Induction Combination Therapy with Guselkumab and Golimumab Followed by Guselkumab Monotherapy Maintenance: Results of the Phase 2a Randomized, Double-blind, Proof-of-concept VEGA Study

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Background and Objective

- Week (wk) 12 data from the Phase 2a VEGA proof-of-concept study demonstrated that dual blockade of interleukin (IL)-23 and tumor necrosis factor α (TNFα) more effectively induced clinical response, clinical remission, endoscopic improvement, and composite histologic-endoscopic outcomes than either monotherapy alone.[1]
- Guselkumab, an IL-23p19 subunit antagonist, is being studied in inflammatory bowel disease
- Golimumab, a TNFα antagonist, is approved for the treatment of ulcerative colitis
- Comparative efficacy and safety were evaluated through Week 38 in adults with moderately-to-severely active ulcerative colitis who received
  - Combination induction therapy with guselkumab plus golimumab followed by guselkumab for maintenance, or
  - Guselkumab or golimumab alone for induction and maintenance

[1]Sands B.E., et al. J Crohns Colitis. 2022;16: i042-i043. Abstract OP36.

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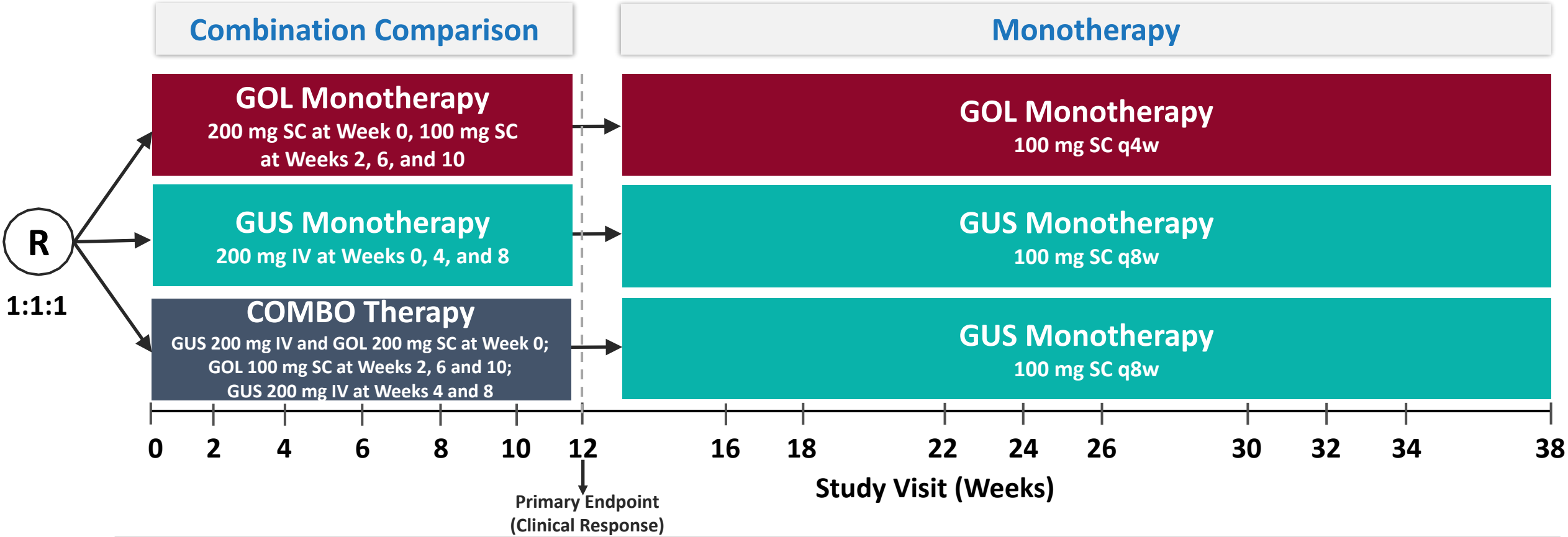
Study Design



Patient Population and Medications

- Moderately-to-severely active UC (Mayo score 6-12, inclusive, and an endoscopy subscore ≥2 by central review)
- Naïve to TNFα, IL-12/23, and Il-23p19 antagonists and have had an inadequate response or intolerance to conventional therapy (immunosuppressants [AZA, 6-MP] and/or corticosteroids)
- Immunosuppressants must have been discontinued prior to randomization
- Corticosteroids up to a dose of prednisone of 20 mg/day (or equivalent) permitted with mandatory tapering beginning at Week 6

R=Randomization; GUS=Guselkumab; GOL=Golimumab; COMBO=Combination Guselkumab + Golimumab

