

Long-Term Efficacy and Safety of Icotrokinra, a First-in-class Targeted Oral Peptide That Precisely Blocks the IL-23 Receptor, In Ulcerative Colitis: Results From the ANTHEM-UC Long-Term Extension

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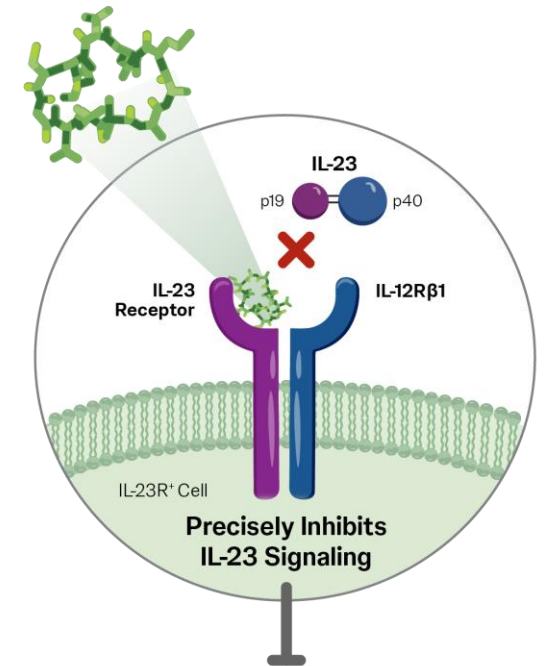
Background and Objective

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 delivered clinically meaningful improvements across key secondary endpoints at Week 12, which were maintained or improved at Week 28²

