

Histology Outcomes Over Time in Patients With Moderately to Severely Active Ulcerative Colitis Treated With Guselkumab in the QUASAR Long-Term Extension Study

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Background and Objective



Although histologic outcomes are frequently reported in clinical trials of moderately to severely active ulcerative colitis (UC), long-term changes over multiple years are not well characterized

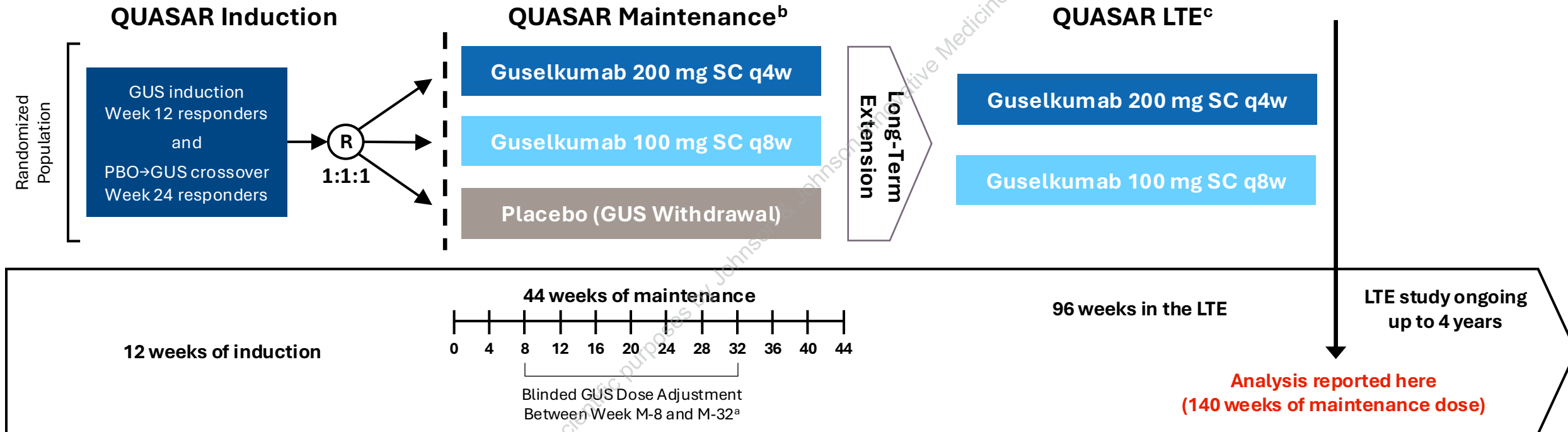


Guselkumab (GUS), a dual-acting interleukin (IL)-23p19 subunit inhibitor that potently neutralizes IL-23 and binds to CD64 (a receptor on cells that produce IL-23), is highly efficacious in UC



Objective: This post hoc analysis presents histology outcomes of GUS treatment in patients with moderately to severely active UC through 3 years of the phase 3 QUASAR study

QUASAR Study Design



^aRandomized patients meeting loss of clinical response criteria (based on the mMayo score and required an endoscopic assessment) were eligible for a blinded dose adjustment as follows: PBO SC → GUS 200 mg SC q4w; GUS 100 mg SC q8w → GUS 200 mg SC q4w; GUS 200 mg SC q4w → GUS 200 mg SC q4w (sham adjustment). ^bPatients who completed the safety and efficacy evaluations (including the required endoscopy procedure) at maintenance Week M-44 and who may benefit from continued study intervention, in the opinion of the investigator, had the opportunity to participate in the LTE of the maintenance study. ^cThe study blinding was maintained during the LTE until the last patient in the maintenance study completed the M-44 visit. After the maintenance study was unblinded, patients had their study visits scheduled to coincide with their dose regimen (either q4w or q8w) and patients receiving PBO were terminated from study participation. LTE=long-term extension; M=maintenance; mMayo=modified Mayo; PBO=placebo; q4w=every 4 weeks; q8w=every 8 weeks; SC=subcutaneous.