Baseline Patient Characteristics

	GOL	GUS	COMBO (Golimumab + Guselkumab) →GUS	Total
Number of Patients	72	71	71	214
Mean age (SD), years	38.1 (10.47)	39.1 (13.67)	37.8 (11.69)	38.4 (11.96)
Male, n (%)	42 (58.3%)	40 (56.3%)	34 (47.9%)	116 (54.2%)
UC duration, years, mean (SD)	4.7 (4.48)	5.4 (5.70)	4.6 (4.61)	4.9 (4.94)
Disease limited to left side of colon, n (%)	38 (52.8)	36 (50.7)	50 (70.4)	124 (57.9)
Full Mayo score (0-12), mean (SD)	8.7 (1.44)	8.9 (1.33)	8.8 (1.37)	8.8 (1.38)
Endoscopy subscore (0-3), n (%)				
Subscore of 2 (moderate)	35 (48.6)	24 (33.8)	28 (39.4)	87 (40.7)
Subscore of 3 (severe)	37 (51.4)	47 (66.2)	43 (60.6)	127 (59.3)
Patients receiving corticosteroids at baseline, n (%)	31 (43.1)	28 (39.4)	29 (40.8)	88 (41.1)

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Disposition Through Final Study Drug Administration Visit

	GOL	GUS	COMBO→GUS	Total
Number of Patients	72	71	71	214
Discontinued study treatment prior to Week 34[a], n (%)	13 (18.1%)	6 (8.5%)	9 (12.7%)	28 (13.1%)
Reason for discontinuation, n (%)				
Adverse event	4 (5.6%)	1 (1.4%)	6 (8.5%)	11 (5.1%)
Worsening of UC	3 (4.2%)	0	4 (5.6%)	7 (3.3%)
Adverse event - other	1 (1.4%)	1 (1.4%)	2 (2.8%)	4 (1.9%)
Due to COVID-related events	0	0	0	0
Lack of efficacy	2 (2.8%)	2 (2.8%)	1 (1.4%)	5 (2.3%)
Withdrawal by patient	6 (8.3%)	1 (1.4%)	1 (1.4%)	8 (3.7%)
Lack of improvement	4 (5.6%)	0	0	4 (1.9%)
Death	0	0	0	0
Pregnancy	0	0	1 (1.4%)	1 (0.5%)
Other	1 (1.4%)	2 (2.8%)	0	3 (1.4%)
Due to COVID-19 related events	1 (1.4%)	2 (2.8%)	0	3 (1.4%)

[a]Final dose of study intervention was administered at Week 34 and final efficacy visit was at Week 38.