Icotrokinra Blocks IL-23 From Binding to its Receptor

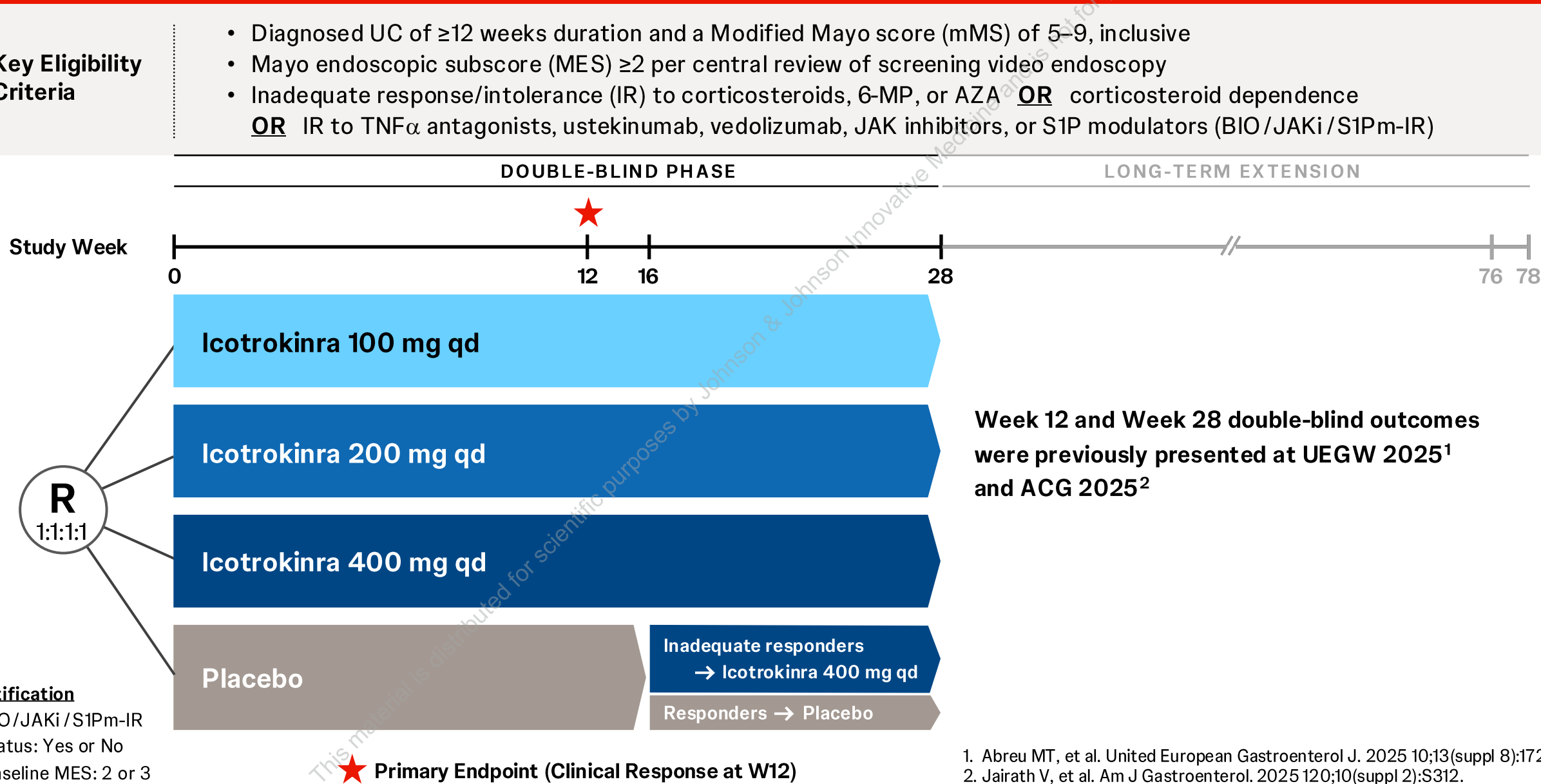


Inhibits IL-17A, IL-17F, and IL-22 Production

Here we present final efficacy and safety outcomes with icotrokinra from the ANTHEM-UC long-term extension (LTE)

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.

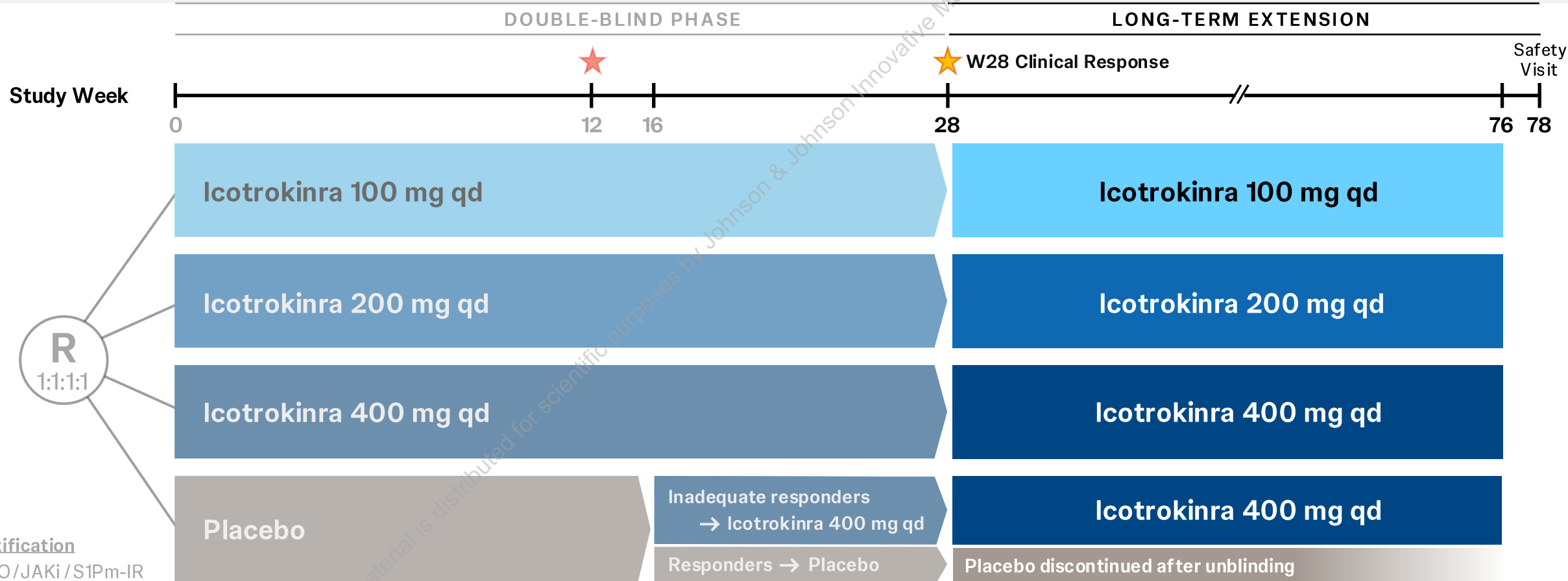
ANTHEM-UC Design



ANTHEM-UC 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 TNF α antagonists, ustekinumab, vedolizumab, JAK inhibitors, or S1P modulators (BIO/JAKi/S1Pm-IR)