Endpoints and Statistical Considerations

Sankey diagrams of Geboes score categories were created for patients randomized to GUS in the maintenance study, continued in the LTE study, and had Geboes score evaluations at all timepoints from induction baseline through M-140 (100 mg q8w or dose adjusted, N=137; 200 mg q4w, N=130)

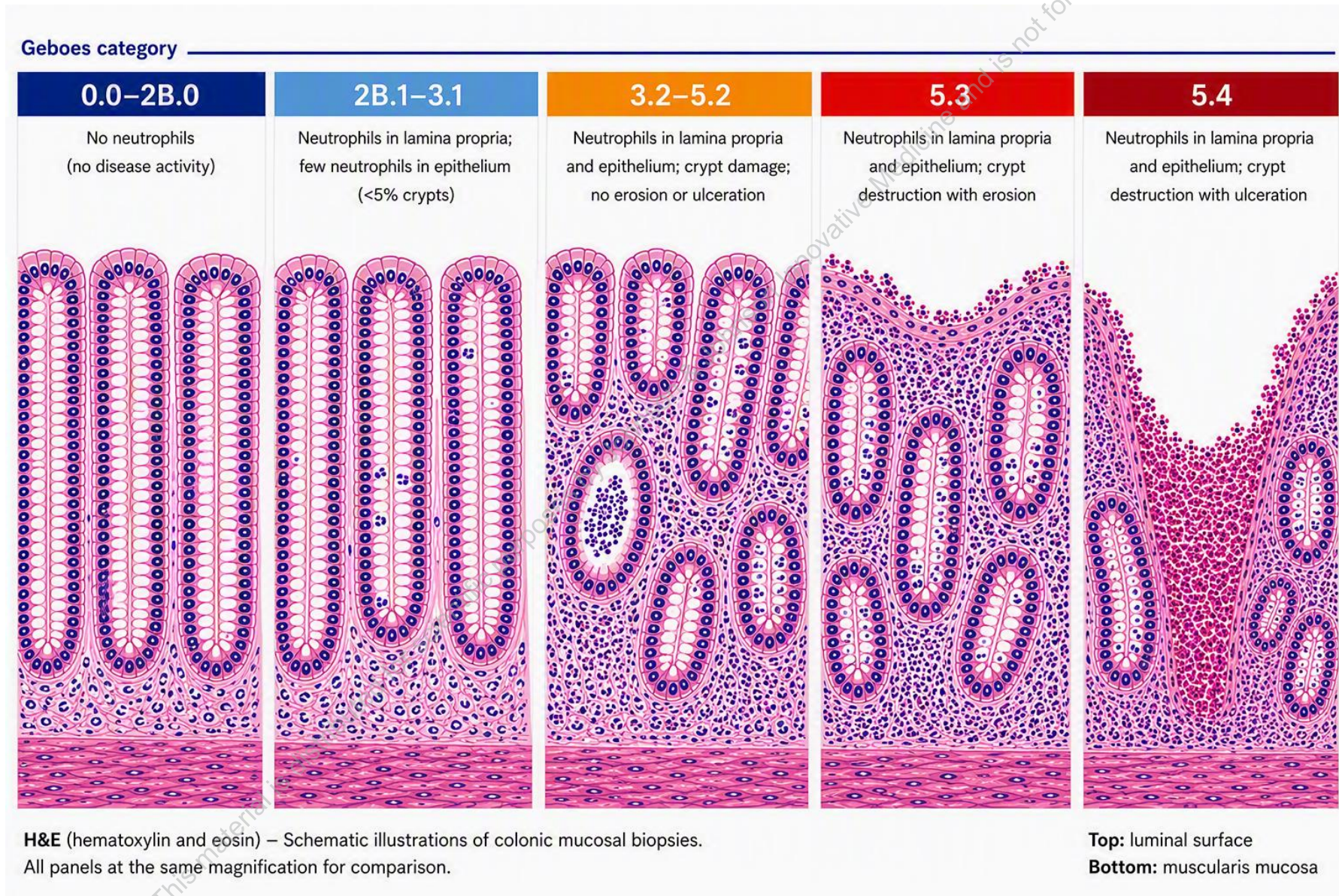
Geboes score categories

- 5.4: neutrophils in lamina propria and epithelium; crypt destruction with ulceration
- 5.3: neutrophils in lamina propria and epithelium; crypt destruction with erosion of the surface epithelium
- 3.2-5.2: neutrophils in lamina propria and epithelium; varying degrees of crypt damage, possibly including surface epithelium; no erosion or ulceration
- 2B.1-3.1: neutrophils in lamina propria, few neutrophils in epithelium in <5% of crypts
- 0.0-2B.0: no neutrophils (no disease activity)

Statistical considerations

- Patients who had an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an adverse event of worsening UC before the designated post-maintenance baseline timepoint had their induction baseline value carried forward from the time of the event onward
- For patients who discontinued study agent for any other reason before the designated post-maintenance baseline timepoint, their observed values were used, if available
- After accounting for these events, patients missing any histology components at any timepoint were excluded

