

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

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# Presenter Disclosures

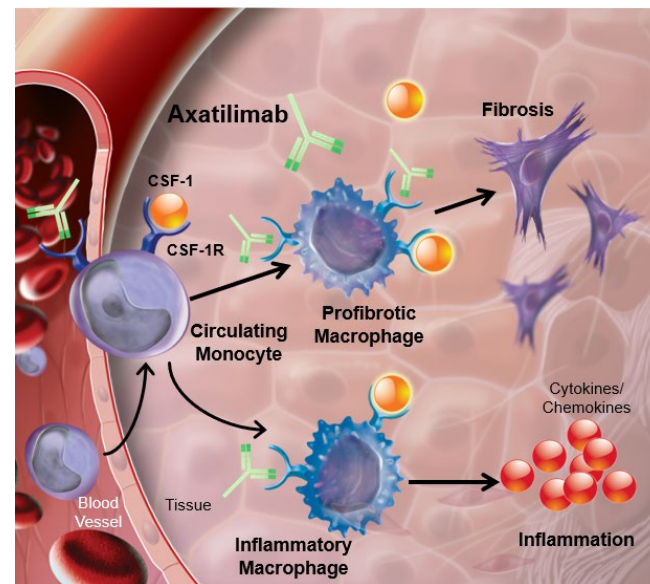
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- Honoraria: Novartis and Sanofi

# Axatilimab for cGVHD

- CSF-1R–dependent monocytes and macrophages contribute to the multiorgan inflammation and fibrosis that drives cGVHD<sup>1</sup>
- Axatilimab is an investigational, high-affinity anti–CSF-1R monoclonal antibody<sup>2</sup>
- In the AGAVE-201 study, axatilimab 0.3 mg/kg Q2W resulted in the highest response rate and most manageable safety profile<sup>3</sup>
- 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<sup>1,2,4</sup>



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  $\geq 2$  years with  $\geq 2$  prior lines of systemic therapy
- Active cGVHD defined per 2014 NIH consensus criteria<sup>1</sup>
- Concomitant use of the following therapies was permitted but not required
  - Corticosteroids
  - Calcineurin inhibitors
  - mTOR inhibitors

Randomization (1:1:1)\*  
N=241 (ITT population)

Axatilimab 0.3 mg/kg Q2W  
n=80

Axatilimab 1.0 mg/kg Q2W  
n=81

Axatilimab 3.0 mg/kg Q4W  
n=80

**Primary endpoint:** ORR in the first 6 cycles<sup>†,2</sup>

**Secondary endpoints:** mLSS, organ-specific response rates, safety

**Exploratory endpoints:** Physician and patient-reported symptom changes<sup>‡</sup>

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 <sup>†</sup>	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 <sup>‡</sup>	8 (25)	10 (26)	8 (23)	26 (25)
FEV1 ≤39% <sup>§</sup>	14 (47)	15 (42)	7 (26)	36 (39)
Esophagus	23 (29)	18 (22)	20 (25)	61 (25)

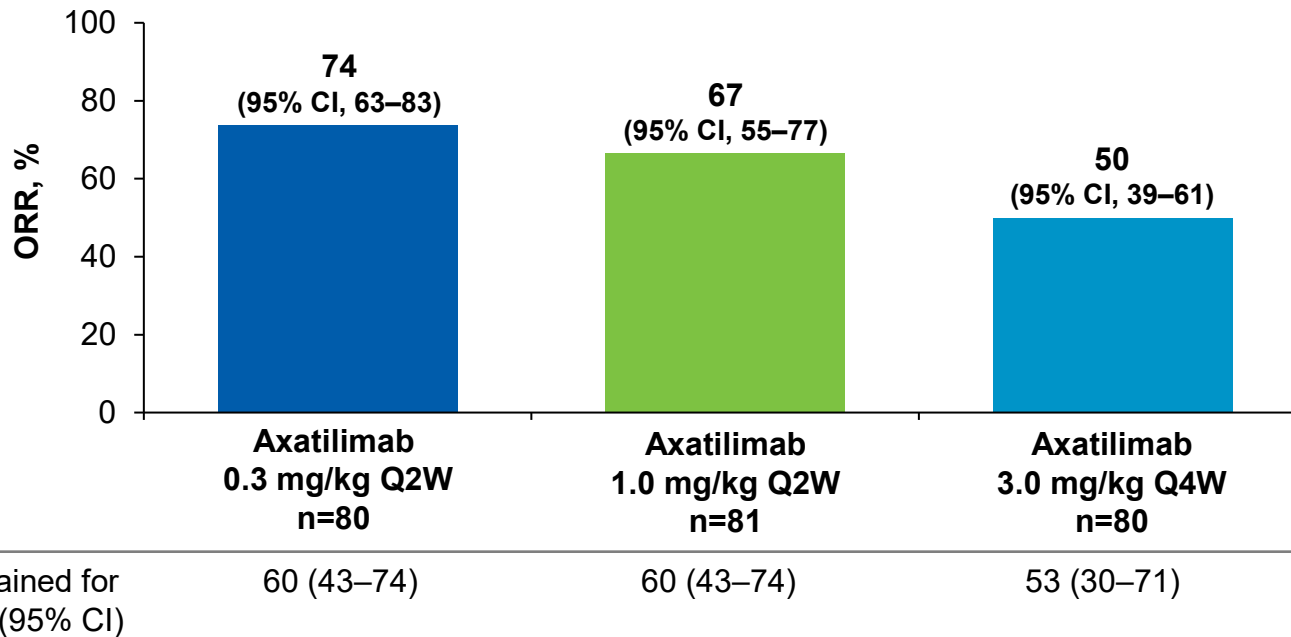
FEV1, forced expiratory volume in first second.