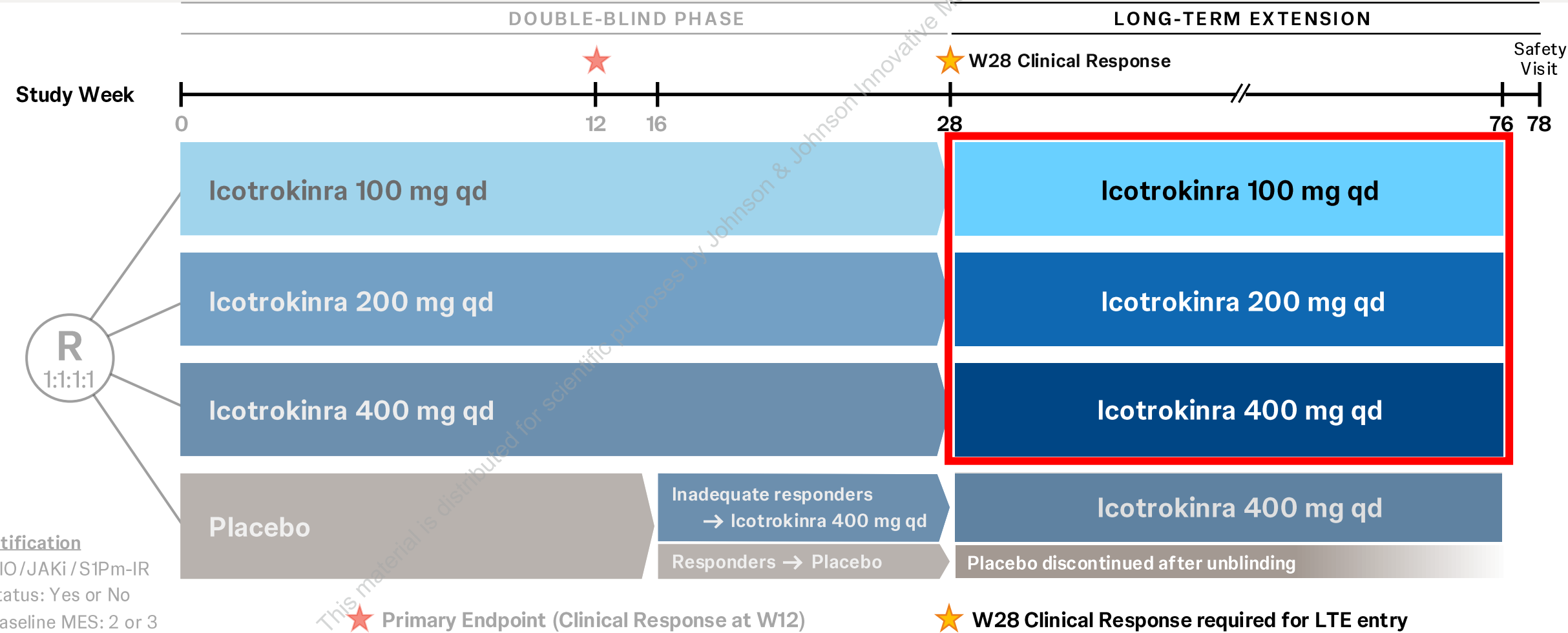
★ Primary Endpoint (Clinical Response at W12)

★ W28 Clinical Response required for LTE entry

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Endpoints and Statistical Considerations

➤ **LTE endpoints included:**

- Clinical response at Week 76
- Clinical remission at Week 76
- Corticosteroid-free clinical remission at Week 76
- Endoscopic improvement at Week 76
- Symptomatic remission through Week 76

➤ All endpoints were prespecified, exploratory, and assessed in participants who entered and received study treatment in the LTE (LTE analysis set). Analyses in ADT subgroups were not prespecified.

