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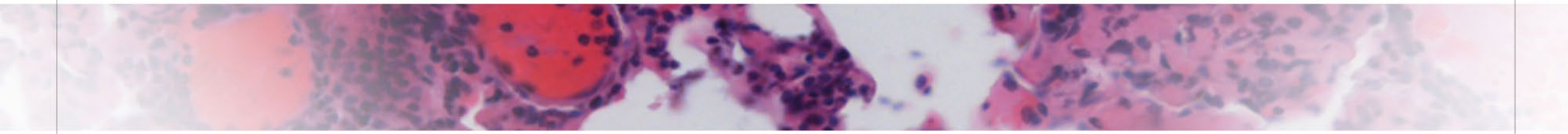

Safety and Efficacy of Axatilimab at 3 Different Doses in Patients with Chronic Graft-Versus-Host Disease (AGAVE-201)

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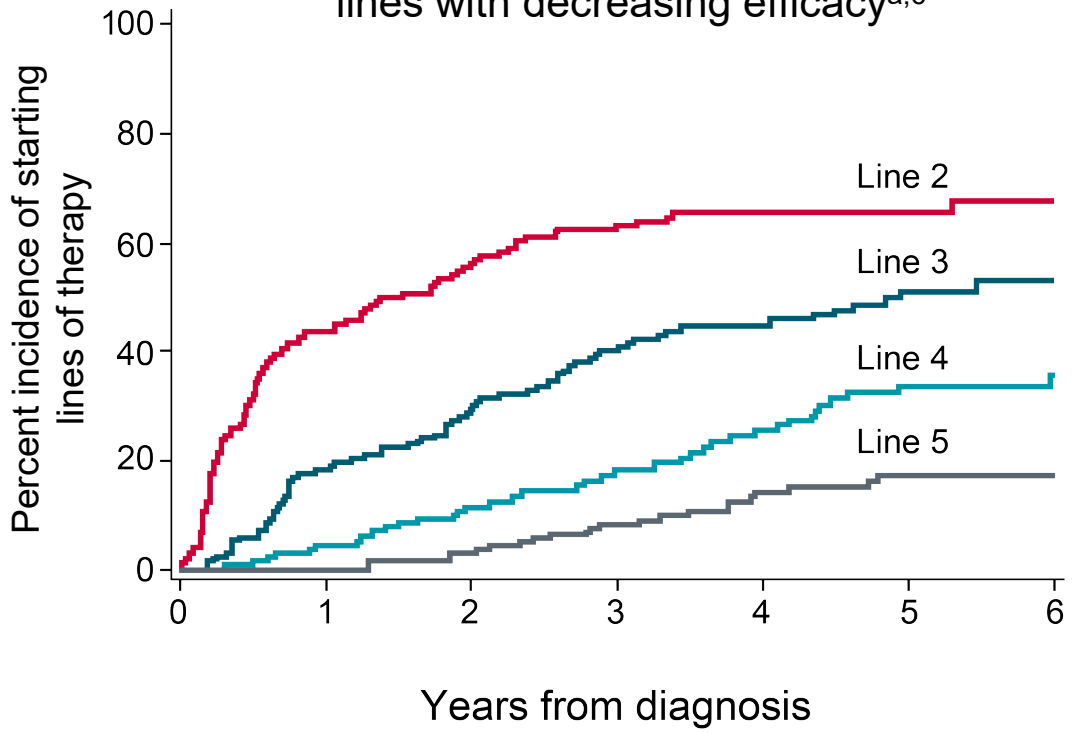
ASH Plenary Session, December 10, 2023

Chronic Graft-Versus-Host Disease Is a Heterogeneous Immune-Mediated Complication of allo-HSCT

- Major cause of late morbidity in 30% to 50% of patients[1-3]
- Inflammatory and fibrotic multiorgan disease[2,4]
- Significant impairment in QOL[5]

There is an unmet need for novel treatments that are well tolerated and provide rapid, durable responses as well as improved QOL

More than 50% of patients receive ≥3 therapy lines with decreasing efficacy[a,6]



allo-HSCT, allogeneic hematopoietic stem cell transplant; QOL, quality of life.
[a]A line of therapy was defined as 1 or more treatments prescribed at the same time.