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



ORR was defined by NIH 2014 consensus criteria. The primary endpoint was met if lower bound of 95% CI >30%.

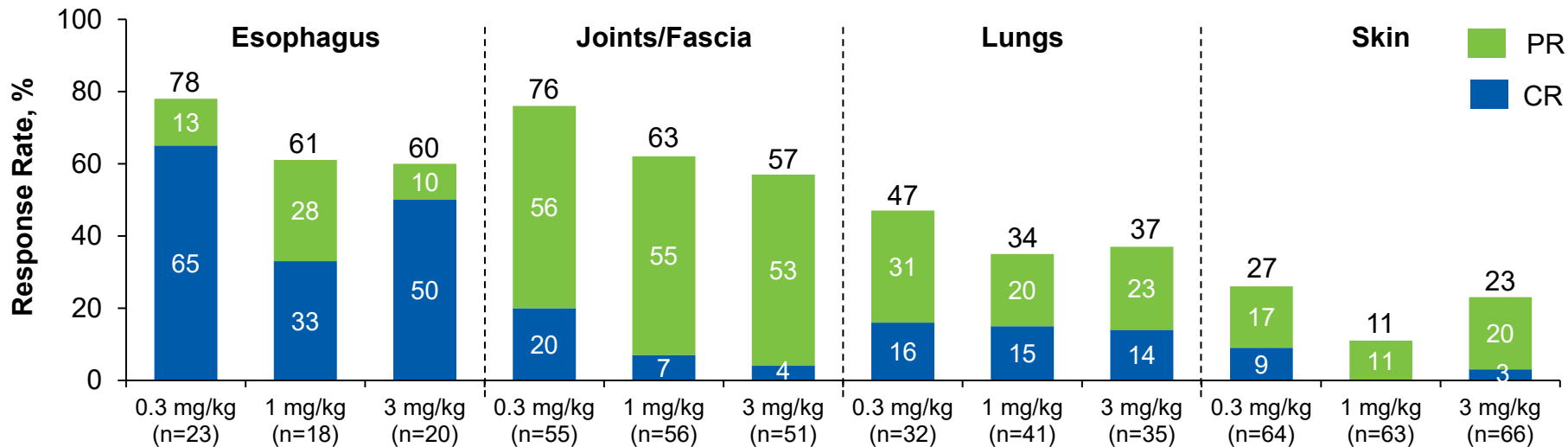
\* Based on Kaplan-Meier estimate of 12-month event-free probability.