➤ Statistical testing was not performed

- ✔ Participants with intercurrent events of ostomy or colectomy 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
- ✔ 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
- ✔ Week 76 efficacy endpoints based on the Mayo score were determined using the local Mayo endoscopy subscore

Characteristics of the LTE Population at Baseline

	Icotrokinra 100 mg qd	Icotrokinra 200 mg qd	Icotrokinra 400 mg qd
LTE analysis set, N	48	44	44
Age, years, mean (SD)	46.3 (14.6)	43.4 (15.3)	39.8 (15.2)
Sex, male, n (%)	30 (62.5%)	24 (54.5%)	26 (59.1%)
Race, White, n (%)	34 (70.8%)	29 (65.9%)	30 (68.2%)
UC disease duration, years, mean (SD)	7.4 (5.7)	7.8 (8.2)	7.8 (8.2)
Extensive disease, n (%)	17 (35.4%)	13 (29.5%)	20 (45.5%)
Modified Mayo score [max = 9], mean (SD)	6.5 (1.2)	6.9 (1.2)	6.6 (1.3)
Mayo endoscopic subscore of 3 (severe), n (%)	26 (54.2%)	25 (56.8%)	25 (56.8%)
Fecal calprotectin, mg/kg, median [IQR]	1638.2 [603.7; 3713.0]	2532.1 [644.2; 4183.6]	1534.6 [597.2; 4825.8]
CRP, mg/L, median [IQR]	2.9 [1.1; 6.6]	4.0 [1.0; 11.9]	4.2 [1.5; 8.8]
Baseline corticosteroid use, n (%)	16 (33.3%)	23 (52.3%)	14 (31.8%)
No history of BIO/JAKi/S1Pm-IR, n (%)	29 (60.4%)	30 (68.2%)	25 (56.8%)
BIO/JAKi/S1Pm-IR, n (%)	19 (39.6%)	14 (31.8%)	19 (43.2%)
IR to 1 class / mechanism ^a	14 (73.7%)	13 (92.9%)	11 (57.9%)
IR to 2 classes / mechanisms ^a	5 (26.3%)	1 (7.1%)	8 (42.1%)

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 = TNF α antagonists, ustekinumab, or vedolizumab; IR = prior inadequate response or intolerance.

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85% of participants (LTE analysis set) remained on treatment through Week 76

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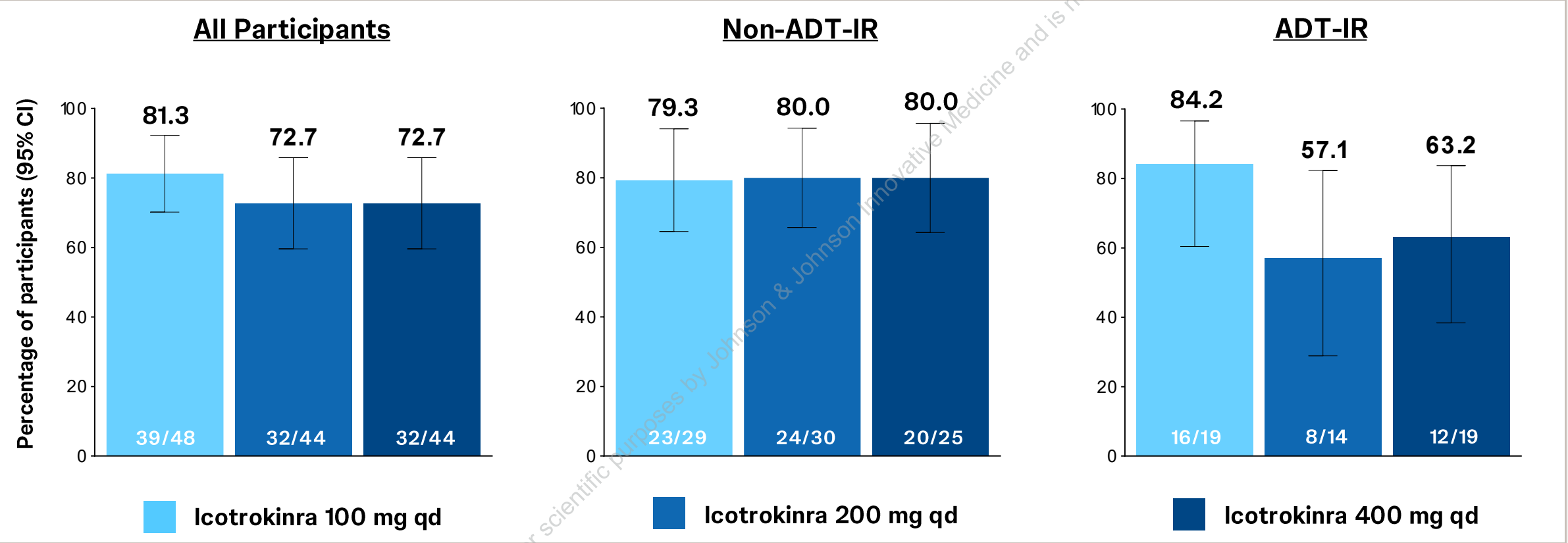
Clinical Response at Week 76