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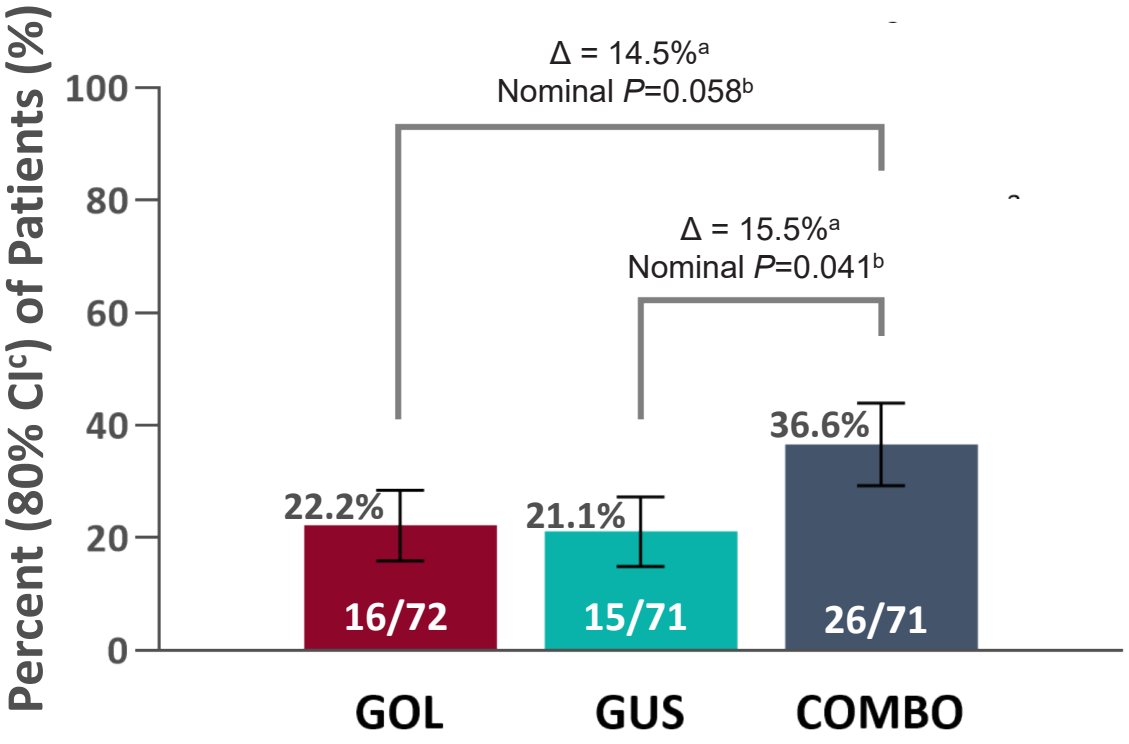
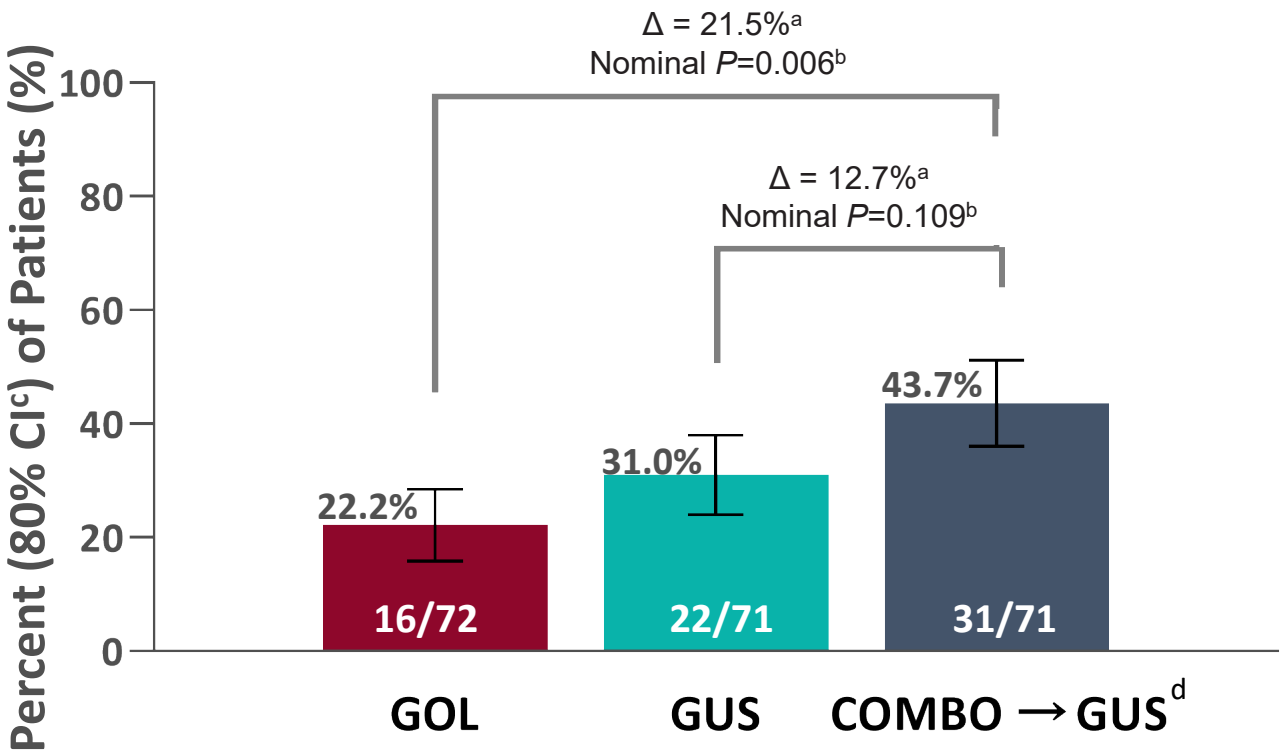
Clinical Remission

Mayo Score ≤2 with No Individual Subscore >1

Week 12



Week 38



[a]The adjusted treatment difference between the combination therapy vs. the monotherapy groups were based on the Wald statistic with the CMH weight.
[b]P-value was based on the CMH chi-square test, stratified by corticosteroid use at baseline (Yes, No).
[c]The 80% confidence intervals (CIs) for were based on the Wald statistic.
[d]Patients in the combination therapy group switched to guselkumab monotherapy beginning at Week 12.

