

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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Disclosure of Conflicts of Interest

I, Britta Siegmund, declare the following activities: consultant for AbbVie, Abivax, AltruBio, Boehringer Ingelheim, Bristol Myers Squibb, Dr. Falk Pharma, Eli Lilly, Endpoint Health, Galapagos, Johnson & Johnson, Materia Prima, MSD, Pfizer, Takeda, Wedbush Securities; speaker fees from AbbVie, AlfaSigma, Bristol Myers Squibb, CED Service GmbH, Dr. Falk Pharma, Eli Lilly, MD Education, MSD, Galapagos, Johnson & Johnson, Pfizer, Tr1X Bio; grant from Pfizer

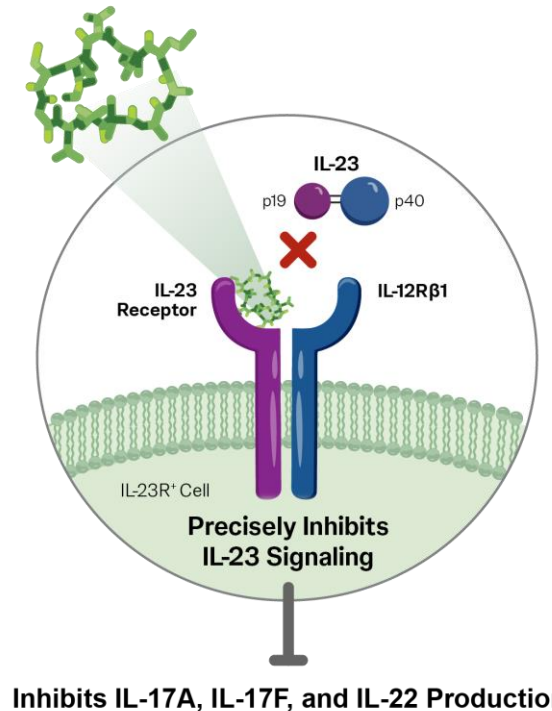
Background and Objective

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 endpoint¹ 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 28¹

Icotrokinra Blocks IL-23 From Binding to its Receptor



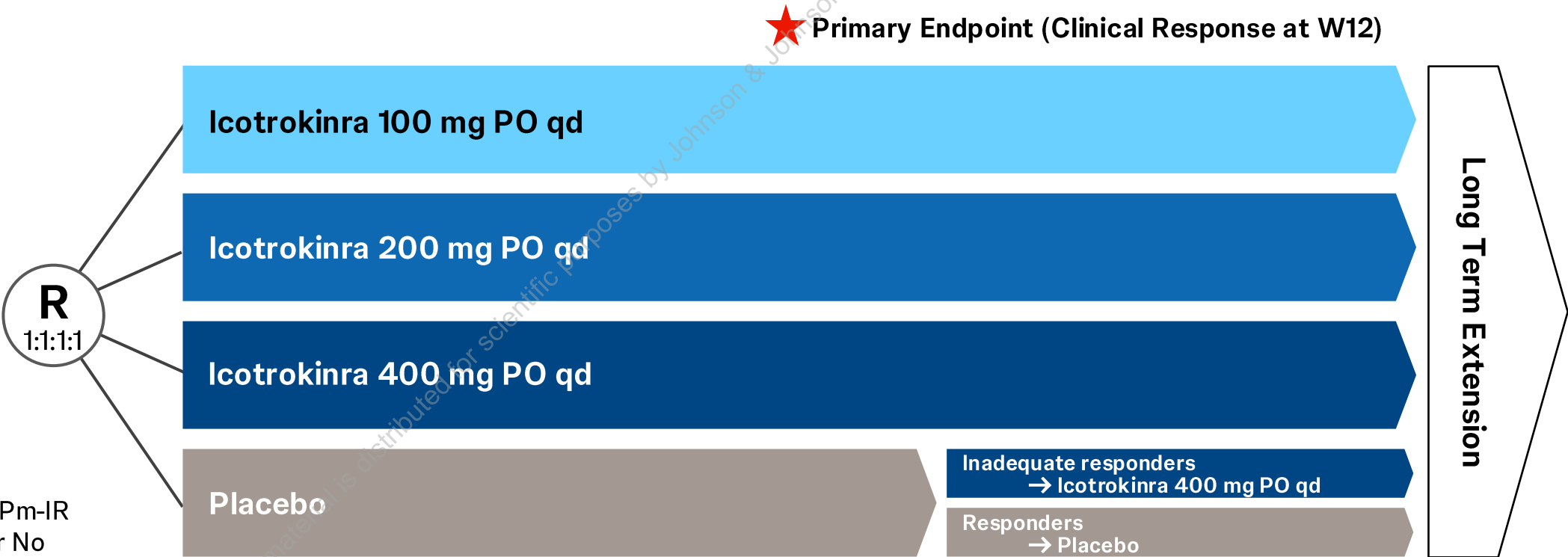
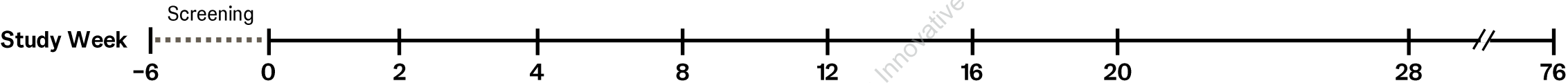
Here we report the impact of icotrokinra treatment on exploratory histologic and endoscopic outcomes in ANTHEM-UC study participants

