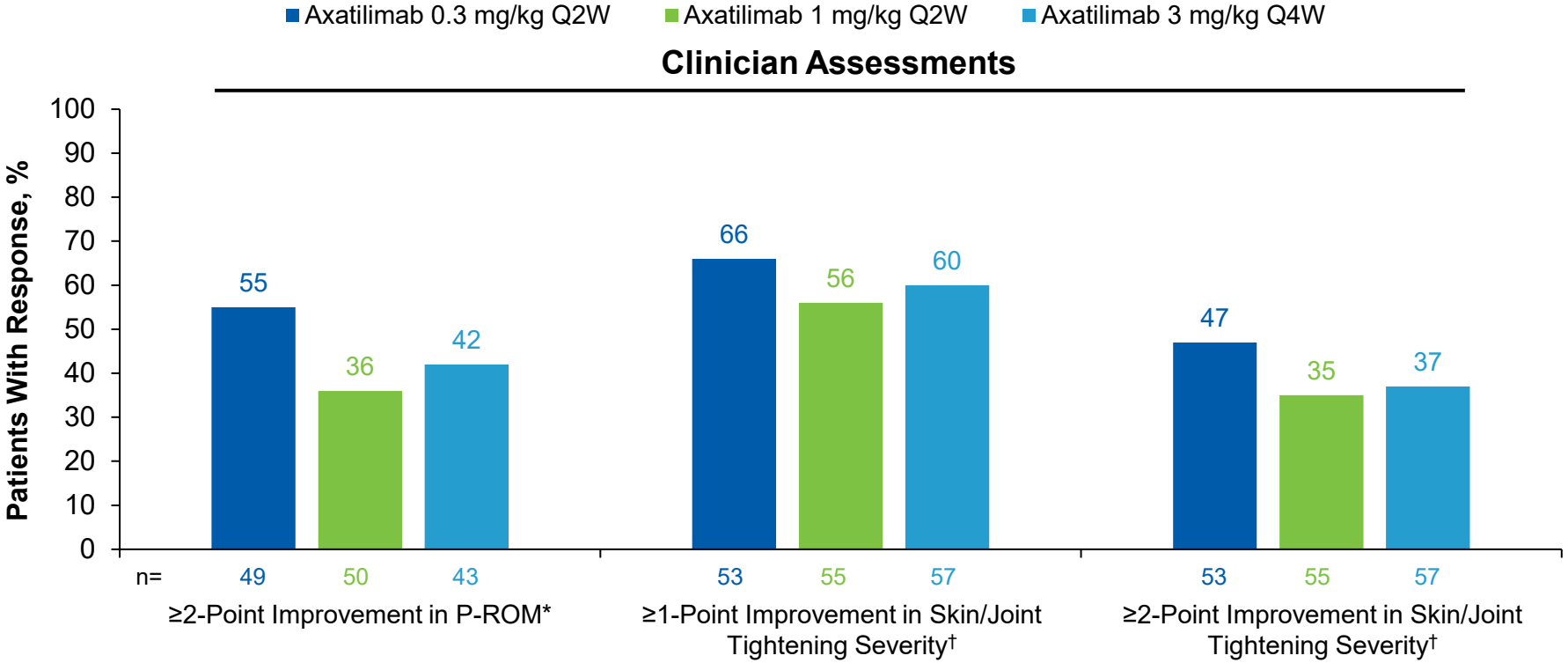
Best Responses at Any Time



SOB, shortness of breath.
Denominator is the number of patients with corresponding organ involvement and assessment at baseline.
* mLSS item with score range of 0–4. † Combined mLSS items with a score range of 0–8.