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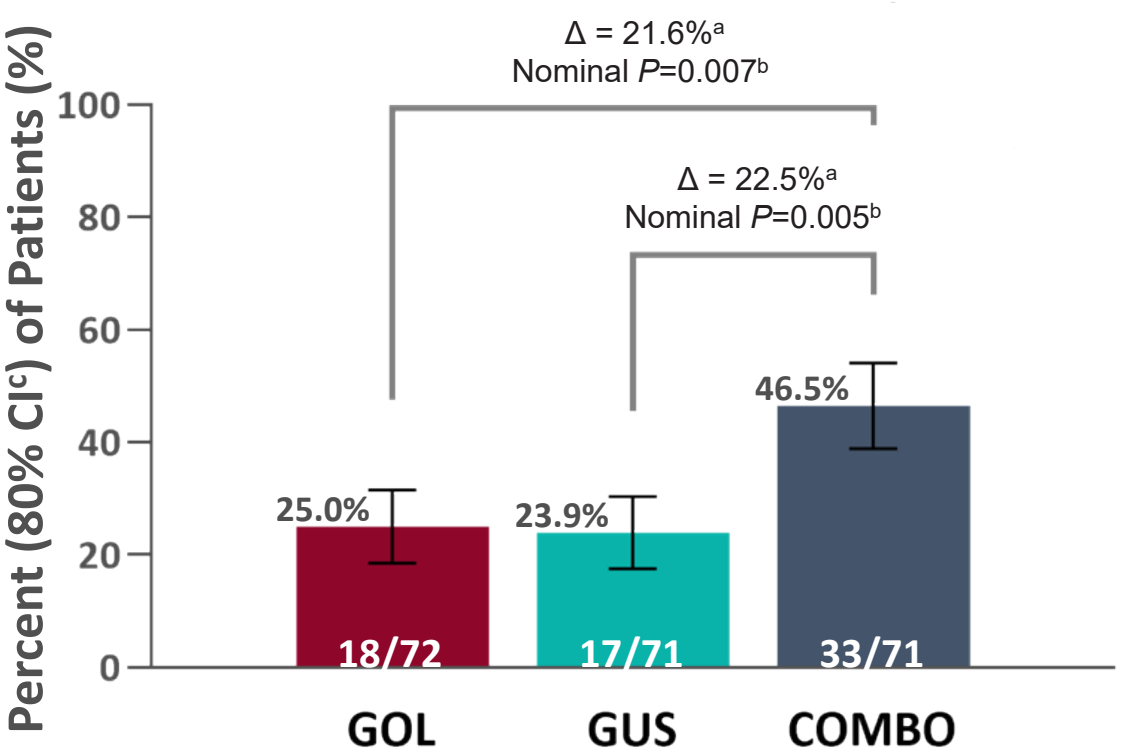
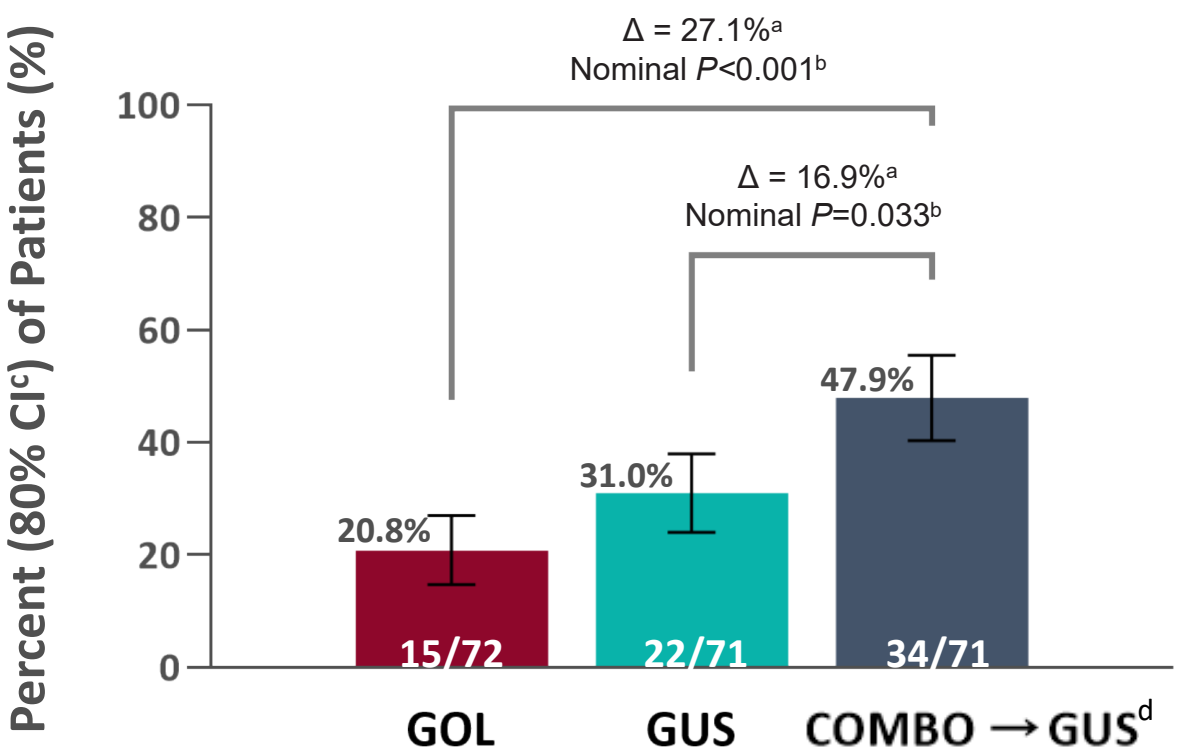
Clinical Remission (Modified Mayo Score)

Mayo Stool Frequency Subscore of 0 or 1 and Not Increased from Baseline, a Rectal Bleeding Subscore of 0, and an Endoscopy Subscore of 0 or 1 with No Friability Present on the Endoscopy