1. Abreu MT, Siegmund B, Surace L, et al. N Engl J Med 2026;395:1495-504.

ANTHEM-UC Study Design

Key Eligibility Criteria

- Diagnosed UC of ≥12 weeks duration and a Modified Mayo score (mMS) of 5–9, inclusive
- Mayo endoscopic subscore (MES) ≥2 per central review of screening video endoscopy
- Inadequate response/intolerance (IR) to corticosteroids, 6-MP, or AZA **OR** corticosteroid dependence **OR** IR to TNFα antagonists, ustekinumab, vedolizumab, JAK inhibitors, or S1P modulators (BIO/JAKi/S1Pm-IR)



Stratification

- BIO/JAKi/S1Pm-IR status: Yes or No
- Baseline MES: 2 or 3

Endpoints and Statistical Considerations

➤ **Exploratory endpoints* 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 16
 - 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.¹ Exploratory endpoints were not controlled for multiple comparisons.

1. Abreu MT, Siegmund B, Surace L, et al. N Engl J Med 2026;395:1495-504.

Demographics and Baseline Disease Characteristics

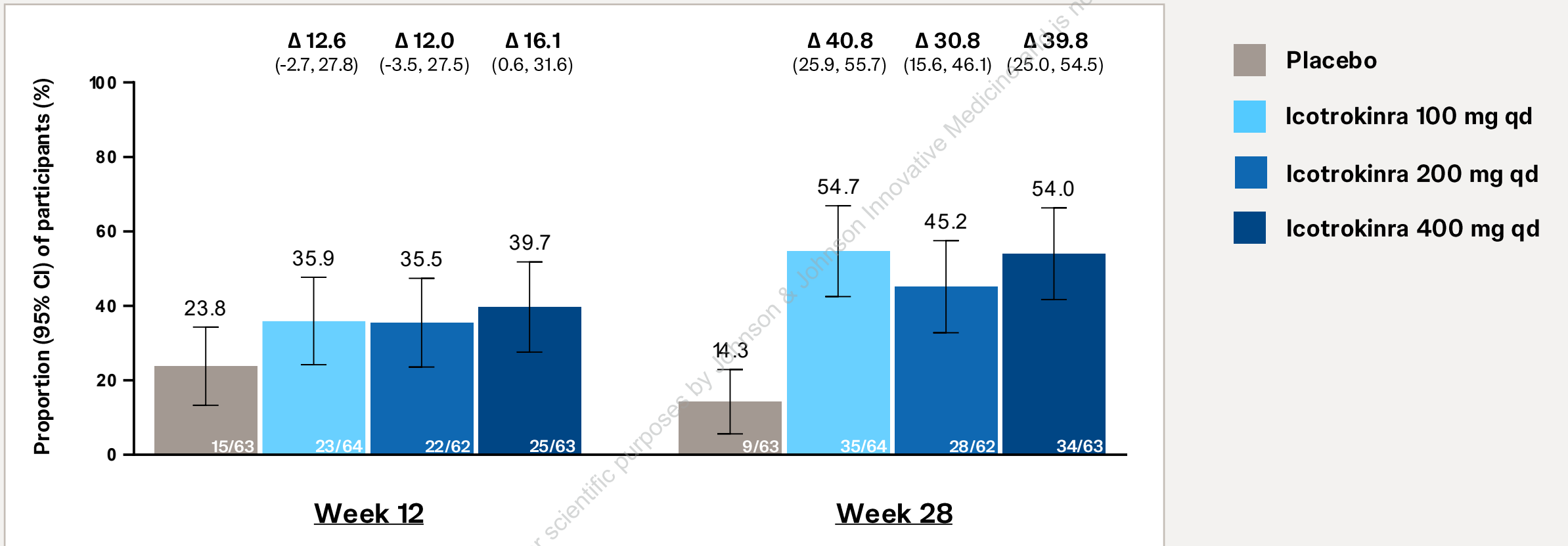
	Placebo	Icotrokinra 100 mg qd	Icotrokinra 200 mg qd	Icotrokinra 400 mg qd	Total
Full analysis set, n	63	64	62	63	252
Age, years, mean (SD)	38.3 (13.8)	45.8 (14.6)	41.8 (14.6)	40.6 (14.8)	41.6 (14.7)
Sex, male, n (%)	35 (55.6%)	40 (62.5%)	32 (51.6%)	40 (63.5%)	147 (58.3%)
Race, White, n (%)	44 (69.8%)	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 (severe), 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 Medications for Ulcerative Colitis

	Placebo	lcotrokinra 100 mg qd	lcotrokinra 200 mg qd	lcotrokinra 400 mg qd	Total
Full analysis set, n	63	64	62	63	252
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/S1Pm-IR, n (%)	35 (55.6%)	38 (59.4%)	36 (58.1%)	34 (54.0%)	143 (56.7%)
BIO/JAKi/S1Pm-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 S1P modulators (BIO/JAKi/S1Pm-IR)
BIO = TNFα antagonists, ustekinumab, or vedolizumab; IR = prior inadequate response or intolerance.