Clinical Improvements in Skin and Joints

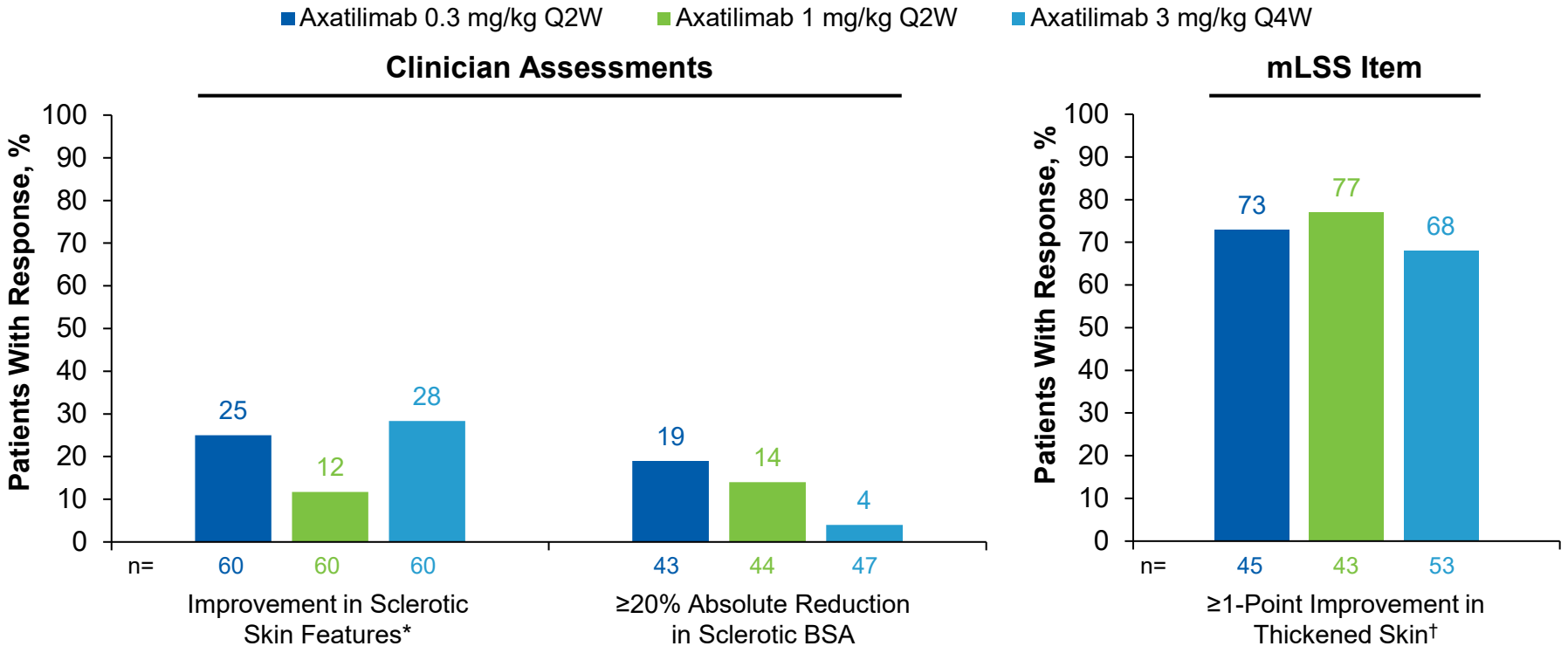
Best Responses at Any Time



P-ROM, photographic range of motion.
Denominator is the number of patients with corresponding organ involvement and assessment at baseline.
* Score range of 0–25. † Clinician assessment with a score range of 0–10.

Clinical and Patient-Reported Improvements of Sclerotic Skin

Best Responses at Any Time



BSA, body surface area.
Denominator is the number of patients with corresponding organ involvement and assessment at baseline.
* Any improvement in skin features score. † mLSS item with score range of 0–4.

No CMV, EBV, or Invasive Fungal Infections at 0.3 mg/kg Q2W

- AEs were mostly low grade, reversible, and increased with higher doses

n (%)	Axatilimab 0.3 mg/kg Q2W n=79		Axatilimab 1.0 mg/kg Q2W n=81		Axatilimab 3.0 mg/kg Q4W n=79	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Viral infection	33 (42)	10 (13)	34 (42)	12 (15)	30 (38)	12 (15)
COVID-19*	13 (16)	3 (4)	19 (23)	6 (7)	12 (15)	7 (9)
EBV	0	0	0	0	4 (5)	1 (1)
CMV†	0	0	1 (1)	0	2 (3)	0
Bacterial infection	10 (13)	5 (6)	12 (15)	6 (7)	12 (15)	6 (8)
Fungal infection	3 (4)	0	7 (9)	3 (4)	6 (8)	0
Invasive fungal‡	0	0	3 (4)	2 (2)	0	0
Mycobacterial infection	1 (1)	1 (1)	0	0	0	0
Unspecified pathogen§	43 (54)	10 (13)	39 (48)	17 (21)	33 (42)	12 (15)
Pneumonia	9 (11)	8 (10)	12 (15)	7 (9)	8 (10)	5 (6)
Treatment-related infections	15 (19)	6 (8)	19 (23)	11 (14)	11 (14)	6 (8)

AE, adverse event; CMV, cytomegalovirus; EBV, Epstein-Barr virus.
Safety population includes all patients who received ≥1 dose of axatilimab. * Includes COVID-19 pneumonia. † Includes CMV infection, CMV infection reactivation, and cytomegaloviral pneumonia. ‡ Includes bronchopulmonary aspergillosis or *Aspergillus* infection. § Includes infections with unspecified etiology.

Conclusions

- Responses were noted in all fibrosis-dominant organs
- Clinical activity in fibrosis-dominant organs is supported by clinician-reported changes and patient-reported reductions in organ-specific symptom burden
- Axatilimab had a generally well-tolerated safety profile
  - Opportunistic infections, which are typically common in patients with cGVHD under heavy immunosuppression, were infrequent

Acknowledgments

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