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

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

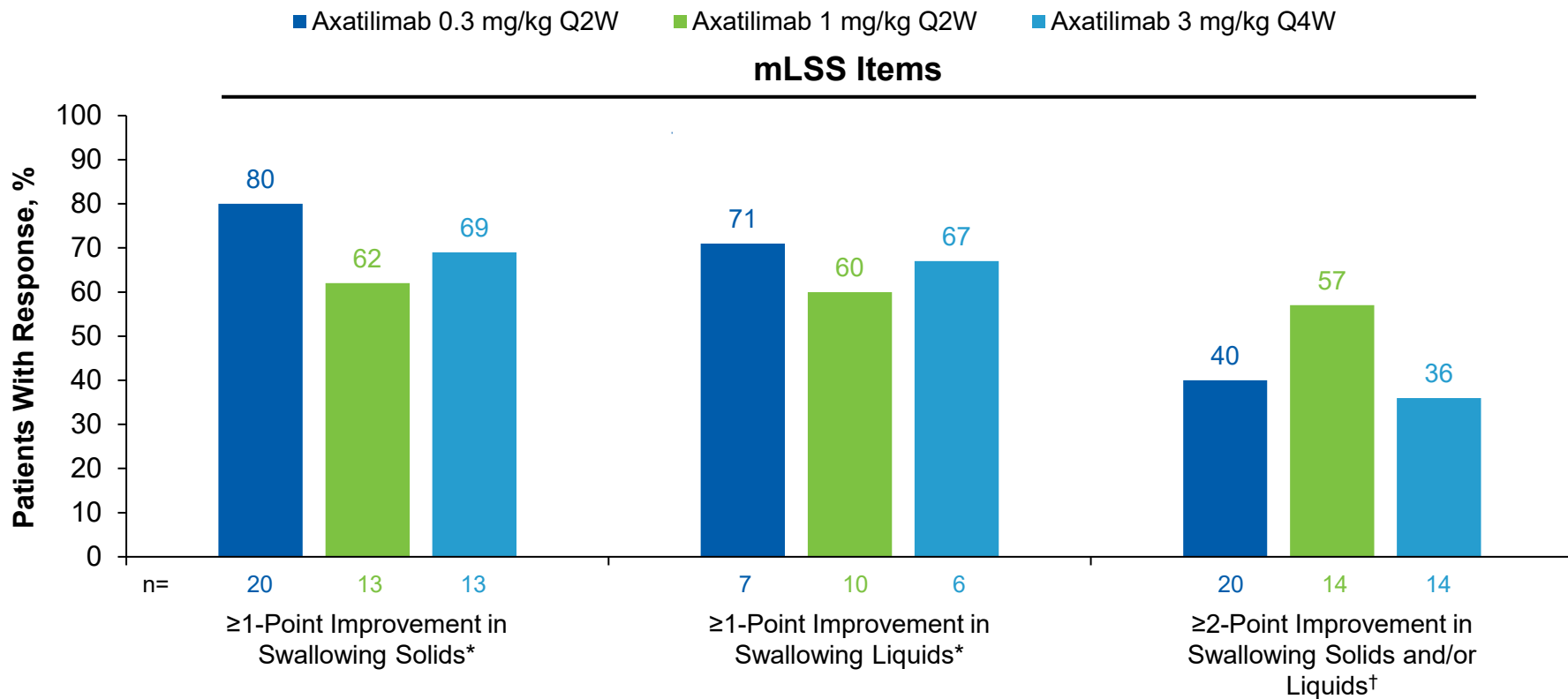
CR, complete response; PR, partial response.

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



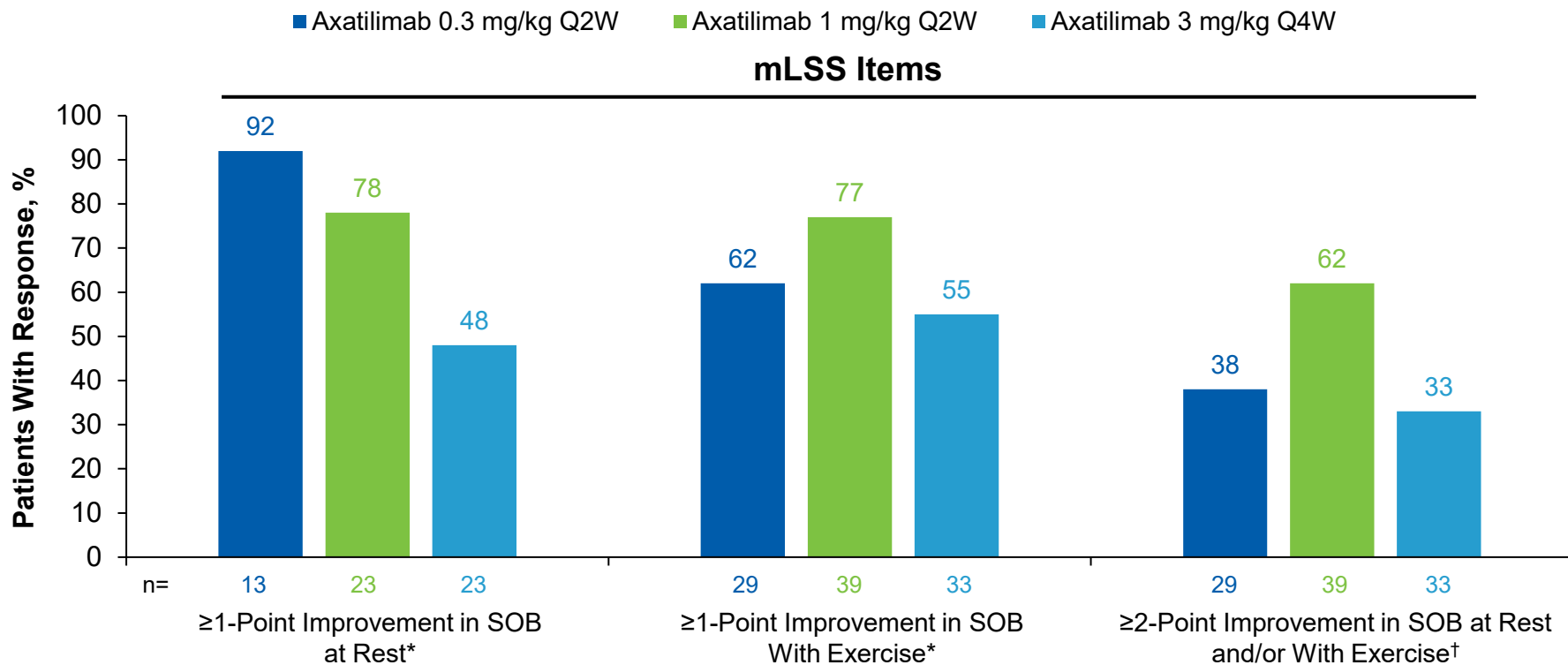
Denominator is the number of patients with corresponding organ involvement and assessment at baseline.