Week 12



Week 38



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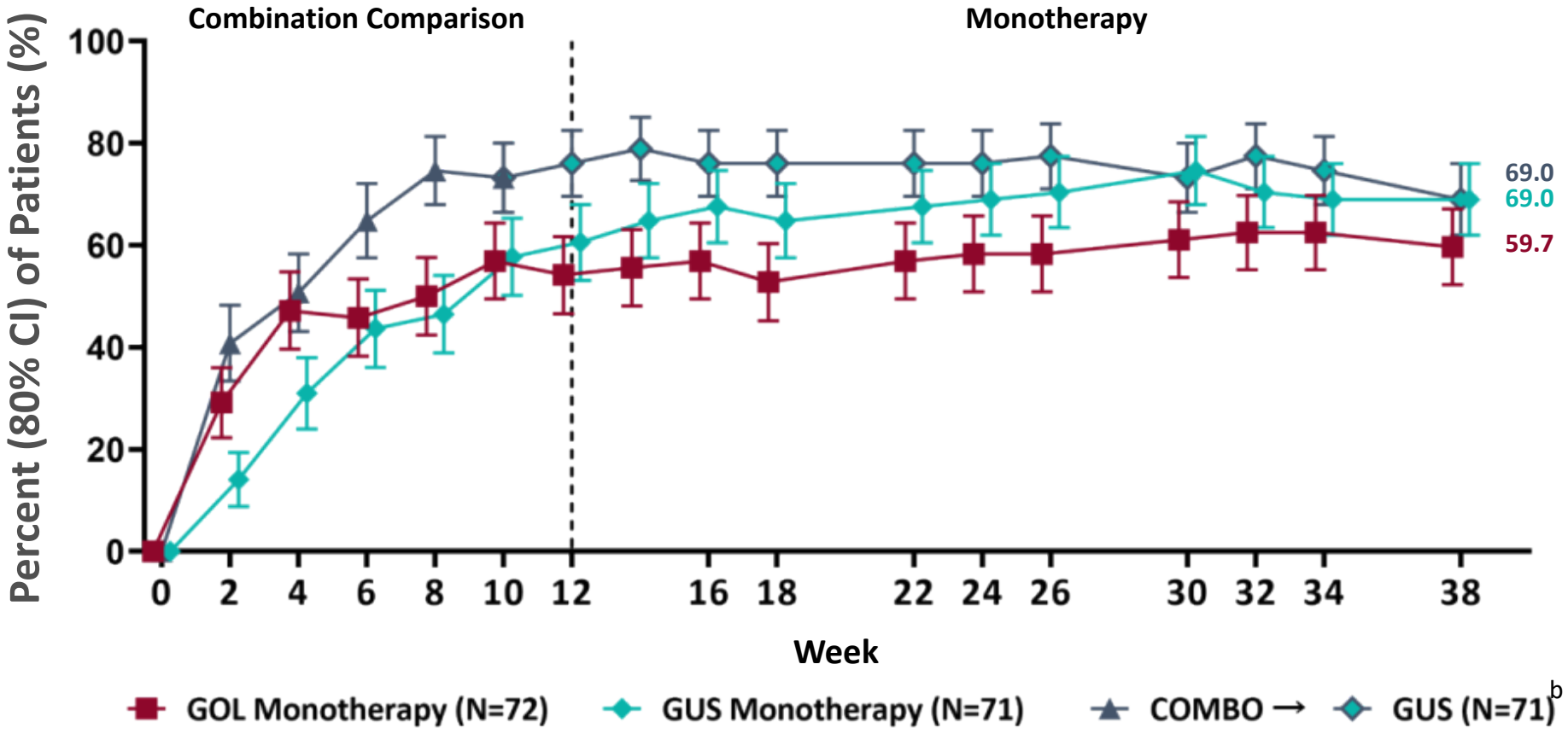
Symptomatic Remission Through Week 38[a]

Mayo Stool Frequency Subscore of 0 or 1, Where the Stool Frequency Subscore Has Not Increased from Baseline, and a Rectal Bleeding Subscore of 0