Clinical response: a decrease from baseline in the modified Mayo score by $\geq 30\%$ 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

Data presented as percentage of participants in the LTE analysis set attaining the endpoint (with NRI). No biopsies were collected at Week 76. Nonresponder imputation (NRI): Participants with intercurrent events of ostomy or colectomy 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, as were those who were missing data for the endpoint. Week 76 efficacy endpoints based on the Mayo score were determined using the local Mayo endoscopy subscore.

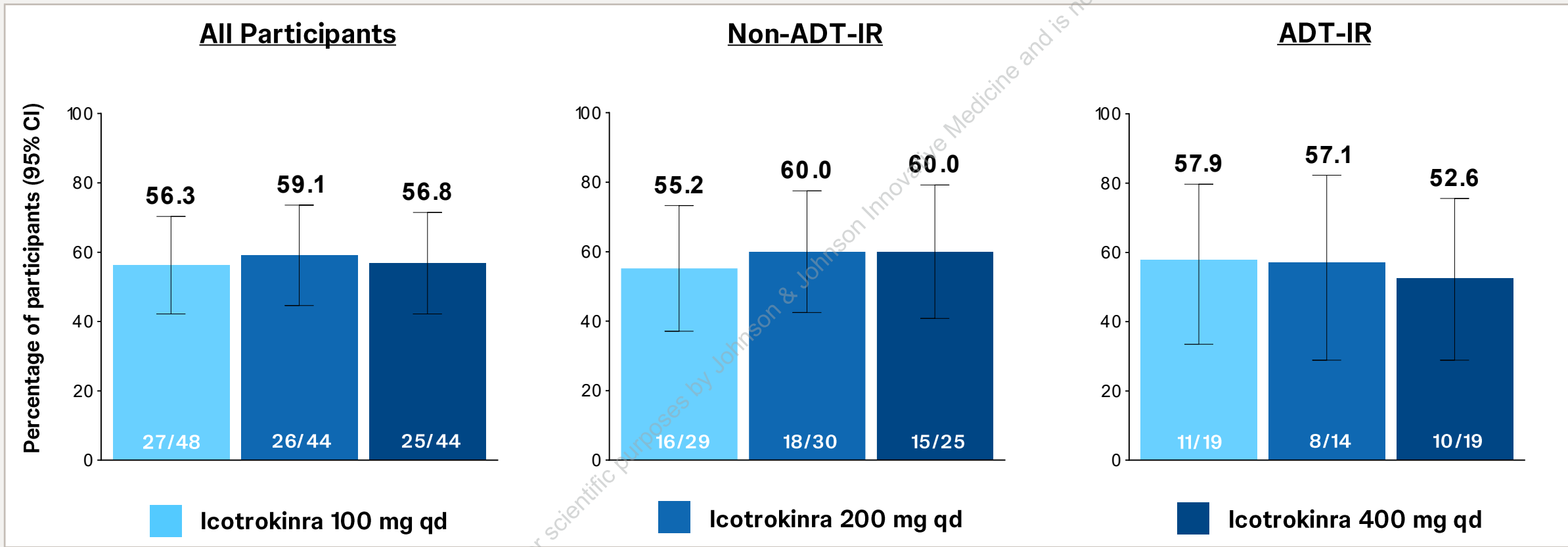
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Clinical Remission at Week 76