\* 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



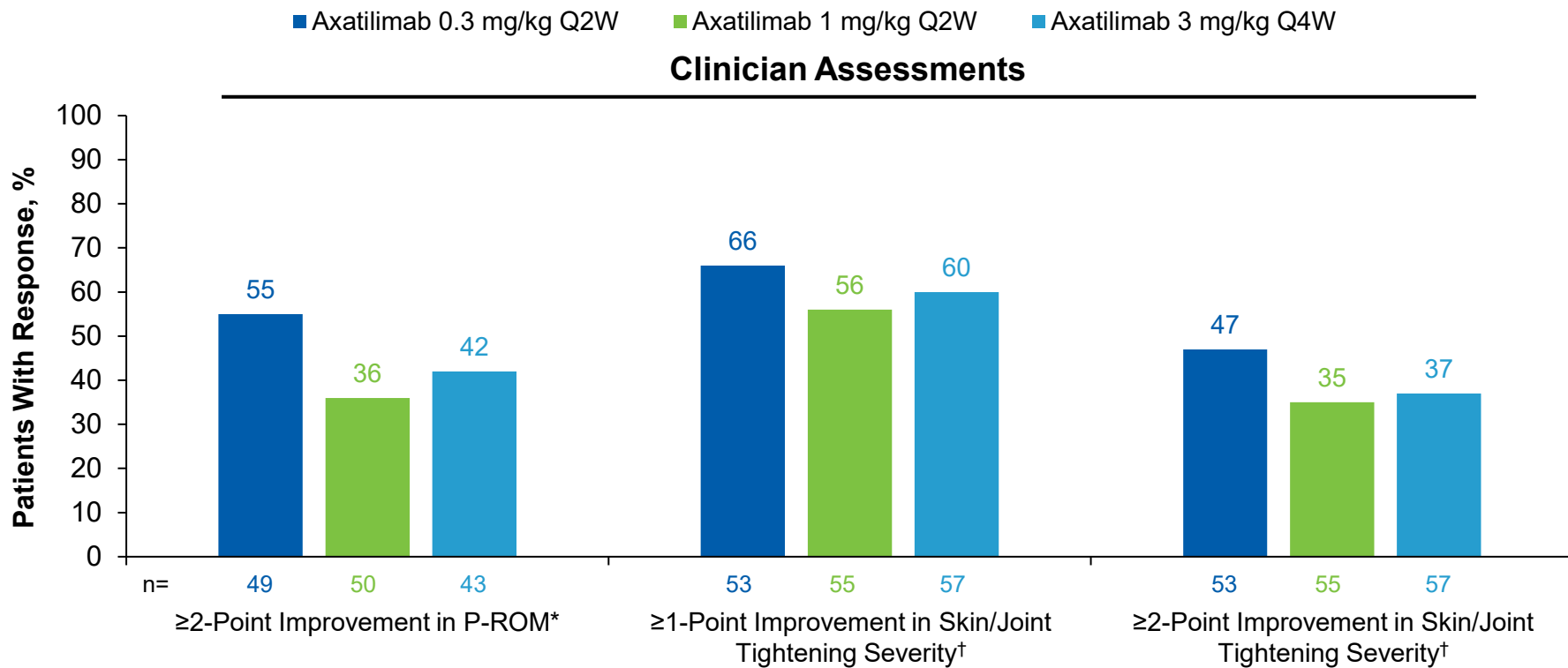
SOB, shortness of breath.

