

Unsupervised Machine Learning to Identify Distinct Patient-Level Response Patterns to Guselkumab in Ulcerative Colitis: Post Hoc Analysis from the ASTRO Trial

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Background

- Typically, ulcerative colitis (UC) trials report efficacy on a cohort level using binary endpoints (i.e., clinical remission, endoscopic improvement), aggregating outcomes of all participants at specified timepoints
- Analysis of individual longitudinal trends of efficacy based on participant-level clinical data provides a better understanding of response to treatment, and may help optimize personalized treatment in UC
- Artificial intelligence, including machine learning, may be useful in a clinical setting to possibly identify patterns and predictors of individual treatment response in patients with UC
- Guselkumab is a selective, dual-acting interleukin (IL)-23p19 subunit inhibitor that potently blocks IL-23 and binds to CD64, a receptor on immune cells that produce IL-23¹

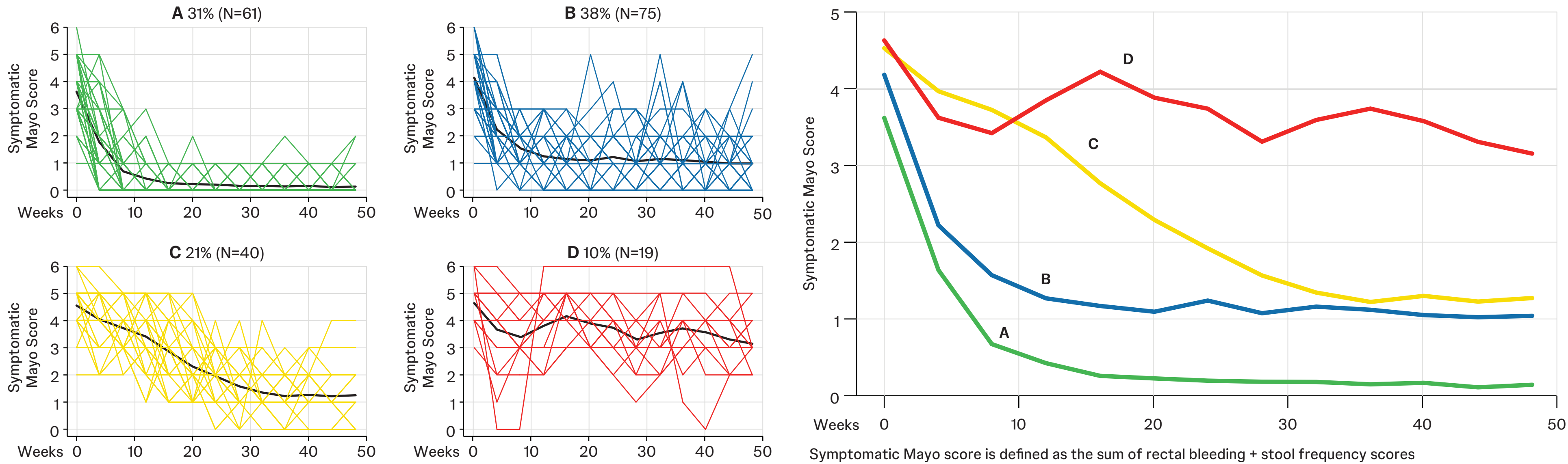
Objective

- To identify distinct subpopulations of guselkumab-treated participants with UC from the Phase 3 ASTRO study² based on the individual Symptomatic Mayo Score (SMS) response trajectories using unsupervised machine learning

Results

- Four distinct participant subpopulations (A-D) were detected by unsupervised machine learning, representing clusters with different SMS response dynamics (Figure 1)
- The clusters were arranged by greatest SMS response indicated by lower SMS scores (cluster A) to partial SMS response (cluster D):
 - A (N=61; 31% of participants), B (N=75; 38%), C (N=40; 21%), and D (N=19; 10%)

Figure 1. Four Distinct Clusters Identified by Unsupervised Machine Learning Using Symptomatic Mayo Scores From Baseline to Week 48