Histologic Improvement

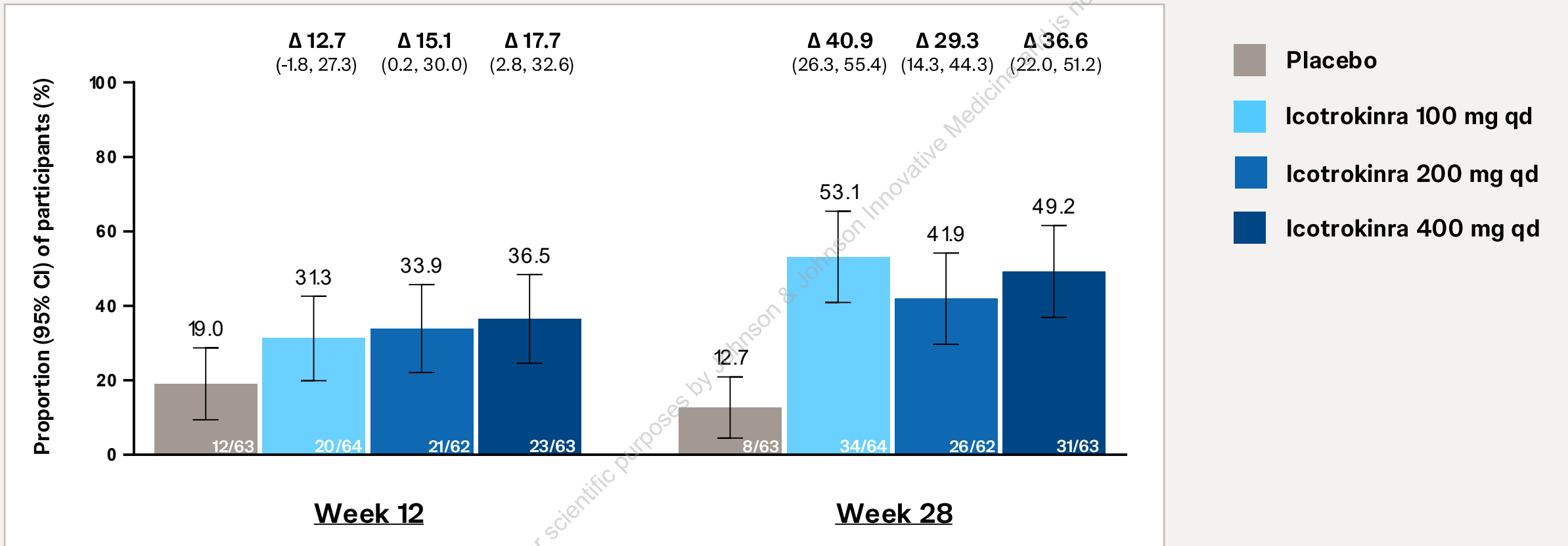


Histologic improvement: neutrophil infiltration in <5% of crypts [Geboes Grade 3 ≤1], no crypt destruction [Geboes Grade 4=0], and no erosions, ulcerations, or granulation tissue [Geboes Grade 5=0]

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/S1Pm-IR status (Yes or No) and Mayo endoscopic subscore (moderate [2] or severe [3]).

Participants with intercurrent events of ostomy or colectomy, prohibited changes in UC medication, 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), or (for the Week 28 endpoints) meeting Week 16 inadequate response criteria were considered nonresponders, as were participants who had missing data for the endpoint.

