

Histologic and Endoscopic Efficacy of Icotrokinra, a First-in-Class Targeted Oral Peptide That Precisely Blocks the IL-23 Receptor, in Ulcerative Colitis: Outcomes from the ANTHEM-UC Study

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Background

Icotrokinra is a first-in-class, investigational, targeted oral peptide that precisely blocks the interleukin-23 (IL-23) receptor

All icotrokinra doses met the Week 12 primary endpoint of ANTHEM-UC, a Phase 2b, randomized, double-blind, placebo-controlled, treat-through, dose-ranging study in adults with moderate to severe ulcerative colitis

Icotrokinra also delivered clinically meaningful improvements across key secondary endpoints at Week 12, which were maintained or improved at Week 28

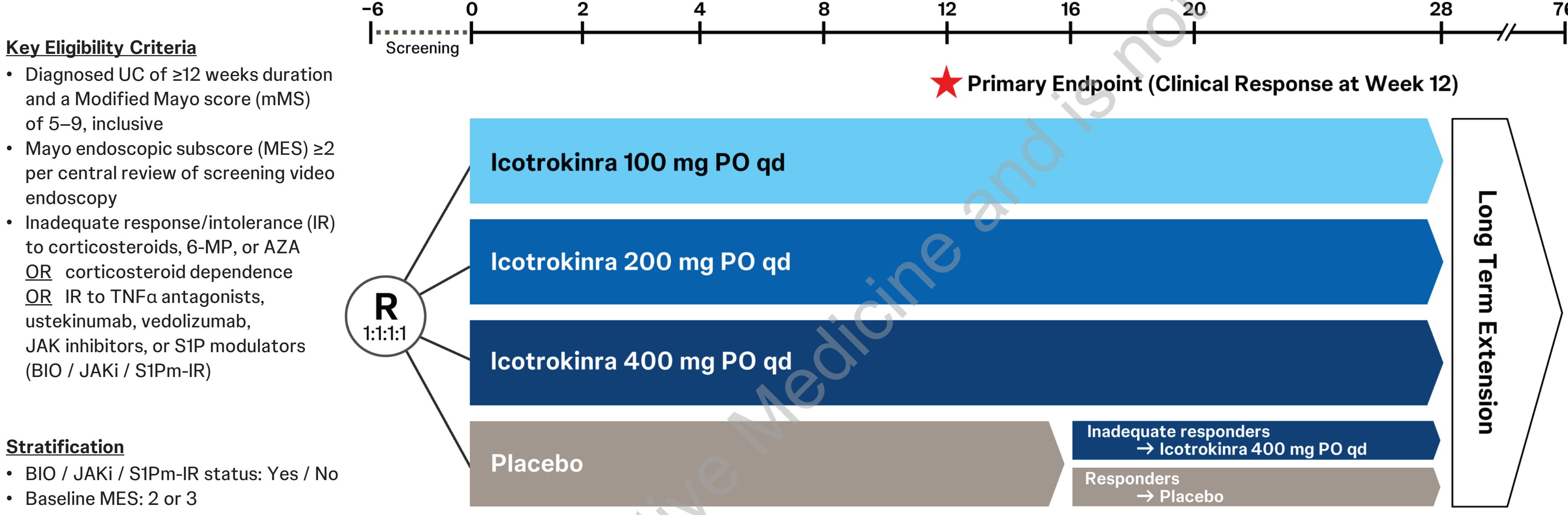
Objective

Here we report the impact of icotrokinra treatment on exploratory histologic and endoscopic outcomes in ANTHEM-UC study participants

Methods

- In this Phase 2b, randomized, double-blind, dose-ranging, placebo-controlled study, participants were randomized 1:1:1 to placebo or icotrokinra at once-daily oral doses of 100 mg, 200 mg, or 400 mg
- Exploratory endpoints* (not controlled for multiple comparisons) included:
 - Histologic improvement
 - Histologic remission
 - Endoscopic remission
 - Composite of histologic and clinical remission
- Inadequate responders at Week 16 in the placebo group were treatment adjusted to icotrokinra 400 mg, while those in the icotrokinra groups received a sham adjustment and continued their randomized doses
- Participants with intercurrent events of ostomy or colectomy, prohibited changes in UC medication, or discontinuation of study intervention for any reason except those due to major disruptions (e.g., COVID-19–related reasons or regional crisis, excluding COVID-19 infection) were considered non-responders moving forward; participants meeting inadequate response criteria at Week 16 were considered non-responders at Week 28
- After accounting for intercurrent events strategies, participants who were missing data necessary to determine the outcome at the assessment timepoint were considered non-responders at that timepoint