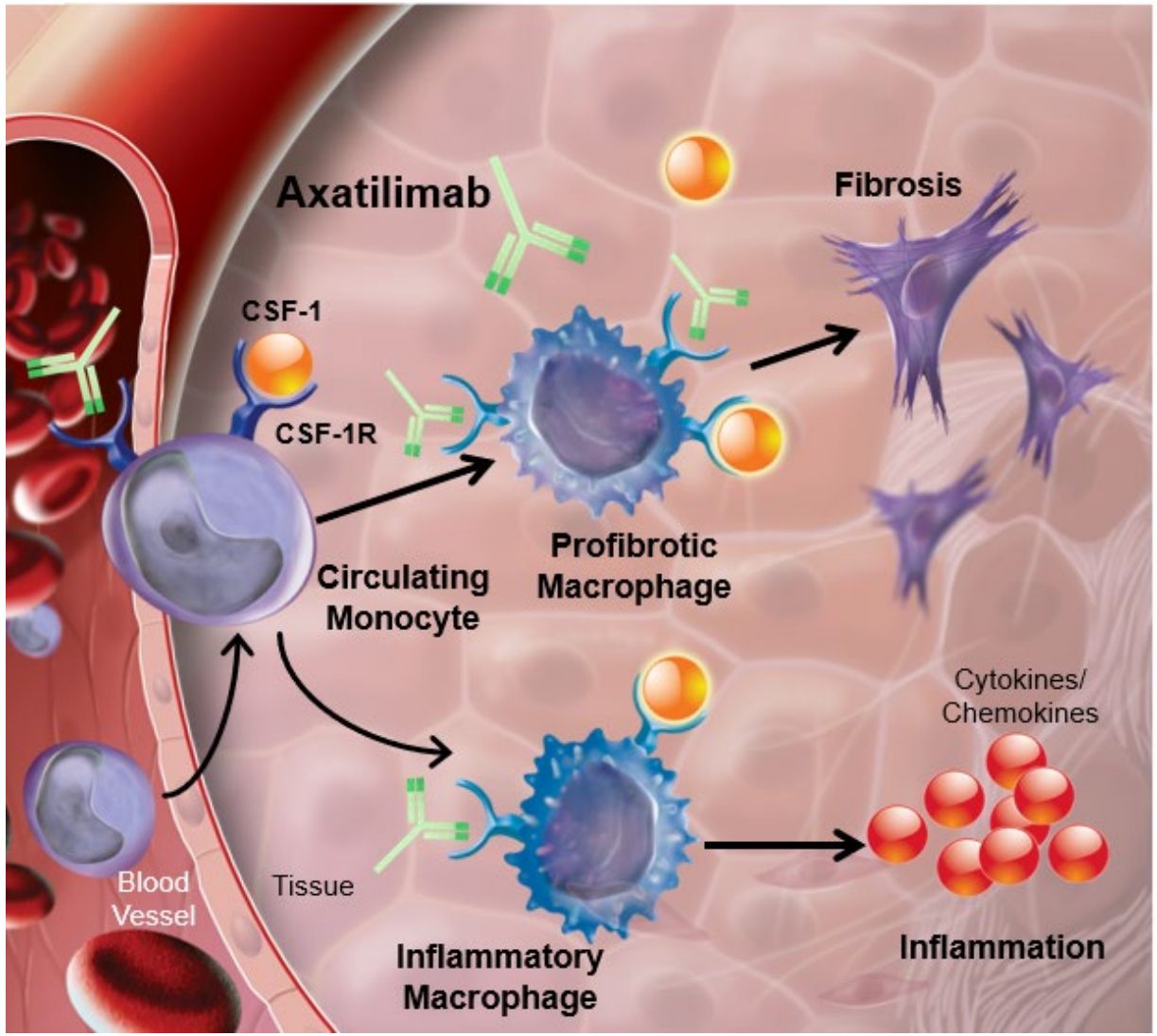
1. Arai et al. *Biol Blood Marrow Transplant.* 2015;21:266-274. **2.** Arora et al. *Biol Blood Marrow Transplant.* 2016;22:449-455. **3.** Velickovic et al. *Ther Adv Hematol.* 2020;11:1-18. **4.** Wood et al. *Bone Marrow Transplant.* 2013;48:1429-1436. **5.** Yu et al. *Cancer Med.* 2023;12:3623-3633. **6.** Lee et al. *Biol Blood Marrow Transplant.* 2018;24:555-562.

Axatilimab Targets Key Mediators of cGVHD Pathology

- CSF-1R–dependent monocytes and macrophages mediate inflammation and fibrosis[1,2]
- Axatilimab is an investigational monoclonal antibody that targets CSF-1R on monocytes and macrophages[2]
- Axatilimab has shown favorable safety and promising efficacy in recurrent/refractory cGVHD, with an ORR of 67% in the first 6 cycles[2]

cGVHD, chronic graft-versus-host disease; CSF-1R, colony-stimulating factor 1 receptor; ORR, overall response rate.