Histologic Remission

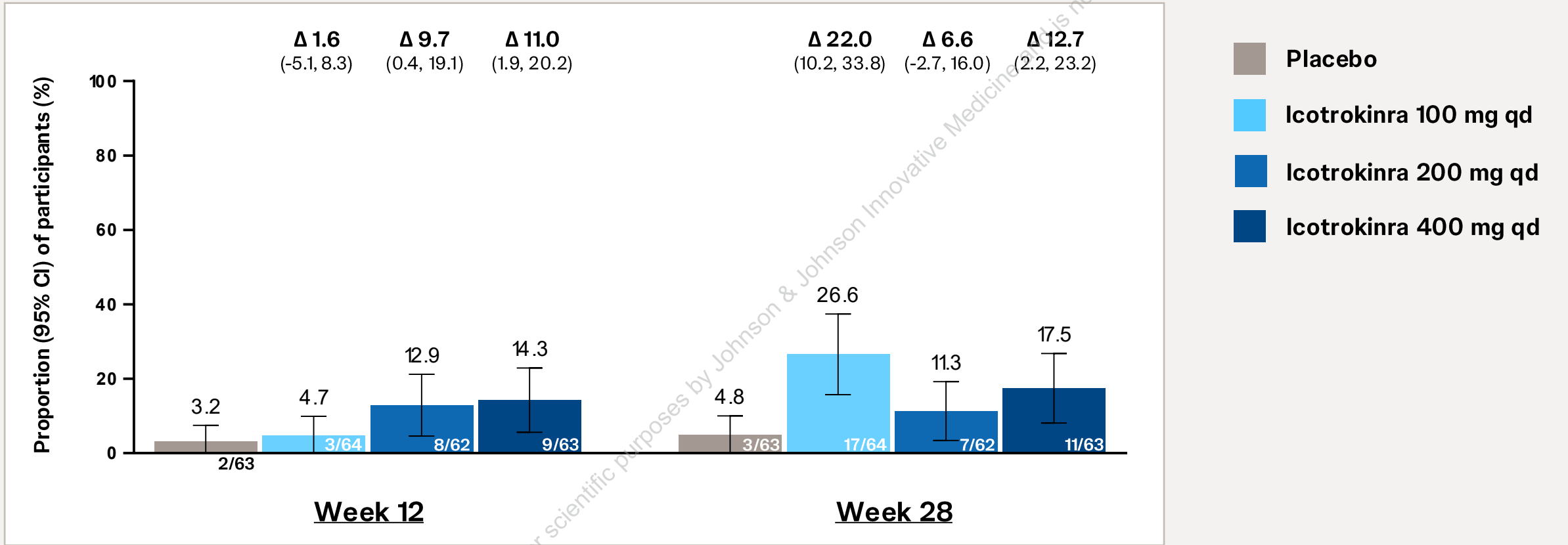


Histologic remission: absence of neutrophils from the mucosa (both lamina propria and epithelium) [Geboes Grades 2B and 3=0], no crypt destruction [Geboes Grade 4=0], and no erosions, ulcerations, or granulation tissue [Geboes Grade 5=0]

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/S1Pm-IR status (Yes