* Secondary endpoints of endoscopic improvement and histologic–endoscopic mucosal improvement were previously reported



Results

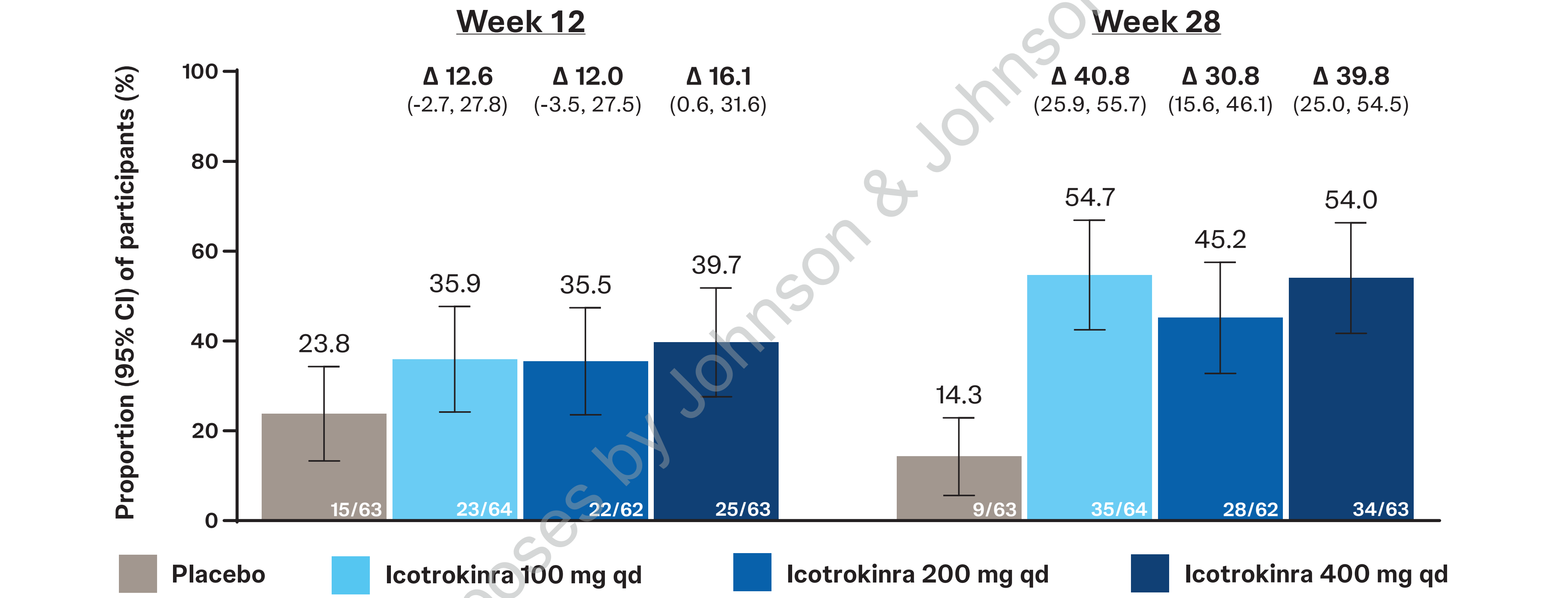
These findings should be interpreted in the context of the small sample size and baseline imbalances—including more extensive disease and a greater proportion of participants with an inadequate response or prior intolerance to ≥ 2 classes of advanced therapies—suggesting greater disease severity in the group treated with icotrokinra 400 mg