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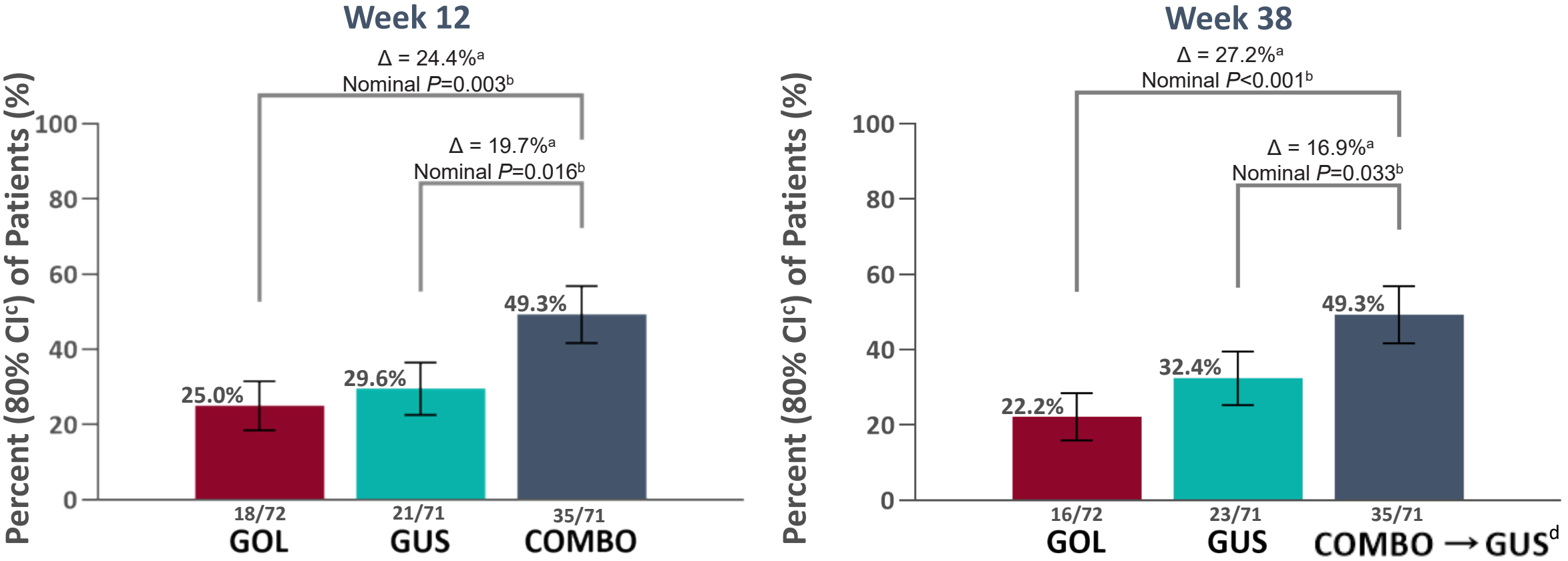
Endoscopic Improvement

Endoscopy Subscore of 0 or 1 with No Friability Present on the Endoscopy



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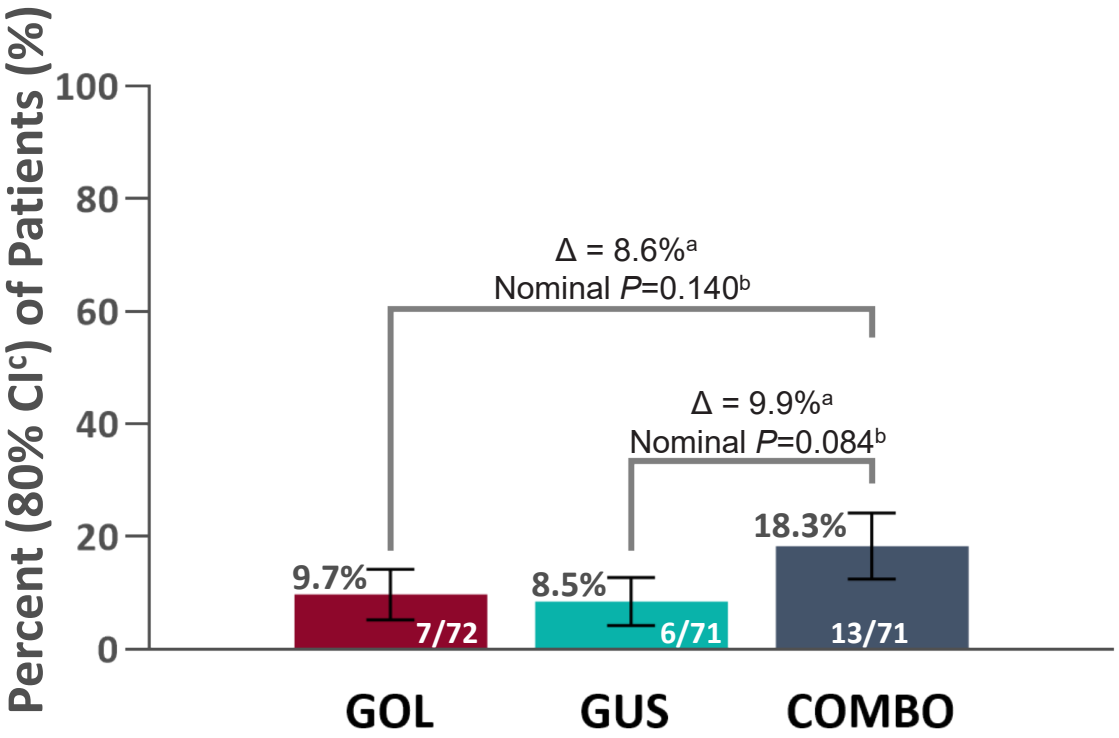
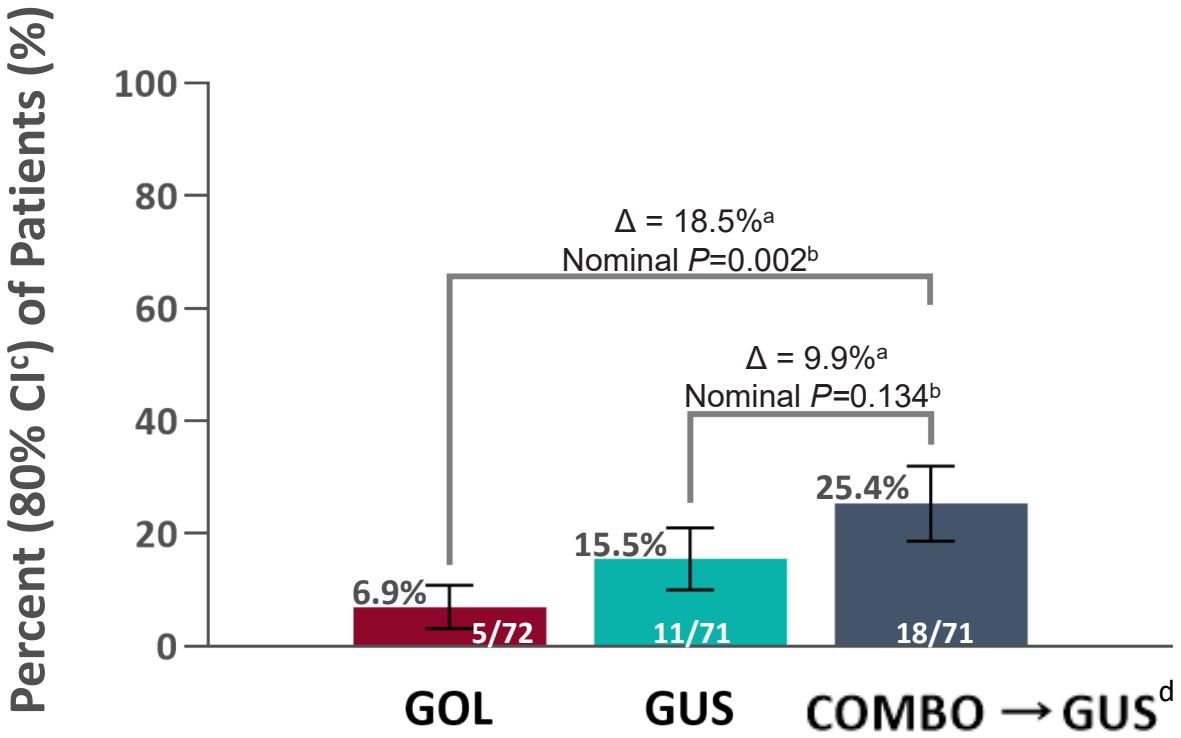
Endoscopic Normalization

Endoscopy Subscore of 0

Week 12



Week 38



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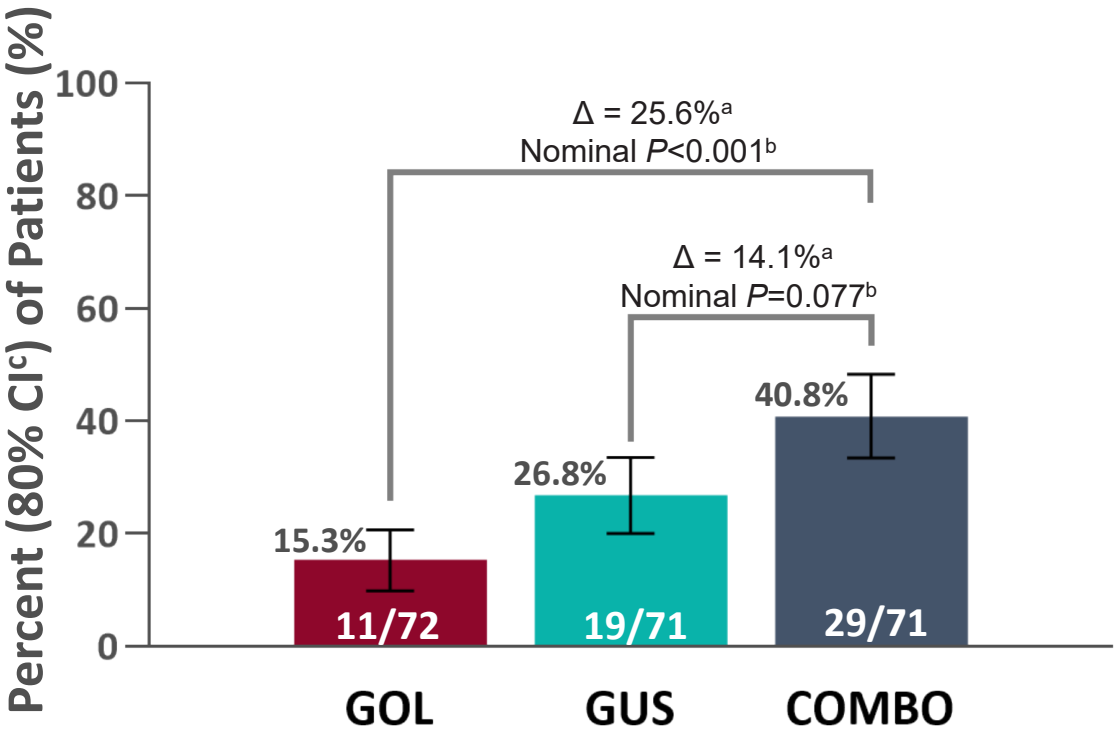
Both Histologic Remission and Endoscopic Improvement