Geboes Histologic Activity Categories



Induction Baseline Characteristics

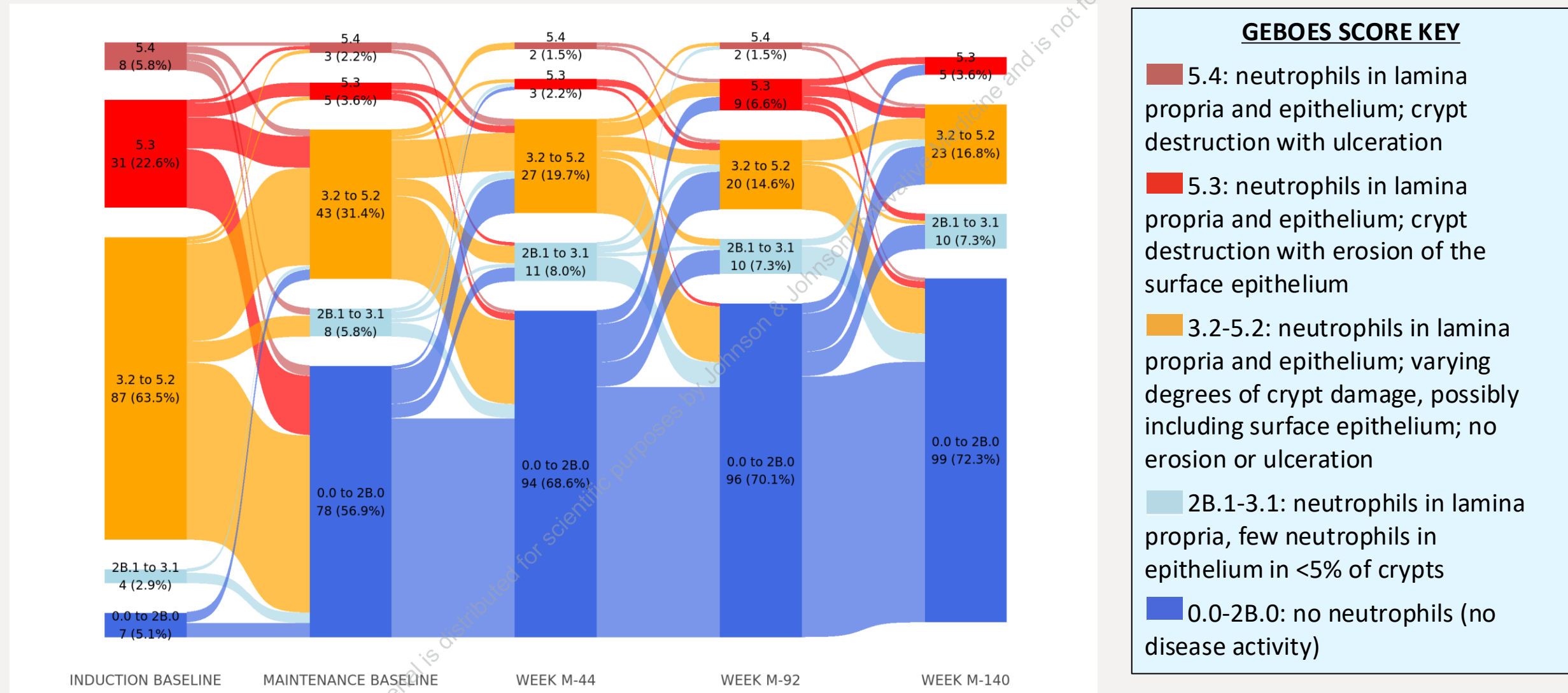
LTE Randomized Full Analysis Set

		Guselkumab	
		100 mg q8w N=155	200 mg q4w N=148
Demographics			
	Age, years, mean (SD)	40.2 (12.8)	40.6 (15.1)
	Male, n (%)	83 (53.5)	75 (50.7)
Disease Characteristics			
	UC disease duration, years, mean (SD)	8.2 (9.0)	8.2 (8.5)
	mMayo score (0-9), mean (SD)	6.8 (1.2)	6.9 (1.1)
	mMayo score of 7-9 (severe), n (%)	94 (60.6)	97 (65.5)
	C-reactive protein, mg/L, median (IQR)	4.0 (1.4-10.4) ^a	3.9 (1.5-9.5) ^b
	Fecal calprotectin, mg/kg, median (IQR)	1709.0 (815.0-3607.0) ^c	1605.5 (596.0-3253.0) ^d
	Prior inadequate response/intolerance to ADT, n (%)	60 (38.7)	62 (41.9)
	ADT-naïve, n (%)	90 (58.1)	81 (54.7)
Concomitant UC Medications			
	Oral corticosteroids, n (%)	56 (36.1)	54 (36.5)
	Immunomodulatory drugs, n (%)	39 (25.2)	36 (24.3)

^aN=153; ^bN=145; ^cN=133; ^dN=134. ADT=advanced therapy.

Geboes Score Categories Through 3 Years

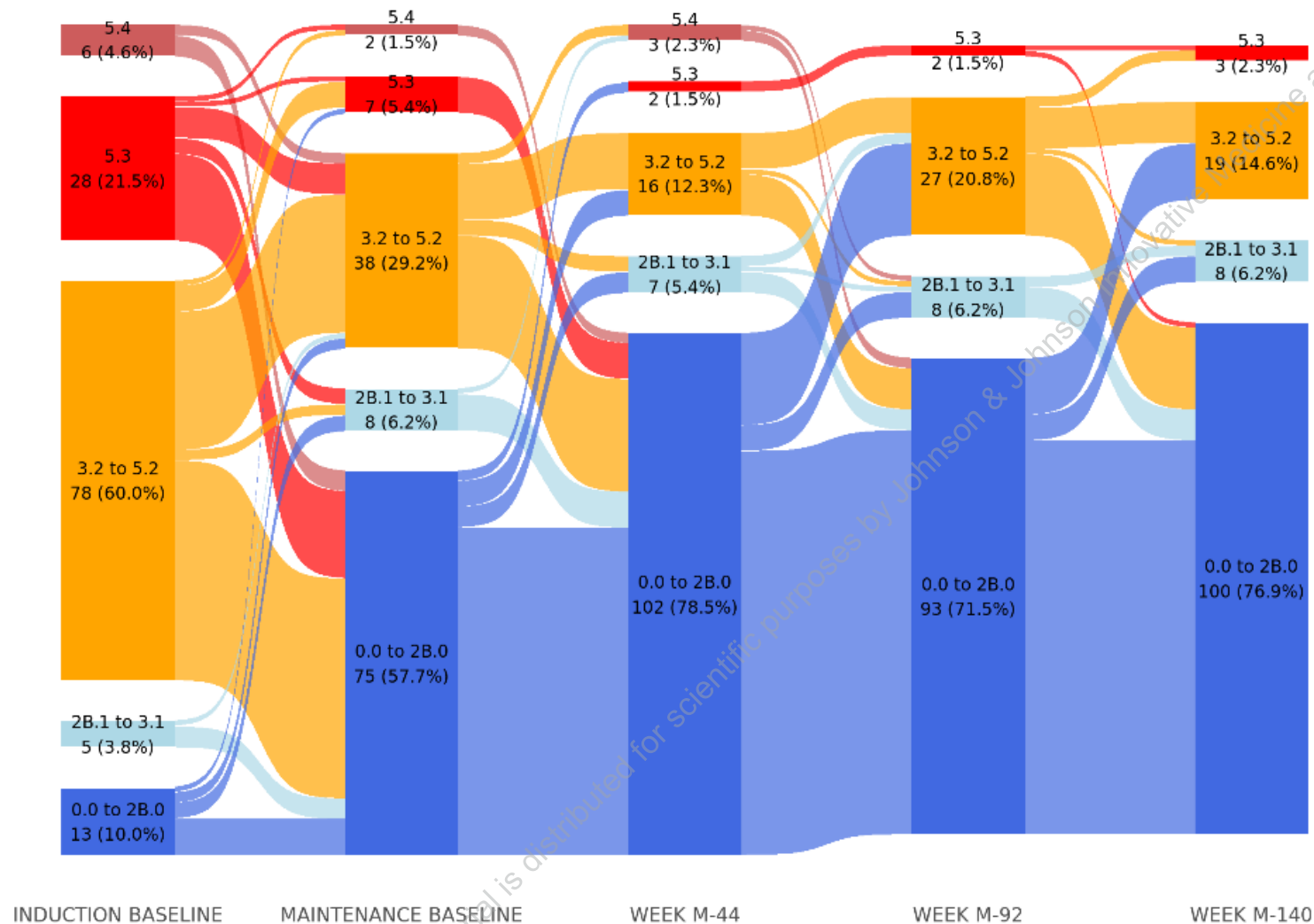
Guselkumab SC 100 mg q8w (n=131), or 200 mg q4w after dose adjustment (n=6)^a



^aSix of 137 patients (4.4%) had a dose adjustment to guselkumab SC 200 mg q4w.

Geboes Score Categories Through 3 Years

Guselkumab SC 200 mg q4w (n=130)



GEBOES SCORE KEY

5.4: neutrophils in lamina propria and epithelium; crypt destruction with ulceration

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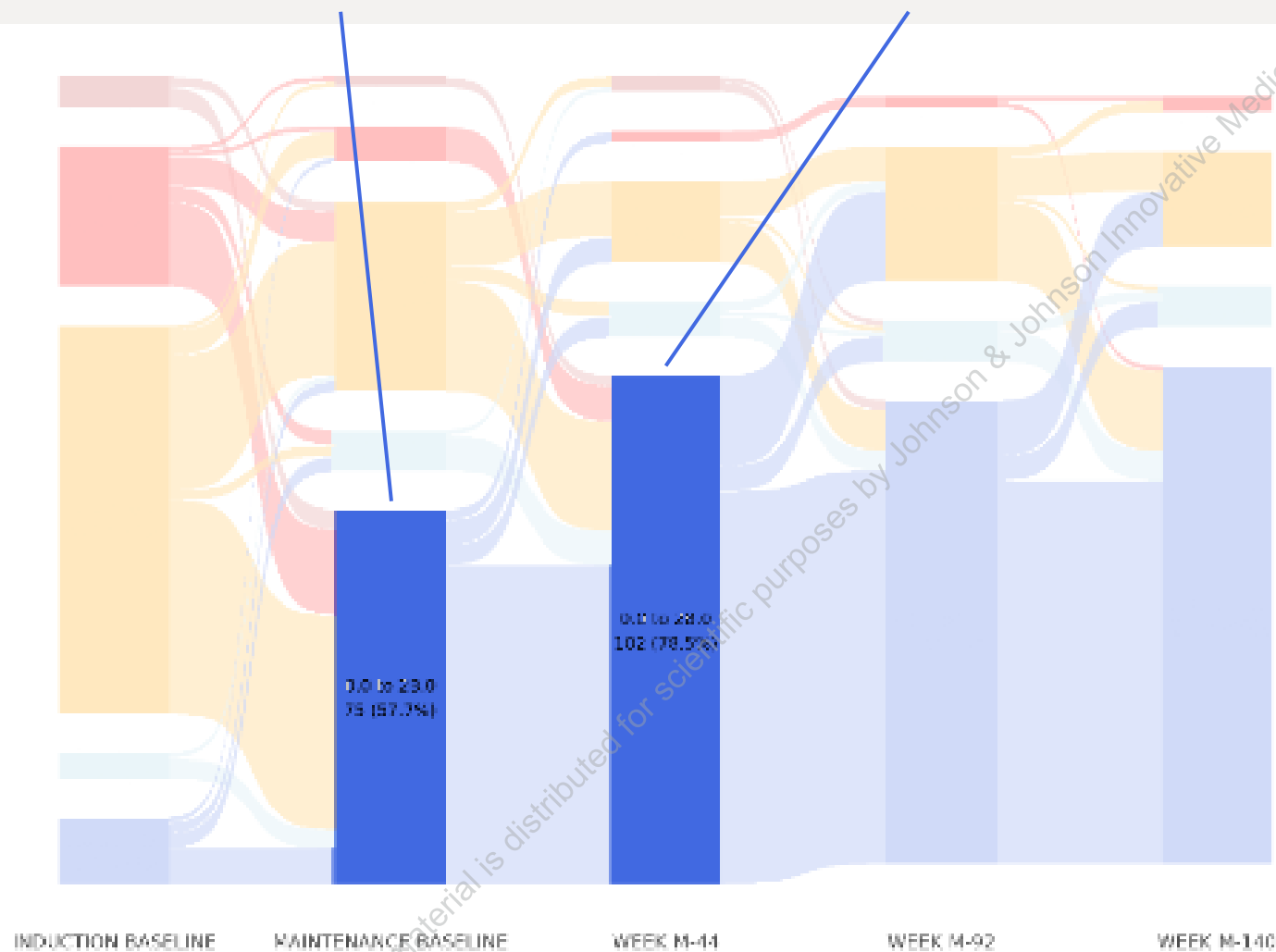
0.0-2B.0: no neutrophils (no disease activity)