Axatilimab Mechanism of Action[1-3]

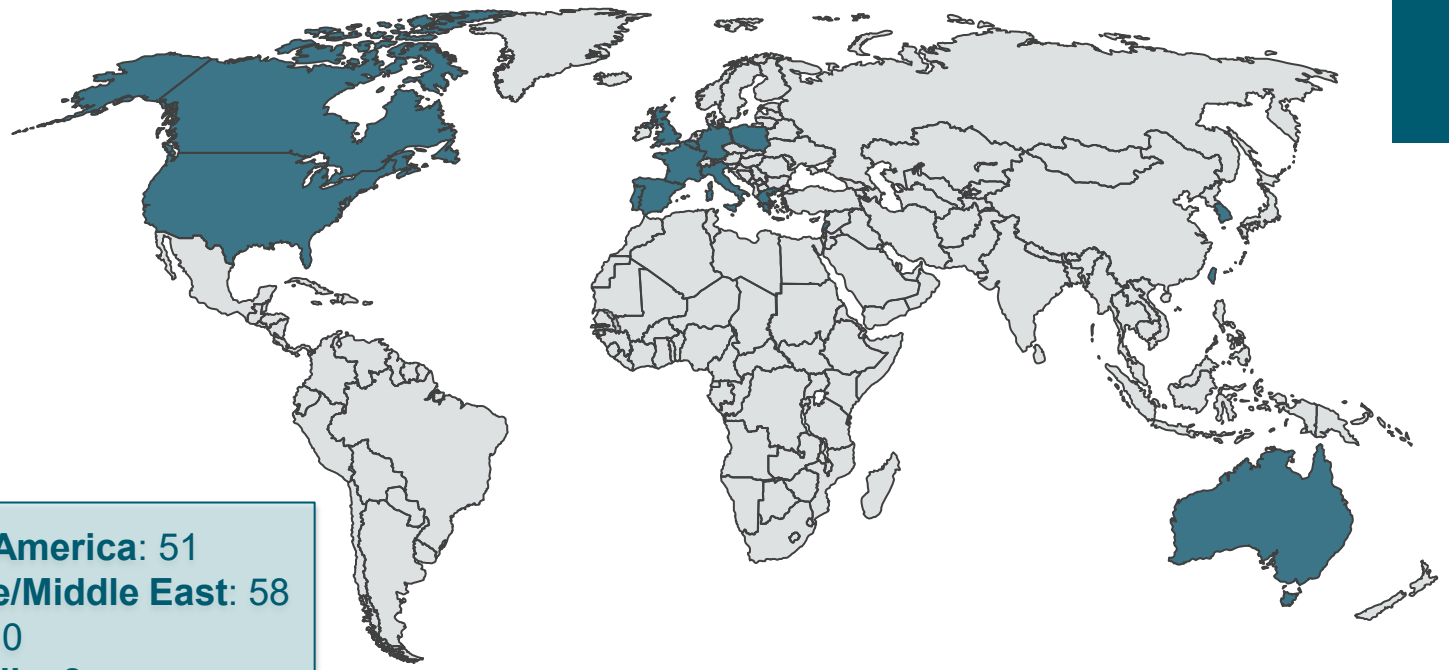


1. MacDonald et al. *Blood.* 2017;129:13-21. **2.** Kitko et al. *J Clin Oncol.* 2022;41:1864-1875. **3.** Jardine et al. *J Clin Invest.* 2020;130:4574-4586.

AGAVE-201: Study Design and Methods

Phase 2 study evaluated safety and efficacy of axatilimab in patients with cGVHD[1]

121 Global Study Sites



North America: 51
Europe/Middle East: 58
Asia: 10
Australia: 2

Randomization
3 axatilimab doses[a]
N=241

- **0.3 mg/kg Q2W**
  n=80
- **1.0 mg/kg Q2W**
  n=81
- **3.0 mg/kg Q4W**
  n=80

Q2W, every 2 weeks; Q4W, every 4 weeks.
[a]Patients were randomized 1:1:1 and stratified by severity of cGVHD and prior use of ibrutinib, ruxolitinib, or belumosudil.

1. ClinicalTrials.gov. https://www.clinicaltrials.gov/study/NCT04710576. Accessed October 13, 2023.

AGAVE-201: Study Design and Methods

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 corticosteroids (65%), calcineurin inhibitors (28%), or mTOR inhibitors (12%) was allowed but not required
- No additional systemic cGVHD therapy was allowed

Primary endpoint

- ORR in the first 6 cycles as defined by NIH 2014 Consensus Criteria[1]
- Endpoint was met if lower bound of 95% CI >30%

Secondary and exploratory endpoints

- Clinically meaningful improvement in mLSS (≥7 points)
- Organ-specific response rates, DOR, FFS, OS
- Safety

DOR, duration of response; FFS, failure-free survival; mLSS, modified Lee Symptom Scale; mTOR, mammalian target of rapamycin; NIH, National Institutes of Health; OS, overall survival.

