

ICOTROKINRA, THE FIRST TARGETED ORAL PEPTIDE THAT SELECTIVELY BLOCKS THE INTERLEUKIN-23 RECEPTOR, REDUCES SYSTEMIC AND TISSUE INFLAMMATORY BURDEN IN ULCERATIVE COLITIS: RESULTS FROM THE ANTHEM-UC STUDY



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Digestive Disease Week®

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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

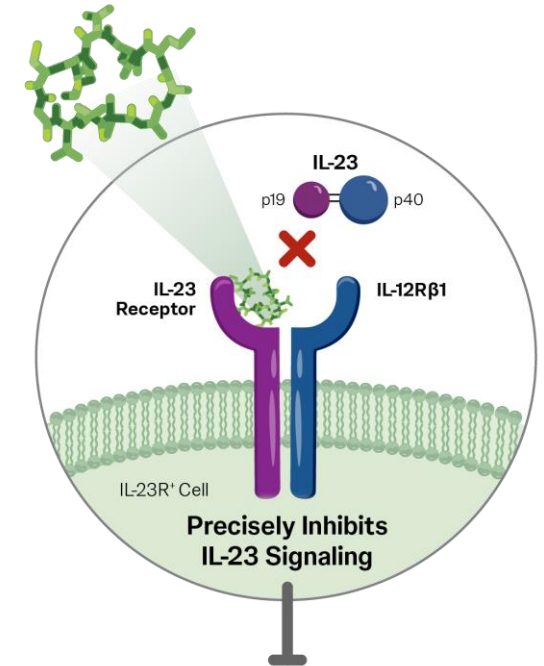
Background and Objective

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 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 28²

Icotrokinra Blocks IL-23 From Binding to its Receptor

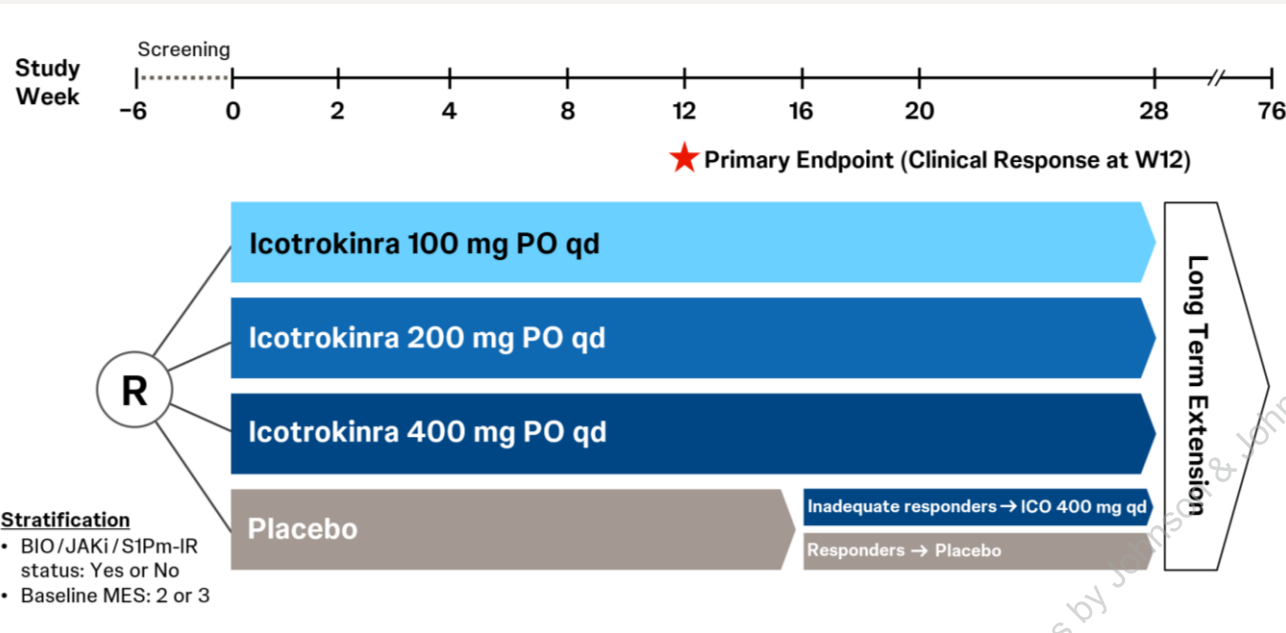


Inhibits IL-17A, IL-17F, and IL-22 Production

Here we report the impact of icotrokinra treatment on systemic and tissue biomarkers of inflammatory burden in ANTHEM-UC study participants

