OP 487

EFFICACY OF ICOTROKINRA, THE FIRST TARGETED ORAL PEPTIDE THAT SELECTIVELY BLOCKS THE IL-23 RECEPTOR, IN ULCERATIVE COLITIS PATIENTS WITH OR WITHOUT PRIOR INTOLERANCE OR INADEQUATE RESPONSE TO ADVANCED THERAPIES: RESULTS FROM THE ANTHEM-UC STUDY

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DDW2026
Digestive Disease Week®
MAY 2–5, 2026 | CHICAGO, IL
EXHIBIT DATES: MAY 3–5, 2026
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SPEAKER DISCLOSURE

Edward V. Loftus, Jr.

I disclose the following financial relationships with a commercial interest:

Consulting for AbbVie, Abivax, Astellas, Avalo Therapeutics, Biocon, Bristol Myers Squibb, Celltrion Healthcare, Eli Lilly, Genentech, Gilead, HanAll Biopharma, Iota Biosciences, Iterative Health, Johnson & Johnson, Merck, Morphic, Ono, Shattuck Labs, Spyre Therapeutics, Takeda, Tr1X Bio; research support from AbbVie, Gilead, Johnson & Johnson, Merck, Takeda, Tr1X Bio; shareowner of Exact Sciences, Moderna

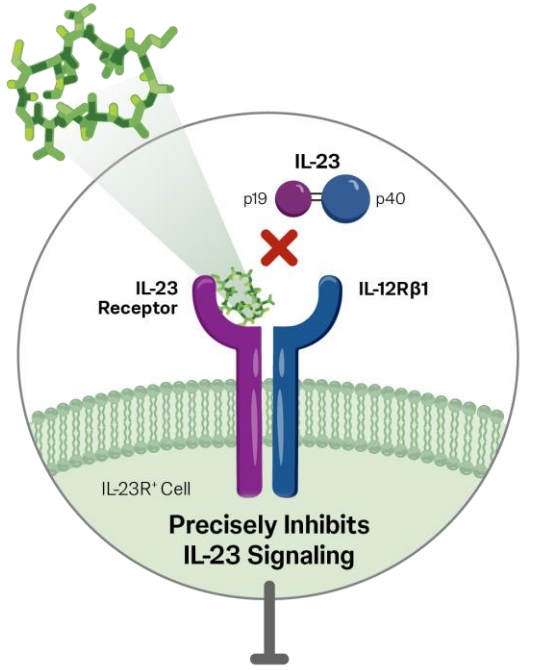
Background and Objective

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 endpoint[1] 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 in clinical, endoscopic, and histologic endpoints at Week 12, which were maintained or improved at Week 28[2]