1. Jagasia et al. *Biol Blood Marrow Transplant.* 2015;21:389-401.

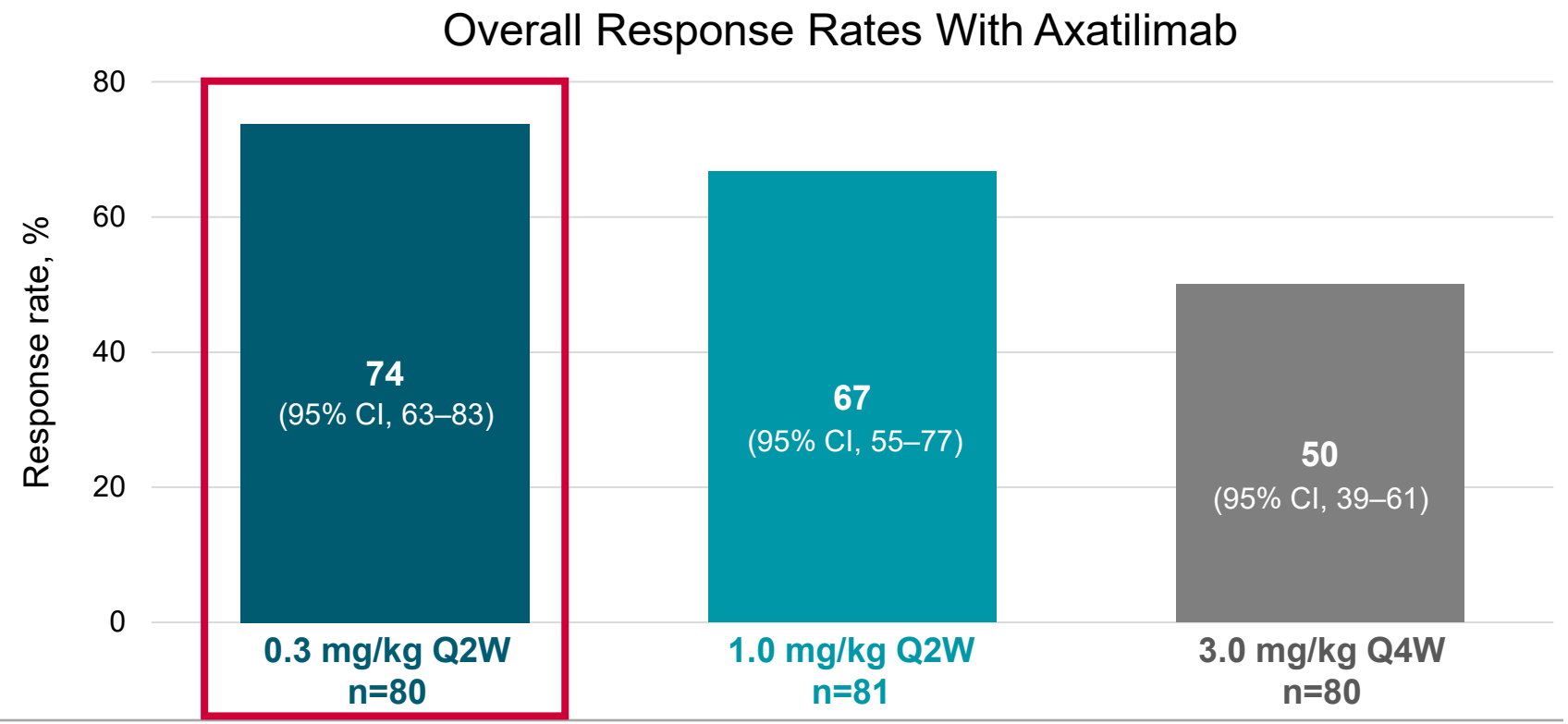
Baseline Characteristics (ITT Population)

Patient characteristic	Total cohort (N=241)
Age, median (min, max), y	53 (7, 81)
Sex, male, n (%)	151 (63)
Race, White, n (%)	200 (83)
Time from cGVHD diagnosis to randomization, median (max), y	4 (18)
Patients with severe disease, n (%)	192 (80)
Number of organs involved at baseline, median (max)	4 (8)
≥ 4 organs involved, n (%)	130 (54)
Number of prior systemic cGVHD therapies, median (max)	4 (15)
Refractory to last prior cGVHD treatment,[a] n (%)	132 (55)
Prior ibrutinib, ruxolitinib, and/or belumosudil, n (%)	204 (85)
Prior ibrutinib, n (%)	75 (31)
Prior ruxolitinib, n (%)	179 (74)
Prior belumosudil, n (%)	56 (23)

Patient characteristics were well balanced among cohorts

ITT, intention to treat. [a]Defined as patients with a best response to last prior treatment of no change or progressive disease reported at baseline.