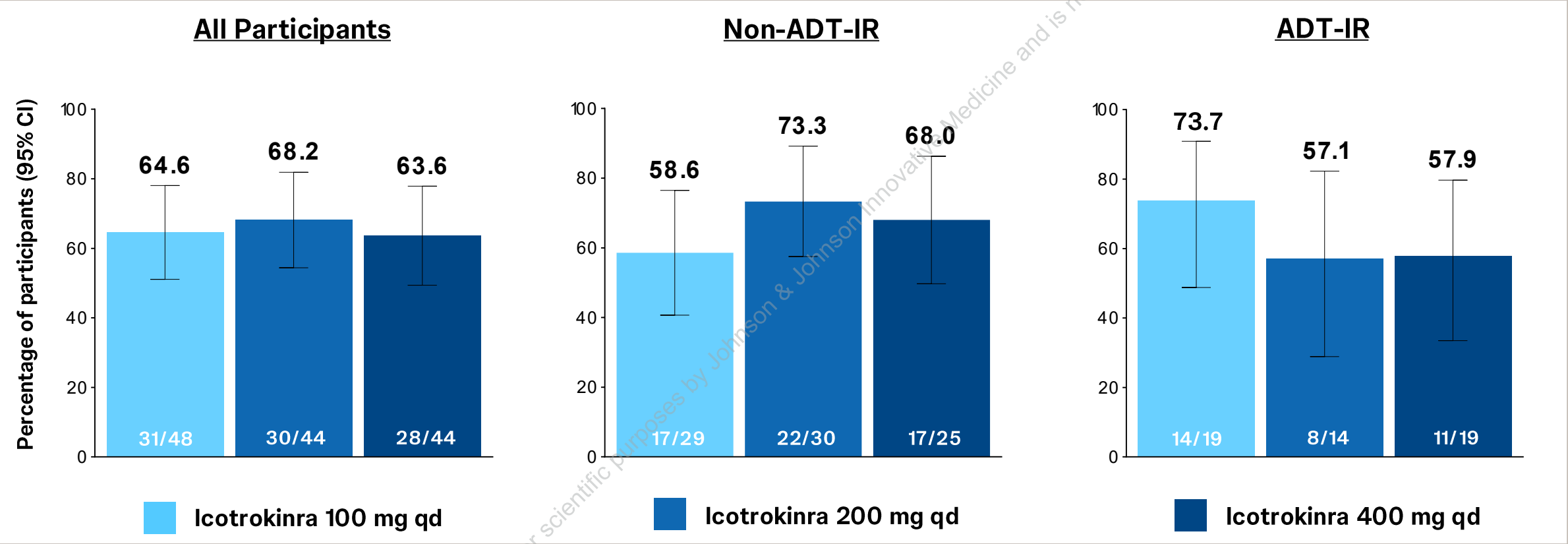
Clinical remission: stool frequency subscore of 0 or 1, rectal bleeding subscore of 0, and Mayo endoscopy subscore of 0 or 1



97% of icotrokinra participants who achieved clinical remission at W76 were also corticosteroid-free at W76

Data presented as percentage of participants in the LTE analysis set attaining the endpoint (with NRI). No biopsies were collected at Week 76. Nonresponder imputation (NRI): Participants with intercurrent events of ostomy or colectomy 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, as were those who were missing data for the endpoint. Week 76 efficacy endpoints based on the Mayo score were determined using the local Mayo endoscopy subscore.