Icotrokinra Blocks IL-23 From Binding to its Receptor



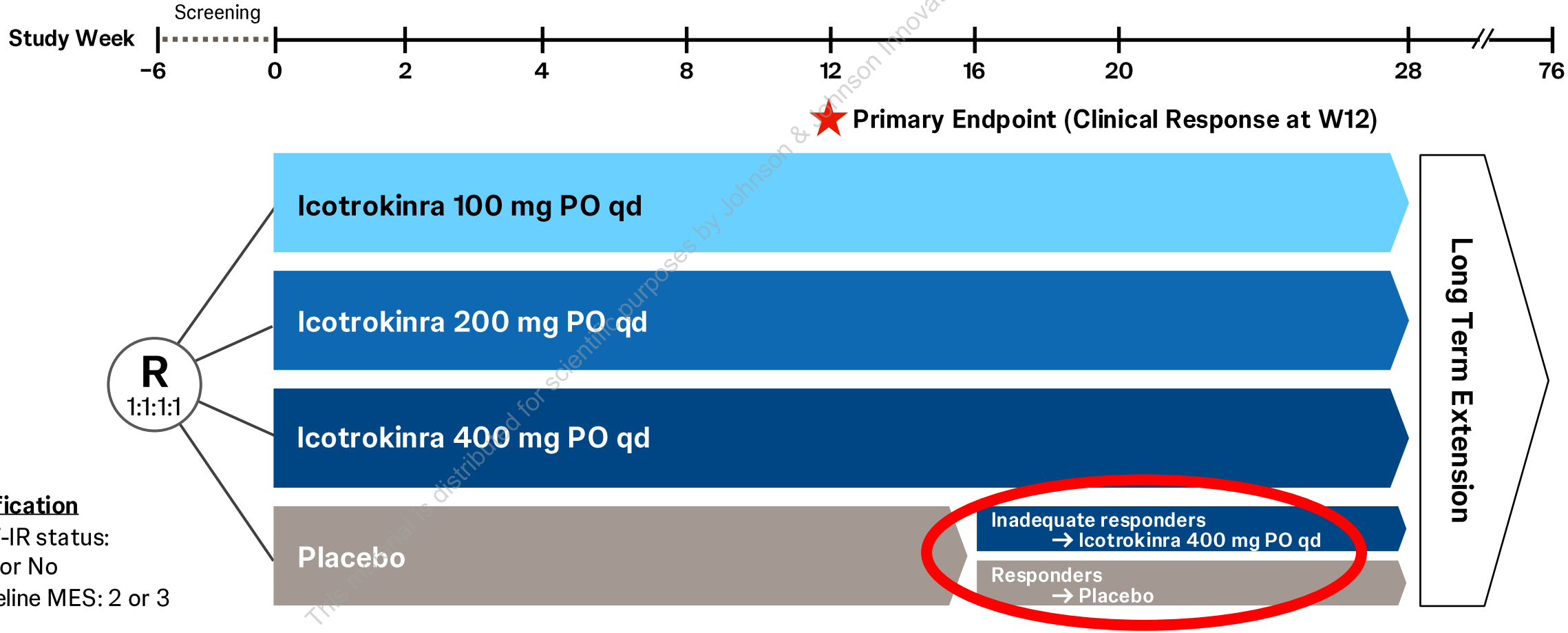
Here, we report the efficacy of icotrokinra in ANTHEM-UC participants with and without prior inadequate response or intolerance to advanced therapies for UC

1. Abreu MT, et al. United European Gastroenterol J. 2025 10;13(suppl 8):172-3.
2. Jairath V, et al. Am J Gastroenterol. 2025 120;10(suppl 2):S312.

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
- **ADT-IR**: inadequate response or intolerance (IR) to TNFα blockers, IL-12/23 antagonists, integrin receptor antagonists, JAK inhibitors or S1P modulators *OR*
  Non-ADT-IR: IR to corticosteroids, 6-MP, or AZA or corticosteroid dependence (exposure to ADT without IR is permitted)



Stratification

- ADT-IR status: Yes or No
- Baseline MES: 2 or 3

Endpoints and Statistical Considerations

- **Key Endpoints** (Week 12)
  - Primary: clinical response
  - Secondary: clinical remission, symptomatic remission, endoscopic improvement, histologic-endoscopic mucosal improvement (HEMI)
  - Analyses were controlled for multiple comparisons (overall population only)
- Analyses in subpopulations by ADT-IR history were prespecified and exploratory (not controlled for multiple comparisons)
- Analyses at Week 28 were prespecified and exploratory (not controlled for multiple comparisons)

