Dynamics of Overall and Organ-Specific Responses to Axatilimab in Chronic Graft-Versus-Host Disease: Analysis From the AGAVE-201 Study

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66th American Society of Hematology (ASH) Annual Meeting and Exposition; December 7–10, 2024; San Diego, CA, USA

Background

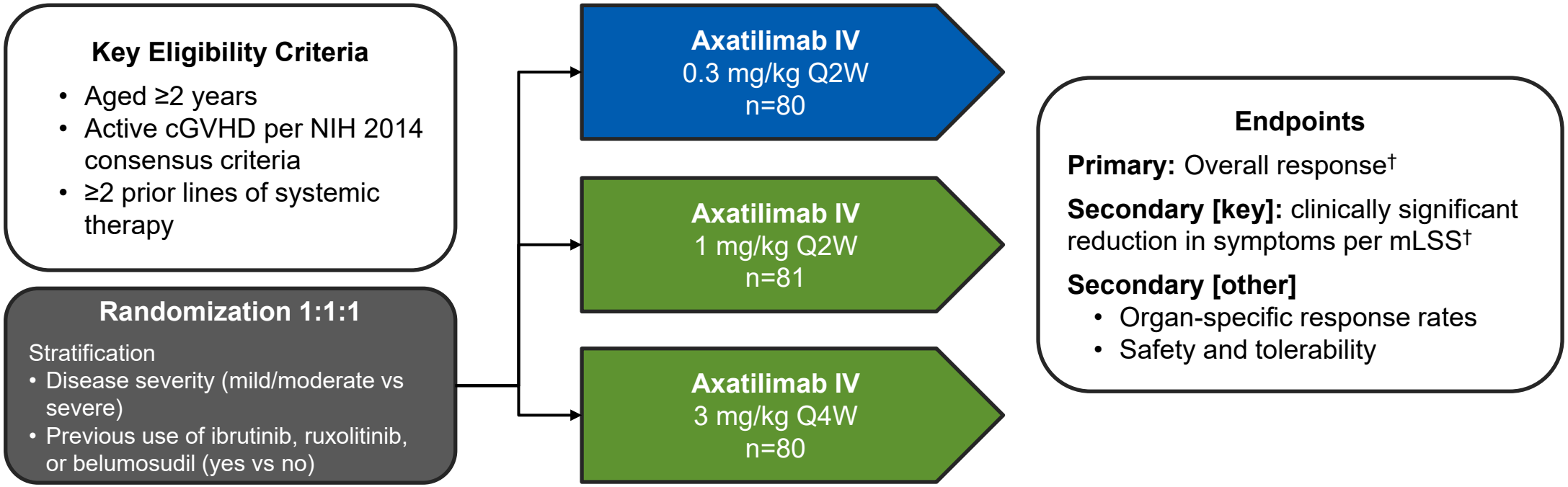
- cGVHD is characterized by inflammatory and fibrotic pathology affecting multiple organs and leading to significant impairment[1-3]
- Axatilimab, an anti–CSF-1R monoclonal antibody, targets monocytes and macrophages that are critical for inflammation and fibrosis in cGVHD[4]
- In the pivotal AGAVE-201 study (NCT04710576), axatilimab 0.3 mg/kg Q2W had robust clinical activity and was generally well tolerated in patients with cGVHD, with treatment-related adverse events that were mostly low grade and reversible[5]
- Dynamics of clinical responses and symptom improvements following axatilimab treatment for cGVHD needs further investigation
- **Objective:** To assess the timing/dynamics of clinical responses and symptom improvements among patients with cGVHD who achieved responses with axatilimab in AGAVE-201

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

1. Yu J, et al. *Cancer Med.* 2023;12(3):3623-3633. 2. Kurosawa S, et al. *Biol Blood Marrow.* 2019;25(9):1851-1858. 3. Bevans, et al. *Biol Blood Marrow.* 2017;23(4):538-551. 4. Ordentlich P, et al. Targeting colony stimulating factor-1 receptor (CSF-1R) with SNDX-6352, a novel anti-CSF-1R targeted antibody. Presented at: SITC Annual Meeting; November 9–13, 2016; National Harbor, MD. 5. Wolff D, et al. *N Engl J Med.* 2024;391(11):1002-1014.