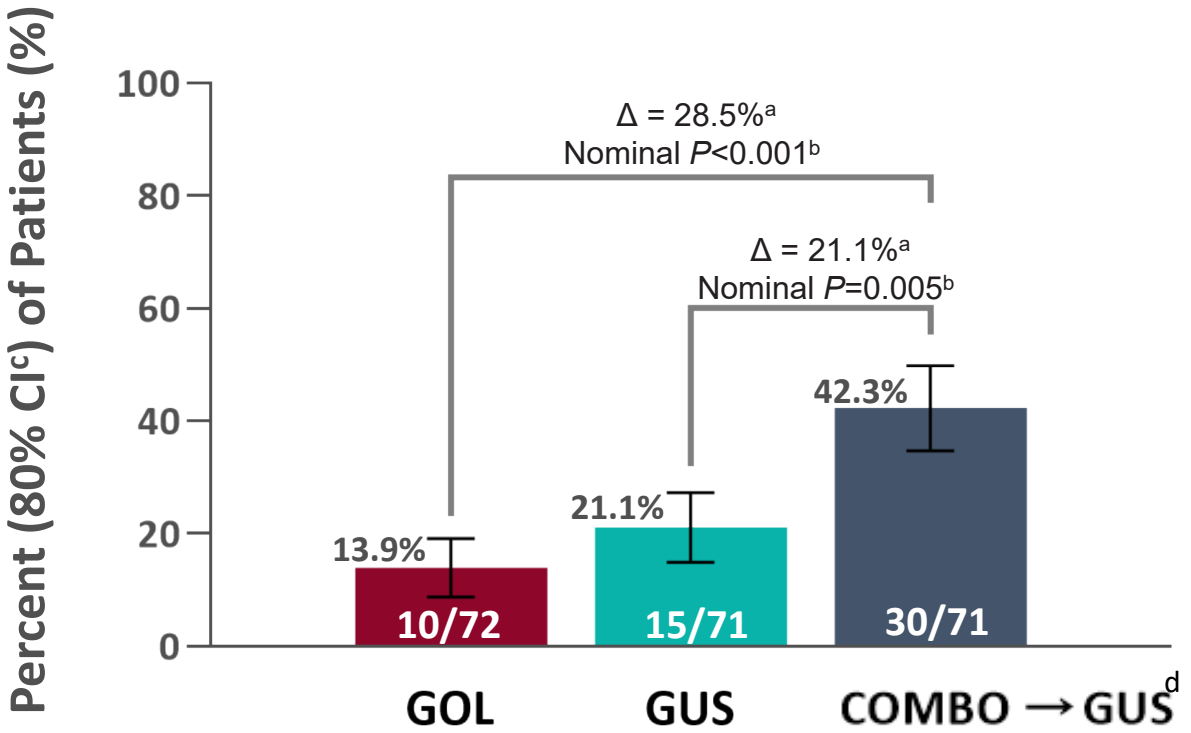
Histologic Remission: Absence of Neutrophils from the Mucosa (Both Lamina Propria and Epithelium), No Crypt Destruction, and No Erosions, Ulcerations or Granulation Tissue According to the Geboes Grading System

Endoscopic Improvement: Endoscopy Subscore of 0 or 1 with No Friability Present on the Endoscopy

Week 12



Week 38



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Key Safety Findings Through Final Safety Visit

	GOL	GUS	COMBO→GUS
Number of Patients	72	71	71
Patients with ≥1, n (%)			
Adverse event (AEs)	55 (76.4%)	46 (64.8%)	45 (63.4%)
Serious adverse event (SAEs)	4 (5.6%)	4 (5.6%)	4 (5.6%)
AEs leading to discontinuation of study intervention	4 (5.6%)	1 (1.4%)	7 (9.9%)
Infection[a]	23 (31.9%)	17 (23.9%)	22 (31.0%)
Serious infection[a]	2 (2.8%)	2 (2.8%)	2 (2.8%)
Opportunistic infection[a,b]	0	0	2 (2.8%)
COVID-19 infection	1 (1.4%)	3 (4.2%)	2 (2.8%)
Malignancy	0	1 (1.4%)	0
AEs leading to death	0	1 (1.4%)	1 (1.4%)

Note: final dose of study intervention was administered at Week 34, followed by a 16-week safety follow-up period (Week 50).
[a]As assessed by the investigator.
[b]Extrapulmonary TB and cytomegalovirus colitis.
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Conclusions

- Patients treated with combination induction therapy with guselkumab plus golimumab, followed by guselkumab monotherapy, achieved higher rates of the following endpoints at Week 38 as compared to either guselkumab or golimumab alone:
  - Clinical remission
  - Endoscopic improvement and endoscopic normalization
  - Composite endpoint of histologic remission and endoscopic improvement
- Adverse event rates were comparable among the treatment groups
- The combination treatment paradigm evaluated in VEGA warrants further investigation