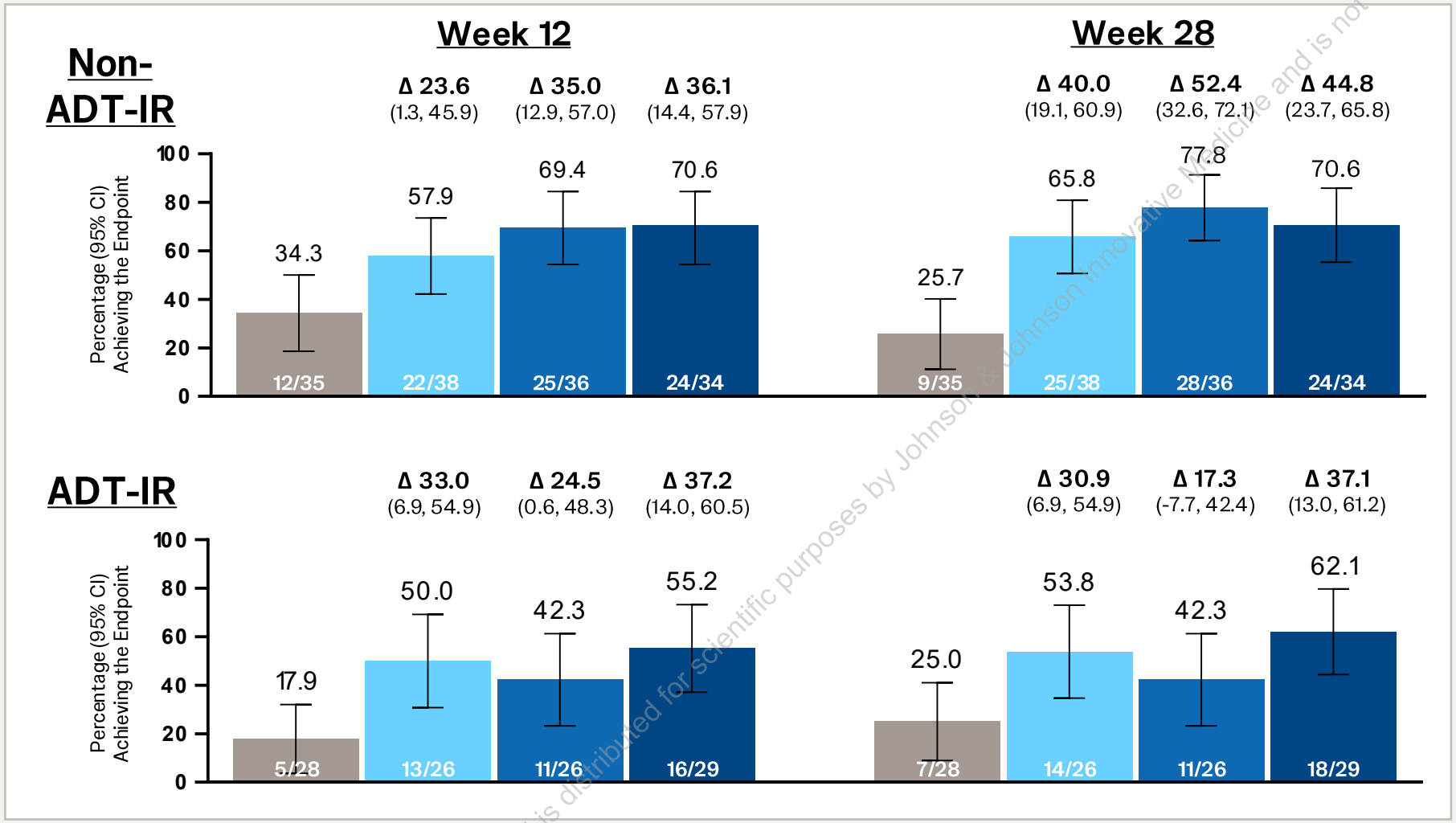
- Participants meeting inadequate response criteria at Week 16 received a treatment adjustment (placebo to icotrokinra 400 mg; sham adjustment for icotrokinra participants) and were considered non-responders at Week 28
- Participants with intercurrent events of ostomy or colectomy, prohibited changes 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
- 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