AGAVE-201 Study Design

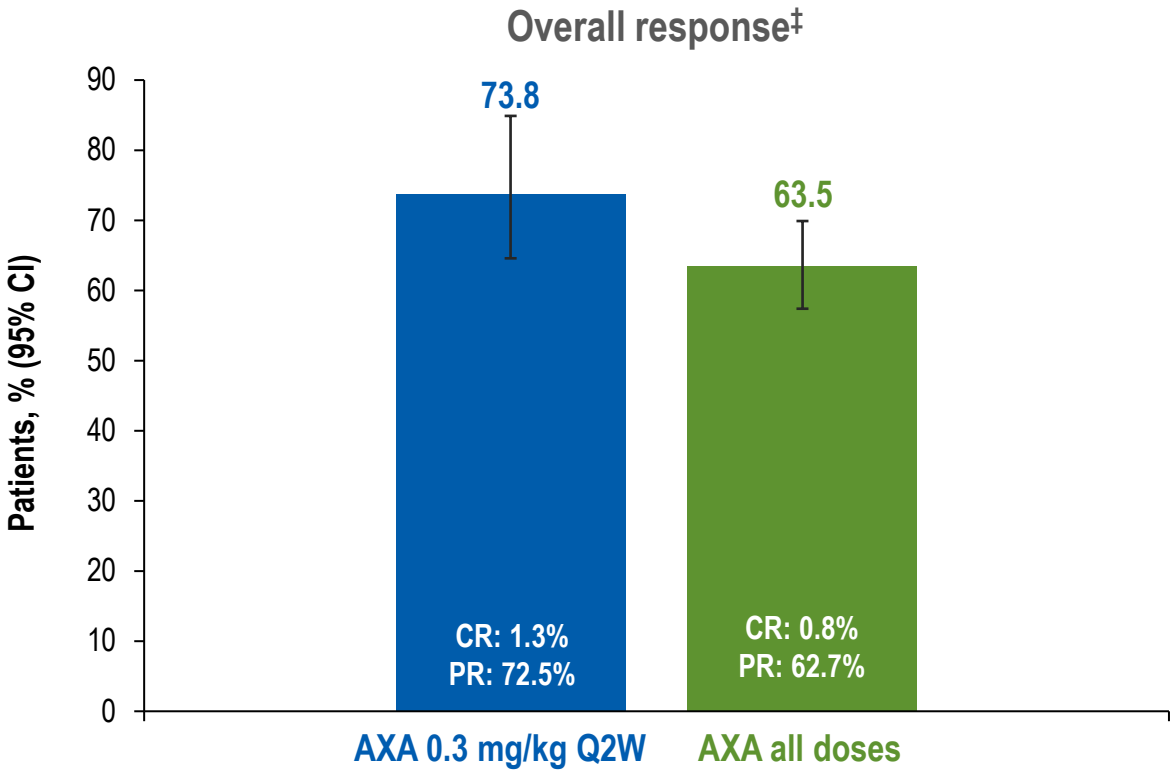
- Phase 2, open-label, multicenter, randomized study to evaluate safety and efficacy of axatilimab in patients with recurrent/refractory cGVHD (NCT04710576)



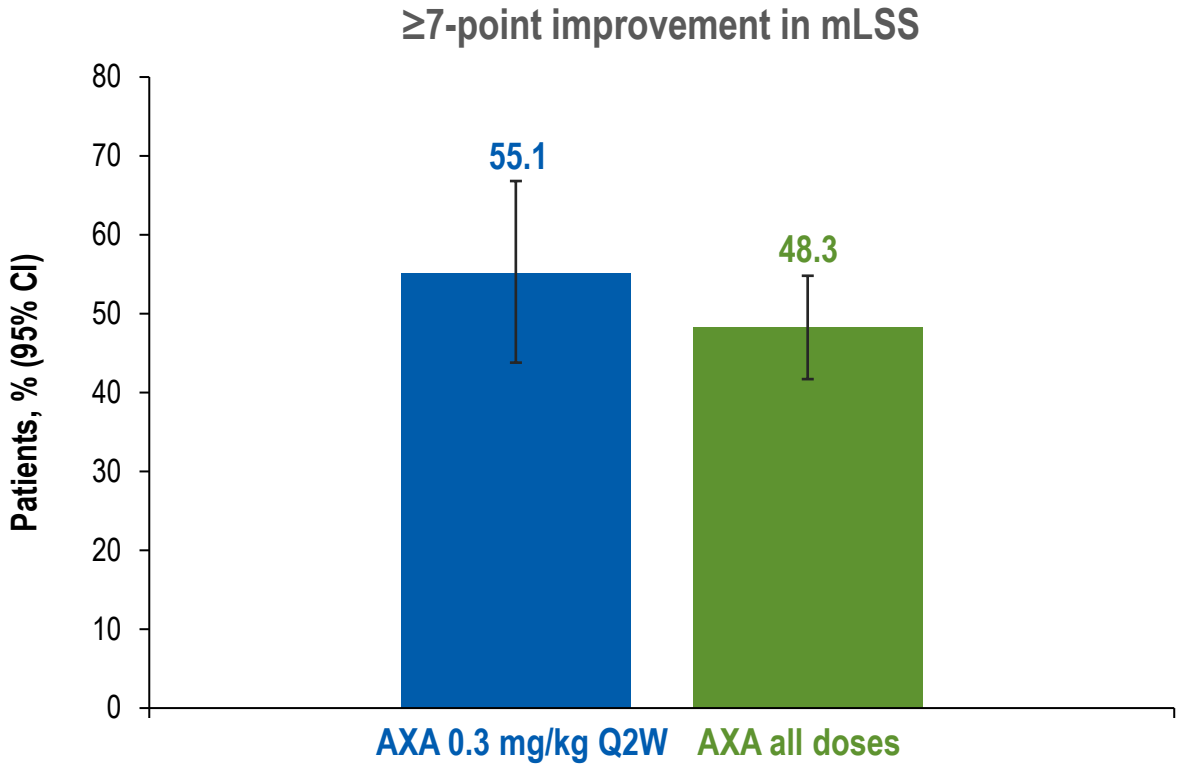
This analysis focuses on patients who achieved overall, organ-specific, or mLSS responses

mLSS, modified Lee Symptom Scale; IV, intravenous; NIH, National Institutes of Health; Q4W, every 4 weeks.
† Complete or partial response per NIH 2014 consensus criteria, within the first 6 cycles (from randomization to Day 169 or the beginning of Cycle 7, whichever is later).
‡ In this analysis, a reduction of ≥7 points was assessed (linearly transformed range of 0–100, with 100 indicating worst symptoms).