or No) and Mayo endoscopic subscore (moderate [2] or severe [3]).

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Endoscopic Remission

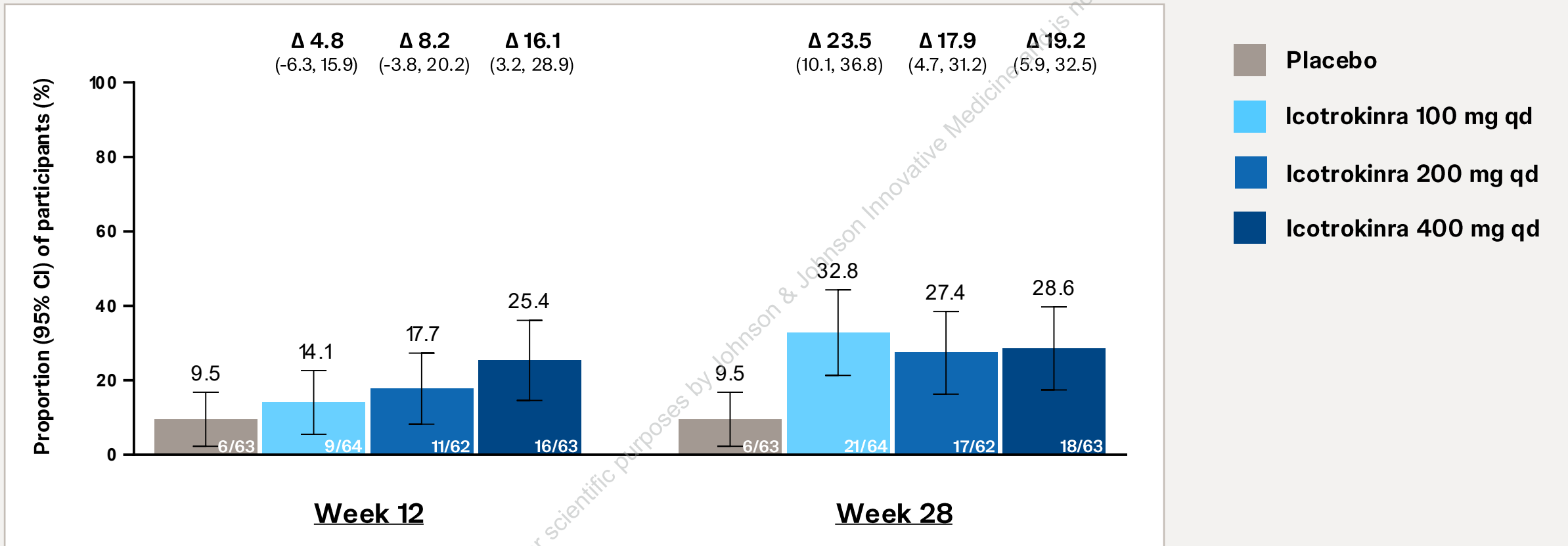


Endoscopic remission: Mayo endoscopy subscore of 0

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/S1Pm-IR status (Yes or No) and Mayo endoscopic subscore (moderate [2] or severe [3]).