	Placebo	Icotrokinra 100 mg qd	Icotrokinra 200 mg qd	Icotrokinra 400 mg qd	Total
Full analysis set, n	63	64	62	63	252
Age, years, mean (SD)	38.3 (13.8)	45.8 (14.6)	41.8 (14.6)	40.6 (14.8)	41.6 (14.7)
Sex, male, n (%)	35 (55.6%)	40 (62.5%)	32 (51.6%)	40 (63.5%)	147 (58.3%)
Race, White, n (%)	44 (69.8%)	45 (70.3%)	39 (62.9%)	42 (66.7%)	170 (67.5%)
UC disease duration, years, mean (SD)	8.2 (8.1)	7.4 (6.1)	7.8 (7.5)	7.6 (7.6)	7.8 (7.3)
Extensive disease, n (%)	27 (42.9%)	23 (35.9%)	23 (37.1%)	29 (46.0%)	102 (40.5%)
Modified Mayo score [max=9], mean (SD)	6.75 (1.231)	6.55 (1.296)	6.75 (1.386)	6.49 (1.401)	6.63 (1.327)
Mayo endoscopic subscore of 3, n (%)	36 (57.1%)	38 (59.4%)	37 (59.7%)	37 (58.7%)	148 (58.7%)
Fecal calprotectin, mg/kg, median [IQR]	1467.0 [420.5; 3622.0]	1433.3 [698.0; 3121.2]	2467.0 [646.4; 4599.6]	1421.3 [584.6; 4978.6]	1523.0 [587.0; 3816.7]
CRP, mg/L, median [IQR]	3.0 [0.9; 7.0]	3.0 [1.1; 6.7]	5.3 [1.5; 11.3]	4.0 [1.5; 8.1]	3.6 [1.3; 8.1]
Baseline corticosteroid use, n (%)	21 (33.3%)	21 (32.8%)	29 (46.8%)	23 (36.5%)	94 (37.3%)
Baseline immunomodulator use, n (%)	16 (25.4%)	10 (15.6%)	10 (16.1%)	6 (9.5%)	42 (16.7%)
No history of BIO/JAKi/SIPm-IR, n (%)	35 (55.6%)	38 (59.4%)	36 (58.1%)	34 (54.0%)	143 (56.7%)
BIO/JAKi/SIPm-IR, n (%)	28 (44.4%)	26 (40.6%)	26 (41.9%)	29 (46.0%)	109 (43.3%)
IR to 1 class / mechanism ^a	22 (78.6%)	19 (73.1%)	21 (80.8%)	15 (51.7%)	77 (70.6%)
IR to 2 classes / mechanisms ^a	6 (21.4%)	6 (23.1%)	5 (19.2%)	14 (48.3%)	31 (28.4%)
IR to >2 classes / mechanisms ^a	0	1 (3.8%)	0	0	1 (0.9%)

a. Denominator was number of participants with a history of inadequate response or intolerance to biologics, JAK inhibitors, or SIP modulators (BIO/JAKi/SIPm-IR)
BIO = TNF α antagonists, ustekinumab, or vedolizumab; IR = prior inadequate response or intolerance