ORR† (Primary Endpoint) and ≥7-Point Improvement in mLSS in the First 6 Cycles



	AXA 0.3 mg/kg Q2W	AXA all doses
n=	80	241
Median TTR on study, median (range), mo	1.7 (0.9–8.1)	1.6 (0.9–8.6)



	AXA 0.3 mg/kg Q2W	AXA all doses
n=	78	236
Median TTR on study, median (range), mo	1.5 (1.0–7.2)	1.4 (0.9–18.5)

AXA, axatilimab; CR, complete response; PR, partial response; TTR, time to response.
† NIH 2014 consensus criteria.
‡ Overall response (CR+PR) at any time point up to Day 176 or the beginning of Cycle 7, whichever is later.

Responder Analyses

- Cumulative incidences of clinical responses per NIH 2014 consensus criteria (overall and organ-specific) and a ≥7-point improvement in mLSS summary score† were assessed among patients who achieved a response
- Comparisons of TTR for 2014 NIH consensus criteria and individual mLSS items were assessed among patients with both responses

Organ	Patient-reported mLSS assessments‡ (≥1-point improvement)
Esophagus	• Swallowing liquids • Swallowing solids
Eyes	• Visual clarity • Eye dryness
Joints/fascia	• Joint/muscle aches • Joint movement
Lung	• SOB at rest • SOB with exercise
Mouth	• Oral ulcers
Skin	• Skin thickening

SOB, shortness of breath.
† Threshold considered to be clinically meaningful
‡ mLSS items are not validated as single measures.

Patient Demographics and Baseline Clinical Characteristics

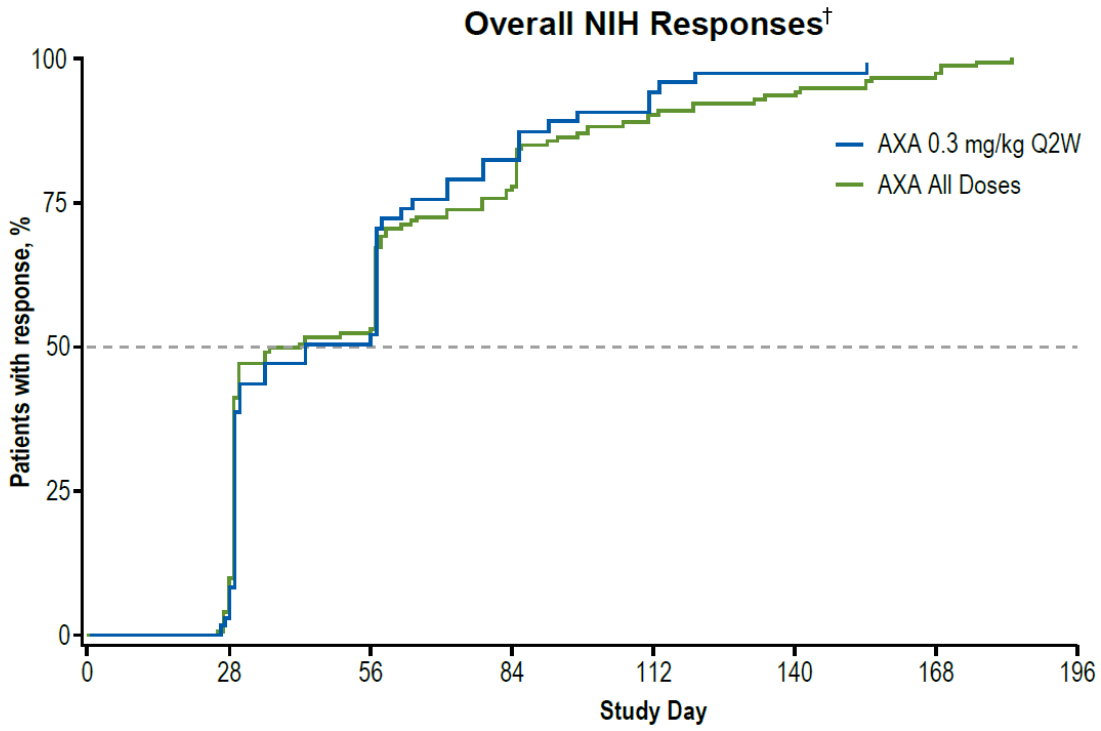
- Demographics and baseline characteristics were similar across treatment groups and between responders and the overall patient population