Primary Efficacy Endpoint[a] Met in All Cohorts

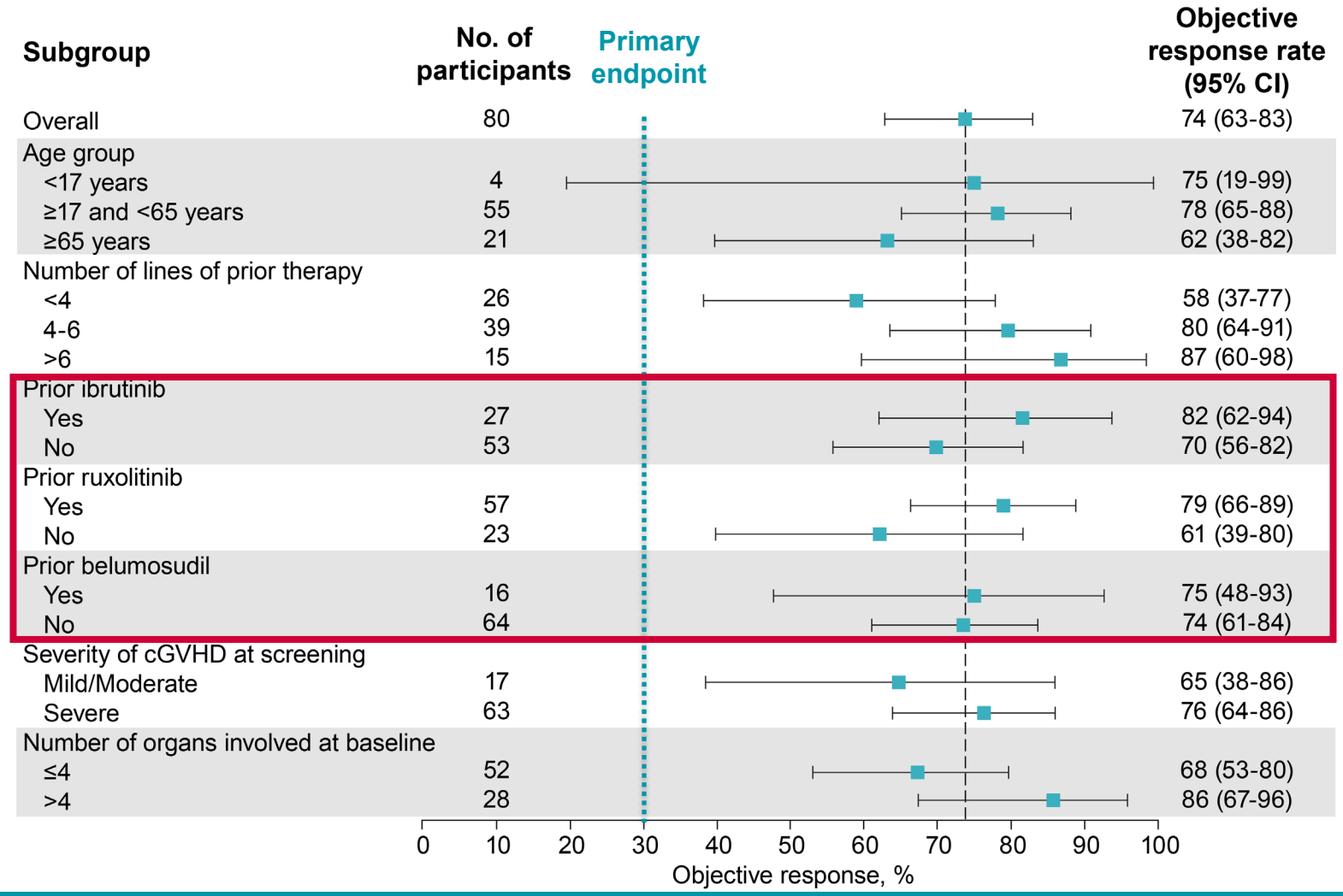


	0.3 mg/kg Q2W n=80	1.0 mg/kg Q2W n=81	3.0 mg/kg Q4W n=80
Time to response, median months (range)	1.7 (0.9–8.1)	1.9 (0.9–8.6)	1.4 (0.9–5.6)
Response maintained for ≥12 months, % (95% CI)	60 (43–74)	60 (43–74)	53 (30–71)