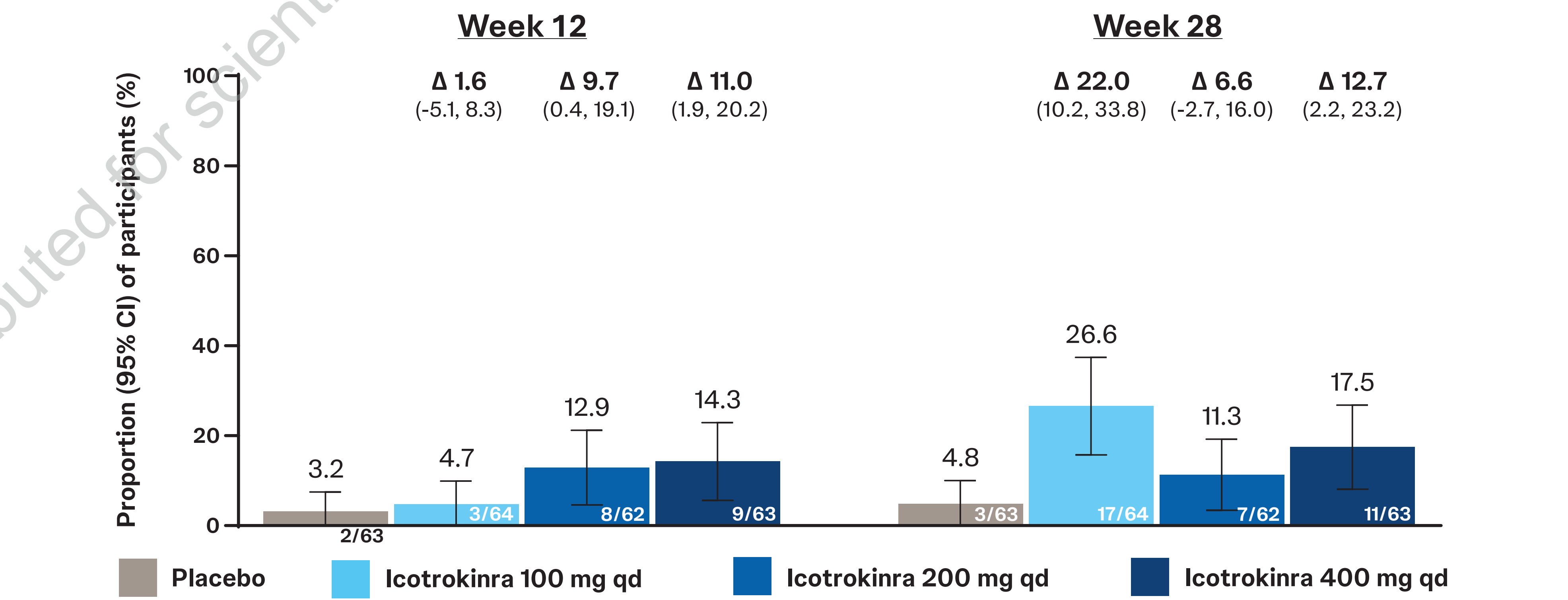
Histologic Improvement

Neutrophil infiltration in <5% of crypts [Geboes Grade 3 ≤ 1], no crypt destruction [Geboes Grade 4=0], and no erosions, ulcerations, or granulation tissue [Geboes Grade 5=0]



Endoscopic Remission

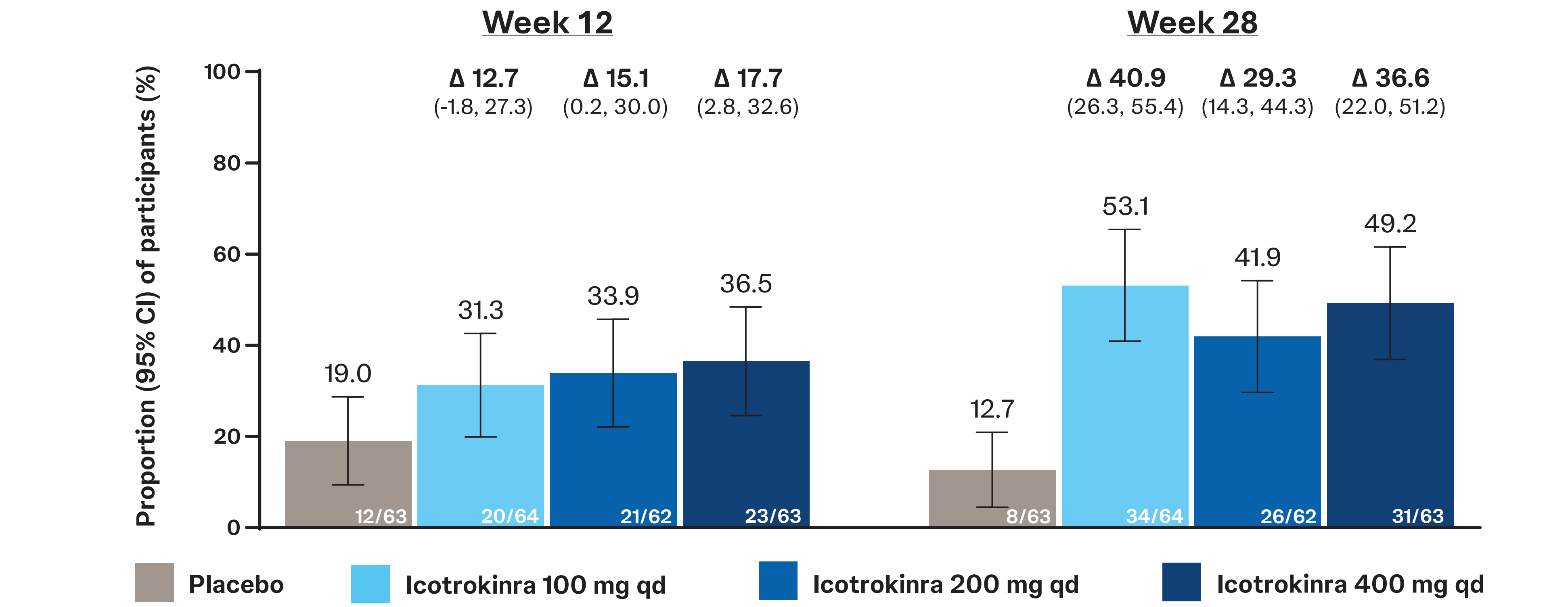
Mayo endoscopy subscore of 0



Δ = adjusted treatment difference (95% confidence interval) vs placebo. Adjusted treatment differences and 95% CIs were based on the common risk difference by use of Mantel-Haenszel stratum weights and the Sato variance estimator, using stratification factors of BIO/JAKi/SIPm-IR status (Yes or No) and Mayo endoscopic subscore (moderate [2] or severe [3]).