Geboes Score Categories Through 3 Years

Guselkumab SC 200 mg q4w (n=130)

In histologic remission at M-0
75 patients

In histologic remission at M-44
102 patients



Maintenance of Histologic Remission

Guselkumab 100 mg SC q8w, or 200 mg q4w after dose adjustment^a

Most patients in remission at M-0 or M-44 were also in remission at M-140

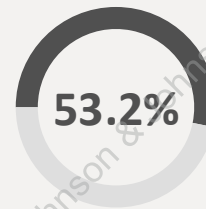
Starting cohort

Also at every follow-up visit

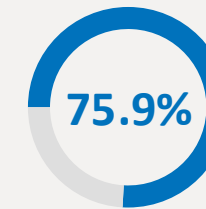
Also at Week M-140

Maintenance baseline (M-0)

79 patients in remission



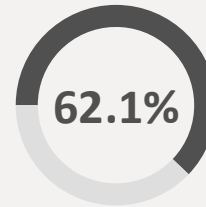
42/79 patients
M-44, M-92 and M-140



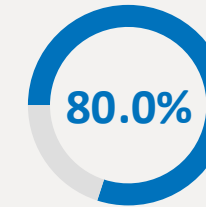
60/79 patients

Week M-44

95 patients in remission



59/95 patients
M-92 and M-140



76/95 patients

Histologic remission: Absence of neutrophils from the mucosa (both lamina propria and epithelium), no crypt destruction, and no erosions, ulcerations, or granulation tissue

^aSix of 137 patients (4.4%) had a dose adjustment to guselkumab SC 200 mg q4w.

Maintenance of Histologic Remission

Guselkumab 200 mg SC q4w

Most patients in remission at M-0 or M-44 were also in remission at M-140

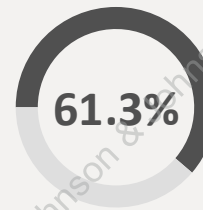
Starting cohort

Also at every follow-up visit

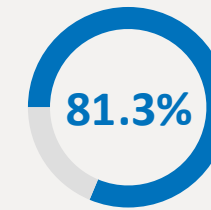
Also at Week M-140

Maintenance baseline (M-0)

75 patients in remission



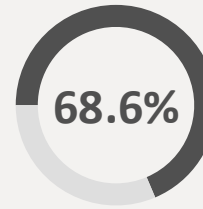
46/75 patients
M-44, M-92 and M-140



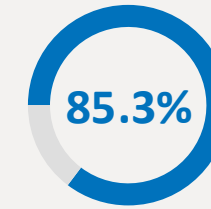
61/75 patients

Week M-44

102 patients in remission



70/102 patients
M-92 and M-140



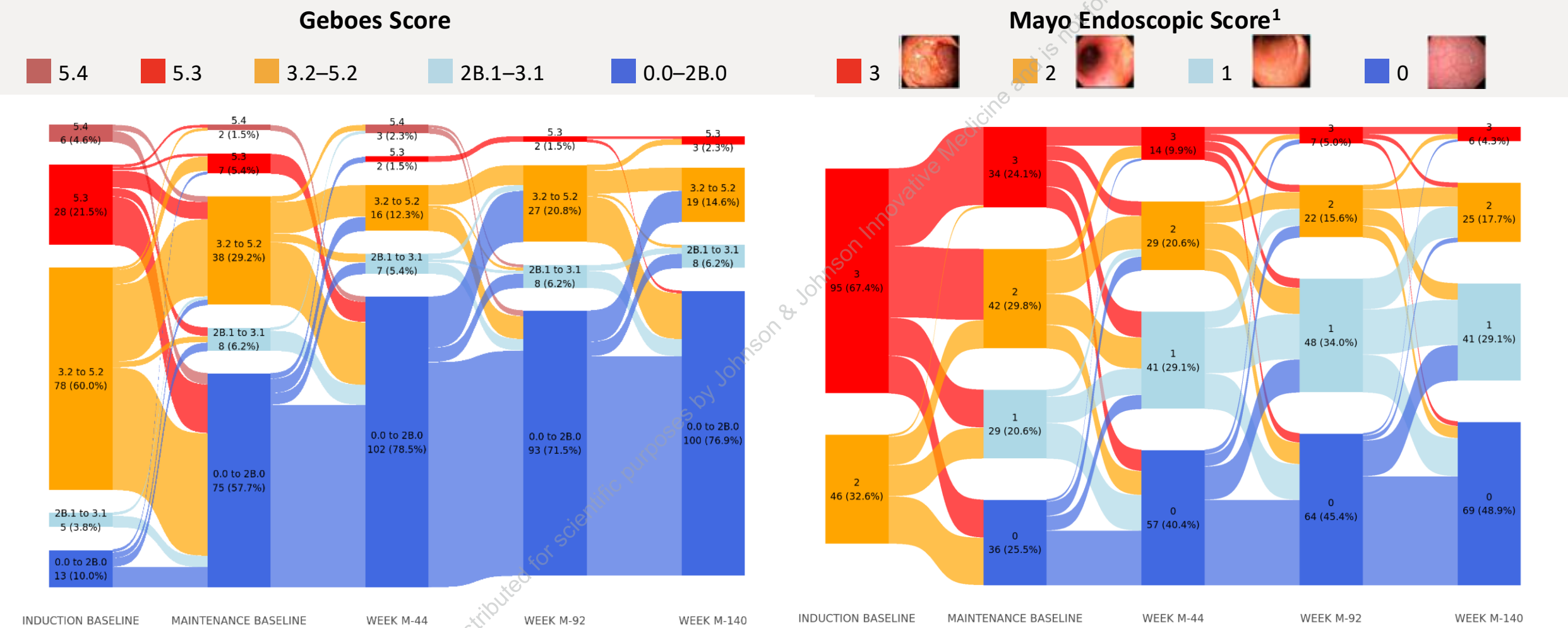
87/102 patients

Results refer to the specified visits, not continuous remission between visits. M-0 is maintenance baseline.

Histologic remission: Absence of neutrophils from the mucosa (both lamina propria and epithelium), no crypt destruction, and no erosions, ulcerations, or granulation tissue