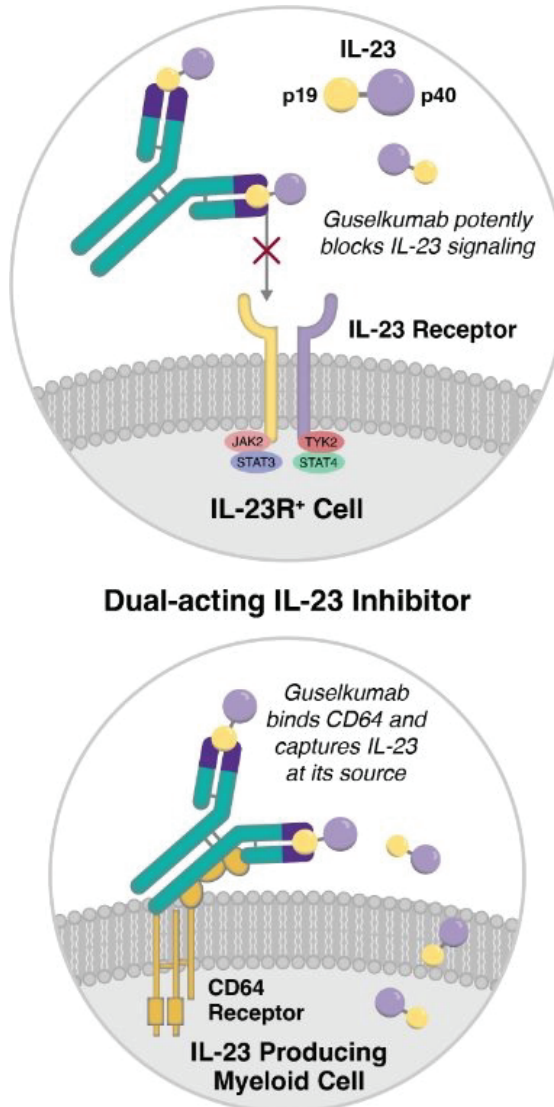
Only guselkumab-treated participants with Symptomatic Mayo Scores available at each of the 13 visits were included in the analysis (N=195).

- Baseline demographics and disease characteristics were similar among clusters, except that fewer participants in cluster A (13/61 [21.3%]) had a prior inadequate response or intolerance to advanced therapies (ADT) at baseline

Table 1. ASTRO identified clusters by baseline characteristics

	A (N=61)	B (N=75)	C (N=40)	D (N=19)	Overall (N=195)
Demographics					
Men, n (%)	35 (57.4%)	49 (65.3%)	23 (57.5%)	12 (63.2%)	119 (61.0%)
Age, years median (IQR)	43.0 (35.0 - 53.0)	43.0 (30.0 - 54.0)	44.5 (28.5 - 54.5)	44.0 (30.0 - 62.0)	44.0 (32.0 - 54.0)
White, n (%)	33 (54.1%)	48 (64.0%)	27 (67.5%)	11 (57.9%)	119 (61.0%)
Characteristics					
UC disease duration, years, median (IQR)	6.69 (2.62 - 13.75)	6.25 (2.43 - 13.95)	7.18 (3.35 - 9.71)	5.38 (2.97 - 9.49)	6.54 (2.55 - 12.41)
Modified Mayo Score, median (IQR)	6.0 (5.0-7.0)	7.0 (6.0-7.0)	7.0 (7.0-8.0)	7.0 (7.0-8.0)	7.0 (6.0-8.0)
ADT-IR, n (%)	13 (21.3%)	30 (40.0%)	18 (45.0%)	10 (52.6%)	71 (36.4%)
ADT naïve, n (%)	48 (78.7%)	44 (58.7%)	21 (52.5%)	9 (47.4%)	122 (62.6%)

ADT-IR=prior inadequate response or intolerance to advanced therapies (ADT), IQR=interquartile range, UC=ulcerative colitis.



Methods

- ASTRO was a randomized, double blind, treat-through, Phase 3 study in which participants with moderately to severely active UC were treated with subcutaneous (SC) guselkumab during induction and maintenance
- For these analyses, the guselkumab 100 mg and guselkumab 200 mg groups were combined
- An unsupervised machine learning approach with latent class trajectory modeling was applied using individual guselkumab-treated participants' SMS (the sum of rectal bleeding + stool frequency scores) from Week 0 (baseline) through Week 48
- Guselkumab-treated participants with SMS data available at all 13 timepoints were included (N=195) to analyze if participants separated into groups with similar SMS response dynamics
- The optimal number of clusters was determined by evaluating multiple clustering metrics
- Participant characteristics and clinical outcomes at Weeks 0 through 48 were evaluated for association with response patterns
- All post hoc analyses are descriptive

- Mayo endoscopic subscores (Figure 2), achievement of clinical remission (Figure 3), median fecal calprotectin levels (Figure 4), and median CRP levels (Figure 5) through Week 48 by predicted clusters are presented

Figure 2. Endoscopic Subscore of Mayo Score Through Week 48

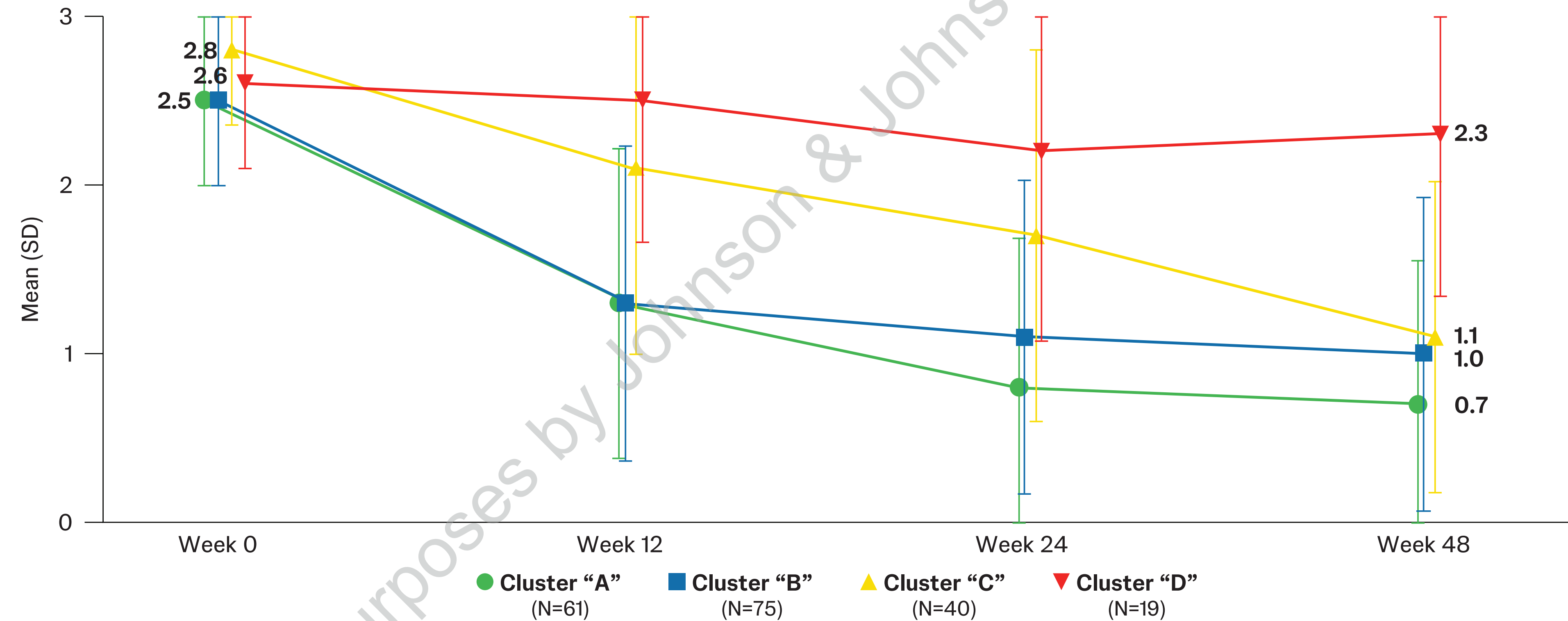
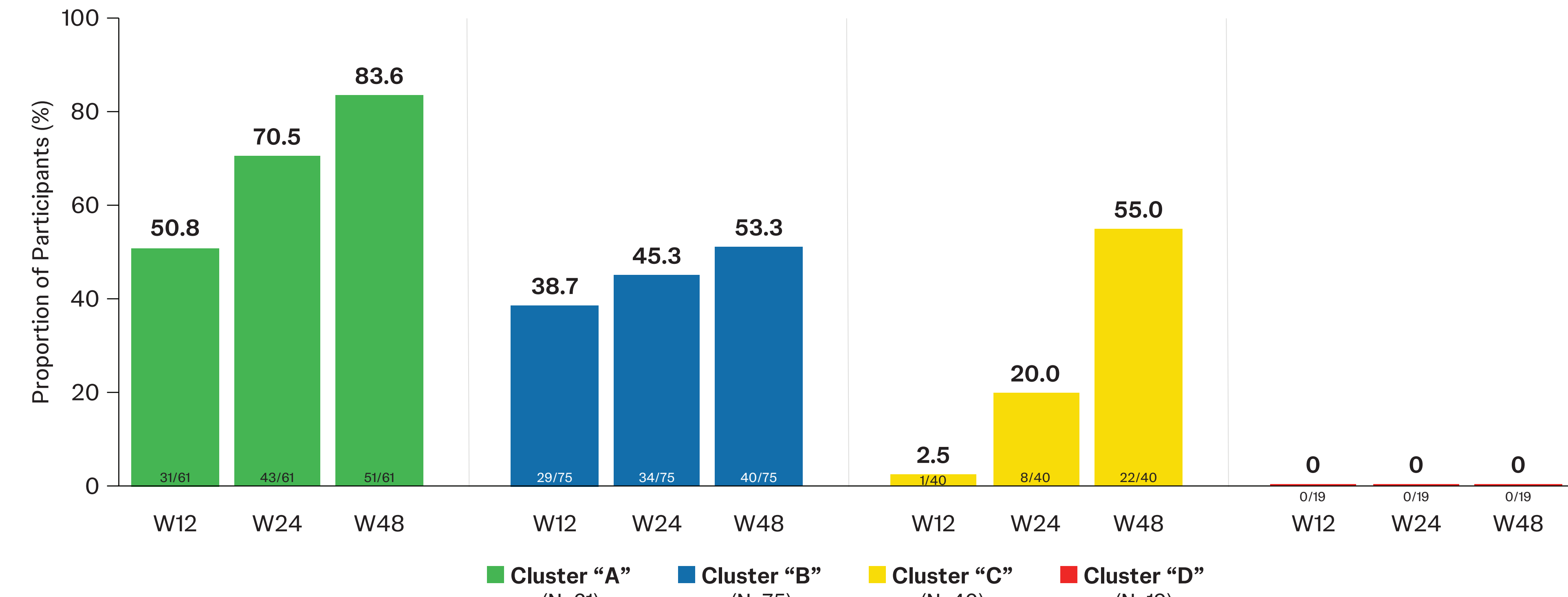
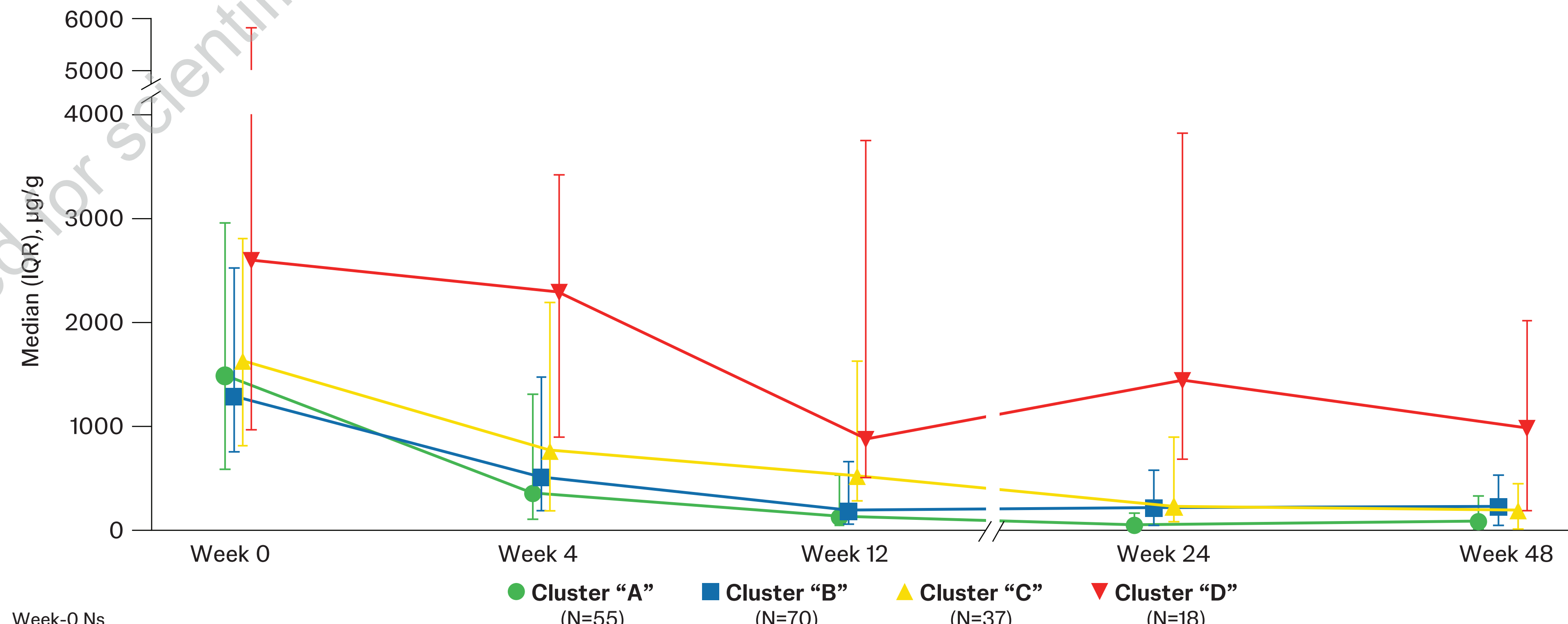


Figure 3. Participants in Clinical Remission Through Week 48



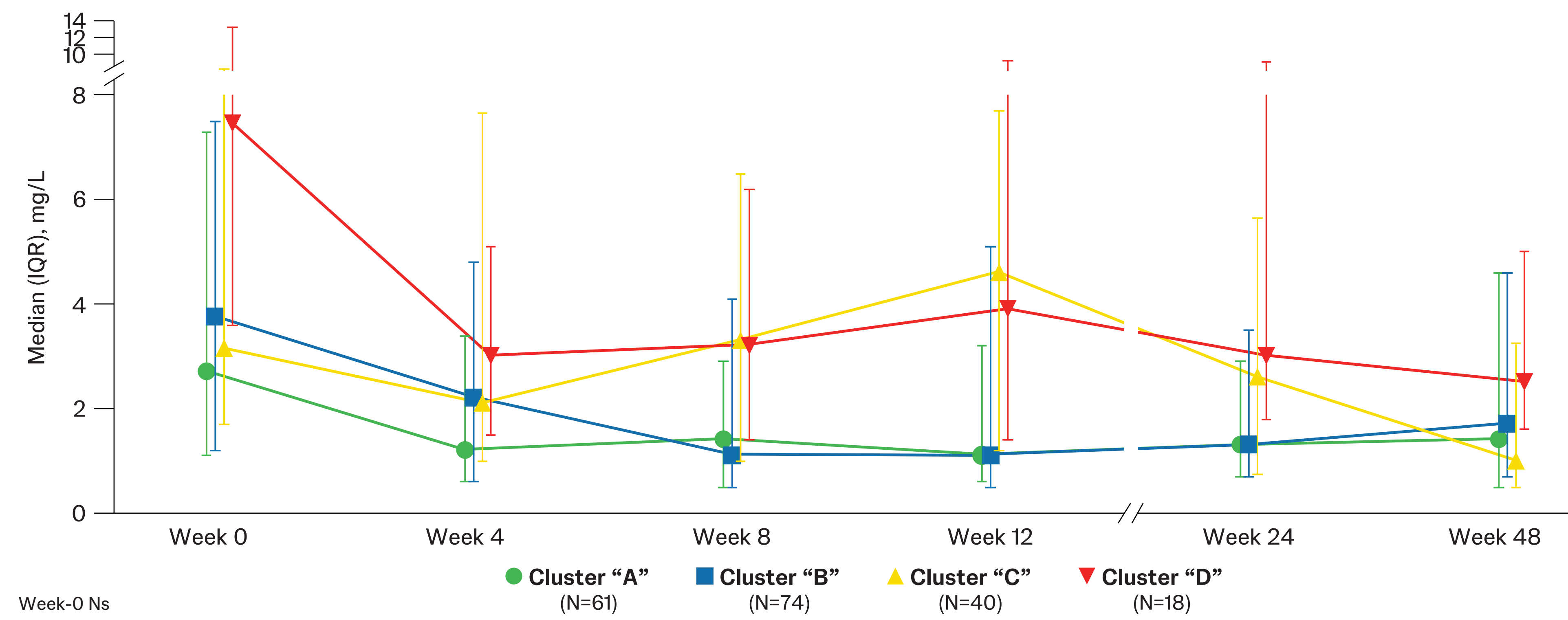
W=week. Clinical remission=a Mayo stool frequency subscore of 0 or 1 and not increased from baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1 with no friability present on the endoscopy.

Figure 4. Fecal Calprotectin Concentrations Through Week 48



Week-0 Ns
IQR=interquartile range. Ns vary because not all participants had samples available at each timepoint.

Figure 5. C-reactive Protein Concentrations Through Week 48



Week-0 Ns
IQR=interquartile range. Ns vary because not all participants had samples available at each timepoint.