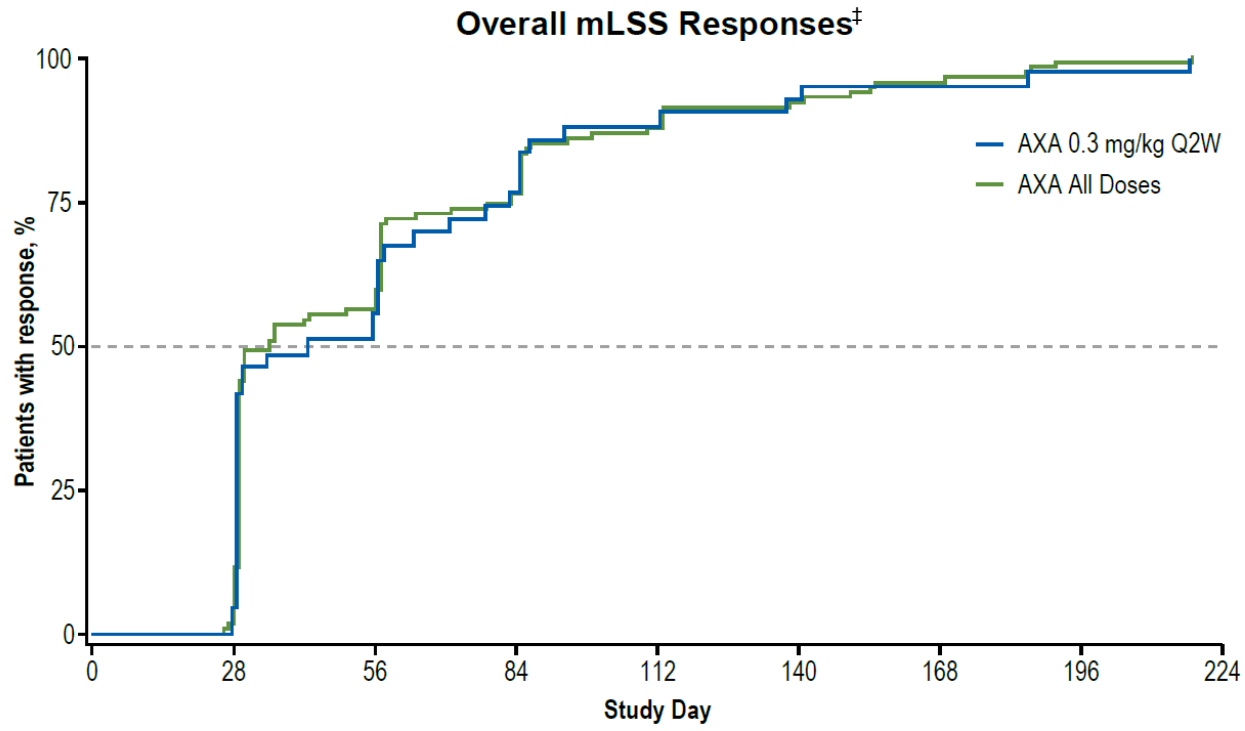
Characteristic	Responders† (n=153)	All patients (N=241)
Age, median (range), y	52.0 (7–76)	53.0 (7–81)
Male, n (%)	95 (62.1)	151 (62.7)
Race, n (%)		
White	133 (86.9)	200 (83.0)
Asian	7 (4.6)	16 (6.6)
Black	1 (0.7)	5 (2.1)
Not reported	10 (6.5)	16 (6.6)
Other‡	2 (1.3)	4 (1.7)
Ethnicity, n (%)		
Not Hispanic or Latino	132 (86.3)	215 (89.2)
Hispanic or Latino	17 (11.1)	19 (7.9)
Not reported/unknown	4 (2.6)	7 (2.9)
Prior cGVHD therapy, n (%)	130 (85.0)	204 (84.6)
Ruxolitinib	117 (76.5)	179 (74.3)
Ibrutinib	53 (34.6)	75 (31.1)
Belumosudil	30 (19.6)	56 (23.2)

Characteristic	Responders† (n=153)	All patients (N=241)
Number of organs involved at baseline, median (maximum)	4.0 (8)	4.0 (8)
Involved organs, n (%)		
Skin	130 (85.0)	193 (80.1)
Eyes	121 (79.1)	183 (75.9)
Joints and fascia	117 (76.5)	162 (67.2)
Mouth	75 (49.0)	112 (46.5)
Lungs	65 (42.5)	108 (44.8)
Esophagus	44 (28.8)	61 (25.3)
Liver	28 (18.3)	40 (16.6)
Upper GI	23 (15.0)	28 (11.6)
Lower GI	17 (11.1)	18 (7.5)
Time from cGVHD diagnosis to randomization, median (range), y	4.0 (0.4–17.6)	4.0 (0.4–17.6)
Severe disease, n (%)	121 (79.1)	192 (79.7)

GI, gastrointestinal.
† Subgroup comprises patients who achieved overall response within the first 6 treatment cycles.
‡ Includes American Indian or Alaskan Native, and Native Hawaiian or Pacific Islander.