Similar Histology and Endoscopy Improvement Trends Over Time

Guselkumab SC 200 mg q4w

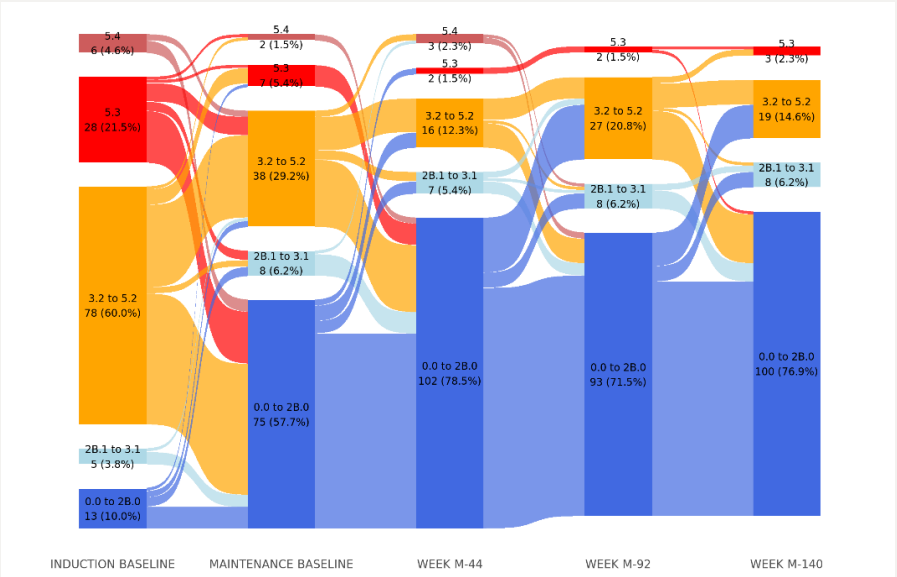


1. Rubin D, et al. *Gastrointestinal Endoscopy*. 2026;103:S1166-S1167.e

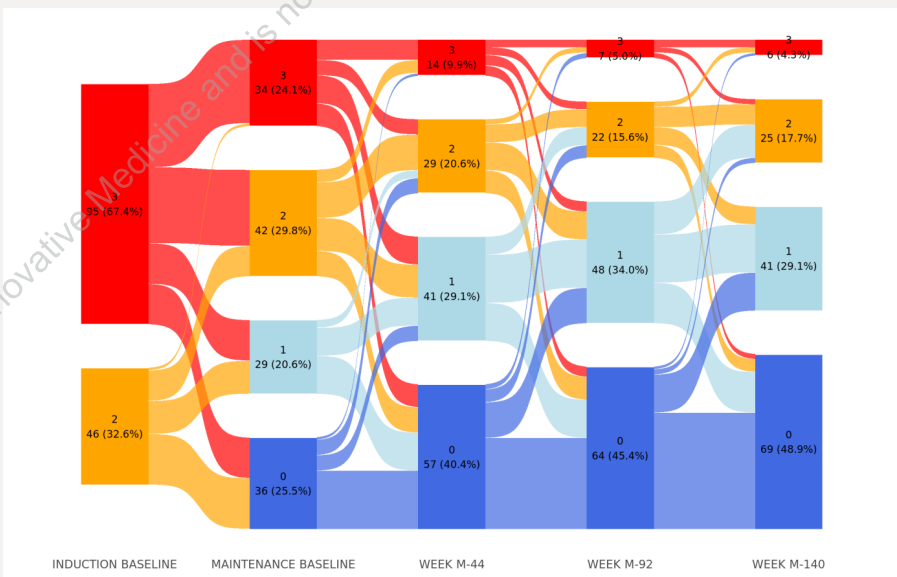
Histology, Endoscopy, and Symptom Trends Over Time

Guselkumab SC 200 mg q4w

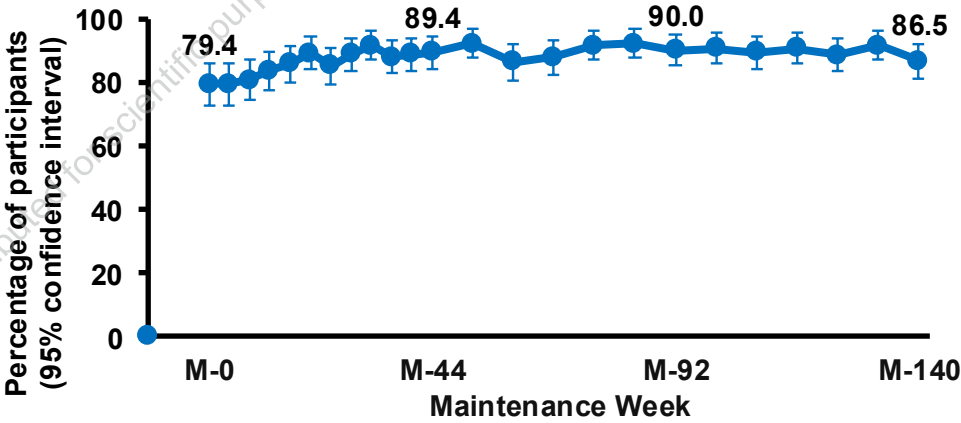
Geboes Score



Mayo Endoscopic Score¹



Symptomatic Remission



—●— Guselkumab 200 mg q4w
n=141

Symptomatic Remission: Stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0, where the stool frequency subscore has not increased from induction baseline

1. Rubin D, et al. *Gastrointestinal Endoscopy*. 2026;103:S1166-S1167.e

Key Takeaways



Both guselkumab maintenance doses were associated with histologic improvements over 3 years



Although approximately 40% of induction clinical responders had moderate to severe histologic disease activity (Geboes score=3.2-5.4) at the beginning of maintenance, histologic improvement was observed after 1 year of guselkumab maintenance treatment and it was generally maintained during long-term extension through 3 years



Histology improvement trends over time were similar to previously reported endoscopy improvement trends over time¹

Acknowledgments

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Disease Characteristics at Maintenance Baseline

	GUS 100 mg SC q8w N=188	GUS 200 mg SC q4w N=190
Clinical remission,^a n (%)	66 (35.1)	69 (36.3)
Endoscopic improvement,^b n (%)	75 (39.9)	79 (41.6)
Endoscopic remission,^c n (%)	41 (21.8)	47 (24.7)
mMayo score (0-9), mean (SD)	2.6 (1.5)	2.5 (1.5)
C-reactive protein, median in mg/L (IQR)	1.4 (0.4; 4.0)	1.4 (0.6; 3.4)
Fecal calprotectin (mg/kg), median in mg/kg (IQR)	308.0 (71.0; 1310.0) ^d	281.0 (89.0; 1233.0) ^e

^aClinical remission was defined as a Mayo stool frequency subscore of 0 or 1 and not increased from baseline, a Mayo RBS of 0, and a Mayo endoscopy subscore of 0 or 1 with no friability; ^bEndoscopic improvement was defined as a Mayo endoscopy subscore of 0 or 1 with no friability; ^cEndoscopic remission was defined as a Mayo endoscopy subscore of 0; ^dN=185; ^eN=187.

IQR=interquartile range; SD=standard deviation.