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 and Methods



Key Eligibility Criteria

- Diagnosed UC of ≥ 12 weeks duration
- Modified Mayo score of 5–9, inclusive
- Mayo endoscopic subscore (MES) ≥ 2 per central review
- Inadequate response/intolerance (IR) to CS, 6-MP, or AZA **OR** CS dependence **OR** IR to TNF α antagonists, ustekinumab, vedolizumab, JAK inhibitors, or S1P receptor modulators (BIO/JAKi/S1Pm-IR)

Clinical inflammatory biomarkers: C-reactive protein and fecal calprotectin

Systemic IL-23 pathway biomarkers: IL-22, IL-17A, and IL-17F

Tissue biomarkers: IL-23 pathway gene expression changes in colonic biopsies

- At screening, biopsies were collected from the colon/rectum (at least 15–20 cm from the anal verge) in a representative area that was consistent with the severity of inflammation
- Subsequent biopsies from the same location were collected at Weeks 12 and 28

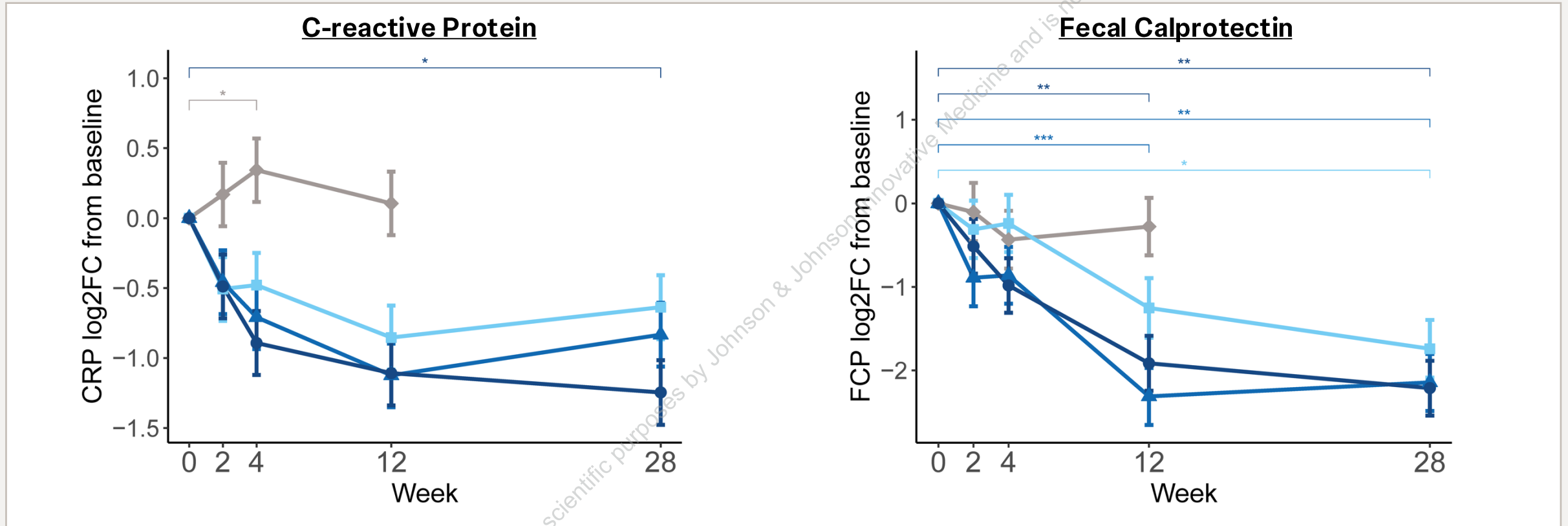
Statistical analyses of these biomarkers were not controlled for multiple comparisons

Demographics and Baseline Disease Characteristics

	Placebo	Icetrokinra 100 mg qd	Icetrokinra 200 mg qd	Icetrokinra 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)	8.3 (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]

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Clinical Inflammatory Biomarkers



◆ Placebo
n = 63

■ Ictrokinra 100 mg qd
n = 64

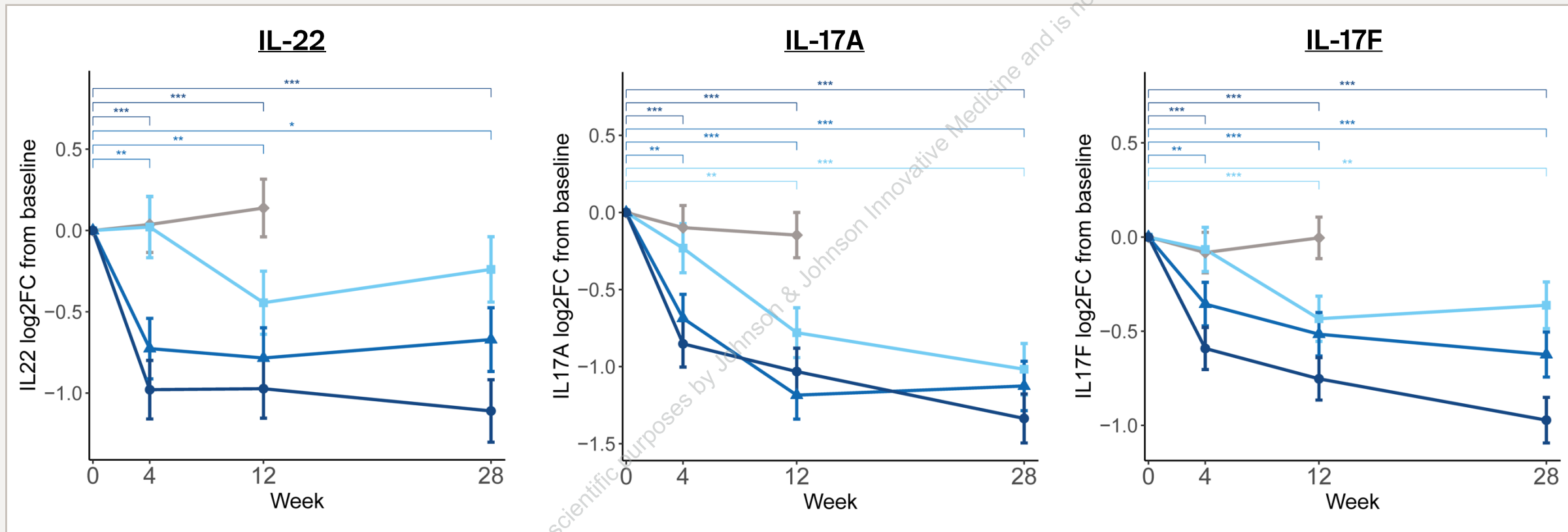
▲ Ictrokinra 200 mg qd
n = 62

● Ictrokinra 400 mg qd
n = 63

Nominal *p < 0.05, **p < 0.001, ***p < 0.001 for log2 fold change from baseline

Plots track mean values (estimated marginal means) using a linear mixed effect model that accounts for treatment*time interaction, age, and sex, with subject as a random effect. Error bars are model-based standard errors.

Systemic IL-23 Pathway Biomarkers



◆ Placebo
n = 44-58

■ Icotrokinra 100 mg qd
n = 44-50

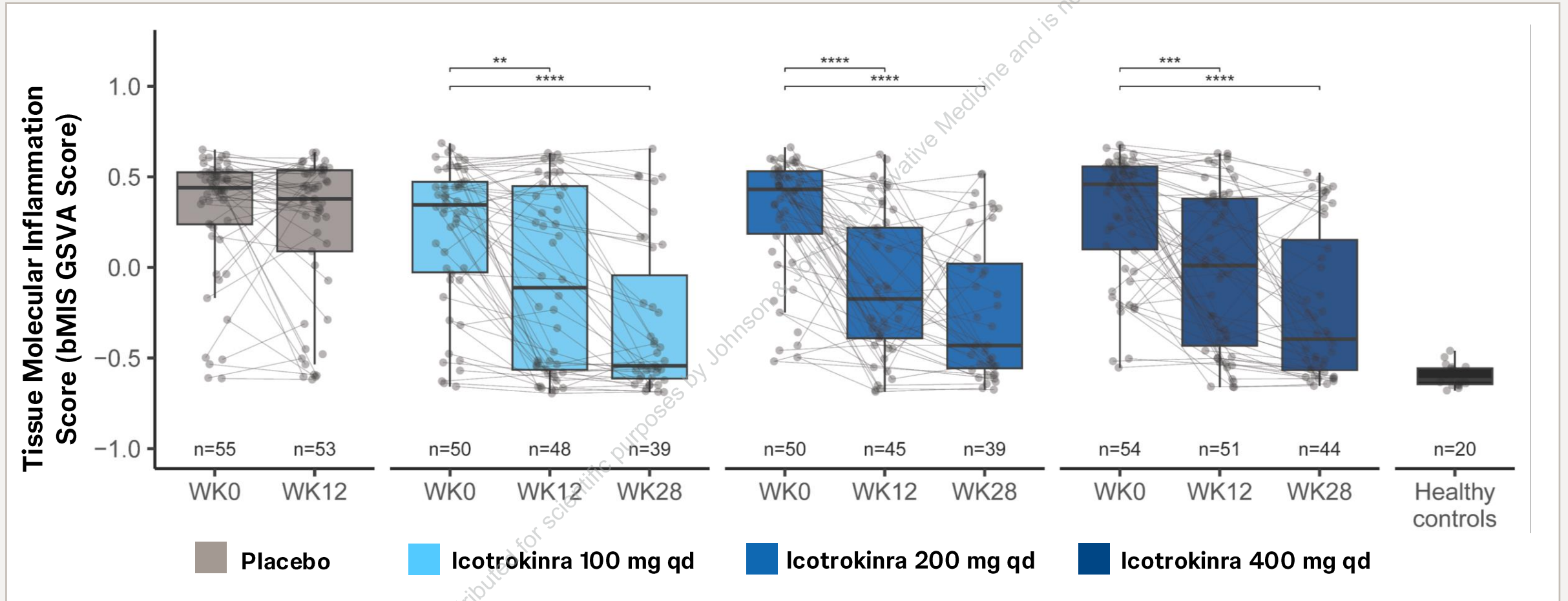
▲ Icotrokinra 200 mg qd
n = 44-49

● Icotrokinra 400 mg qd
n = 46-53

Nominal *p<0.05, **p<0.001, ***p<0.001, ****p<0.0001 for log2 fold change from baseline

Plots track mean values (estimated marginal means) using a linear mixed effect model that accounts for treatment*time interaction, age, and sex, with subject as a random effect. Error bars are model-based standard errors.

Tissue Inflammatory Burden

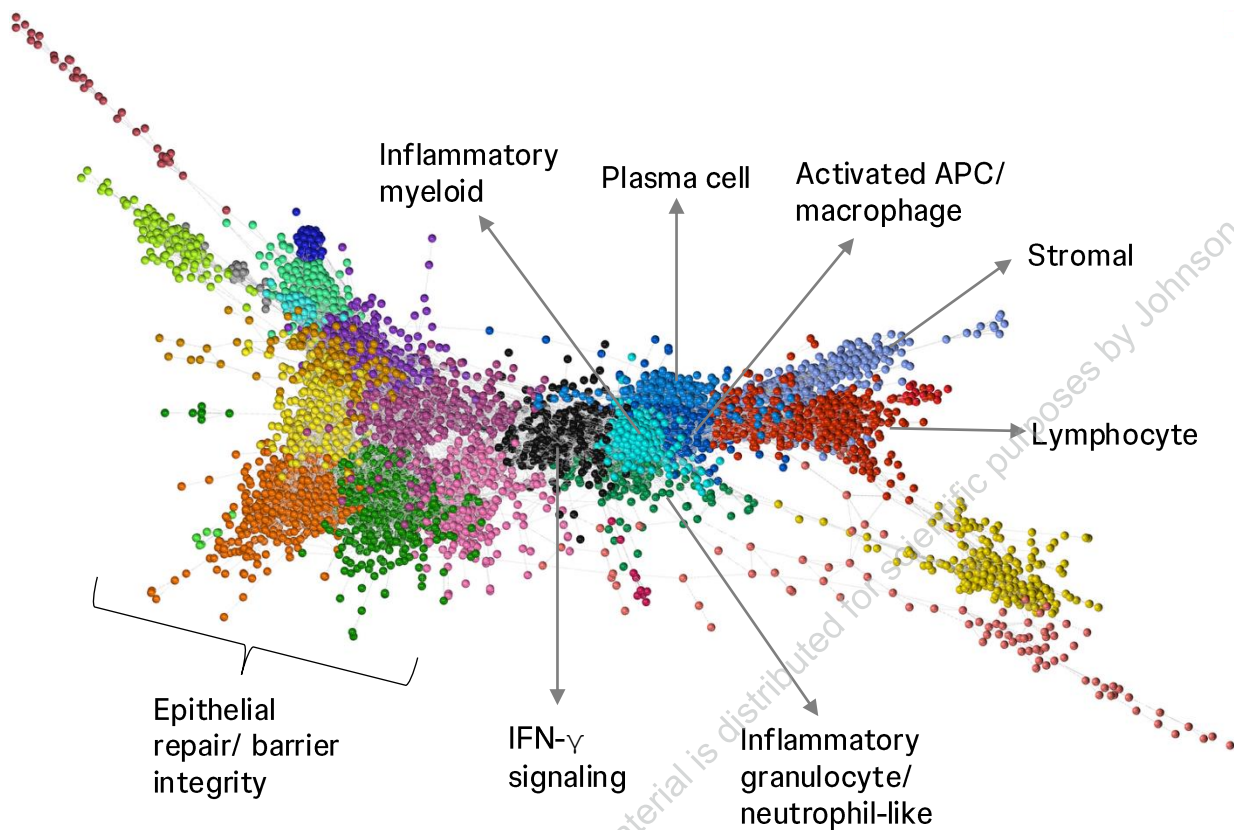


Nominal **p<0.01, ***p<0.001, ****p<0.0001

Quantification of biopsy molecular inflammation score (bMIS) using gene set variation analysis (GSVA) at the indicated time points after placebo or icotrokinra treatment. GSVA scores are depicted and compared at Week 0 and Week 12 or Week 28 with a t-test. Error bars are 95% confidence intervals. Data from healthy controls were generated from commercially obtained colonic biopsies.

Tissue Transcriptome: Impact of Icotrokinra Treatment

Gene correlation network analysis identifies distinct cell clusters in colonic biopsy transcriptomic data



UC patients relative to healthy controls

Downregulated in UC samples

Unchanged in UC samples

Upregulated in UC samples

Icotrokinra treatment effect: Week 12 relative to Week 0

Upregulated with icotrokinra

Unchanged with icotrokinra

Downregulated with icotrokinra

Abs(logFC > 0)
FDR < 0.05

Conclusions



Precisely blocking the IL-23 receptor with once-daily icotrokinra reduced IL-23–mediated inflammatory burden in the systemic circulation and in tissue of patients with ulcerative colitis



Icotrokinra induced transcriptional changes that are consistent with dampening of IL-23–driven inflammation and normalization of the tissue transcriptome



All once-daily doses of icotrokinra attenuated systemic and tissue inflammation; greater reduction of systemic inflammatory burden was observed with the 200 mg and 400 mg doses

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