Time to Overall NIH and mLSS Responses in Cycles 1–6



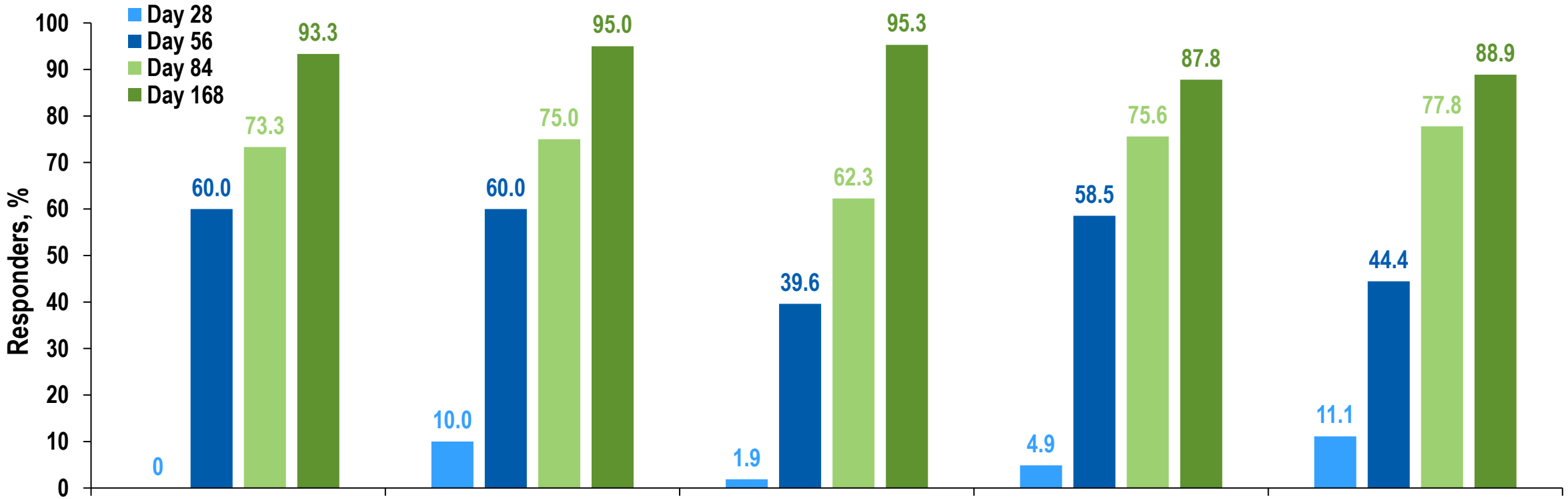


Most patients who achieved an overall clinical response and/or ≥7-point improvement in mLSS in the first 6 treatment cycles did so by Day 56

† Overall response (CR+PR) at any time point up to Day 169 or the beginning of Cycle 7, whichever is later.
‡ ≥7-point improvement from baseline in mLSS.

NIH 2014 Organ-Specific Responders† (All AXA Doses)

- The lower GI, upper GI, joints/fascia, esophagus, and liver were fastest to respond to treatment

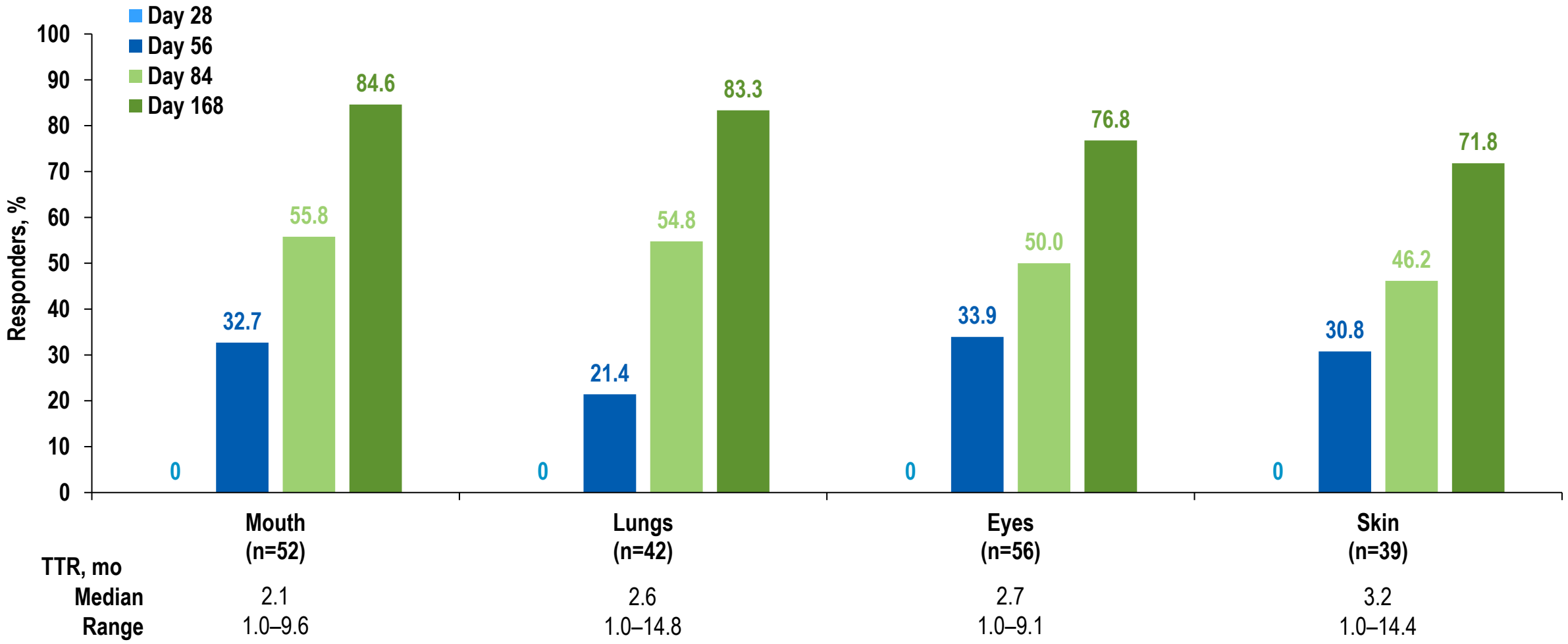


TTR, mo	Lower GI (n=15)	Upper GI (n=20)	Joints/fascia (n=106)	Esophagus (n=41)	Liver (n=9)
Median	1.2	1.0	1.9	1.1	1.9
Range	1.0–10.5	0.9–6.0	0.9–9.5	0.9–10.5	0.9–6.1

† Achieved an organ-specific response on study.

NIH 2014 Organ-Specific Responders† (All AXA Doses)

- Mouth, lungs, eyes, and skin were slower to respond to treatment



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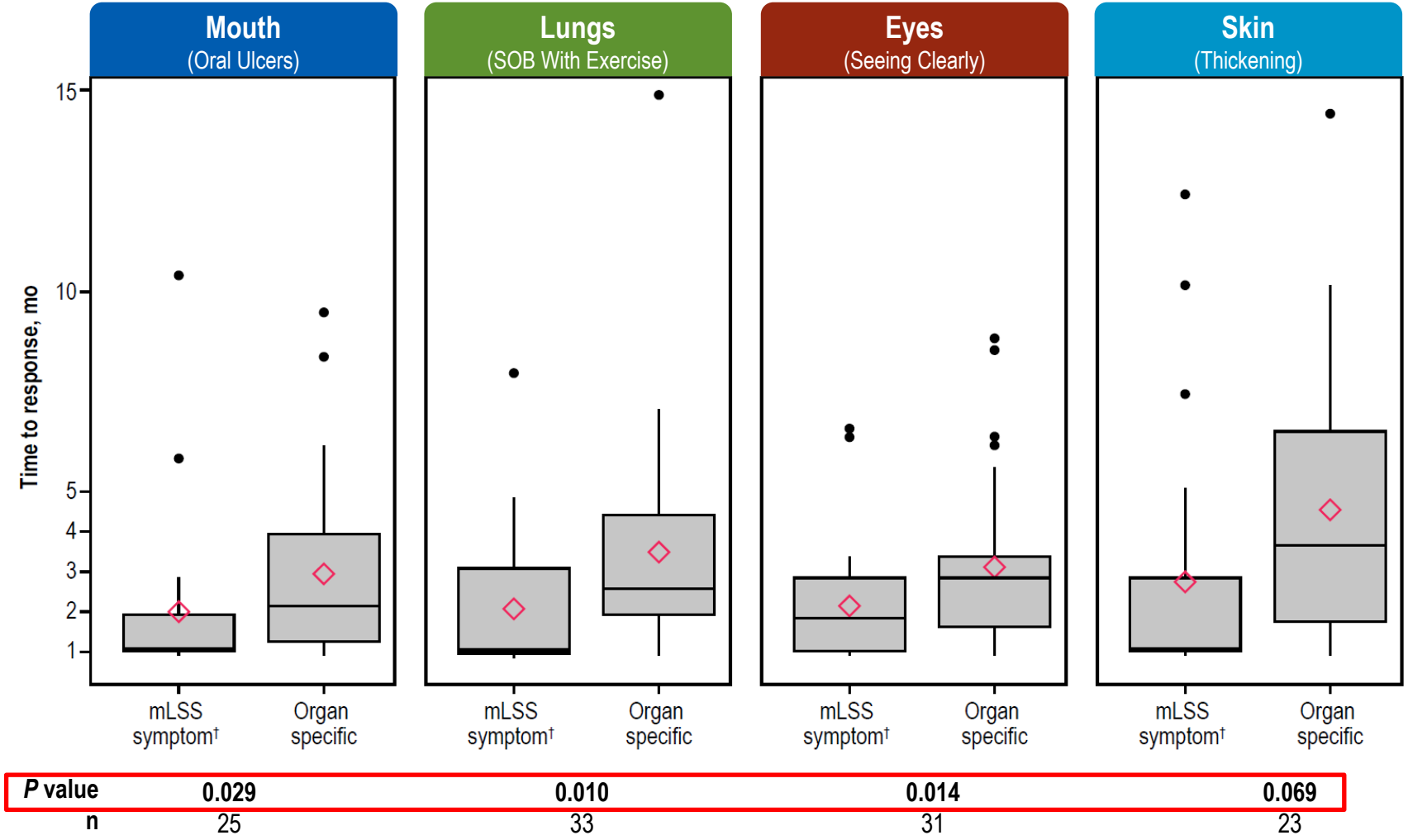
Timing of Symptom Improvement Compared With Organ-Specific NIH Response (All AXA Doses)



Analysis includes all patients who achieved both an organ-specific response by NIH 2014 consensus criteria and a symptom improvement in the corresponding organ in the first 6 cycles. Red diamonds indicate the mean.
P values were calculated by paired *t* test.
† ≥1-point improvement in individual mLSS symptoms.

Safety in Responders†

- Similar to the overall patient population, the safety profile of axatilimab in responders was dose dependent

n (%)	0.3 mg/kg Q2W (n=59)	1 mg/kg Q2W (n=54)	3 mg/kg Q4W (n=40)
TEAE (all grade)	58 (98.3)	53 (98.1)	39 (97.5)
Grade ≥3	28 (47.5)	34 (63.0)	26 (65.0)
TRAEs	42 (71.2)	46 (85.2)	34 (85.0)
Grade ≥3	10 (16.9)	21 (38.9)	17 (42.5)
TEAEs of special interest‡	41 (69.5)	42 (77.8)	28 (70.0)
Grade ≥3	13 (22.0)	20 (37.0)	13 (32.5)
Serious TEAEs	21 (35.6)	24 (44.4)	17 (42.5)
Fatal TEAEs§	0	5 (9.3)	1 (2.5)
TEAEs leading to dose modifications			
Discontinuations	3 (5.1)	16 (29.6)	2 (5.0)
Interruptions	24 (40.7)	20 (37.0)	14 (35.0)
Reductions	4 (6.8)	5 (9.3)	9 (22.5)

TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.
Safety population includes all patients who received ≥1 dose of axatilimab.
† Subgroup comprises patients who achieved overall response within the first 6 treatment cycles.
‡ Defined as infusion-related reactions including hypersensitivity reactions, and infections.
§ 1 mg/kg Q2W: sudden cardiac death, bronchopulmonary aspergillosis, recurrent leukemia, pneumonia (n=2), sepsis; 3 mg/kg Q4W: respiratory syncytial viral pneumonia.

Conclusions

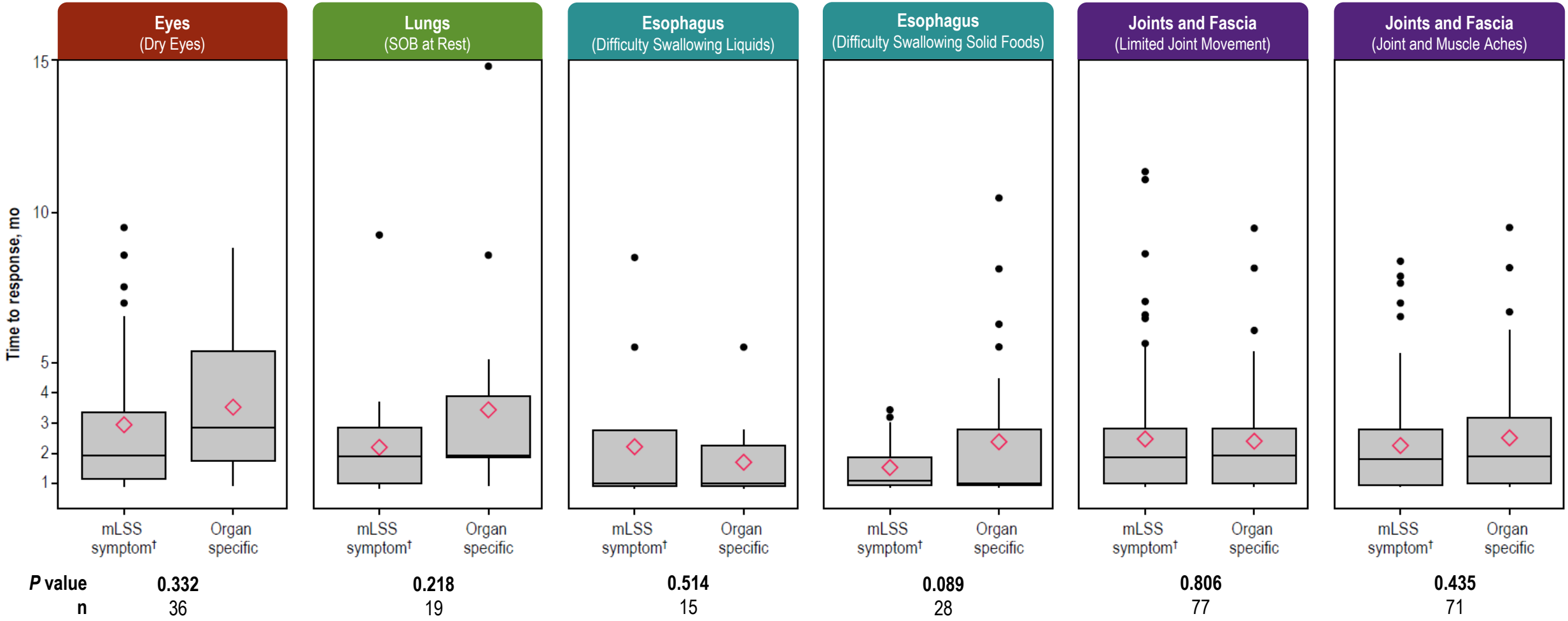
- In the pivotal AGAVE-201 study, axatilimab 0.3 mg/kg Q2W yielded high response rates and was generally well tolerated in patients with cGVHD
- Median times to organ-specific responses with axatilimab ranged from 1.0 to 3.2 months across organs
  - Lower GI, upper GI, esophagus, liver, and joints/fascia were fastest to respond, whereas lung, mouth, eye, and skin responses were slower
- Improvements in specific cGVHD symptoms associated with the lungs, eyes, mouth, and skin were more rapid than the respective organ-specific responses by NIH 2014 response criteria
- Overall, these data highlight the potential for rapid onset of clinical activity and symptom improvement with axatilimab in inflammatory and fibrotic manifestations of cGVHD among a heavily pretreated population with long-standing cGVHD

Acknowledgments

- We thank the patients, their families, and study investigators for their participation in this study
- Special thanks to Eric Xue, PhD, for providing statistical analysis
- For questions, please contact Dr. Hannah Choe (Hannah.Choe@osumc.edu)
- This study was funded by Incyte Corporation and Syndax Pharmaceuticals, Inc.
- Medical writing support was provided by Rob M. Camp, PhD, from The Curry Rockefeller Group, LLC, a Citrus Health Group, Inc., company (Chicago, Illinois), and was funded by Incyte Corporation and Syndax Pharmaceuticals, Inc

Backup

Timing of Organ-Specific NIH Responses and mLSS Symptom Improvements (All AXA Doses; *cont'd*)



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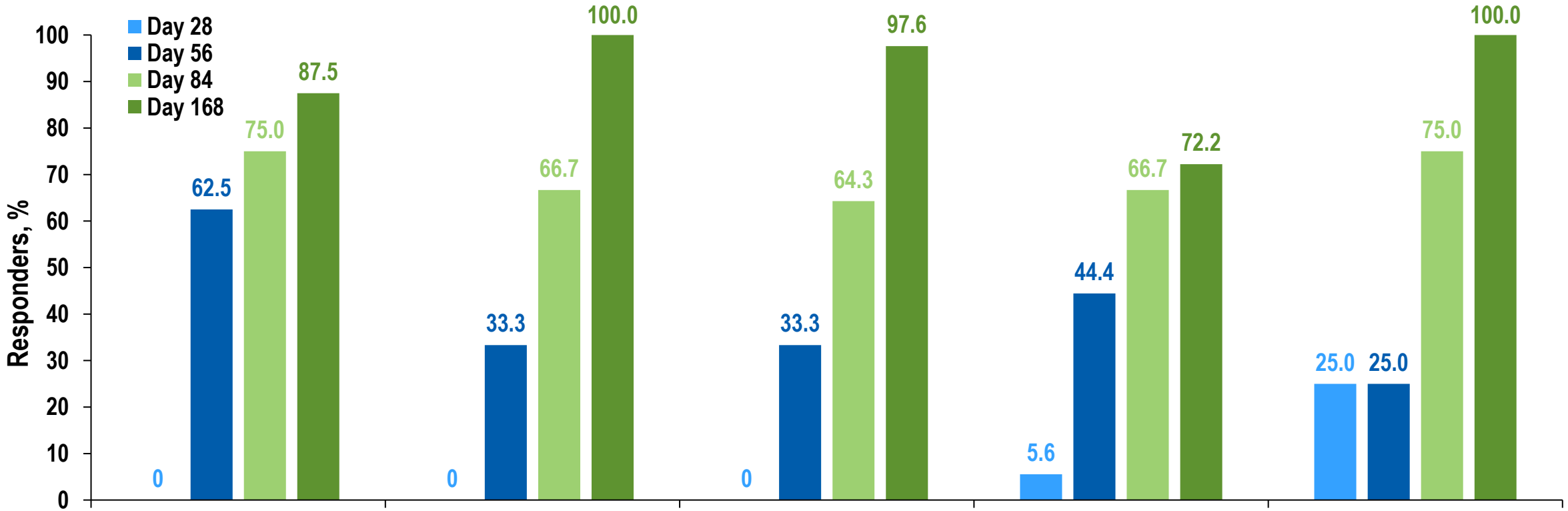
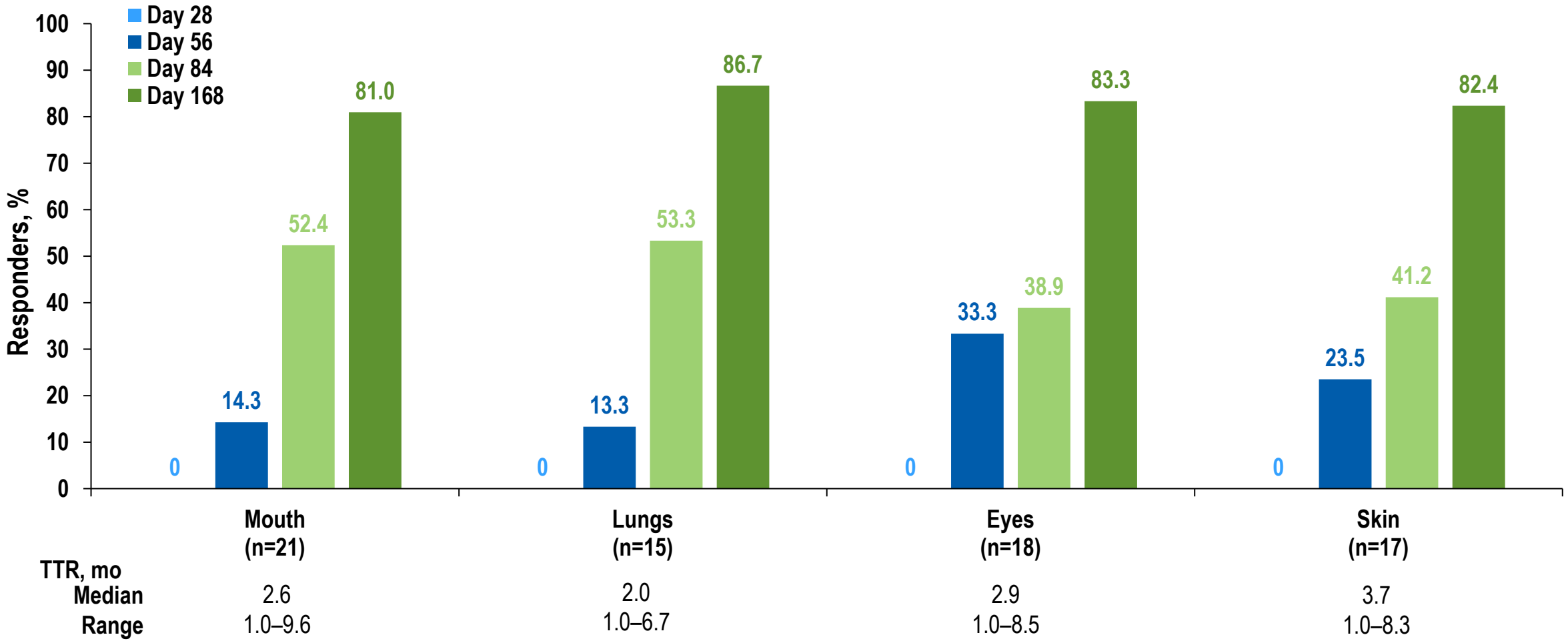


	Lower GI (n=8)	Upper GI (n=9)	Joints/fascia (n=42)	Esophagus (n=18)	Liver (n=4)
TTR, mo					
Median	1.2	1.9	1.9	1.9	1.9
Range	1.0–10.5	1.0–4.0	1.0–9.5	0.9–10.5	0.9–4.4

* Achieved an organ-specific response on study.

NIH 2014 Organ-Specific Responders* (AXA 0.3 mg/kg Q2W)

- Mouth, lung, eye, and skin were slower to respond to treatment



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