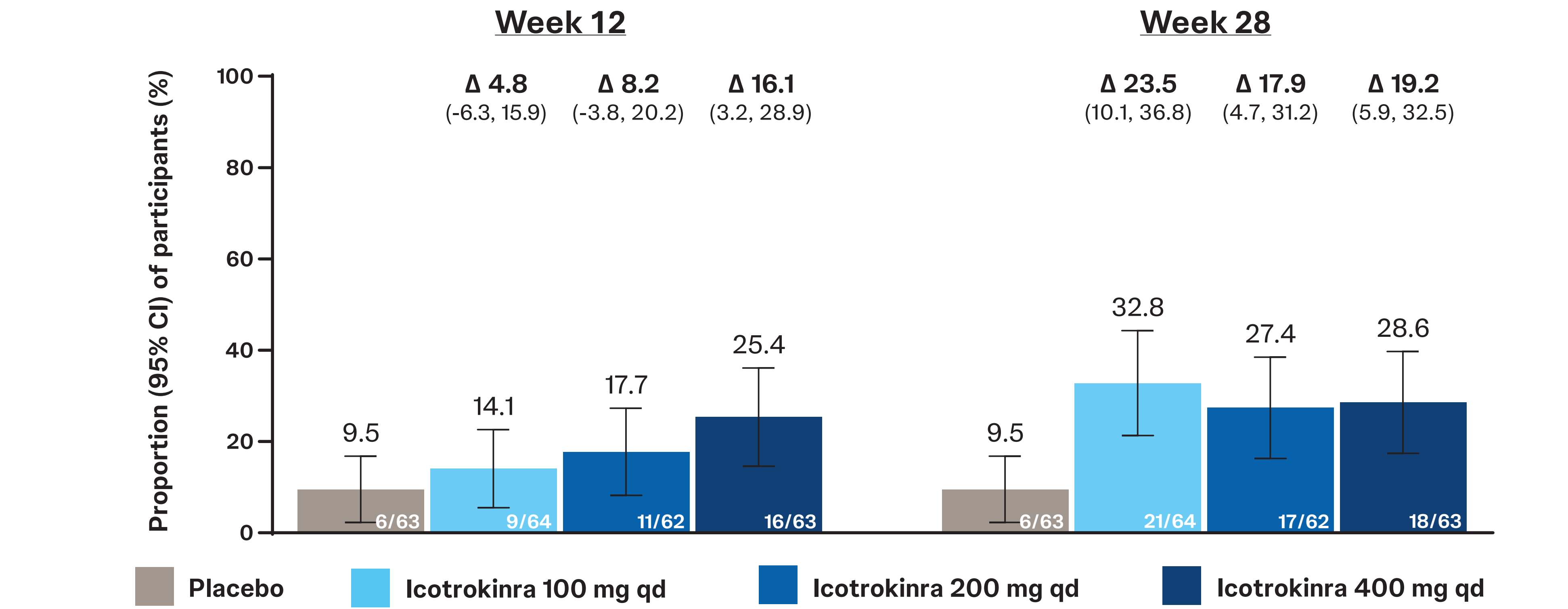
Histologic Remission

Absence of neutrophils from the mucosa (both lamina propria and epithelium) [Geboes Grades 2B and 3=0], no crypt destruction [Geboes Grade 4=0], and no erosions, ulcerations, or granulation tissue [Geboes Grade 5=0]



Composite of Histologic and Clinical Remission

Stool frequency subscore of 0 or 1 and a rectal bleeding subscore of 0 **AND** Mayo endoscopy subscore of 0 or 1 **AND** Absence of neutrophils from the mucosa (both lamina propria and epithelium) [Geboes Grades 2B and 3=0], no crypt destruction [Geboes Grade 4=0], and no erosions, ulcerations, or granulation tissue [Geboes Grade 5=0]



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