Demographics and Baseline Disease Characteristics

	Placebo		Icotrokinra 100 mg qd		Icotrokinra 200 mg qd		Icotrokinra 400 mg qd	
	Non-ADT-IR N=35	ADT-IR N=28	Non-ADT-IR N=38	ADT-IR N=26	Non-ADT-IR N=36	ADT-IR N=26	Non-ADT-IR N=34	ADT-IR N=29
UC disease duration (years), mean (SD)	8.7 (9.4)	7.7 (6.3)	5.8 (5.8)	9.8 (5.8)	6.9 (7.6)	9.0 (7.5)	6.6 (6.5)	8.7 (8.6)
Extensive disease on screening endoscopy, n (%)	15 (42.9%)	12 (42.9%)	13 (34.2%)	10 (38.5%)	14 (38.9%)	9 (34.6%)	16 (47.1%)	13 (44.8%)
Modified Mayo score, mean (SD)	6.66 (1.41)	6.86 (0.97)	6.32 (1.21)	6.88 (1.37)	6.83 (1.18)	6.65 (1.65)	6.44 (1.48)	6.55 (1.33)
Mayo endoscopic subscore = 3 [severe], n (%)	20 (57.1%)	16 (57.1%)	21 (55.3%)	17 (65.4%)	22 (61.1%)	15 (57.7%)	19 (55.9%)	18 (62.1%)
Fecal calprotectin >250 mg/kg, n/N (%)	26/29 (89.7%)	20/23 (87.0%)	28/33 (84.8%)	19/21 (90.5%)	29/31 (93.5%)	20/22 (90.9%)	27/31 (87.1%)	25/27 (92.6%)
CRP >3 mg/L, n (%)	16 (45.7%)	14 (50.0%)	18 (47.4%)	13 (52.0%)	18 (50.0%)	20 (76.9%)	17 (51.5%)	16 (55.2%)
Exposed to ADT without IR, n (%)	3 (8.6%)	---	4 (10.5%)	---	5 (13.9%)	---	3 (8.8%)	---
Prior ADT-IR, n (%)								
1 ADT class	---	22 (78.6%)	---	19 (73.1%)	---	21 (80.8%)	---	15 (51.7%)
2 ADT classes	---	6 (21.4%)	---	6 (23.1%)	---	5 (19.2%)	---	14 (48.3%)
>2 ADT classes	---	0	---	1 (3.8%)	---	0	---	0

Advanced therapy (ADT) classes include TNFα blockers (adalimumab, golimumab, infliximab), IL-12/23 antagonists (ustekinumab), integrin receptor antagonists (vedolizumab), JAK inhibitors (tofacitinib, upadacitinib, filgotinib), and S1P receptor modulators (ozanimod, etrasimod)

Clinical Response (Primary Endpoint at Week 12)