Q2W, every 2 weeks; Q4W, every 4 weeks.
[a]Primary endpoint was overall response rate in the first 6 cycles as defined by NIH 2014 Consensus Criteria[1]

1. Lee at al. *Biol Blood Marrow Transplant*. 2015;21:984-999.

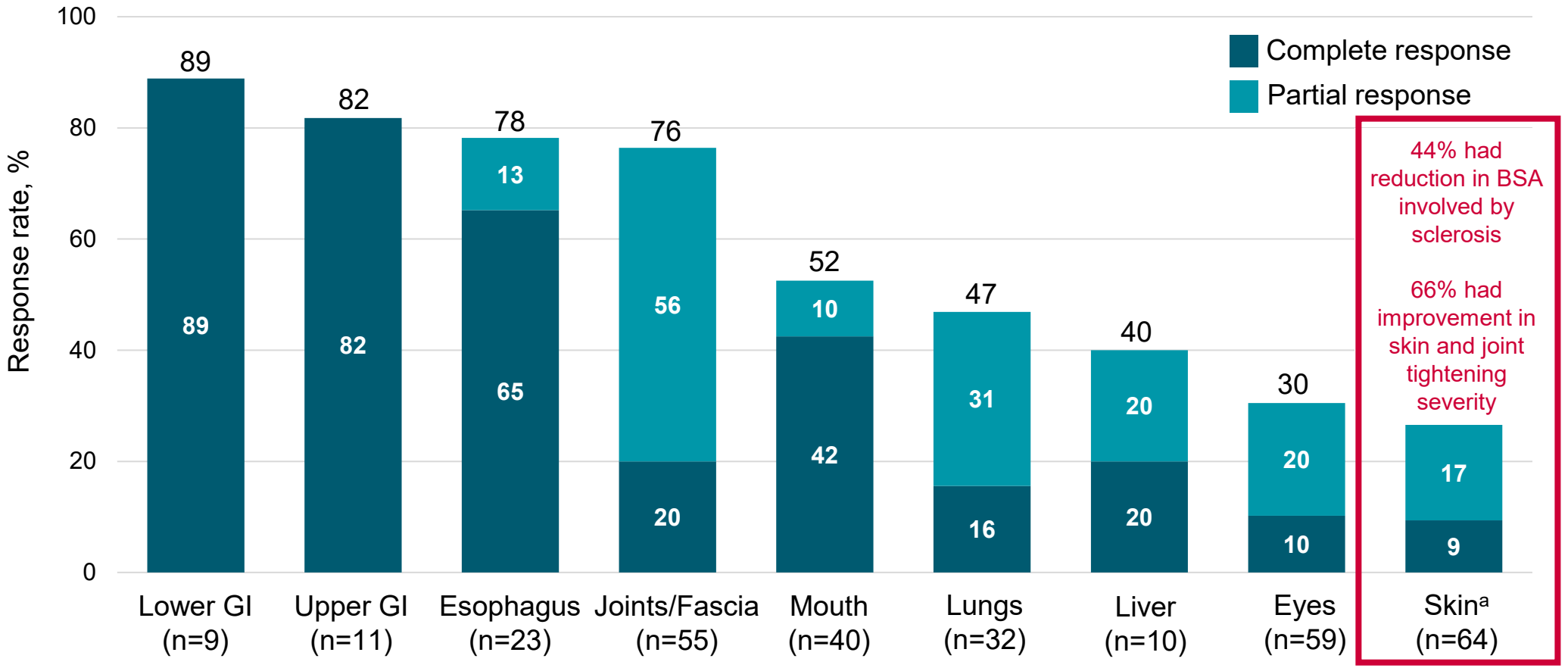
Efficacy Across Subgroups in 0.3 mg/kg Q2W



High response rates (≥75%) were seen in patients who received prior FDA-approved therapies

Q2W, every 2 weeks.