Participants with intercurrent events of ostomy or colectomy, prohibited changes in UC medication, 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), or (for the Week 28 endpoints) meeting Week 16 inadequate response criteria were considered nonresponders, as were participants who had missing data for the endpoint.

Composite of Histologic and Clinical Remission



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]

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/S1Pm-IR status (Yes or No) and Mayo endoscopic subscore (moderate [2] or severe [3]).

Participants with intercurrent events of ostomy or colectomy, prohibited changes in UC medication, 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), or (for the Week 28 endpoints) meeting Week 16 inadequate response criteria were considered nonresponders, as were participants who had missing data for the endpoint.

Conclusions



Participants experienced improvements in stringent, objective histologic and endoscopic outcomes with once-daily oral icotrokinra



Outcomes generally continued to improve between Weeks 12 and 28



At Week 28, all icotrokinra dose groups showed clinically meaningful ($\geq 10\%$) improvements versus placebo across all four endpoints (except the 200-mg group for endoscopic remission)

Acknowledgements

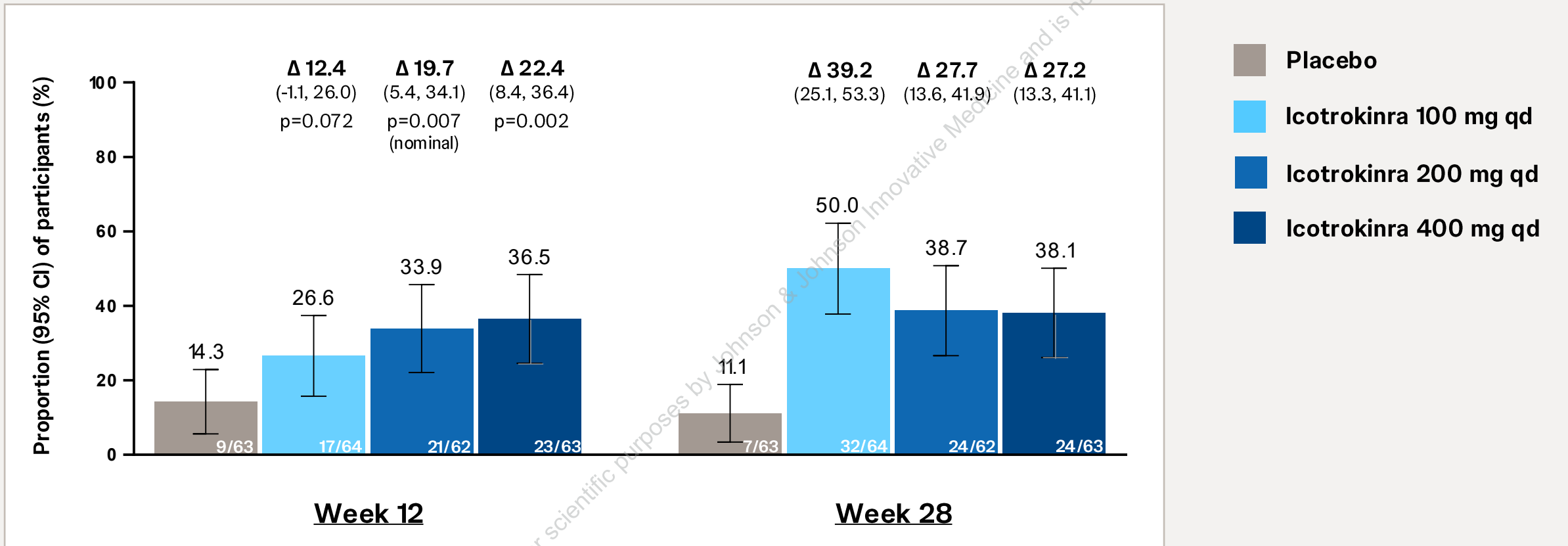
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- This work was supported by Johnson & Johnson