Placebo

Icotrokinra 100 mg qd

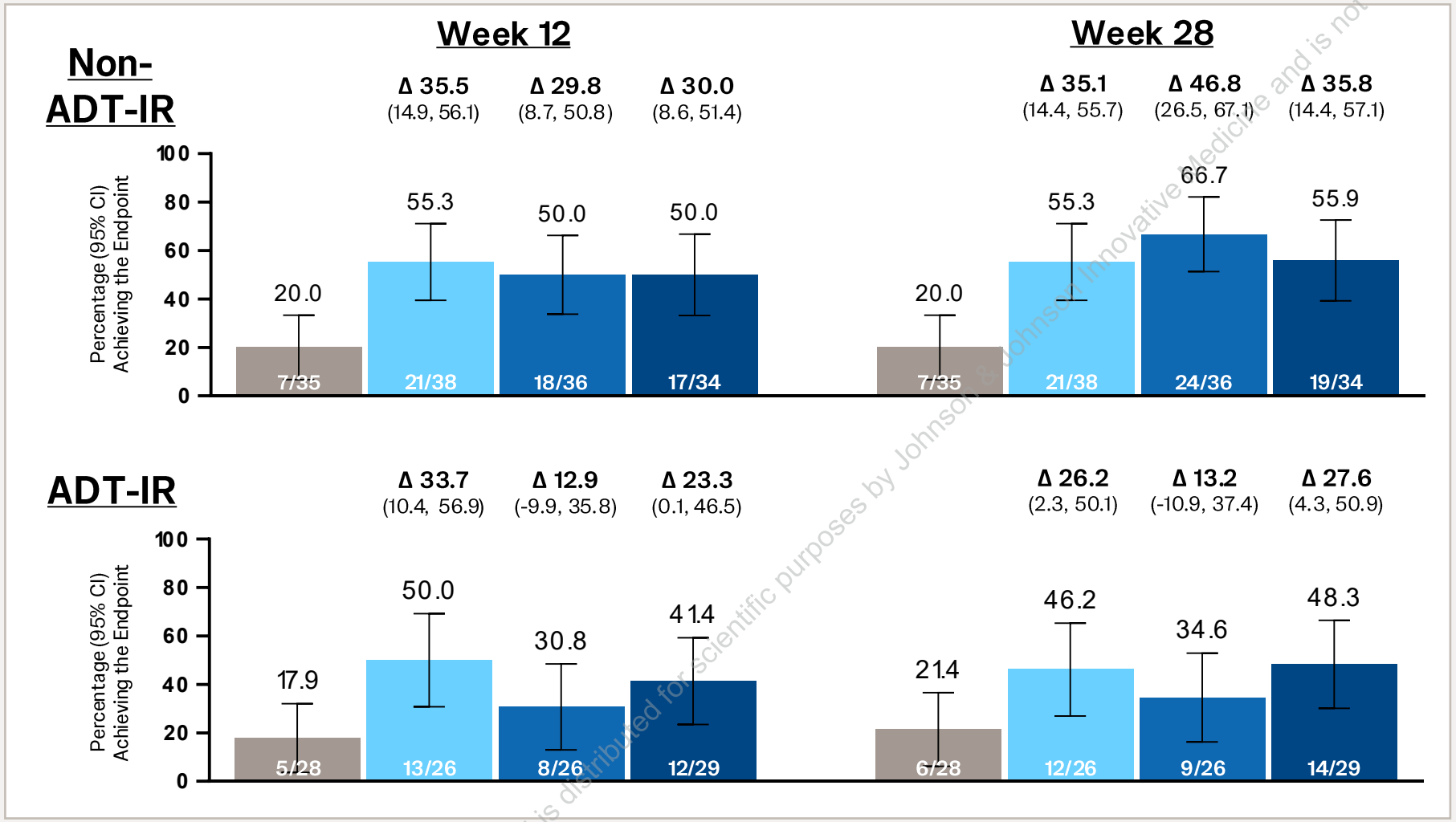
Icotrokinra 200 mg qd

Icotrokinra 400 mg qd

Clinical response: a decrease from baseline in the modified Mayo score by ≥30% and ≥2 points, with either a ≥1-point decrease from baseline in the rectal bleeding subscore or a rectal bleeding subscore of 0 or 1

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 ADT-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. Participants who met inadequate response criteria for dose adjustment at week 16 were also considered non-responders moving forward. 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.