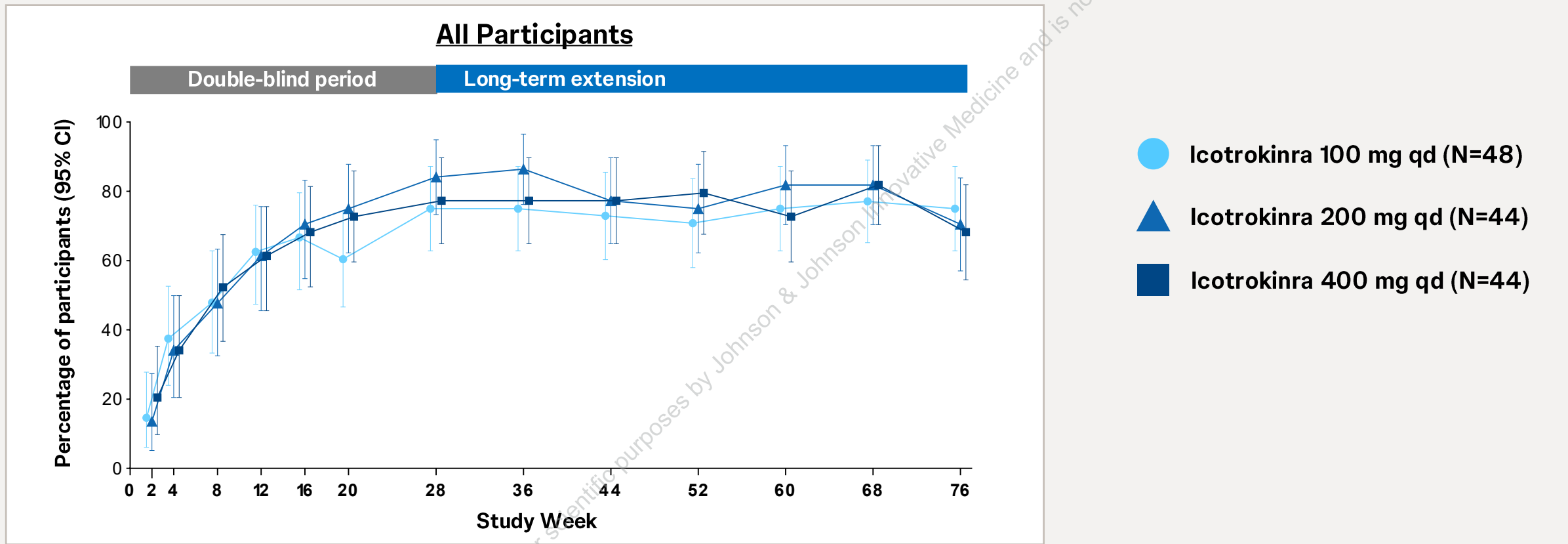
Endoscopic Improvement at Week 76



Endoscopic improvement: Mayo endoscopy subscore of 0 or 1

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Symptomatic Remission Through Week 76



Symptomatic remission: stool frequency subscore of 0 or 1 and rectal bleeding subscore of 0

Data presented as percentage of participants in the LTE analysis set attaining the endpoint (with NRI). No biopsies were collected at Week 76. Nonresponder imputation (NRI): Participants with intercurrent events of ostomy or colectomy 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, as were those who were missing data for the endpoint. Week 76 efficacy endpoints based on the Mayo score were determined using the local Mayo endoscopy subscore.

Summary of Adverse Events Through Week 78

	Placebo ^a	Icotrokinra 100 mg qd	Icotrokinra 200 mg qd	Icotrokinra 400 mg qd
Safety analysis set, N	63	64	62	63
Average duration of follow-up, weeks	27.1	62.3	59.7	58.7
Average duration of treatment, weeks	25.0	59.5	57.5	56.4
Deaths, n	0	0	0	0
Participants with events per 100 participant-years of follow-up [participants with events]				
AEs	122.32 [40]	61.52 [47]	66.29 [47]	73.34 [52]
Serious AEs	18.35 [6]	5.24 [4]	5.64 [4]	2.82 [2]
AEs leading to discontinuation of study agent	21.41 [7]	3.93 [3]	8.46 [6]	4.23 [3]
Infections ^b	58.10 [19]	36.65 [28]	43.72 [31]	31.03 [22]
Serious infections ^b	3.06 [1]	1.31 [1]	0 [0]	0 [0]

-  The most common adverse events with icotrokinra through Week 78 were worsening of ulcerative colitis, upper respiratory tract infection, nasopharyngitis, headache, and arthralgia
-  Through Week 78, no participant experienced active tuberculosis, a potential Hy's law case, drug-induced liver injury, clinically important hepatic disorder, VTE, serious hypersensitivity, MACE, or opportunistic infection
-  During the LTE, a case of in-situ ductal breast carcinoma (not related to study intervention) was reported in the 100-mg group. A participant receiving placebo reported a pulmonary nodule during the study that was confirmed as squamous cell carcinoma (not related) after study completion.

a. Includes participants randomized to placebo excluding data after a participant received dose modification with icotrokinra at Week 16.

b. Infections were defined as any adverse event coded to the MedDRA system organ class 'Infections and infestations'.

Conclusions



The majority of participants with moderately to severely active UC who were randomized to icotrokinra and entered the LTE were in clinical response, clinical remission, or endoscopic improvement at Week 76



Symptomatic remission was observed as early as Week 4 and rates were maintained or improved through Week 76



Icotrokinra was well tolerated, with 85% of participants in the LTE analysis set remaining on treatment through Week 76. Exposure-adjusted adverse events were numerically similar or lower with icotrokinra compared with placebo.



Icotrokinra has the potential to offer therapeutic benefit to patients with UC in a once-daily oral treatment and is being evaluated in Phase 3 trials

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