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IN PARTNERSHIP WITH AIBD

Patient-Centered Management of IBD: Understanding the Current and Evolving Role of IL-23 Inhibitors

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Disclosures

- **Millie D. Long, MD, MPH, FACG:** Consultant – AbbVie, BMS, Celltrion, Eli Lilly, Janssen, Pfizer, Prometheus, Roivant, Sanofi, Takeda, Target Real World Evidence; Research Support – Eli Lilly, Pfizer, Takeda

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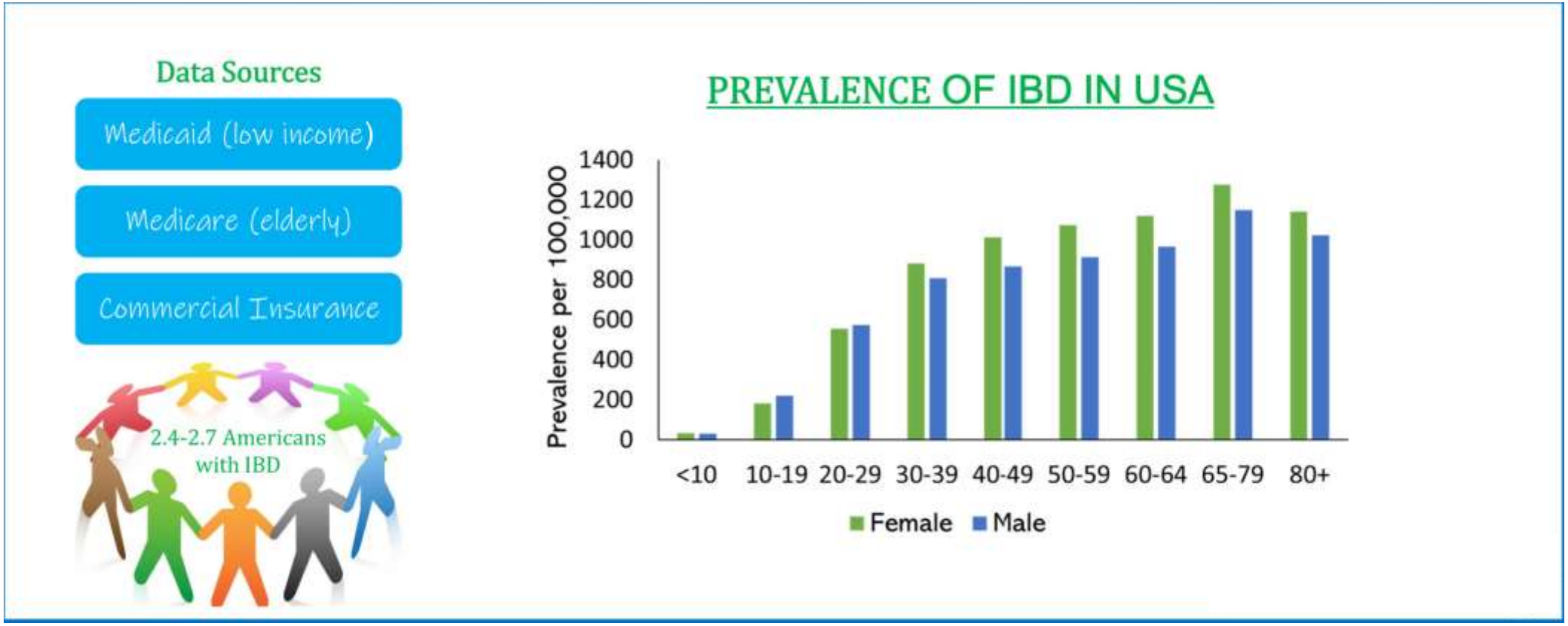
No product promotion or recommendation should be inferred.

Learning Objectives

- Identify and assess the burden associated with suboptimal treatment response and/or unresolved symptoms in IBD
- Describe the role of interleukins in the pathogenesis of IBD and the therapeutic implications of targeting IL-23 and CD64
- Evaluate the mechanisms of action, safety/efficacy data, indications, and patient-centered treatment considerations associated with available and emerging IL-23 inhibitors for IBD

IBD = inflammatory bowel disease; IL = interleukin.

Nearly 1% of Americans Have IBD



Lewis JD, et al. *Gastroenterology*. 2023;165(5):1197-1205.e2.

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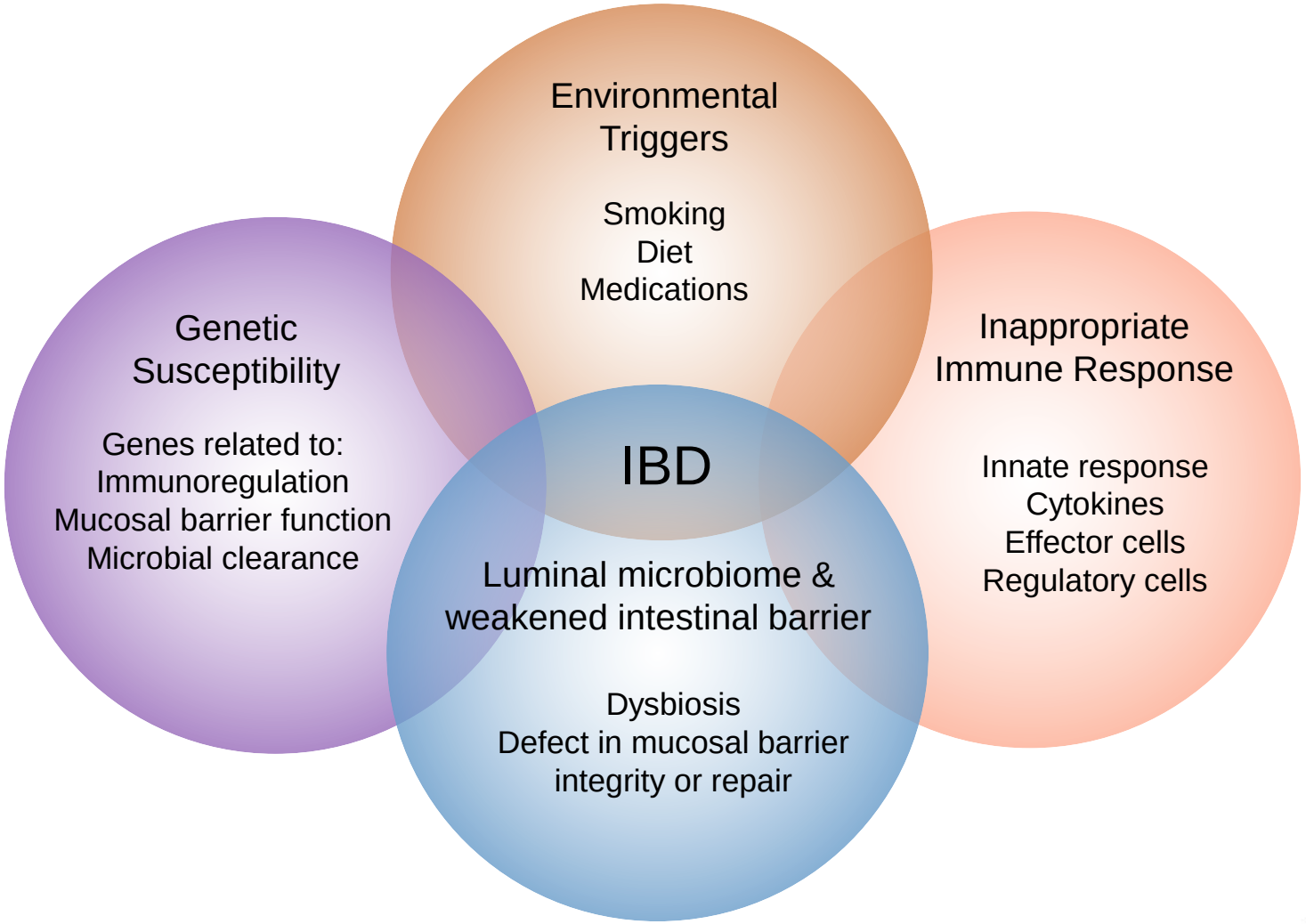
Etiopathogenesis of IBD Is Complex: Targets Multifactorial



Sartor RB. *Nat Clin Pract Gastroenterol Hepatol*. 2006;3(7):390-407.

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Unmet Needs from the Patients' Perspectives

- Symptoms (abdominal pain, bowel frequency, urgency)
- Fatigue
- Risk of surgery, risk of ostomy (#1 graded attribute = prevent surgery)
- Effective, fast-working medication
- Normal social interactions and activities
- Mental and psychological support
- Effect of disease and treatments in the long and short term

Schoefs E, et al. *J Crohns Colitis*. 2023;17(3):379-388.

IBD Complications Remain Prevalent: Requirement for Surgery

- Based on population-based studies
  - Risk of surgery 1, 5, 10 years after CD diagnosis is 16.3%, 33.3%, 46.6%, respectively
  - Risk of surgery 1, 5, 10 years after UC diagnosis is 4.9%, 11.6%, 15.6%, respectively

- Risk of surgery has decreased significantly over the past 6 decades, but remains elevated
  - 5-year risk: CD 24.2%, UC 7.6%

CD = Crohn's disease; UC = ulcerative colitis.

Frolkis AD, et al. *Gastroenterology*. 2013;145(5):996-1006.

Unmet Need: Limitations of Current Therapies

- 1990s optimism (anti-TNFs)
  - RCTs demonstrated lower clinical remission rates than hoped
  - Lower durability
- Since this time, huge gains in number of therapies and mechanisms
- Patients living in the “white space” – somewhere between the 30-60% efficacy seen in populations, and the 100% goal
- Response rates over time
  - 10-40% of patients with IBD may be primary non-responders to anti-TNFs
  - Annual risk for loss of response to TNF is ~13-24% (immunogenicity, suboptimal dosing)

TNF = tumor necrosis factor; RCTs = randomized controlled trials.

Raine T, Danese S. *Gastroenterology*. 2022;162(5):1507-1511. Allez M, et al. *J Crohns Colitis*. 2010;4(4):355-366. D'Haens GR, et al. *Am J Gastroenterol*. 2011;106(2):199-212. Gisbert JP, Panes J. *Am J Gastroenterol*. 2009;104(3):760-767. Billioud V, et al. *Am J Gastroenterol*. 2011;106(4):674-684. Roda G, et al. *Clin Transl Gastroenterol*. 2016;7(1):e135. Marsal J, et al. *Front Med* (Lausanne). 2022;9:897936.

The Therapeutic Landscape in IBD Continues to Evolve to Narrow the "Gaps"…

1950s-2019:

1950s-1970s: Pre-biologics era	1998-2013: Anti-TNF era	2014-2019: Expanding therapeutic targets
Corticosteroids, thiopurines, and aminosalicylates		Anti-integrin $\alpha_4\beta_7$, IL-12/23 inhibitors, and JAK inhibitors

Therapies shown here are approved for use in adults; however, local approvals vary. Please refer to local summary of product characteristics for full prescribing information. The timeline is illustrative and the references are not intended to be exhaustive of all therapies in these classes.
JAK = Janus kinase.

Benchimol EI, et al. *Cochrane Database Syst Rev*. 2008;2008(2):CD006792. Tominaga K, et al. *Front Pharmacol*. 2021;11:582291. de Boer NKH, et al. *J Crohns Colitis*. 2018;12(5):610-620. van Bodegraven AA and Mulder CJJ. *World J Gastroenterol*. 2006;12(38):6115-6123. EMA. Accessed May 2025. https://www.ema.europa.eu/en/medicines.

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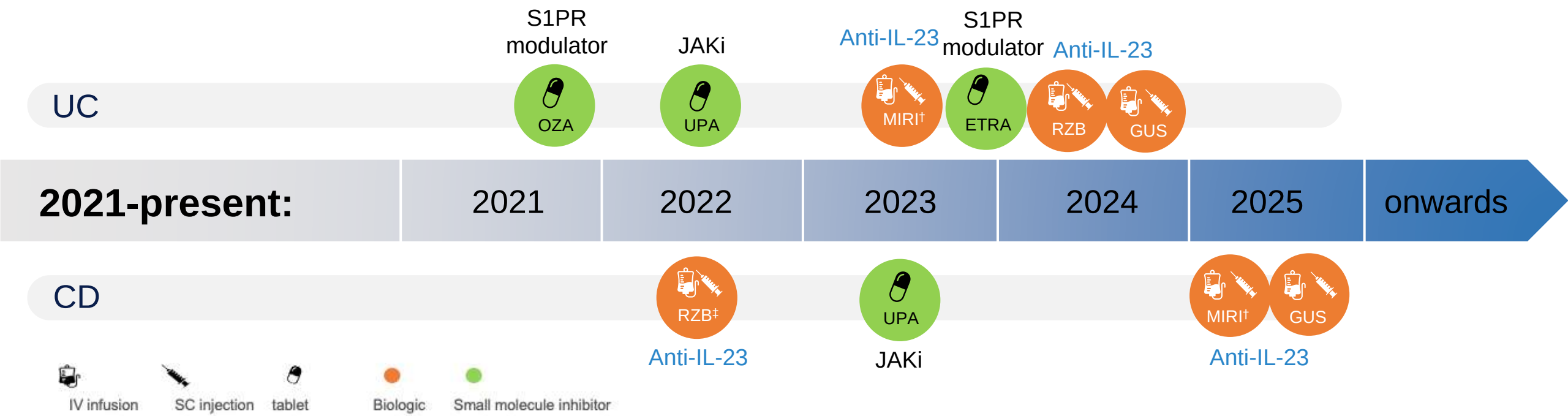
…with More Treatment Options Becoming Available



Therapies shown here are approved for use in adults; however, local approvals vary. Please refer to local summary of product characteristics for full prescribing information. The timeline is illustrative and the references are not intended to be exhaustive of all therapies in these classes.

†MIRI is administered via an IV infusion at weeks 0, 4, and 8, followed by SC injection Q4W; ‡RZB is delivered as IV infusions at weeks 0, 4, and 8, followed by SC injections at week 12 and every 8 weeks thereafter.

ETRA = etrasimod; FILGO = filgotinib; GUS = guselkumab; MIRI = mirikizumab; OZA = ozanimod; OD = once daily; RZB = risankizumab; S1PR = sphingosine-1-phosphate receptor; UPA = upadacitinib.

EMA. Accessed May 2025. https://www.ema.europa.eu/en/medicines. FDA. Accessed July 22, 2025. https://www.accessdata.fda.gov/scripts/cder/daf/.

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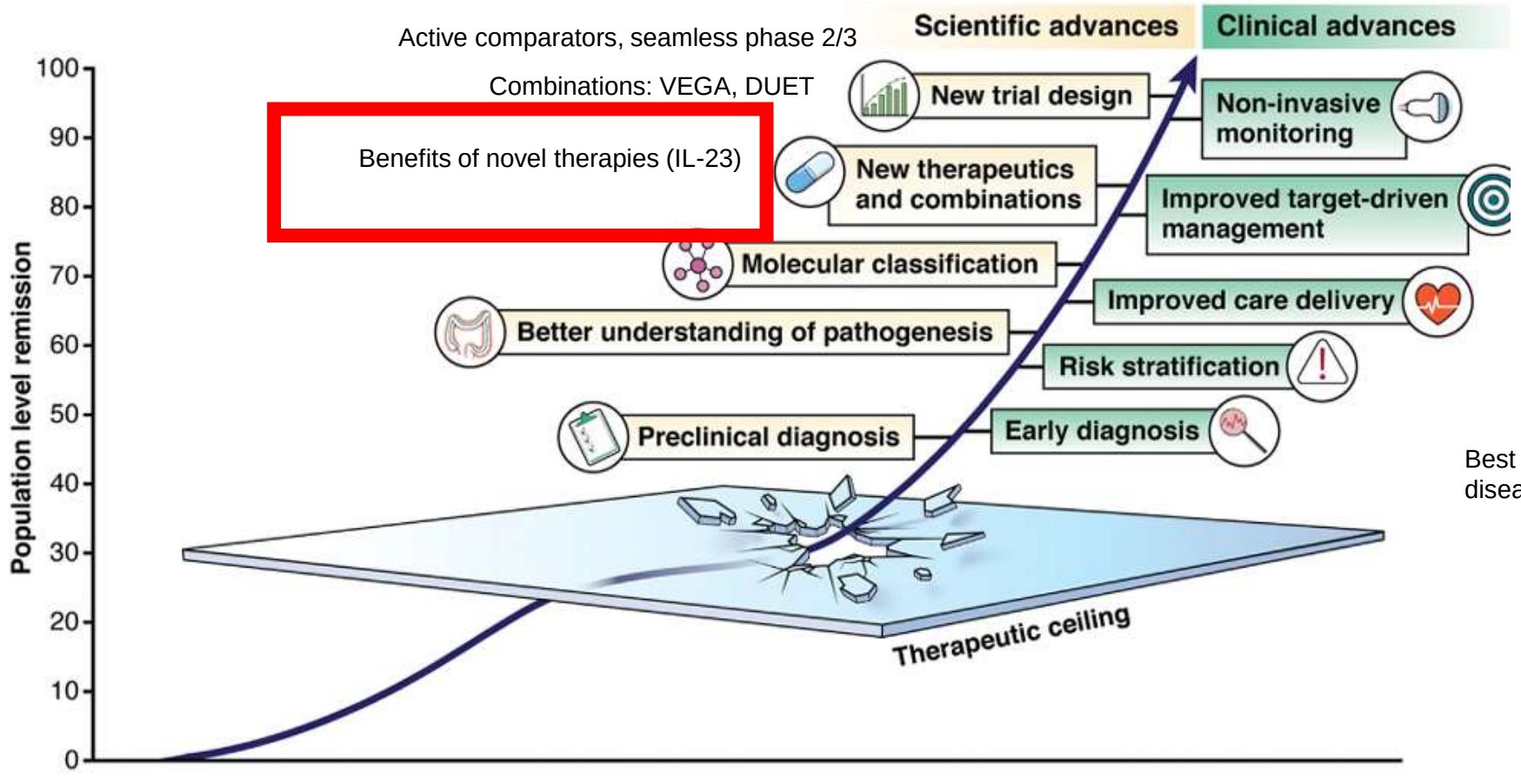
What Is Needed to Break the Therapeutic Glass Ceiling?



Better initial care – no role for mesalamine in CD

Best response seen with shorter disease duration

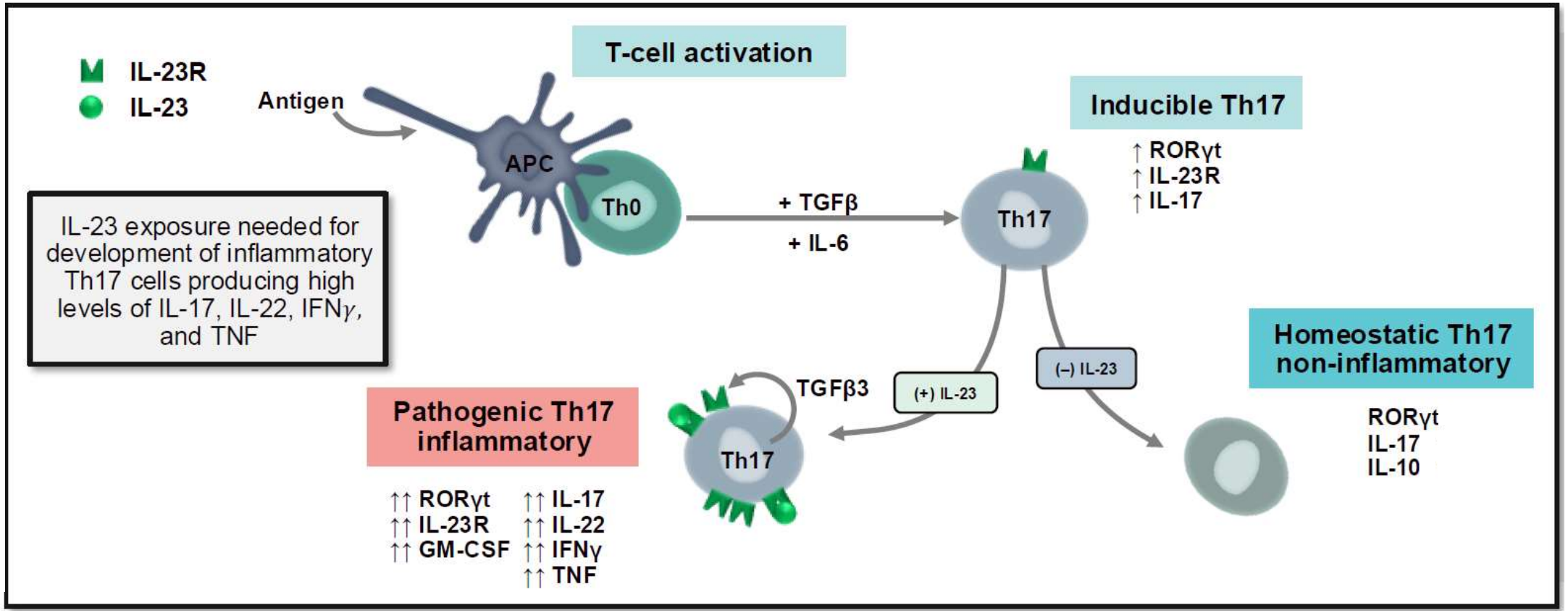
Raine T, Danese S. *Gastroenterology*. 2022;162(5):1507-1511.

Why Target IL-23 in IBD?

- Inhibition of IL-23
  - Decreases mucosal inflammation
  - Improves epithelial barrier integrity
  - Suppresses gut inflammation in T-cell-mediated colitis

Hohenberger M, et al. *J Dermatolog Treat*. 2018;29(1):13-18. Vuyyuru SK, et al. *Drugs*. 2023;83(10):873-891. Wallace KL, et al. *World J Gastroenterol*. 2014;20(1):6-21.

IL-23 Drives Development of Inflammatory Pathogenic Th17 Cells

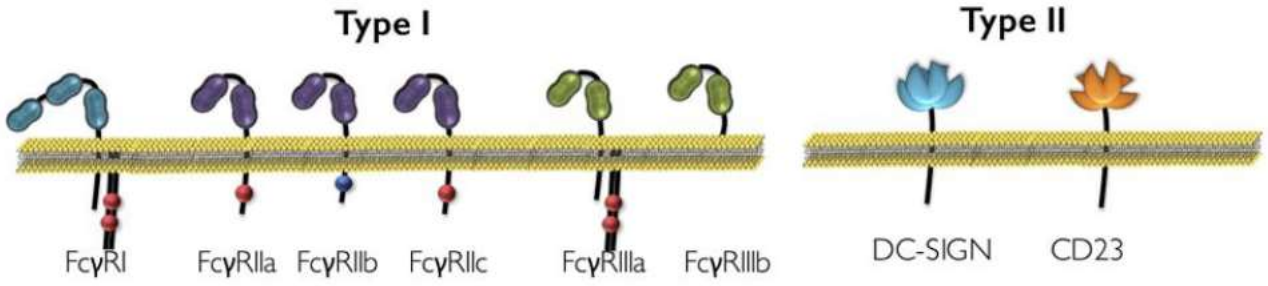


APC = antigen-presenting cell; GM-CSF = granulocyte-macrophage colony-stimulating factor; IFN = interferon; TGF = transforming growth factor.

Adapted from Zuniga LA, et al. *Immunol Rev*. 2013;252(1):78-88. Gaffen SL, et al. *Nat Rev Immunol*. 2014;14(9):585-600. Schmitt H, et al. *Front Immunol*. 2021;12:622934.

Importance of FcY Receptors and CD64 Receptors

- Fcγ receptors—surface receptors on immune cells that recognize the Fc portion of IgG
- CD64 (FcγRI) is the only Fcγ receptor with high affinity for IgG1
- CD64+ cells are the primary cellular source of IL-23 in IBD



	Type I						Type II	
	FcγRI	FcγRIIa	FcγRIIb	FcγRIIIc	FcγRIIIa	FcγRIIIb	DC-SIGN	CD23
Neutrophils	#	+	+	–	–	+	–	#
Eosinophils	#	+	+	–	–	#	–	#
Basophils	#	+	+	–	–	±	–	#
Monocytes	+	+	+	–	±	–	–	#
Macrophages	±	+	+	–	±	–	±	#
Dendritic cells	–/#	+	+	–	–/#	–	+	–
Platelets	–	+	–	–	–	–	–	–

+ Constitutive expression – No expression # Inducible expression

DC-SIGN = dendritic cell-specific intracellular adhesion molecule-3-grabbing nonintegrin; Fc = fragment, crystallizable; IgG = immunoglobulin G.

Bournazos S, et al. *Microbiol Spectr*. 2016;4(6).

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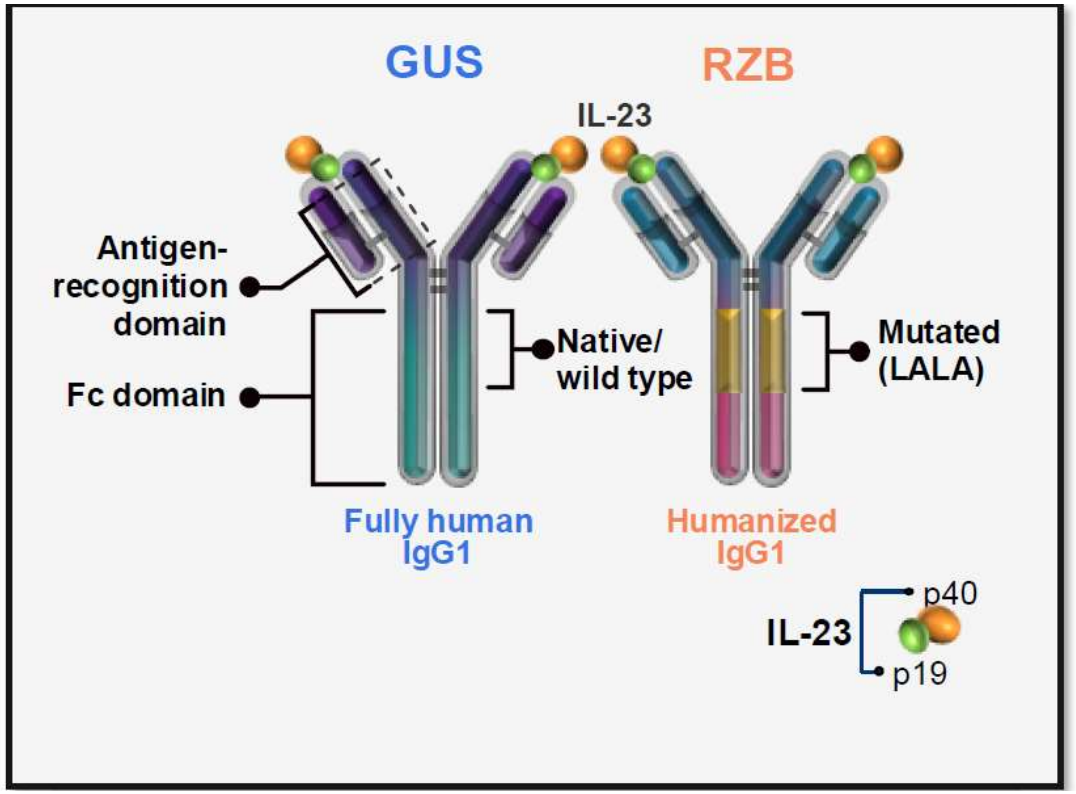
Differences between IL-23 p19 Antibodies (Guselkumab and Risankizumab)

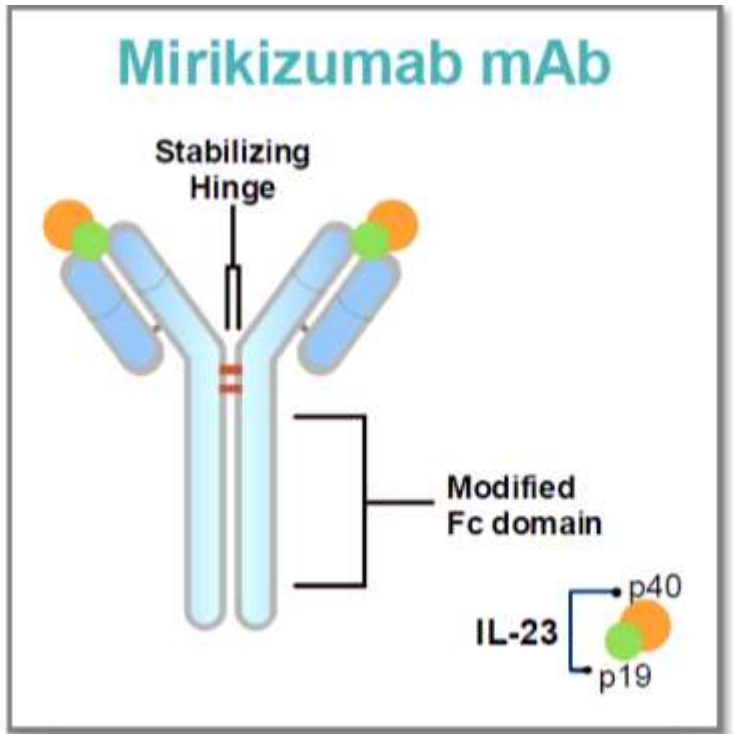
- GUS and RZB are monoclonal antibodies (mAbs) that selectively target the p19 subunit of IL-23
- Both have shown efficacy in the treatment of inflammatory bowel diseases
- GUS and RZB have differences in the Fc region that affect binding to Fc-gamma receptors
  - GUS is a fully human IgG1 with a native Fc region, which allows binding to CD64
  - RZB is a humanized IgG1 processing a mutated LALA Fc region intended to diminish binding to FCyRs



LALA = leucine to alanine substitutions at positions 234 and 235.

D'Haens G, et al. *Lancet*. 2022;399(10340):2015-2030. Ferrante M, et al. *Lancet*. 2022;399(10340):2031-2046. Sachen KL, et al. *Front Immunol*. 2025;16:1532852. Sandborn WJ, et al. *Gastroenterology*. 2022;162(6):1650-1664.e8. Dignass A, et al. *J Crohns Colitis*. 2022;16(Suppl 1):i025-i026. Wojtal KA, et al. *PLoS One*. 2012;7(8):e43361. Pang Y, et al. *Clin Transl Sci*. 2024;17(1):e13706.

Differences between IL-23 p19 Antibodies (Mirikizumab)



- Humanized IgG4 mAb that selectively binds to the p19 subunit of human IL-23 cytokine and inhibits its interaction with the IL-23 receptor
- The Fc domain of MIRI was modified to significantly reduce FcγR binding and interaction

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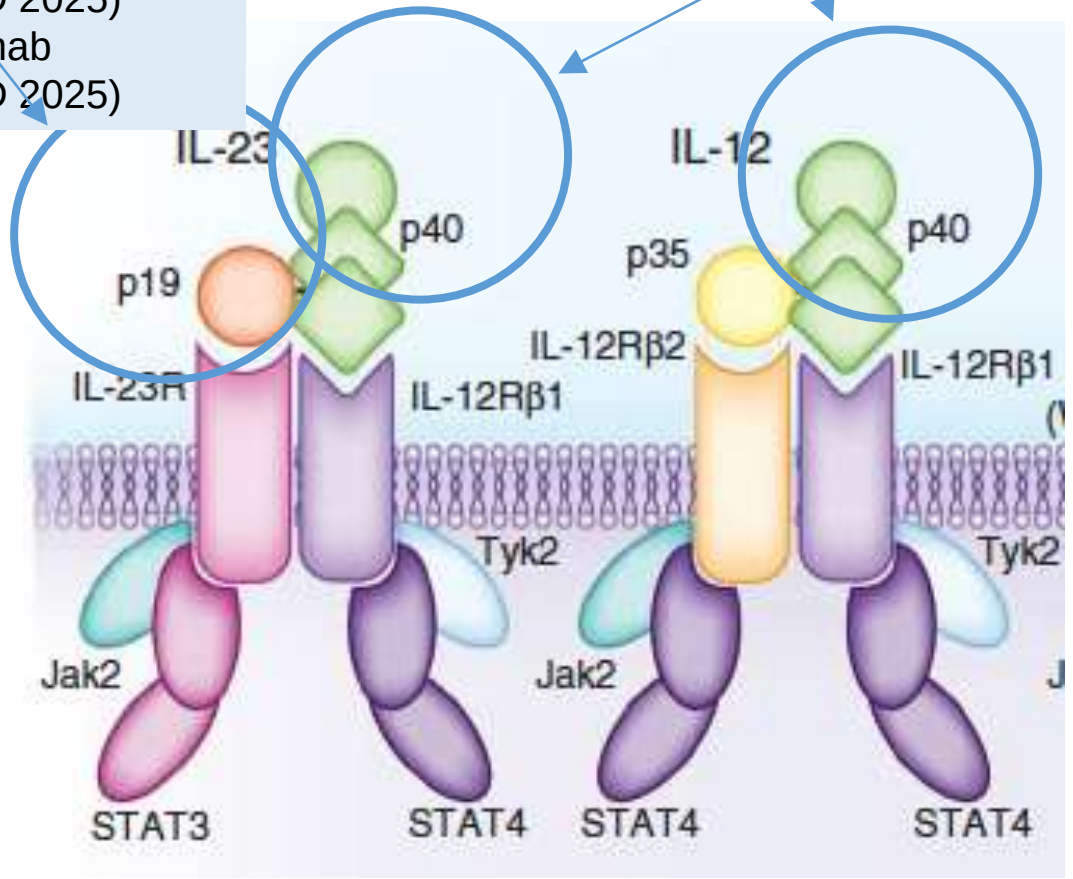
Strohl WR. *Antib Ther*. 2024;7(2):132-156.

Currently Available Anti-Interleukins: Approved for CD and UC

Anti-p19 Antibody
Risankizumab
(CD 2022, UC 2024)
Mirikizumab
(UC 2023, CD 2025)
Guselkumab
(UC 2024, CD 2025)

Anti-p40 antibody
Ustekinumab
(CD 2016, UC 2019)



Risankizumab UC
1200 mg IV weeks 0, 4, 8
180 mg or 360 mg q 8 OBI

Risankizumab CD
600 mg IV weeks 0, 4, 8
180 mg or 360 mg q 8 OBI

Mirikizumab UC
300 mg IV weeks 0, 4, 8
200 mg SC q 4
(2 injections of 100 mg)*

Mirikizumab CD
900 mg IV weeks 0, 4, 8
300 mg SC q 4 (2 injections of 100 and 200 mg)*
*Citrate-free formulations now

Guselkumab UC
200 mg IV weeks 0, 4, 8
100 mg q 8 or 200 mg q 4

Guselkumab CD
200 mg IV weeks 0, 4, 8 OR
400 mg SC weeks 0, 4, 8
100 mg q 8 or 200 mg q 4

OBI = on-body injector.

FDA. Accessed July 22, 2025. https://www.accessdata.fda.gov/scripts/cder/daf/. Rosh J. *Guts and Growth*. April 15, 2024. Accessed July 22, 2025. https://gutsandgrowth.com/2024/04/15/dr-joel-rosh-positioning-therapies-for-pediatric-ulcerative-colitis/.

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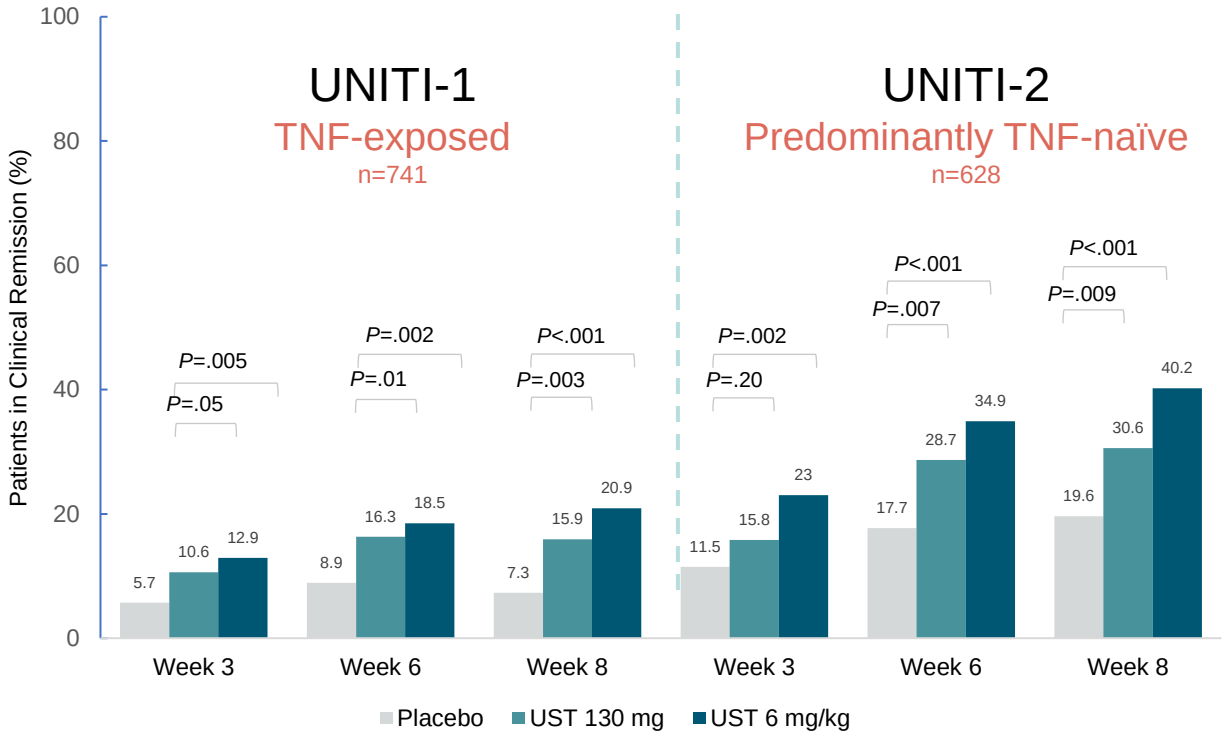
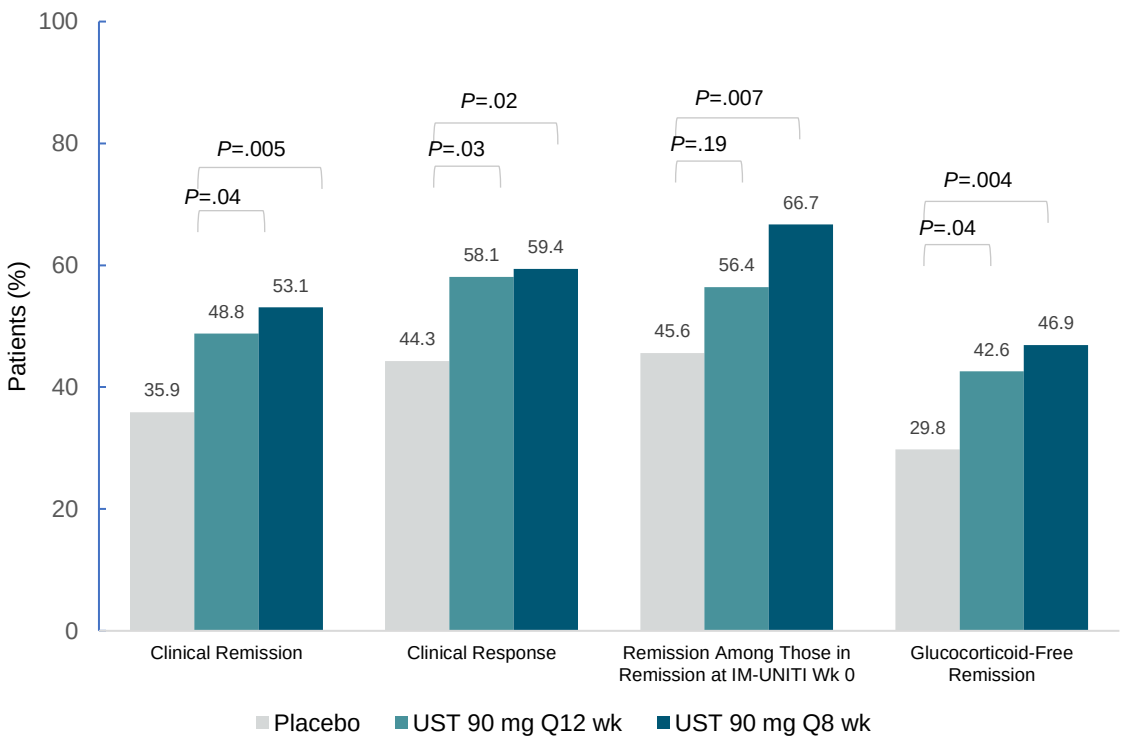
UNITI: Ustekinumab for CD

Induction of remission
UNITI-1 and UNITI-2



Maintenance of remission
IM-UNITI



UST = ustekinumab.

Feagan BG, et al. *N Engl J Med*. 2016;375(20):1946-1960. Sandborn WJ, et al. *Aliment Pharmacol Ther*. 2018;48(1):65-77.

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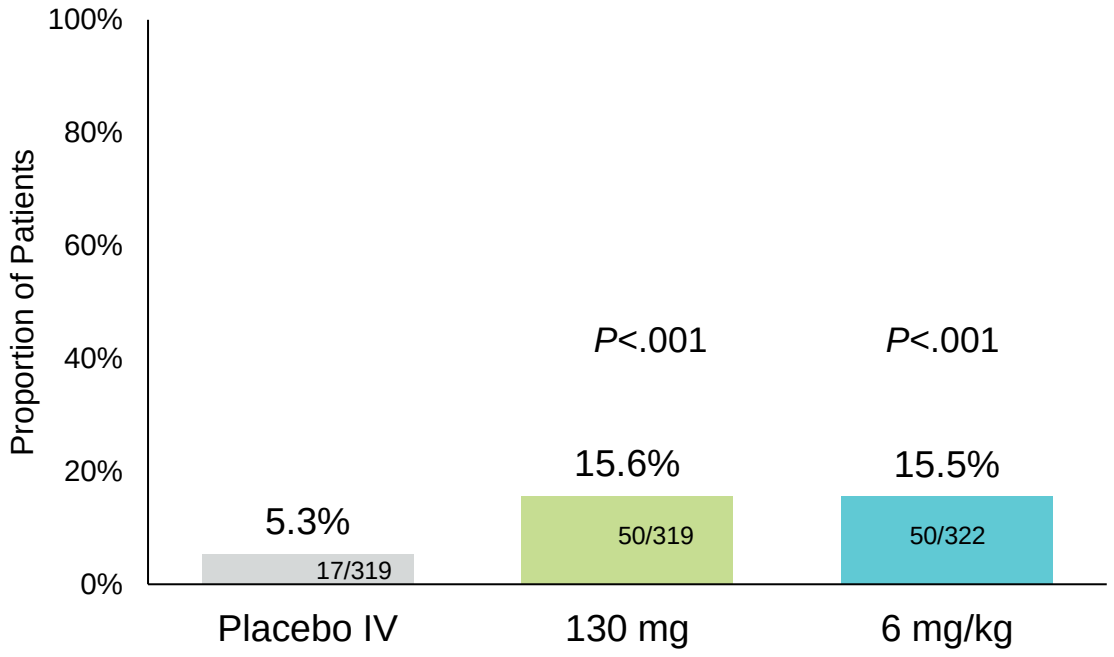
UNIFI: Ustekinumab for UC

Induction

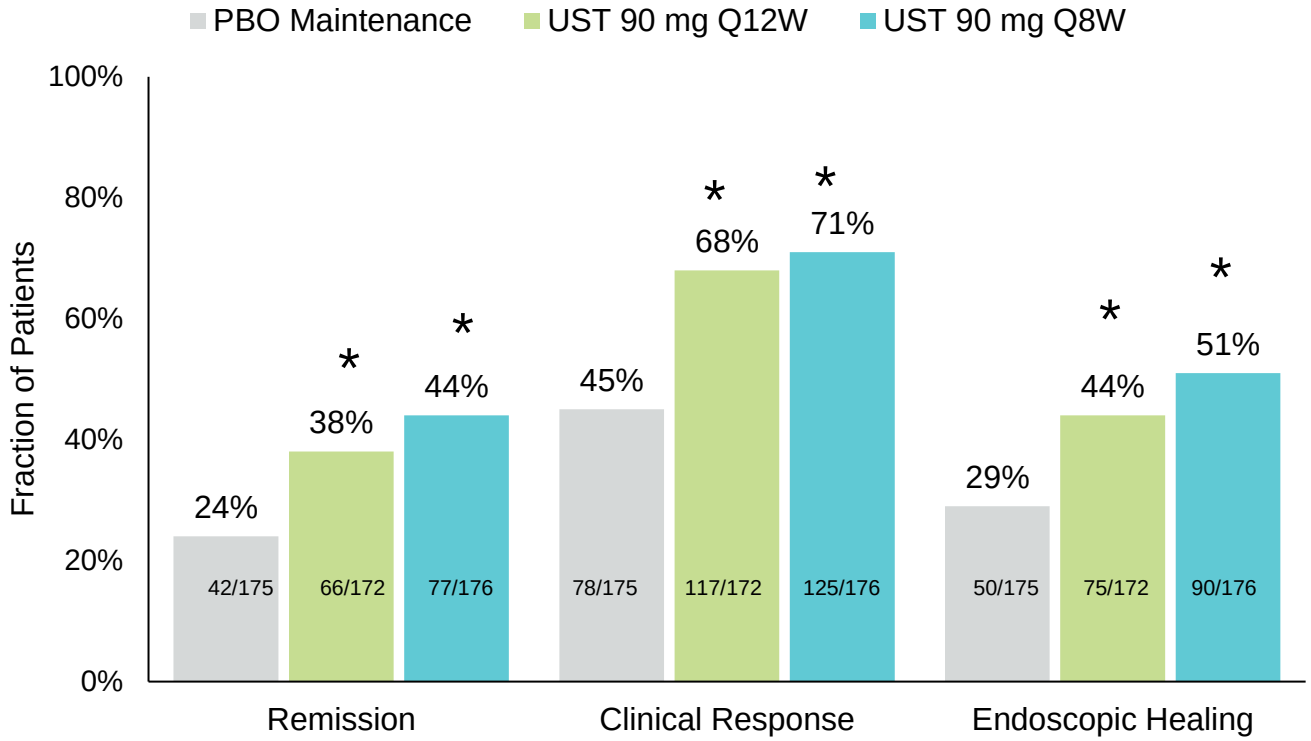
Primary endpoint: Clinical remission at week 8 (n=961)



Ustekinumab IV

Maintenance

Clinical and endoscopic outcomes at week 52 (n=397)



Ustekinumab SC

***P*<.001.**
PBO = placebo.
Clinical remission: Mayo score ≤2 with no individual subscore >1.
Endoscopic healing: Mayo endoscopic subscore 0 or 1.
Sands BE, et al. *N Engl J Med*. 2019;381(13):1201-1214.

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FDA-Approved Biosimilars to Ustekinumab: 2025 (Plaque Psoriasis, Psoriatic Arthritis, CD/UC)

- Wezlana™ (ustekinumab-auub) – interchangeable
- Pyzchiva™ (ustekinumab-ttwe) – interchangeable after 1 year
- Selarsdi™ (ustekinumab-aekn)
- Yesintek™ (ustekinumab-kfce)
- Otulfi™ (ustekinumab-aauz)
- Imuldosa™ (ustekinumab-srlf)
- Steqeyma™ (ustekinumab-stba)
- Starjemza™ (ustekinumab-hmny)

Similar patient assistance programs exist for these products.

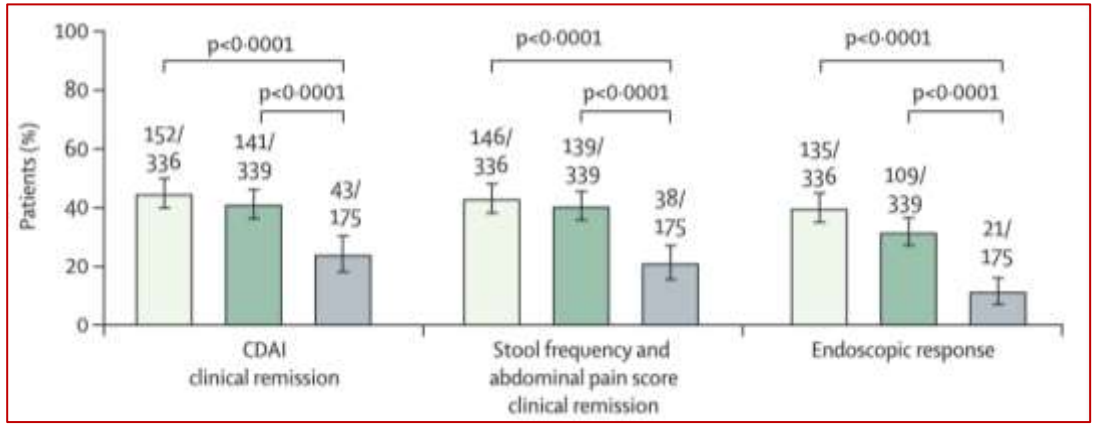
FDA. Accessed July 22, 2025. https://www.fda.gov/drugs/biosimilars/biosimilar-product-information.

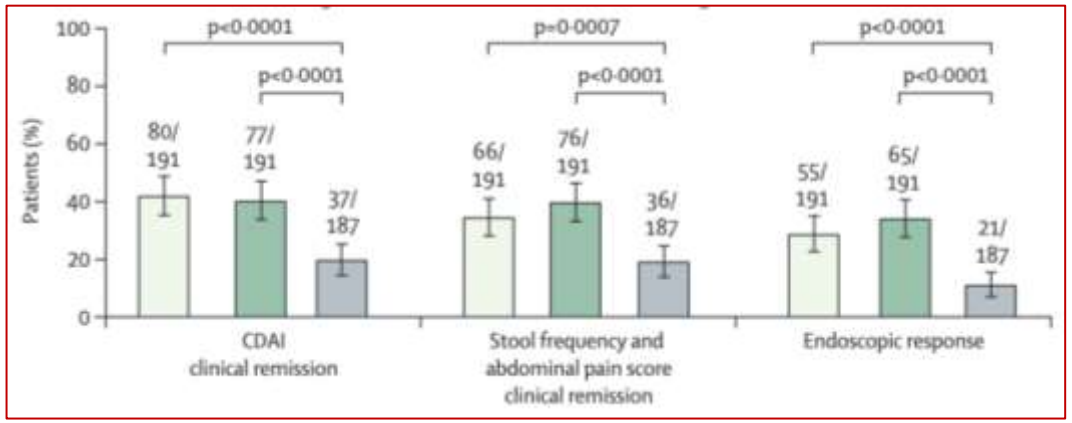
ADVANCE and MOTIVATE: Risankizumab Induction in CD

ADVANCE
Conventional or bio-failure

Risankizumab 600 mg intravenous
Risankizumab 1200 mg intravenous
Placebo

MOTIVATE
Bio-failure





Randomization

- Risankizumab 600 mg IV Q4 weeks
- Risankizumab 1200 mg IV Q4 weeks
- Placebo IV Q4 weeks

Re-randomization of clinical responders

Removal of non-responders

CDAI = CD Activity Index.

D'Haens G, et al. *Lancet*. 2022;399(10340):2015-2030. Ferrante M, et al. *Lancet*. 2022;399(10340):2031-2046.

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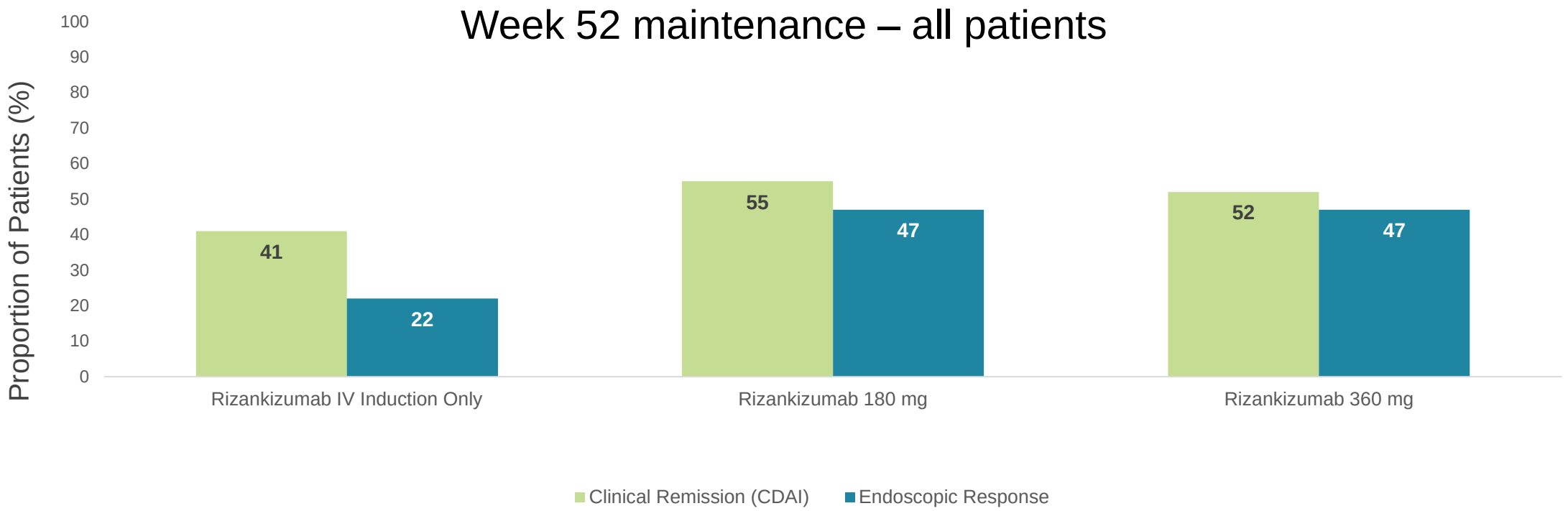
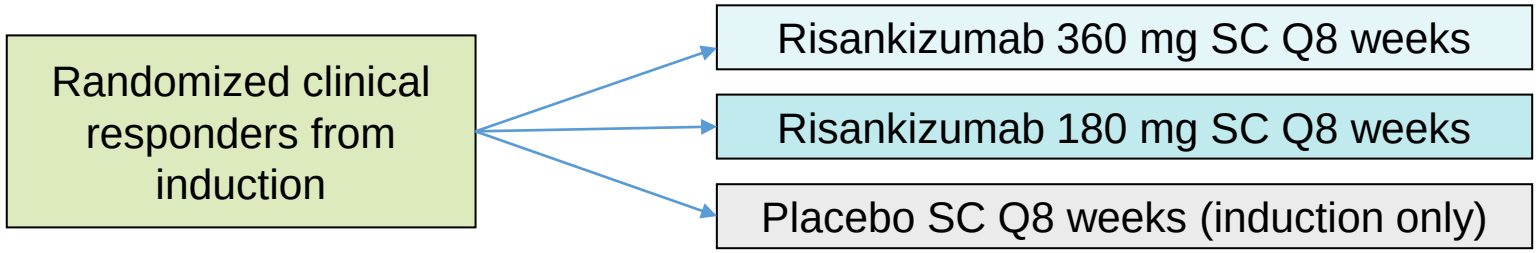
FORTIFY: Risankizumab Maintenance in CD





Ferrante M, et al. *Lancet*. 2022;399(10340):2031-2046.

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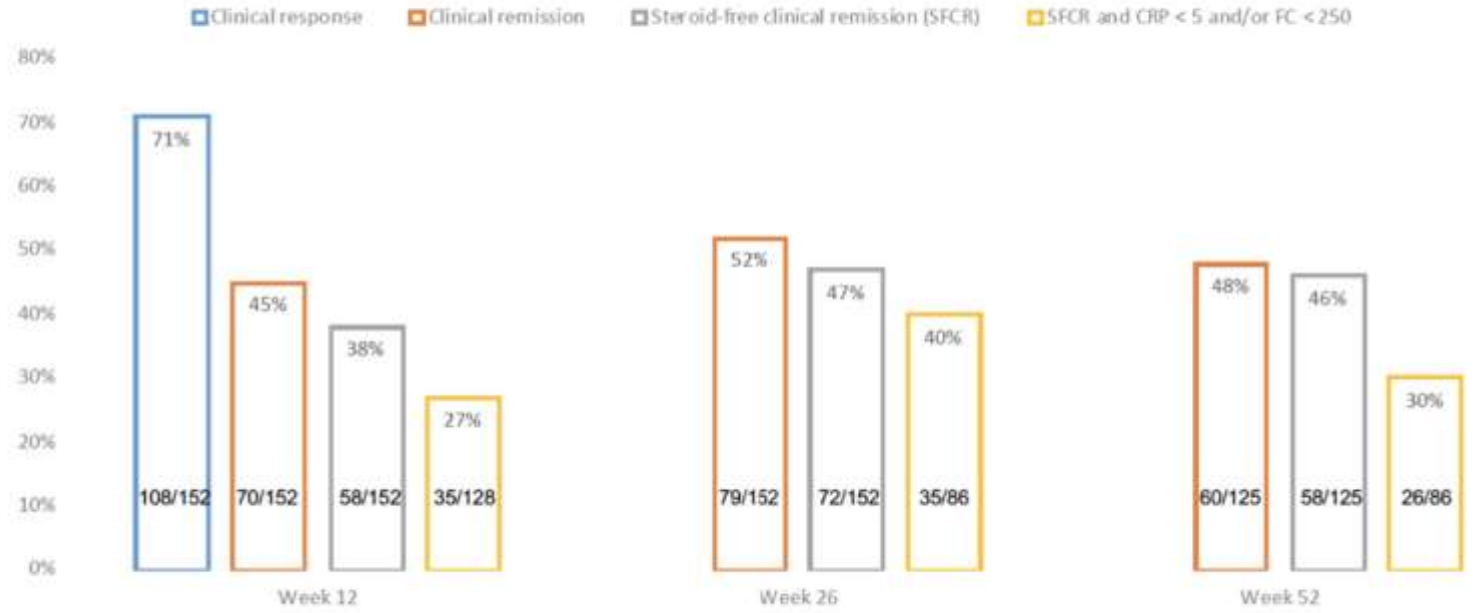
Risankizumab: Real-World Experience (GETAID)

Long-term outcome of risankizumab in Crohn's disease: a real-world GETAID study

174 patients with CD refractory to biologics

Risankizumab 600 mg IV at week 0,4 and 8 and then SC 360 mg every 8 weeks



CRP = C-reactive protein; FC = fecal calprotectin.

Fumery M, et al. *Clin Gastroenterol Hepatol*. 2024;22(12):2451-2458.e1.

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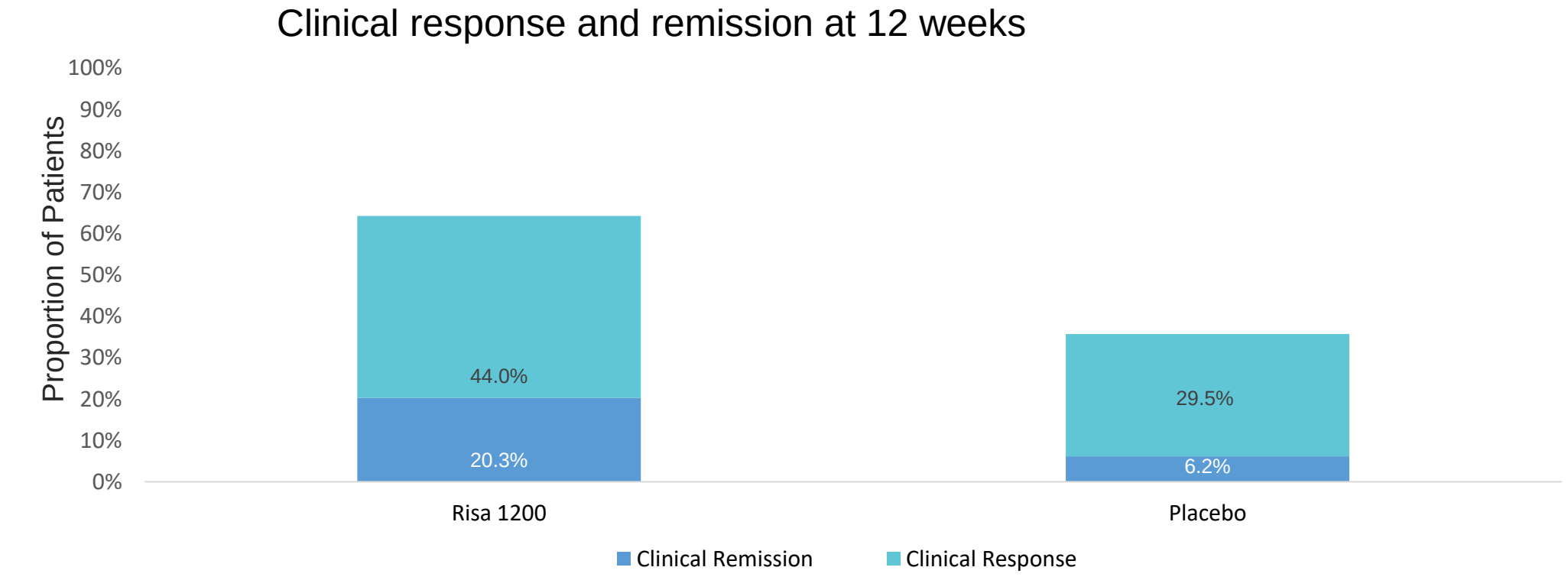
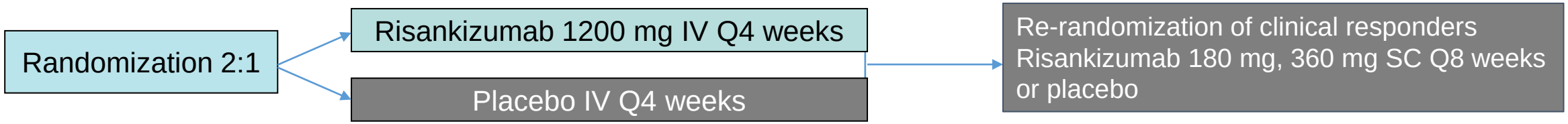
INSPIRE: Risankizumab Induction in UC





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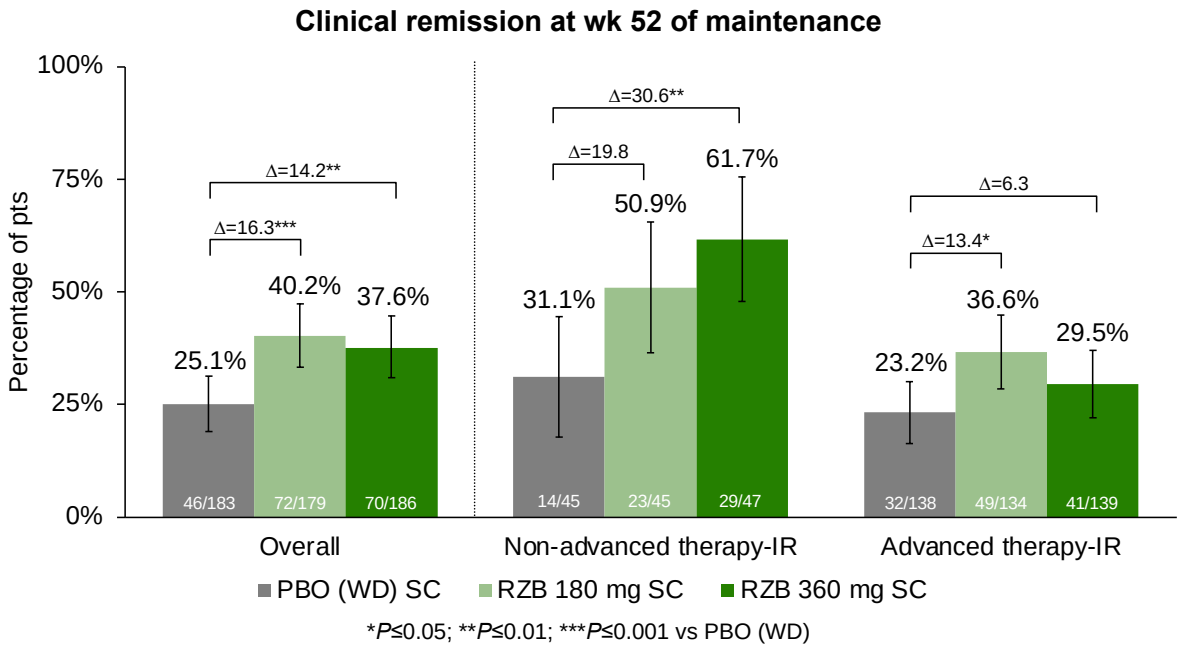
Louis E, et al. *JAMA*. 2024;332(11):881-897.

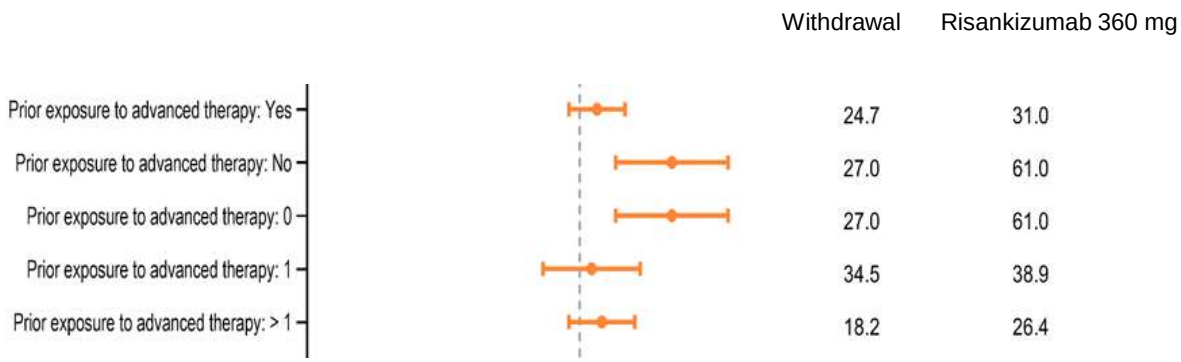
COMMAND: Efficacy and Safety of Risankizumab Maintenance Therapy in Moderate-to-Severe UC

Efficacy population: Week 12 INSPIRE responders; safety population: Week 12 or 24 INSPIRE responders

Primary endpoint: Clinical remission (per MMS) at week 52



Clinical remission by prior advanced therapy at week 52



MMS = modified Mayo score; IR = inadequate response.

Louis E, et al. *JAMA*. 2024;332(11):881-897.

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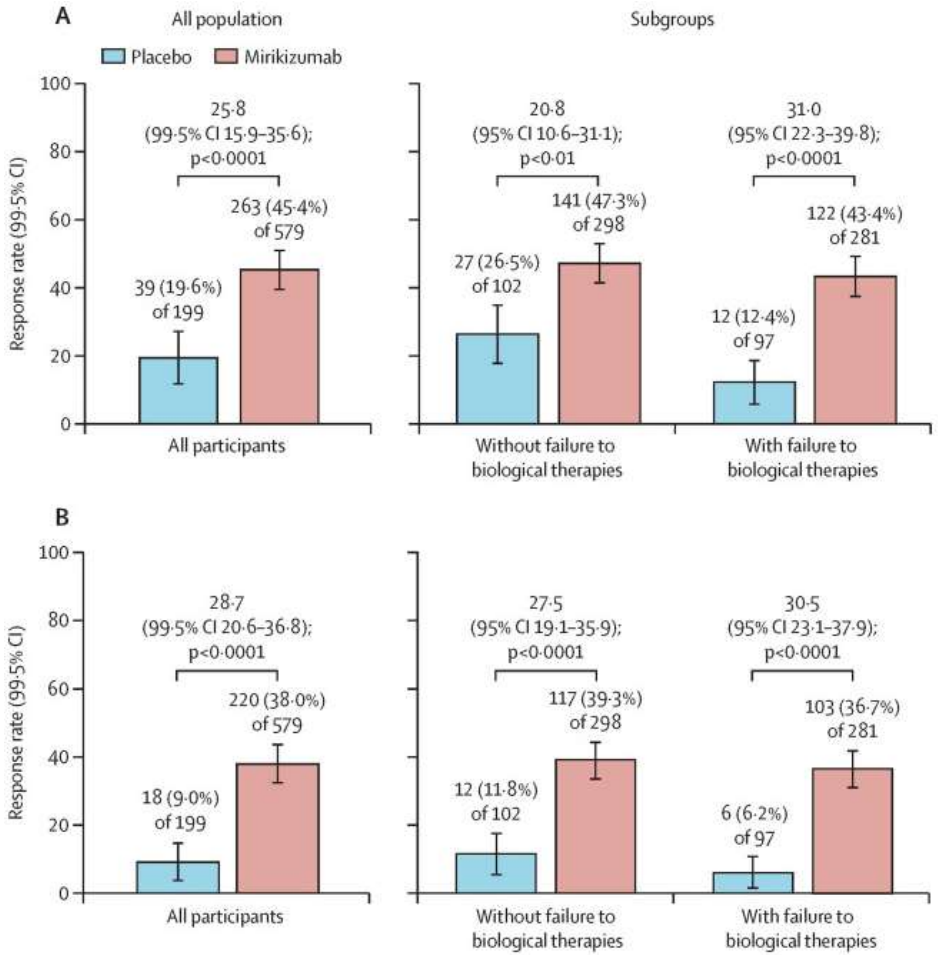
VIVID-1 – Mirikizumab in Crohn's Disease: Treat-Through Design

- Phase 3 RCT of 1150 patients
- Randomized to miri, uste, or placebo (6:3:2)
- Primary outcomes
  - A) PRO clinical response at week 12 + clinical CDAI remission at week 52
  - B) PRO clinical response at week 12 + endoscopic response at week 52



CI = confidence interval.

Ferrante M, et al. *Lancet*. 2024;404(10470):2423-2436.

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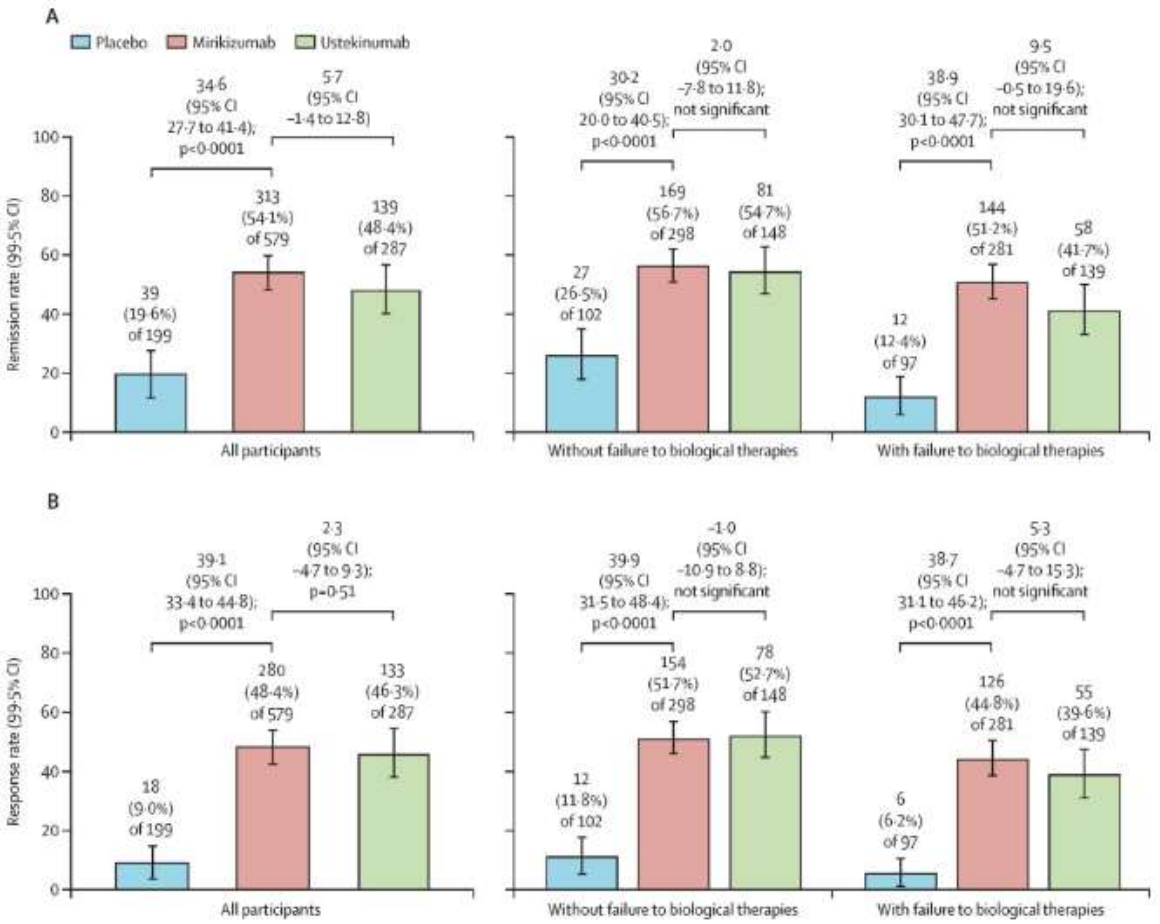
VIVID-1 – Mirikizumab in Crohn's Disease: Treat-Through Design

A) Clinical remission CDAI at week 52

B) Endoscopic response at week 52



Ferrante M, et al. *Lancet*. 2024;404(10470):2423-2436.

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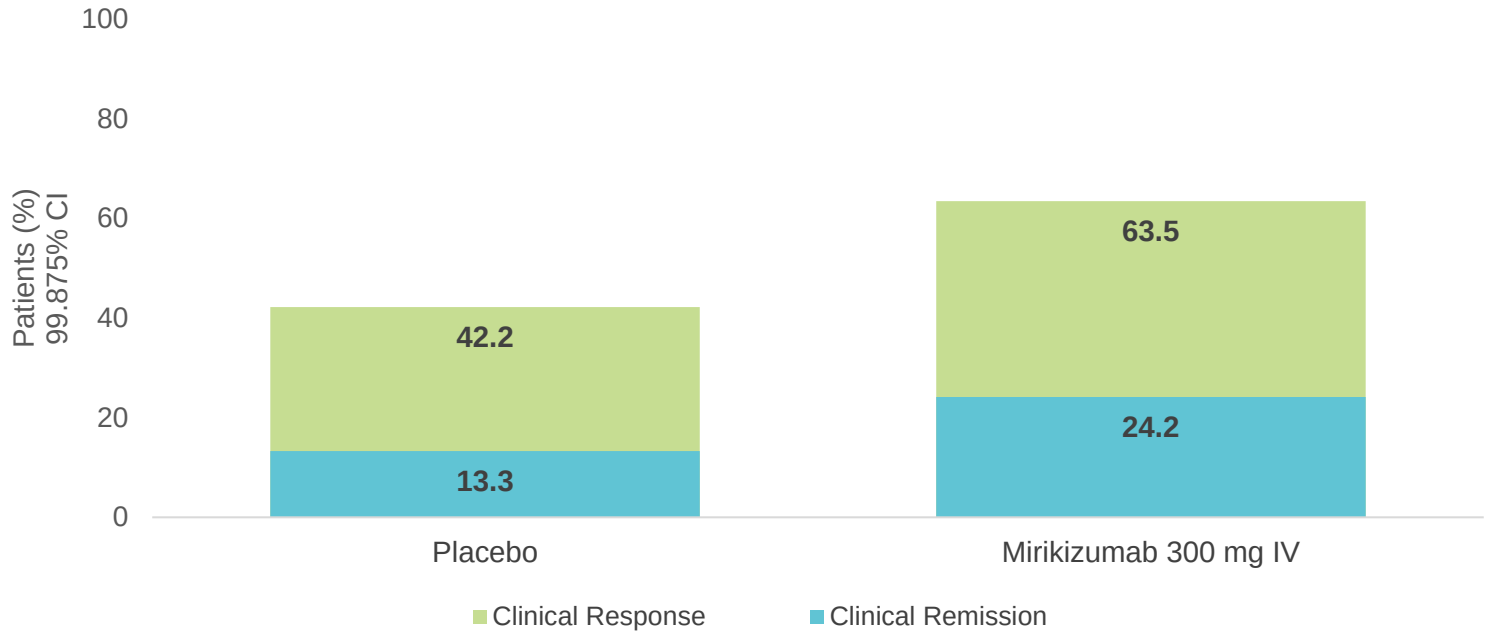
LUCENT-1: Mirikizumab Induction in UC

Clinical remission (primary endpoint) vs clinical response at week 12 (n=1281)



Randomization 3:1

- Mirikizumab 300 mg IV Q4 weeks → Re-randomization of clinical responders 2:1 mirikizumab 200 mg SC or placebo
- Placebo IV Q4 weeks → Non-responders open-label option for mirikizumab extended induction

D'Haens G, et al. *N Engl J Med*. 2023;388(26):2444-2455.

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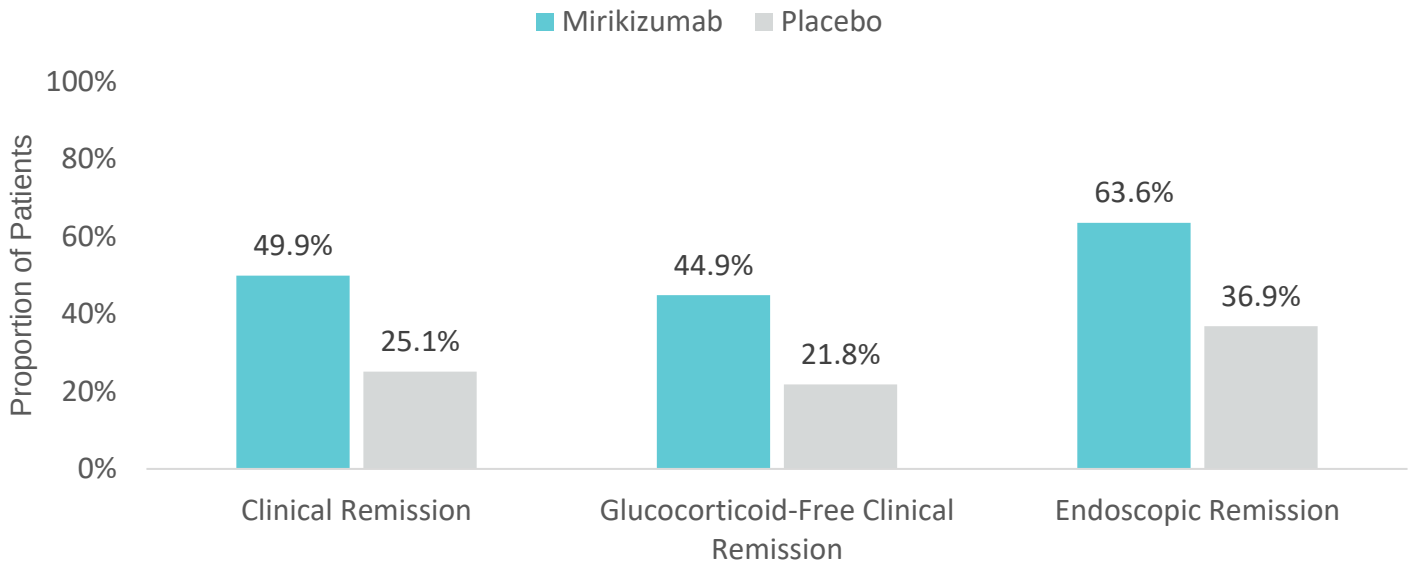
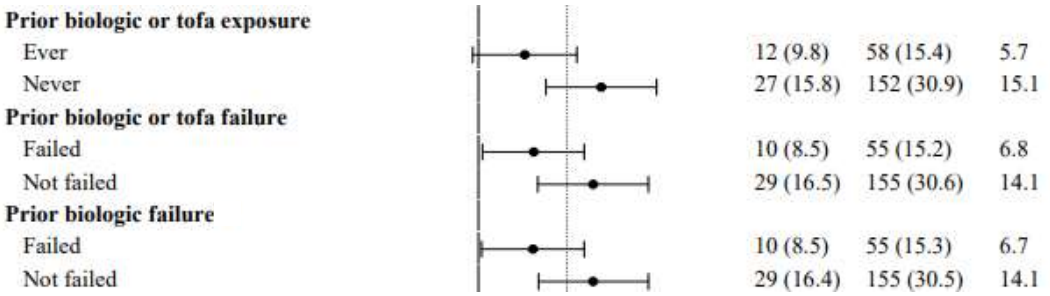
LUCENT-2: Mirikizumab Maintenance in UC

Primary and secondary outcomes at 40 weeks



Miri vs placebo by prior biologic exposure status



D'Haens G, et al. *N Engl J Med*. 2023;388(26):2444-2455.

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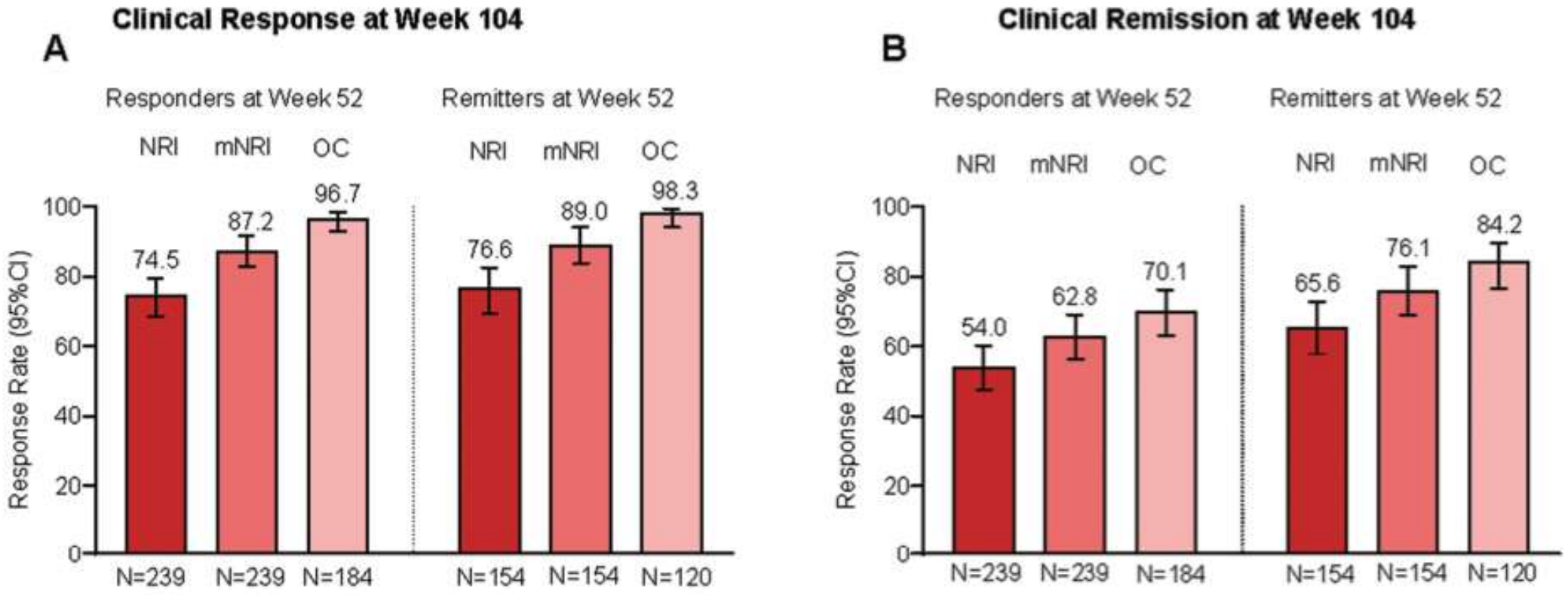
LUCENT-3: Mirikizumab 2-Year Efficacy in UC



NRI = non-responder imputation; mNRI = modified NRI; OC = observed case.

Sands BE, et al. *Inflamm Bowel Dis*. 2024;30(12):2245-2258.

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GALAXI 2/3 – Guselkumab for CD: Treat-Through Design

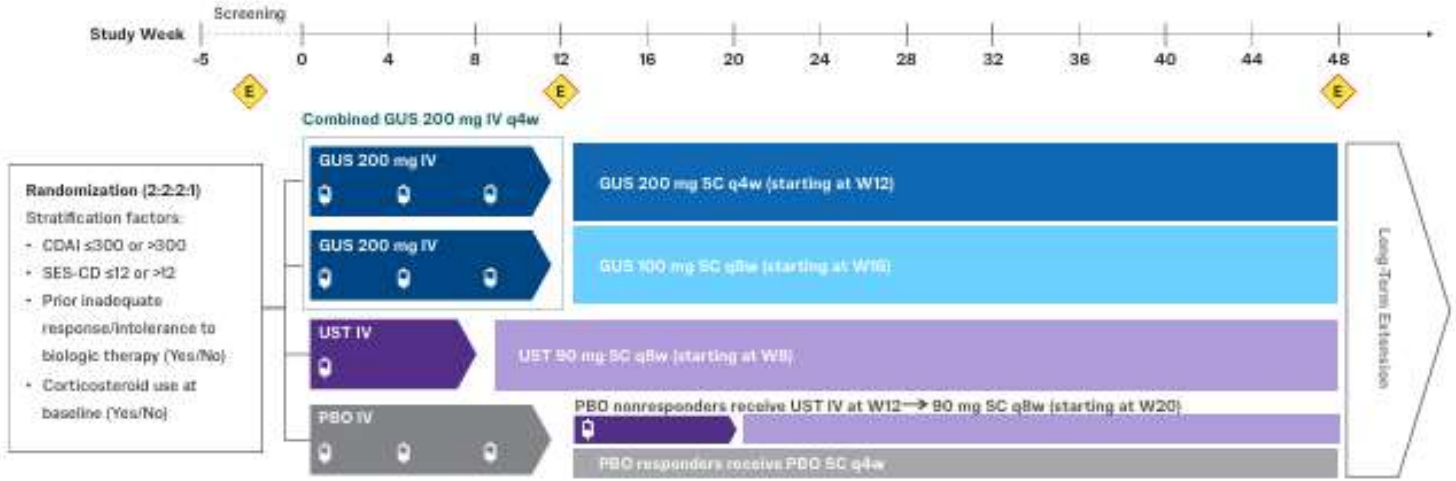
Double-Blind, Treat-Through Design: GALAXI 2 & 3

Primary Analysis Set

- GALAXI 2: 508 participants
- GALAXI 3: 513 participants

Eligibility Criteria

- Moderately to severely active CD (Clinical Disease Activity Index score 220–450 + mean daily Stool Frequency count >3 OR Abdominal Pain score >1) and Simple Endoscopic Score for Crohn's Disease score[a] ≥6 (or ≥4 for isolated ileal disease)
- Inadequate response/intolerance to oral corticosteroids or 6-mercaptopurine/azathioprine/methotrexate, or biologic therapies



SES-CD = Simple Endoscopic Score for CD.

Panaccione R, et al. Presented at: Digestive Disease Week (DDW); May 18-21, 2024; Washington, DC. 1057b.

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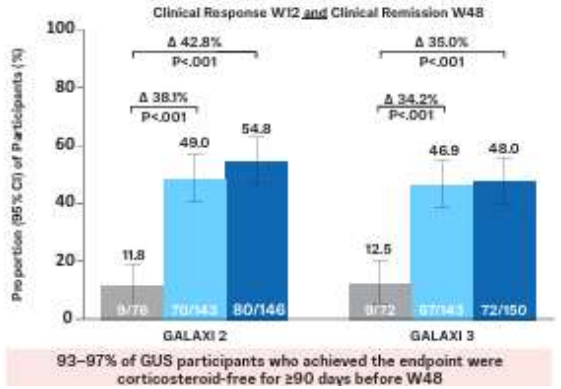
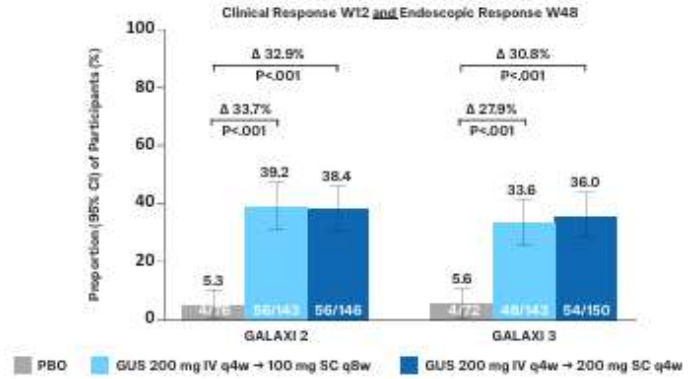
GALAXI 2/3 – Guselkumab for CD: Treat-Through Design

Composite Co-primary Endpoints

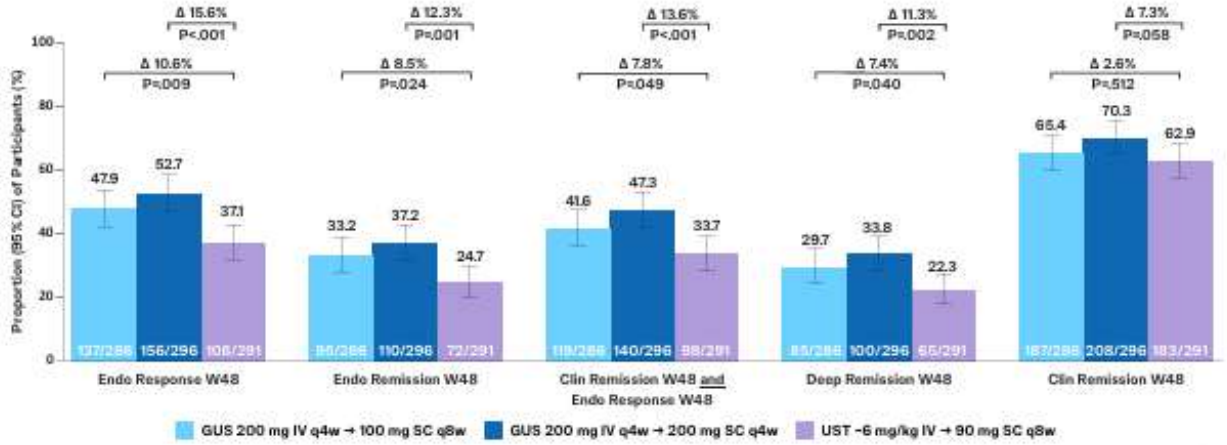


93–97% of GUS participants who achieved the endpoint were corticosteroid-free for ≥90 days before W48



GUS vs UST: Efficacy at W48

Pooled GALAXI 2 & 3: Major Secondary Endpoints



Panaccione R, et al. Presented at: DDW; May 18-21, 2024; Washington, DC. 1057b.

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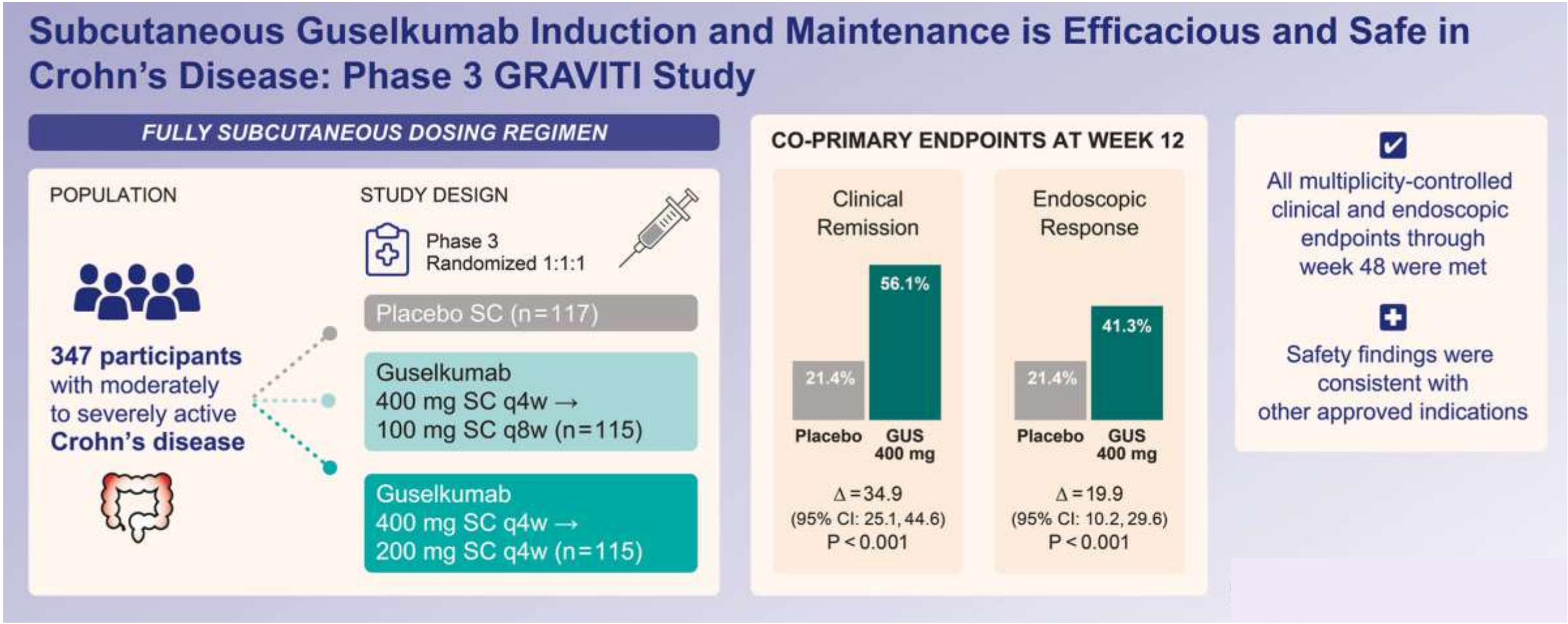
GRAVITI: Phase 3 Study of SC Induction and Maintenance in CD



Hart A, et al. *Gastroenterology*. 2025 [Epub ahead of print].

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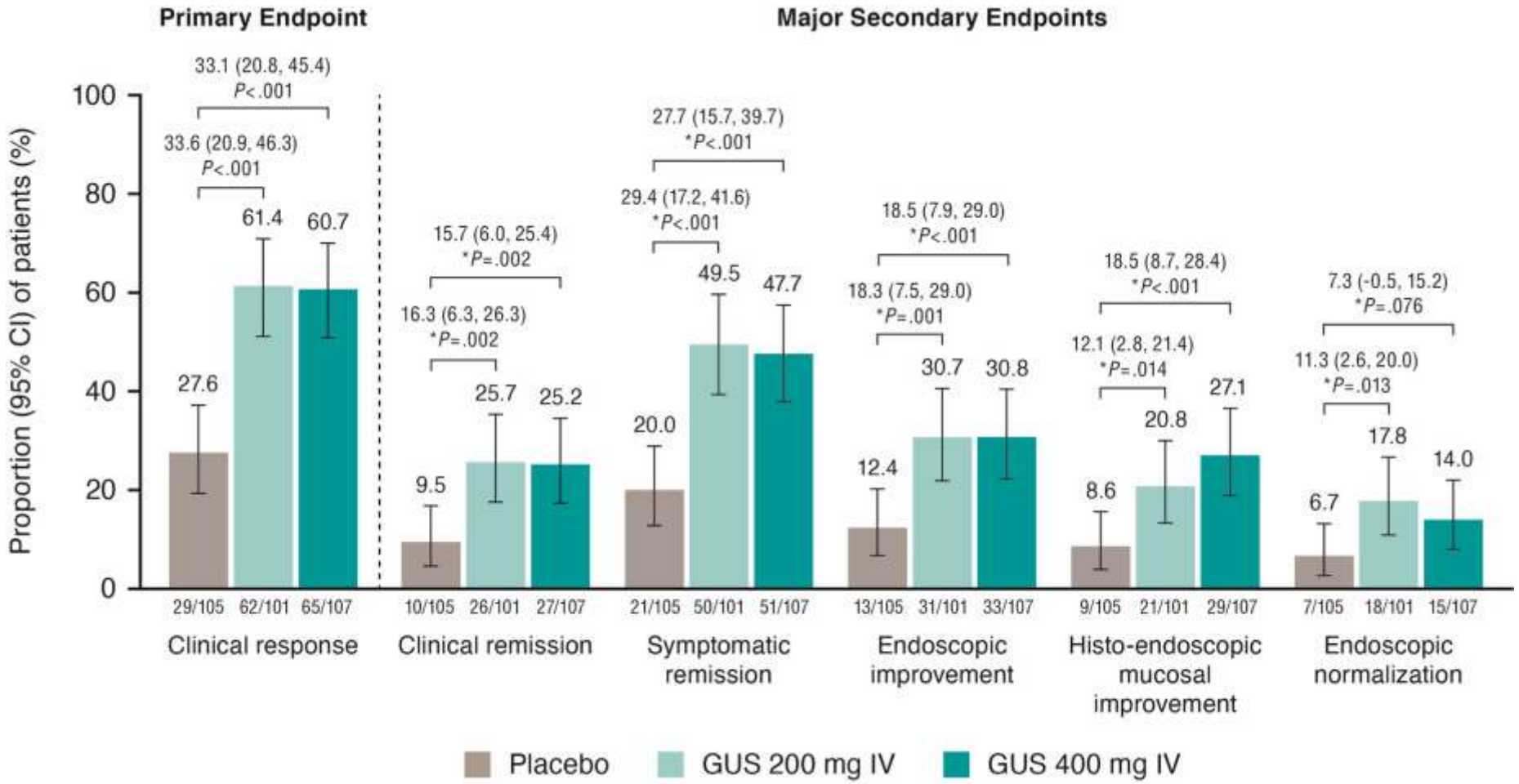
QUASAR: Guselkumab Induction in UC



***Denotes nominal *P*-values.**

Peyrin-Biroulet L, et al. *Gastroenterology*. 2023;165(6):1443-1457.

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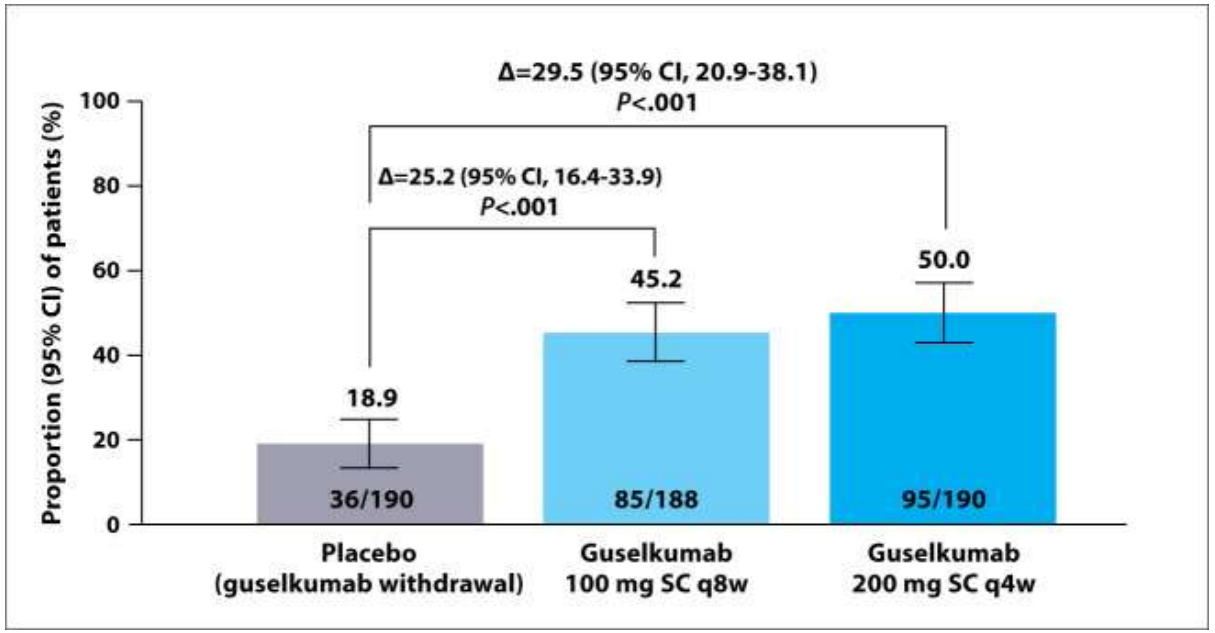
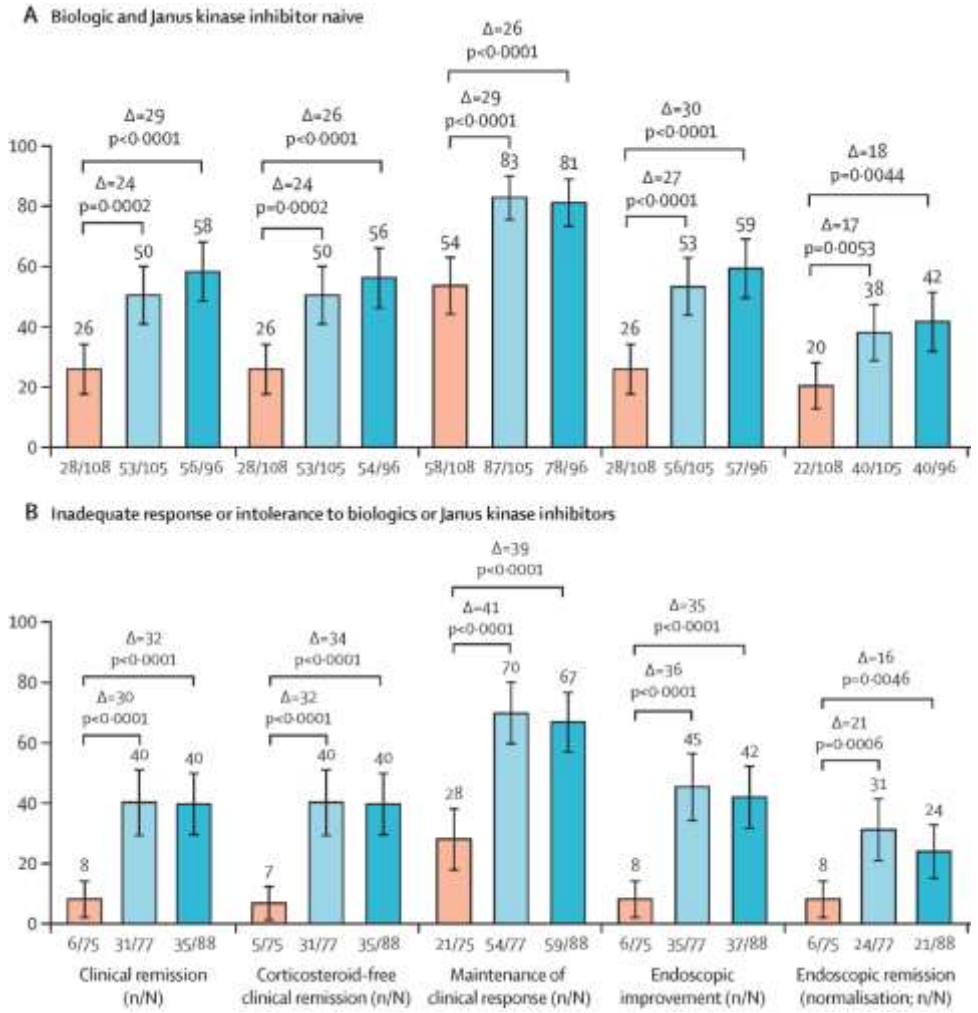
QUASAR: UC Maintenance Outcomes at Week 44



By prior advanced therapy exposure



Rubin DT, et al. *Lancet*. 2025;405(10472):33-49.

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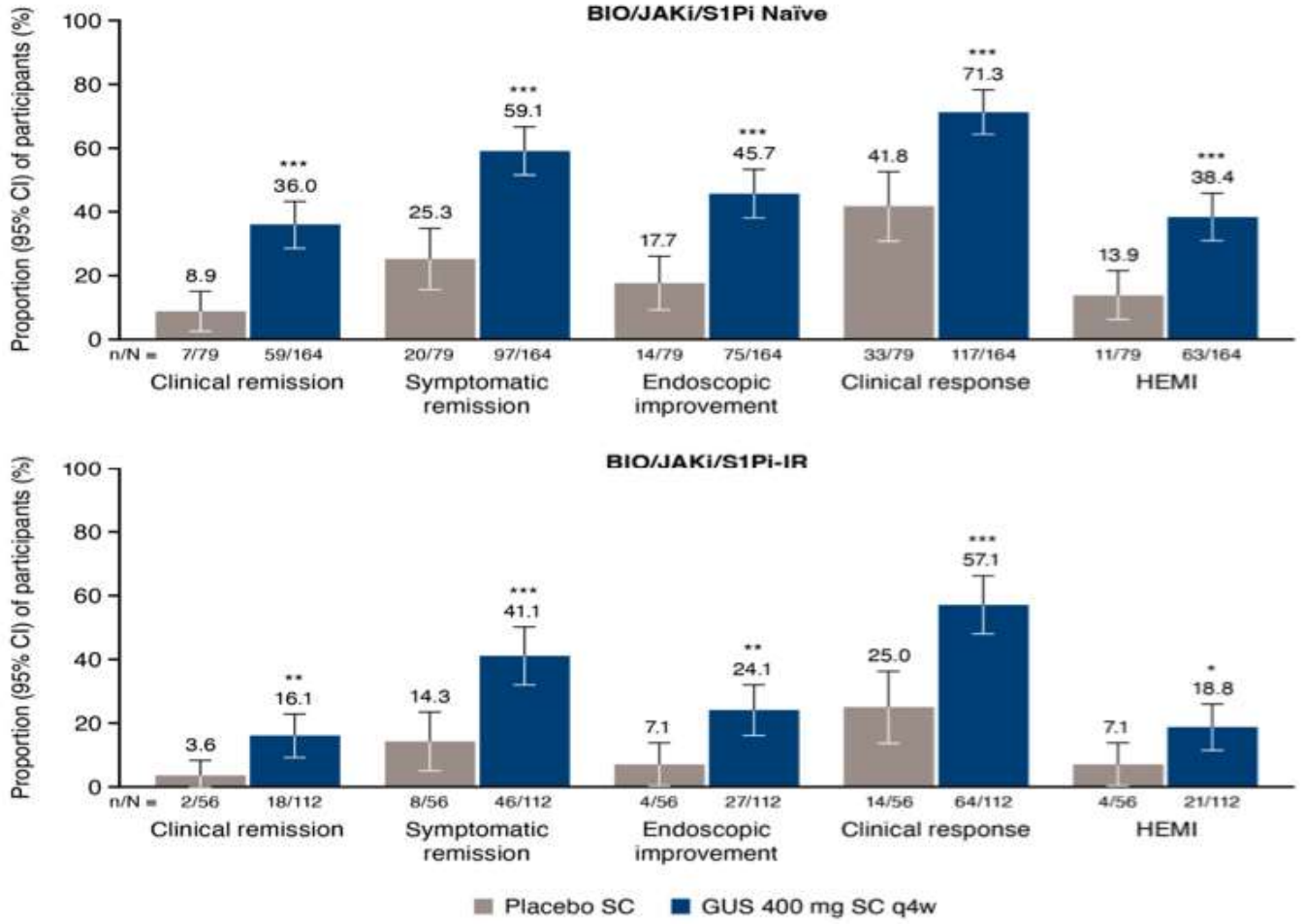
ASTRO: Phase 3 Study of SC Guselkumab Induction in UC

Figure. Primary Endpoint and Week 12 Secondary Endpoints by Biologic, JAK Inhibitor, and/or S1P Inhibitor History



*Nominal *P*<.05; **Nominal *P*<.01; ***Nominal *P*<.001.

Peyrin-Biroulet L, et al. *J Crohns Colitis*. 2025;19(Suppl 1):i19-i20.

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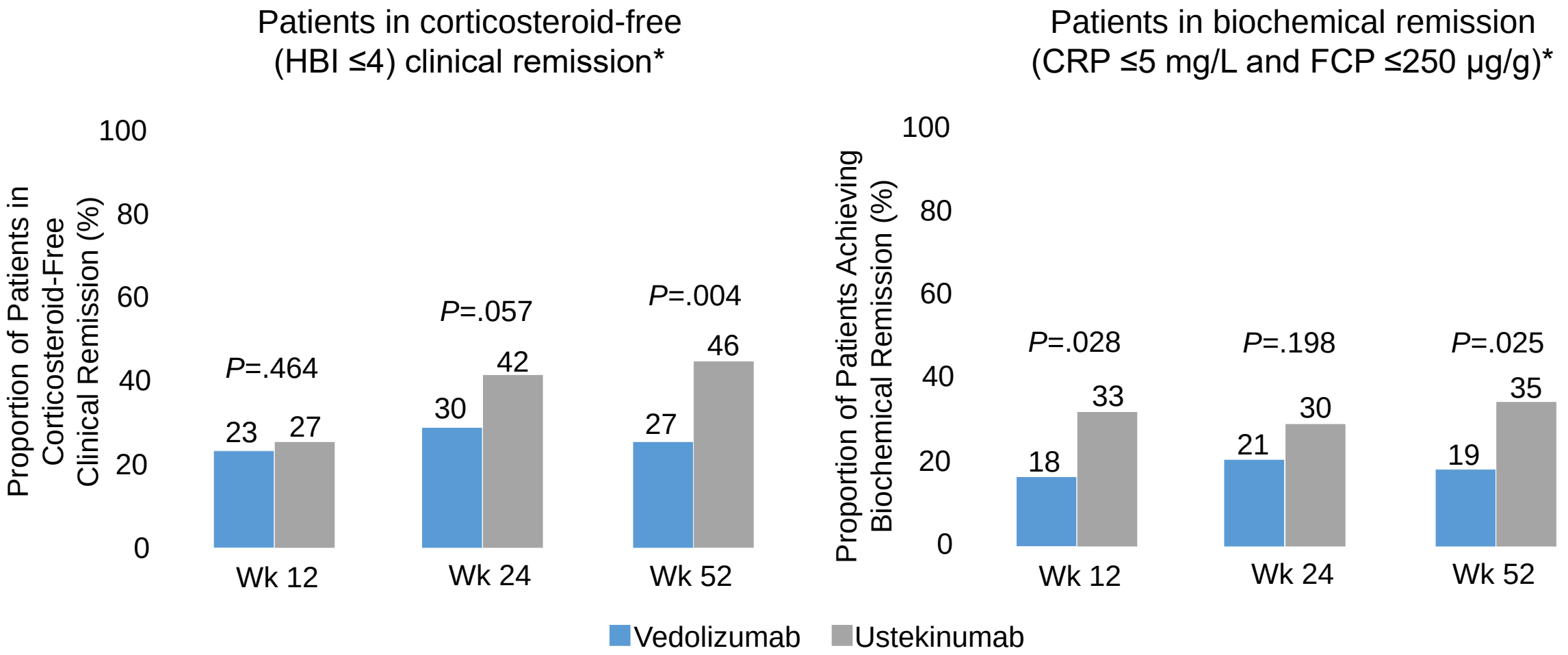
Comparative Studies of Anti-Interleukins

Ustekinumab Associated with Superior Effectiveness vs Vedolizumab in CD with Prior TNF Inhibitor Failure (Dutch Registry)



***Unadjusted data.**
HBI = Harvey-Bradshaw Index; FCP = fecal calprotectin.
Biemans VBC, et al. *Aliment Pharmacol Ther*. 2020;52(1):123-134.

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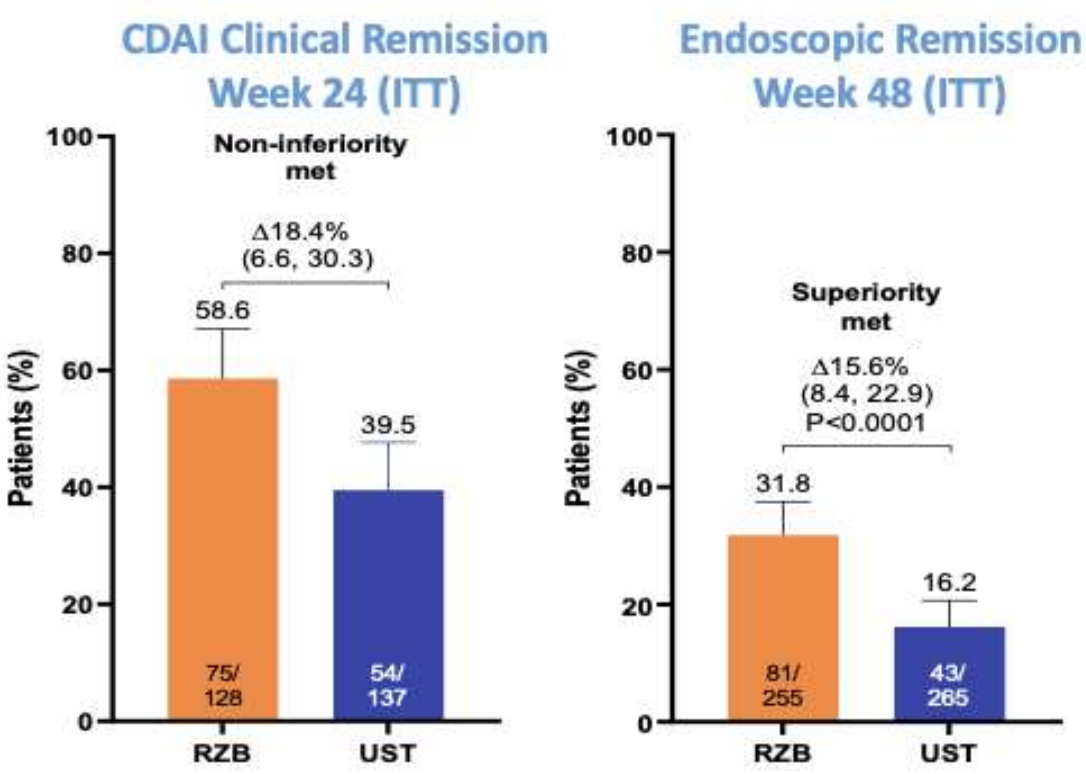
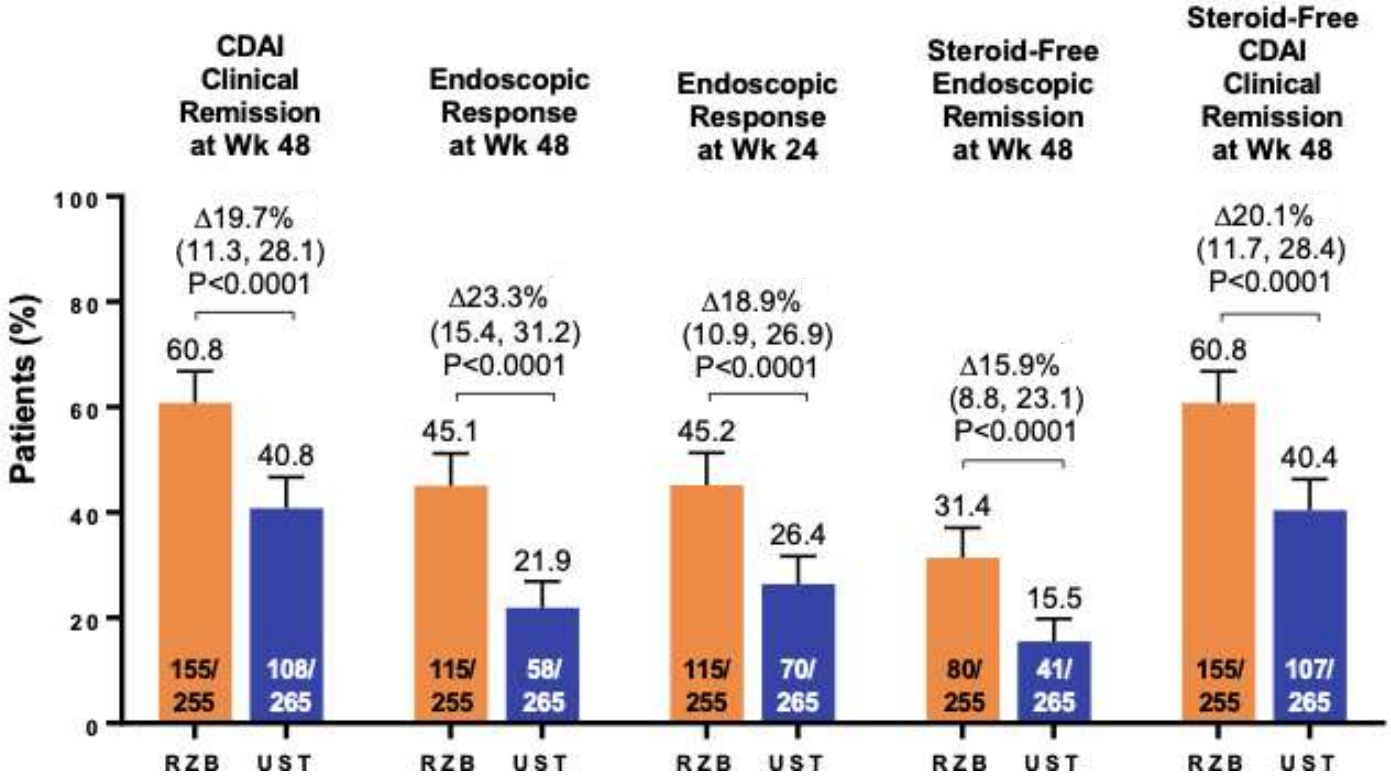
SEQUENCE: Risa vs Uste in TNF-Exposed CD

Open-label RCT w/ blinded assessment of endpoints, n=255 uste, n=265 risa





RCT = randomized controlled trial; ITT = intention-to-treat.

Peyrin-Biroulet L, et al. *N Engl J Med*. 2024;391(3):213-223.

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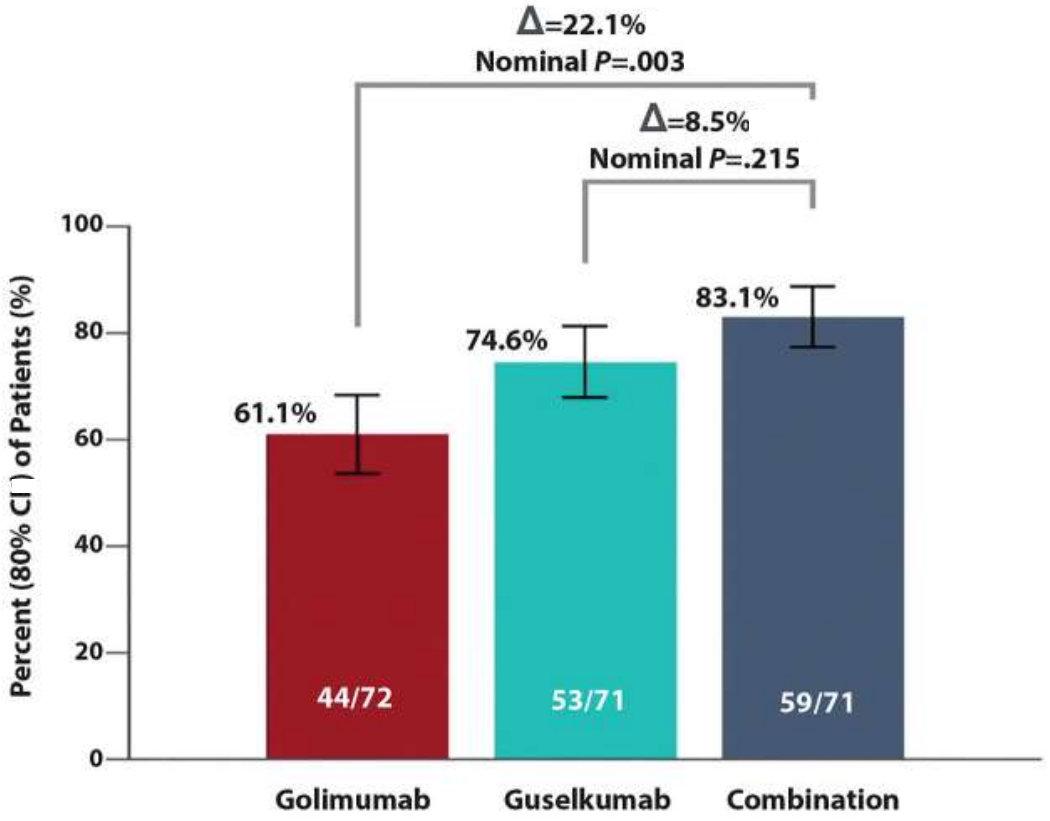
Guselkumab + Golimumab vs Monotherapy in UC: VEGA

- RCT 1:1:1 randomization
- N=214 patients included
- Outcome of clinical response at week 12
  - ≥30% decrease in full Mayo score
  - ≥3 points absolute reduction and rectal bleeding score of 0 or 1
- After induction, SC gusel provided for 32-34 weeks

Week 12 clinical response



Feagan BG, et al. *Lancet Gastroenterol Hepatol*. 2023;8(4):307-320.

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New Oral IL-23: Icotronkinra in UC (ANTHEM-UC)

- First targeted oral peptide to selectively block the IL-23 receptor
- Phase 2b RCT
- 3 doses vs placebo evaluated at week 12
- 63.5% clinical response vs 27% placebo at week 12 (*P*<.001)
- 30.2% of those on highest dose reached clinical remission vs 11.1% placebo (*P*<.01)
- Remission and response rates continued to improve through week 28

Clinical response is defined as decrease from baseline in the modified Mayo score by greater than or equal to (>=) 30 percent (%) 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. Clinical remission is defined as a Mayo stool frequency subscore of 0 or 1 and not increased from induction baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1 with no friability present on the endoscopy.

PR Newswire. March 10, 2025. Accessed July 22, 2025. https://www.prnewswire.com/news-releases/icotrokinra-meets-primary-endpoint-of-clinical-response-in-ulcerative-colitis-study-and-shows-potential-to-transform-the-treatment-paradigm-for-patients-302396524.html.

Patient and Therapy Selection Puzzle

DRUG

Efficacy

Indication
Rapidity of onset
Durability
Pharmacokinetics/TDM
Combination vs monotherapy
Positioning and sequence

Safety

Infection
Cancer
Specific concerns by agent or mechanism

PATIENT

Individual Characteristics

Ages, comorbidities, and preferences

Disease Characteristics

CD extent
Disease behavior/complication
Disease severity
Early vs late
EIMs
Prior treatment success or failure

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TDM = therapeutic drug monitoring; EIMs = extraintestinal manifestations.

Advanced Therapy Choices in IBD

Individual Patient Characteristics

Pregnancy

Young woman with steroid-dependent UC planning to start a family

Any biologic (anti-TNF w/ robust data)

Failed Anti-TNF

Young man with pan-UC who is a primary non-responder to anti-TNF

JAK, IL-23, IL-12/23, surgery

Newly Diagnosed

Newly diagnosed man with moderate CD with a personal history of lymphoma

Vedo, IL-23, IL-12/23

Shared Decision-Making

IL-23 is a choice in nearly all scenarios

Lifestyle Considerations

Businesswoman who travels often for work, with Crohn's ileitis

Ada, IL-23, IL-12/23, IFX SC

Unfavorable Pharmacokinetics

Older woman with pan-UC in whom you want to avoid immunomodulator

Vedo, IL-23, IL-12/23, ozanimod, etrasimod

Perianal Disease

Woman admitted with severe rectal Crohn's with perirectal abscess s/p drainage and seton placement

Anti-TNF (+azathioprine)

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IFX = infliximab.

IBD Patient-Centered Care (Today's Evolving Care Models)

Clinician's and Patient's Goals Are Not Always Aligned

Physician goals:
Objective measures of remission

Steroid-free remission
Endoscopic remission
Prevention of complications

Shared decision-making involves

- Shared goals: Objective + subjective measures
- Patient preferences

Patient goals:
Psychosocial measures of remission

Avoid toileting accidents
Ability to go to school/work
Enjoy relationship and intimacy
Enjoy social and leisure pursuits
Improve emotional health
Restful sleep
Enjoy food
Resolve fatigue
Decrease financial burden
Avoid meds SE

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SE = side effects.

Strategies to Optimize Patient Visits and Care

Establish rapport

Ask questions and establish trust: Make patients comfortable talking about sensitive issues

Educate and activate the patient

Patient becomes a partner in the IBD care journey

Align goals

Patient's concerns about IBD's impact on daily living and clinical/endoscopic endpoints

Balanced discussion of risks/benefits of therapy

In a way that is understandable to patient, use visual or real-life examples

Determine next steps

Choose and adjust treatment plan to meet shared goals

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Team-Based, GI Point of Care: Patient-Centered, Coordinated Care

Start with small team and expand as demands or needs dictate

Regueiro MD, et al. *Inflamm Bowel Dis*. 2016;22(8):1971-1980.

Positioning Interleukin Inhibitors: Our Practice

Crohn's disease

- All IL-23s and ustekinumab effective in bio-naïve patients
- Use in patients with moderate disease; likely not 1st line w/ perianal disease; use w/ derm manifestations (psoriasis, etc); superior safety to TNF
- In anti-TNF-exposed patients, risankizumab/guselkumab preferred over ustekinumab

Ulcerative colitis

- All IL-23s and ustekinumab effective in bio-naïve patients
- Use in patients with moderate disease; use w/ derm manifestations; superior safety to TNF
- In anti-TNF-exposed patients, IL-23 not as differential for risankizumab/mirikizumab as in CD

Differentiation

- ACCESS!
- # of IV infusions for induction vs SC; SC frequency; OBI vs autoinjector vs syringe
  - Guselkumab is currently the only IL-23 inhibitor with both SC and IV induction options

Bourgonje AR, et al. *Gastroenterology*. 2025;168(1):29-52.e3.

Key Learning Points: Unmet Needs in IBD

- Better efficacy regarding symptoms and endoscopic healing
- Prevention of surgery
- Durability

Key Learning Points: IBD Therapies

Ustekinumab

- Established, efficacious, and safe agent for the management of UC and CD
- Biosimilars now available

IL-23

- Mechanism
  - Blocks development of inflammatory pathogenic Th-17 cells
  - Potential for dual role with CD64 (guselkumab)
  - High efficacy/safety
  - Durability
- Mirikizumab, risankizumab, and guselkumab now approved in CD and UC; efficacious and safe agents
- Risankizumab > ustekinumab in TNF-exposed CD populations for endoscopic outcomes
- Guselkumab > ustekinumab for endoscopic outcomes in CD
- Differentiation of IL-23s will likely come down to ACCESS, ease, and type of administration (guselkumab with SC load in CD)

Future will likely include combined agents (IL-23 + anti-TNF) and potential for oral delivery of IL-23

Key Learning Points: Patient-Centered Care in IBD

- Consider patient and drug factors when choosing a therapy
- Shared decision-making is central – ensure that patient and clinician goals are aligned
- Activated patients become partners in their journeys
- Patient-centered care is multi-disciplinary; involve a team for whole-person care