Symptomatic Remission

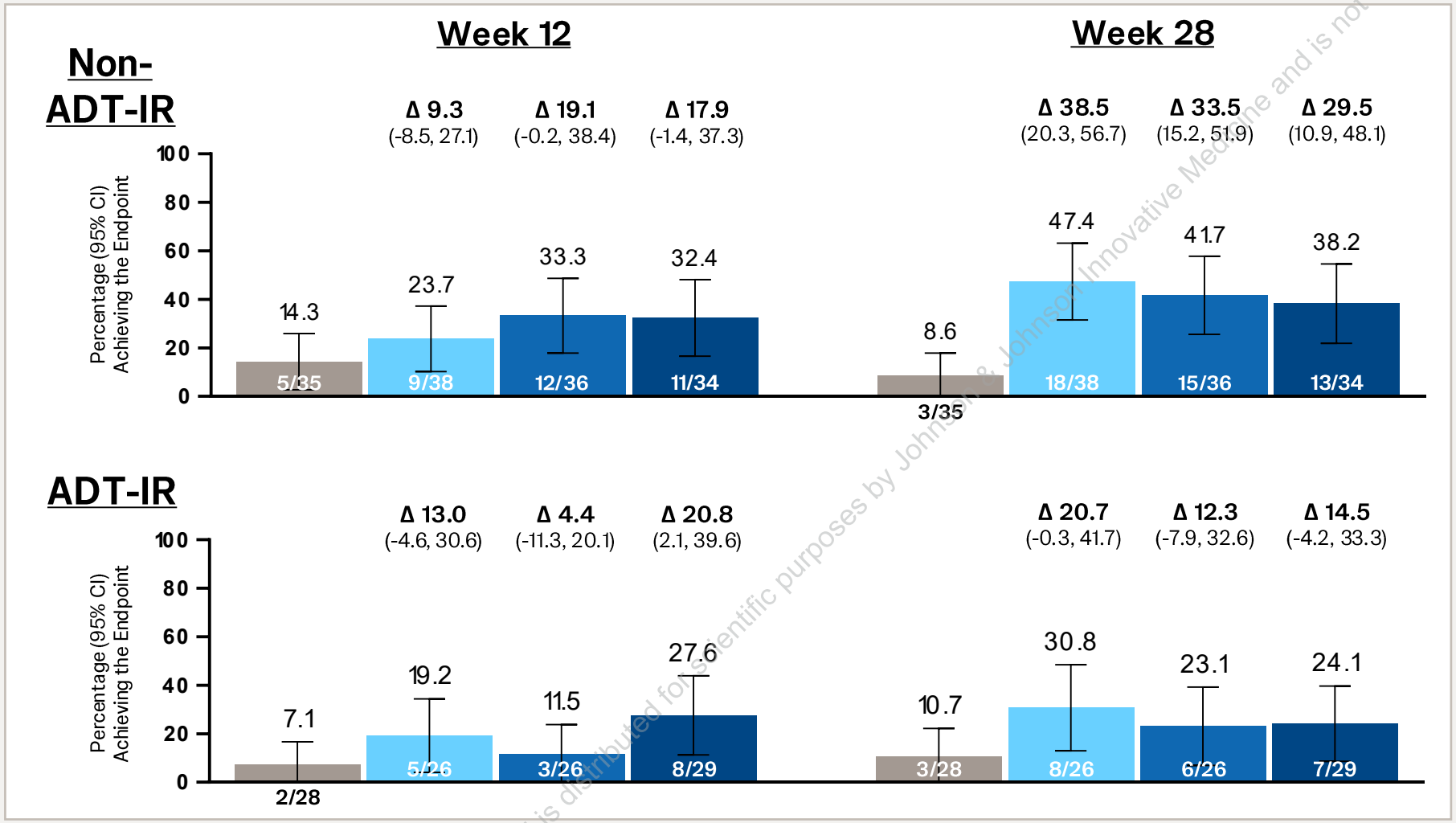


- Placebo
- Icotrokinra 100 mg qd
- Icotrokinra 200 mg qd
- Icotrokinra 400 mg qd

Symptomatic remission: stool frequency subscore of 0 or 1 and rectal bleeding 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 ADT-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. Participants who met inadequate response criteria for dose adjustment at week 16 were also considered non-responders moving forward. 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.

Clinical Remission

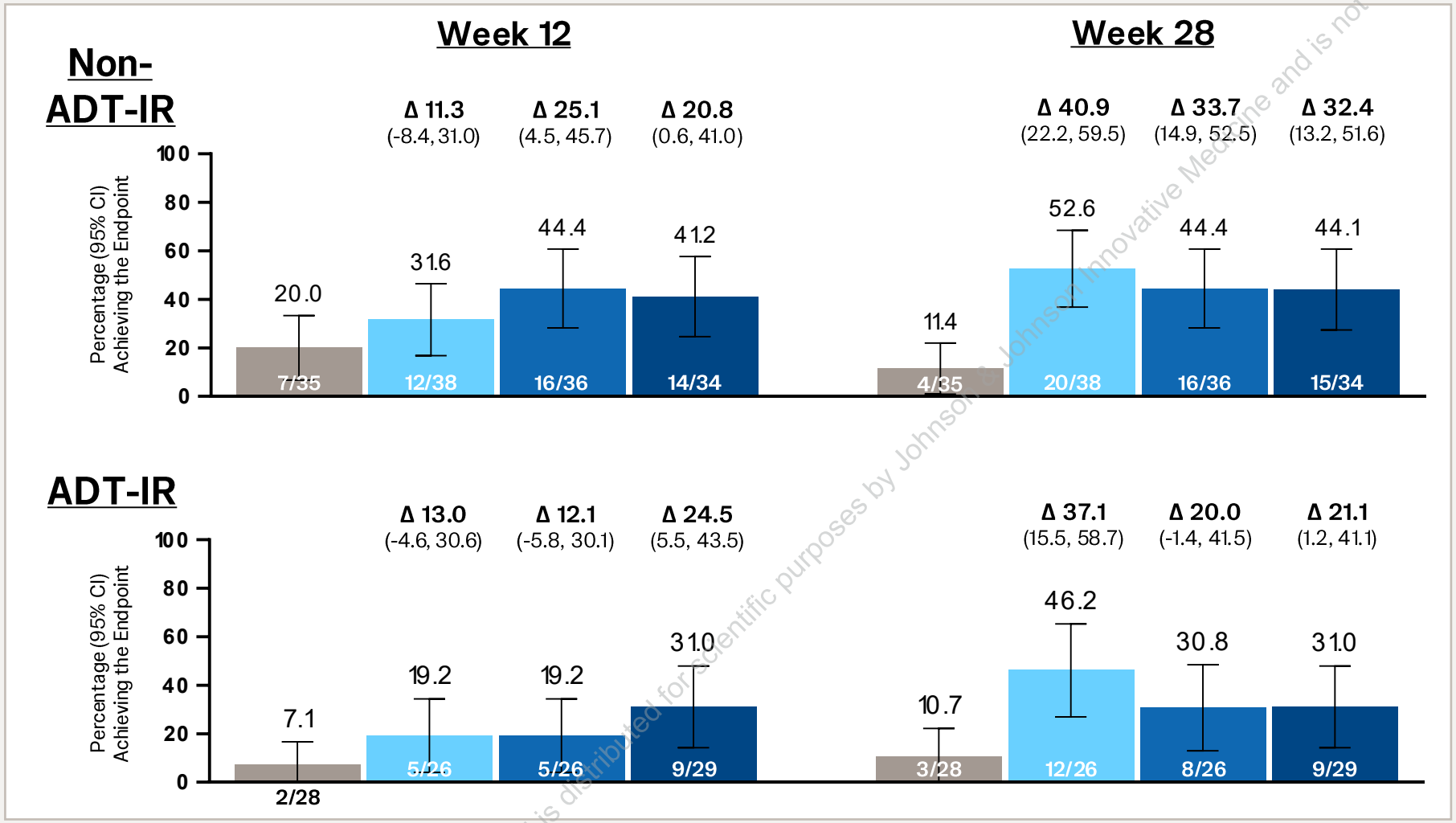


- Placebo
- Icotrokinra 100 mg qd
- Icotrokinra 200 mg qd
- Icotrokinra 400 mg qd

Clinical remission: stool frequency subscore of 0 or 1, rectal bleeding subscore of 0, and Mayo endoscopic subscore of 0 or 1

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 ADT-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. Participants who met inadequate response criteria for dose adjustment at week 16 were also considered non-responders moving forward. 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.

Endoscopic Improvement



Placebo

Icotrokinra 100 mg qd

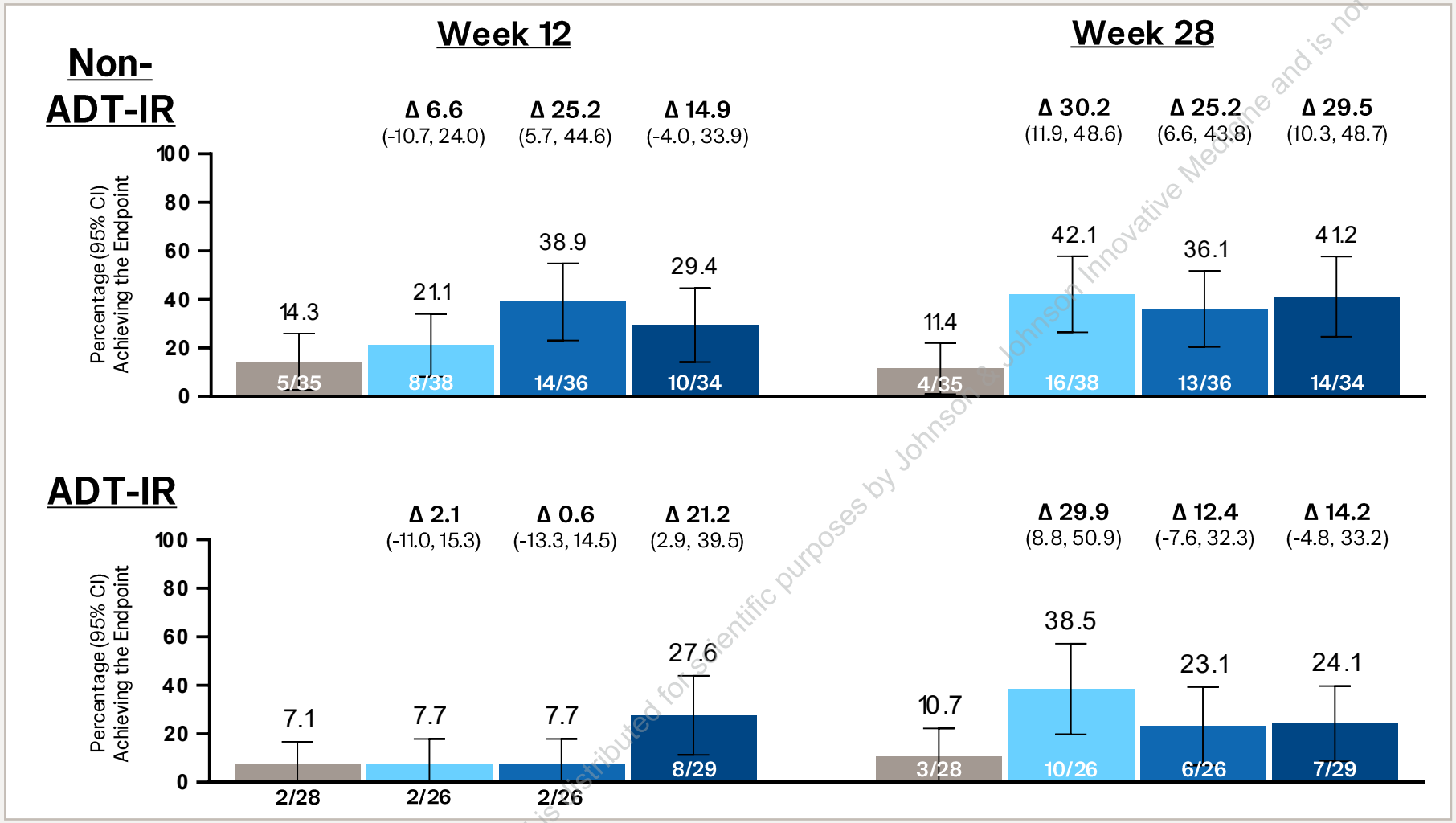
Icotrokinra 200 mg qd

Icotrokinra 400 mg qd

Endoscopic improvement: Mayo endoscopic subscore of 0 or 1

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 ADT-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. Participants who met inadequate response criteria for dose adjustment at week 16 were also considered non-responders moving forward. 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)



Placebo

Icotrokinra 100 mg qd

Icotrokinra 200 mg qd

Icotrokinra 400 mg qd

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

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 ADT-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. Participants who met inadequate response criteria for dose adjustment at week 16 were also considered non-responders moving forward. 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.

Conclusions

- Once-daily icotrokinra demonstrated efficacy in participants with moderately to severely active ulcerative colitis at Week 12 and Week 28, irrespective of prior ADT history
- Within the active treatment groups clinical and endoscopic outcomes (clinical response, symptomatic remission, clinical remission, endoscopic improvement, and HEMI) were generally maintained or improved in both subpopulations from Week 12 to Week 28
- Proportions of participants who met these endpoints were greater in the Non-ADT-IR subpopulation compared with the ADT-IR subpopulation

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- This work was supported by Johnson & Johnson

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