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.

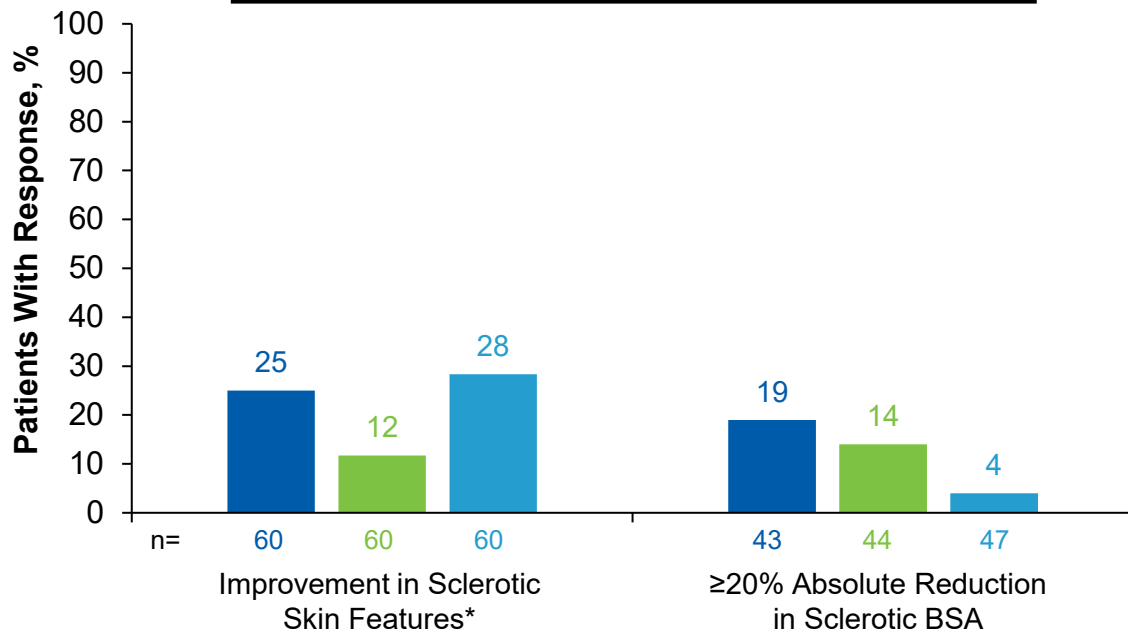
\* Score range of 0–25. † Clinician assessment with a score range of 0–10.

# Clinical and Patient-Reported Improvements of Sclerotic Skin

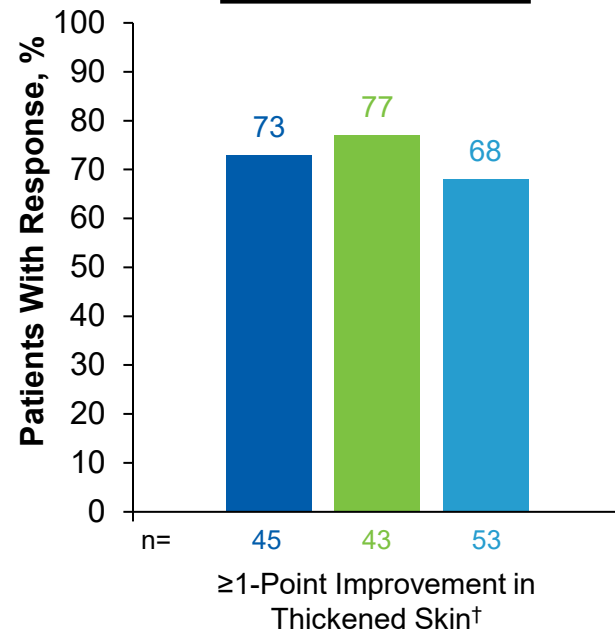
## Best Responses at Any Time

■ Axatilimab 0.3 mg/kg Q2W    ■ Axatilimab 1 mg/kg Q2W    ■ Axatilimab 3 mg/kg Q4W

### Clinician Assessments



### mLSS Item



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

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- 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

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