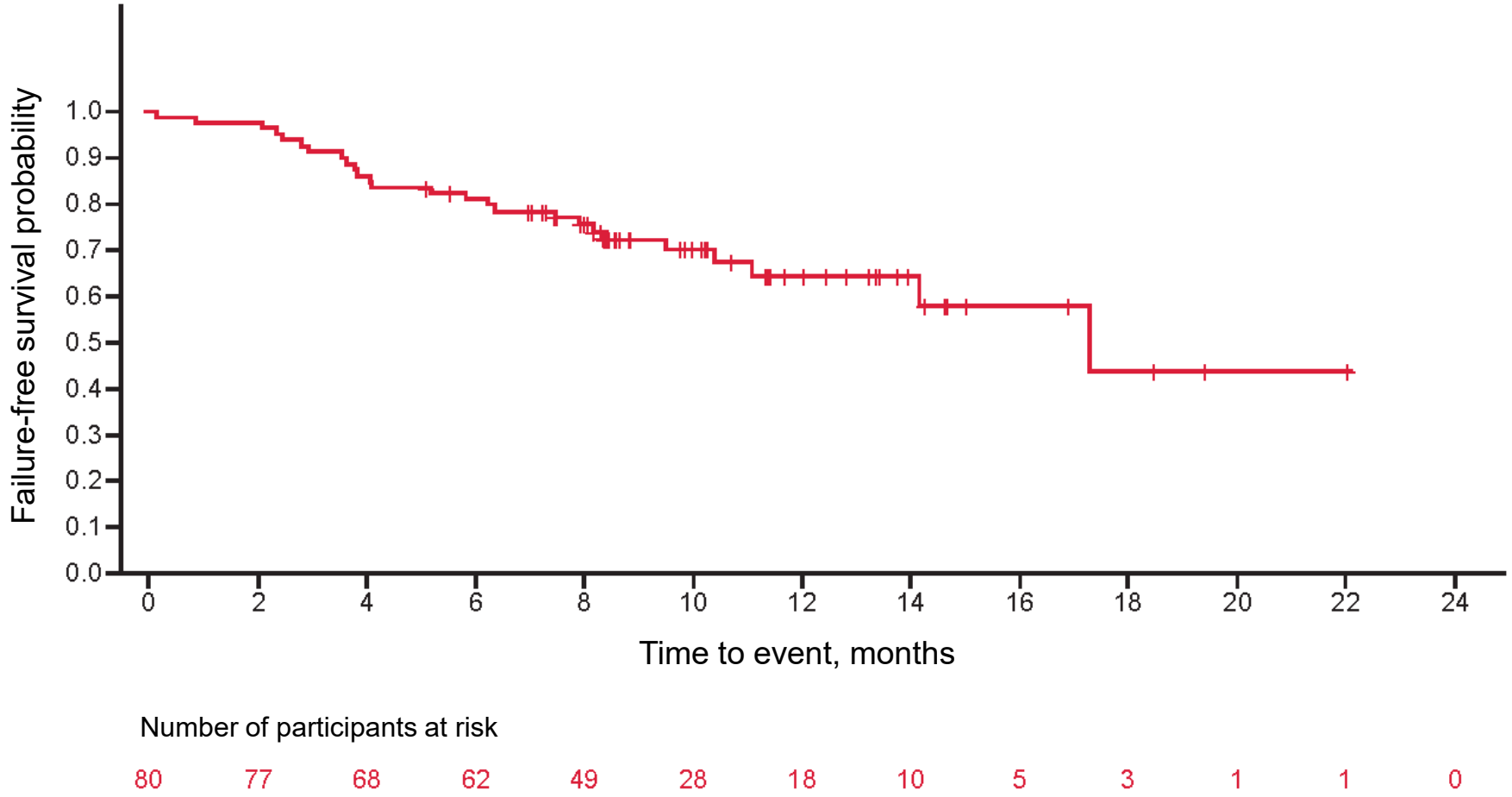
Organ Responses in 0.3 mg/kg Q2W



Responses were notable in fibrosis-dominated organs, including esophagus (78%), joints and fascia (76%), lung (47%), and skin (27%)

BSA; body surface area; GI, gastrointestinal; Q2W, every 2 weeks. [a]Due to rounding, complete response and partial response numbers may not add up to total response rate.