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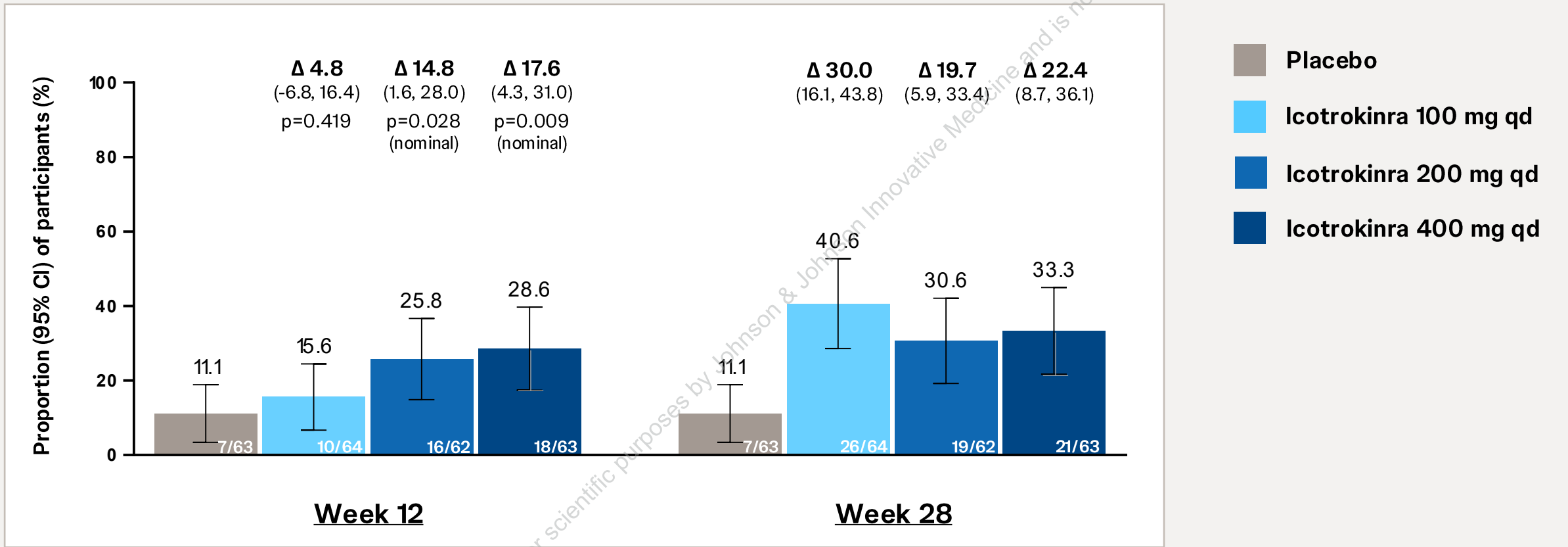
Endoscopic Improvement



Endoscopic improvement: Mayo endoscopic subscore of 0 or 1

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo. Adjusted treatment differences, 95% CIs, and p-values 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]). 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 nonresponders. For participants discontinuing study intervention due to major disruptions, their observed values, if available, were used. After accounting for these scenarios, participants who were missing data necessary for calculation of the outcome measure at the assessment timepoint were considered not to have achieved that endpoint.

Histologic–Endoscopic Mucosal Improvement (HEMI)



Histologic-endoscopic mucosal improvement: histologic remission (absence of neutrophils from the mucosa in both lamina propria and epithelium, no crypt destruction, and no erosions, ulcerations, or granulation tissue according to the Geboes grading system) AND endoscopic improvement (MES of 0 or 1)

Δ = adjusted treatment difference (95% confidence interval) and p-value vs placebo. Adjusted treatment differences, 95% CIs, and p-values 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]). 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 nonresponders. For participants discontinuing study intervention due to major disruptions, their observed values, if available, were used. After accounting for these scenarios, participants who were missing data necessary for calculation of the outcome measure at the assessment timepoint were considered not to have achieved that endpoint.