Failure-free Survival[a] in 0.3 mg/kg Q2W

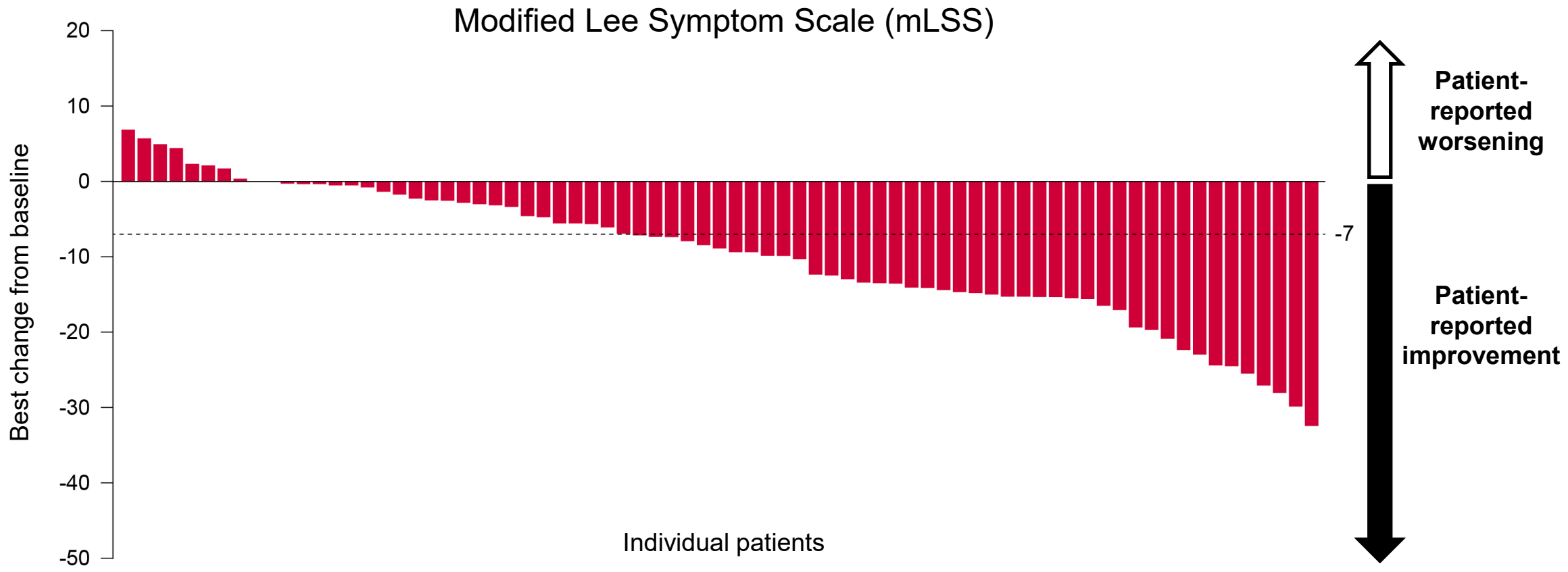


Median FFS was 17.3 (95% CI, 14.2–NE) months

NE, not estimable; Q2W, every 2 weeks.

[a]Defined as time from randomization to death or new systemic cGVHD therapy, where axatilimab dose increase is not considered new therapy.

Patient-Reported Symptom Burden Change in 0.3 mg/kg Q2W



- 55% clinically meaningful change of ≥7-point improvement in mLSS
- Median time to ≥7-point mLSS improvement was 1.5 months
- 73% had improved mLSS skin thickened score from baseline

Q2W, every 2 weeks.

Axatilimab Safety Profile

	Axatilimab 0.3 mg/kg Q2W n=79	Axatilimab 1.0 mg/kg Q2W n=81	Axatilimab 3.0 mg/kg Q4W n=79
Axatilimab dose changes owing to AE, n (%)			
Discontinuation	5 (6.3)	18 (22.2)	14 (17.7)
Dose decrease	5 (6.3)	6 (7.4)	13 (16.5)
Any grade AE in ≥20% of total patients			
Fatigue	18 (22.8)	16 (19.8)	21 (26.6)
Headache	15 (19.0)	14 (17.3)	16 (20.3)
Periorbital edema	2 (2.5)	19 (23.5)	23 (29.1)
COVID-19	13 (16.5)	18 (22.2)	11 (13.9)
Laboratory-based abnormalities			
AST increase	11 (13.9)	31 (38.3)	43 (54.4)
CPK increase	9 (11.4)	26 (32.1)	49 (62.0)
Lipase increased	9 (11.4)	21 (25.9)	39 (49.4)
Lactate dehydrogenase increased	11 (13.9)	22 (27.2)	32 (40.5)
ALT increase	10 (12.7)	18 (22.2)	31(39.2)
Amylase increase	3 (3.8)	10 (12.3)	34 (43.0)
At least 1 related Grade ≥3 AE, n (%)	14 (17.7)	28 (34.6)	37 (46.8)
Fatal AE	1 (1.3)[a]	7 (8.6)[b]	6 (7.6)[c]

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, blood creatine kinase; Q2W, every 2 weeks; Q4W, every 4 weeks. [a]Dyspnea. [b]Sudden cardiac death, bronchopulmonary aspergillosis, pneumonia (n=2), sepsis, leukemia recurrent, respiratory failure. [c]Leukemia recurrent, dyspnea, respiratory failure, shock hemorrhagic, neutropenic sepsis, pneumonia.

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
- Adverse events were mostly low grade, reversible, and increased with higher doses, with no unexpected safety concerns
- Unique mechanism of action may represent a new therapeutic strategy in cGVHD

Q2W, every 2 weeks.

Acknowledgements

- All study patients, their families, and caregivers for participating in this study
- Study teams at the individual sites
- Syndax Pharmaceuticals, Inc., and Incyte Corporation for funding the study

Questions?

For a plain language summary of the presentation, please see: