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Inflammatory Bowel Disease
IN PARTNERSHIP WITH AIBD

Targeting IL-23 in IBD: Personalized Strategies for Sensitive Symptoms and Individual Needs

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- **Marita Kametas, MSN, APN, FNP, CMSRN, COCN:** Consultant/Grant Funding/Speaker's Bureau – AbbVie, Eli Lilly, Johnson & Johnson, Pfizer, Takeda, TKG

Learning Objectives

- Apply best practices in identifying and assessing sensitive symptoms in people with IBD, including bowel urgency, using effective evidence-based and expert-recommended strategies

- Evaluate the most recent safety/efficacy data and therapeutic indications associated with IL-23 inhibitors for IBD

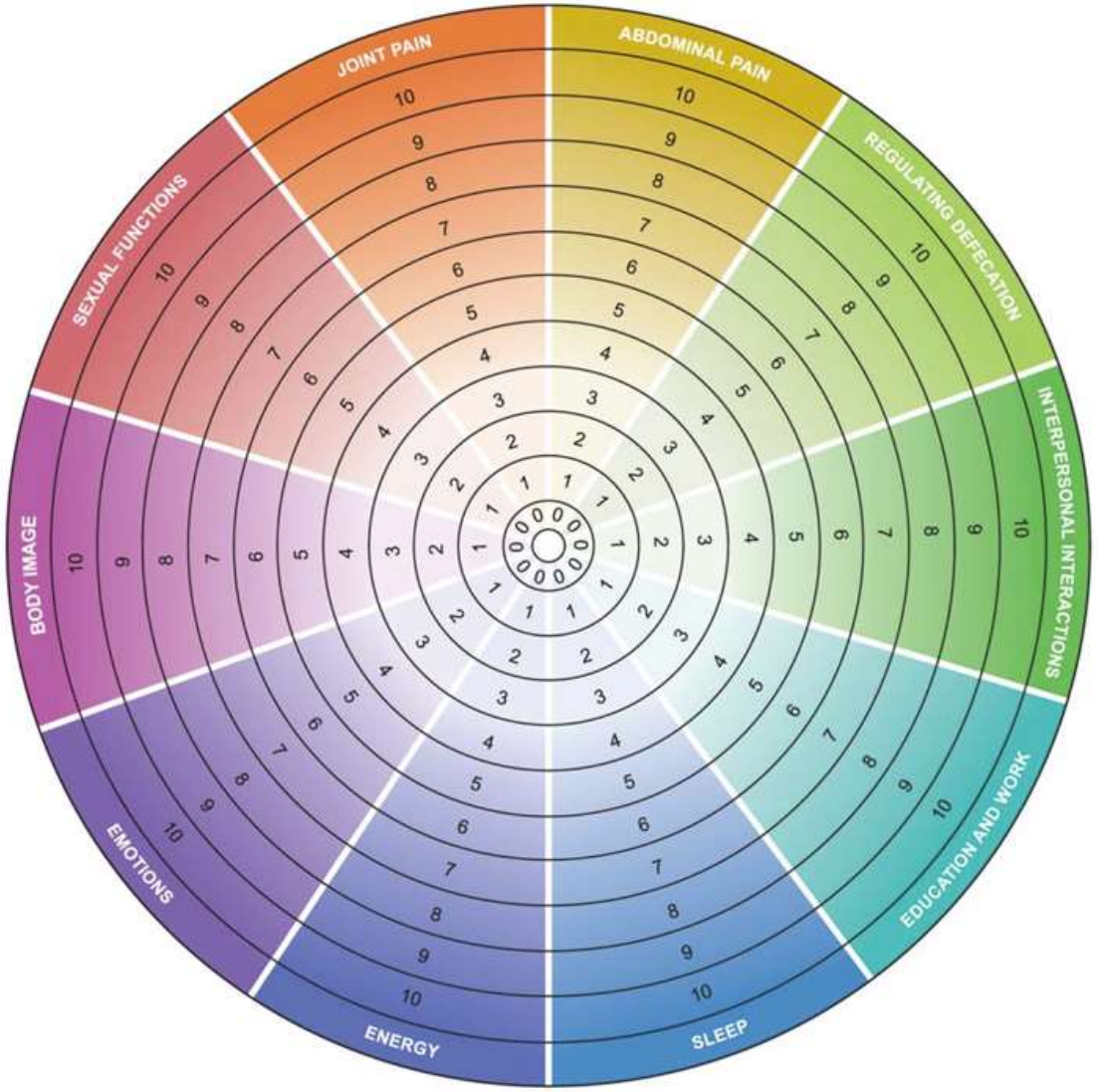
- Implement comprehensive treatment strategies to optimize outcomes for people with IBD, including those who struggle with obesity

IBD = inflammatory bowel disease; IL = interleukin.

Symptom Assessment

IBD Disk

- A shortened, self-administered adaption of the validated IBD Disability Index – to give immediate visual representation of patient-reported IBD-related disability



Ghosh S, et al. *Inflamm Bowel Dis*. 2017;23(3):333-340.

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CD: Crohn's Disease Activity Index

- Range <150 inactive disease, >450 severe disease
- Measured over the past 7 days
- Includes number of liquid stools, abdominal pain, general well-being, anti-diarrhea drug use, abdominal mass on exam, hematocrit, presence of extraintestinal manifestations, and fever

Best WR, et al. *Gastroenterology*. 1976;70(3):439-444.

UC: Mayo Score (Including Modified, Partial)

- Mayo Score developed for clinical trials
- 4-component scoring system – stool frequency, rectal bleeding, physician global assessment, and endoscopic findings – each rated 0-3, collectively producing a total Mayo Score ranging from 0-12
- Modified: No physician global assessment
- Partial: No endoscopy

Schroeder KW, et al. *N Engl J Med*. 1987;317(26):1625-1629.

ACG CD Guideline Assessment Recommendations

- Evaluation of clinical disease activity should include
  - Stool frequency and consistency
  - Abdominal pain
  - Systemic signs of inflammation (eg, fever, weight loss, tachycardia, and anemia)
  - Extraintestinal manifestations of CD
- Confirm disease activity through imaging and/or endoscopic assessments
  - In individuals without any observable mucosal inflammation or ulceration, consideration should be given to the potential differential diagnostic possibilities

ACG = American College of Gastroenterology.

Lichtenstein GR, et al. *Am J Gastroenterol*. 2025;120(6):1225-1264.

ACG UC Guideline Assessment Recommendations

- Primary symptoms to assess include
  - Frequency of bowel movements, including number of nocturnal bowel movements
  - Rectal bleeding; proportion of bowel movements that are mixed with visible blood
- Additional symptoms
  - Bowel urgency
  - Abdominal pain
  - Bowel cramping
  - Weight loss
  - Extraintestinal manifestations

Rubin DT, et al. *Am J Gastroenterol*. 2025;120(6):1187-1224.

ACG UC Guideline Assessment Recommendations

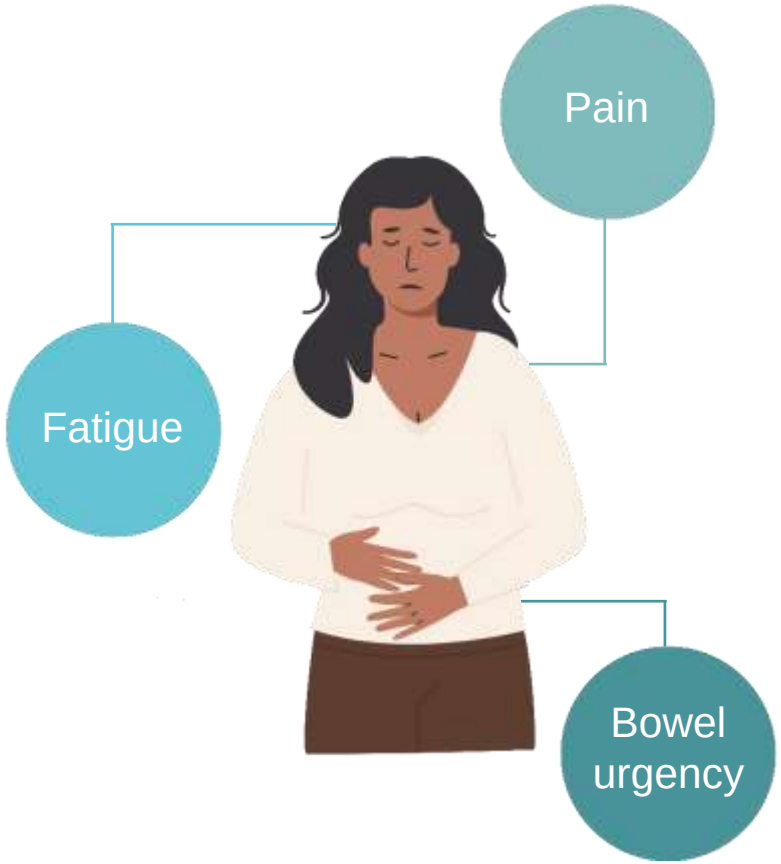
	Remission	Mild	Moderate-severe	Fulminant
Stools (#/day)	Formed stools	<4	>6	>10
Blood in stools	None	Intermittent	Frequent	Continuous
Urgency	None	Mild, occasional	Often	Continuous
Hemoglobin	Normal	Normal	<75% of normal	Transfusion required
ESR	<30	<30	>30	>30
CRP (mg/L)	Normal	Elevated	Elevated	Elevated
Fecal calprotectin (μg/g)	<150–200	>150–200	>150–200	>150–200
Endoscopy (MES)	0–1	1	2–3	3
Endoscopy (UCEIS)	0–1	2–4	5–8	7–8
Intestinal ultrasound	Colonic BWT≤3 mm Rectal BWT ≤4 mm mLimberg = 0		Colonic BWT >3 mm Rectal BWT >4 mm mLimberg >0	

The below factors are general guides for disease activity. With the exception of remission, a patient does not need to have all the factors to be considered in a specific category.

BWT, Bowel Wall Thickness (mucosa, submucosa, muscularis propria, and serosa); CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IVCS, intravenous corticosteroids; mLimberg, Modified Limberg Score of hypervascularity in the submucosa (scored as [0] absent, [1] small spots [single vessels] within the wall, [2] long stretches within the wall, and [3] long stretches within the wall extending into the mesentery) (88); MES, Mayo Endoscopic Subscore (see Figure 2 and Table 5); UCEIS, Ulcerative Colitis Endoscopic Index of Severity (see Figure 2 and Table 7).

Rubin DT, et al. *Am J Gastroenterol*. 2025;120(6):1187-1224.

Symptoms Most Impacting QoL in IBD Differ from Indices



- Multiple aggravators
  - Requires constant planning and adaptation
- Relentless and unpredictable symptoms
  - Creates uncertainty/anxiety
- Far-reaching negative impact
  - Mental health
  - Relationship closeness and intimacy
  - Work or school performance
  - Social isolation and stigma

QoL = quality of life.

Adapted from Dibley L, et al. *Dig Dis Sci*. 2021;66(10):3330-3342.

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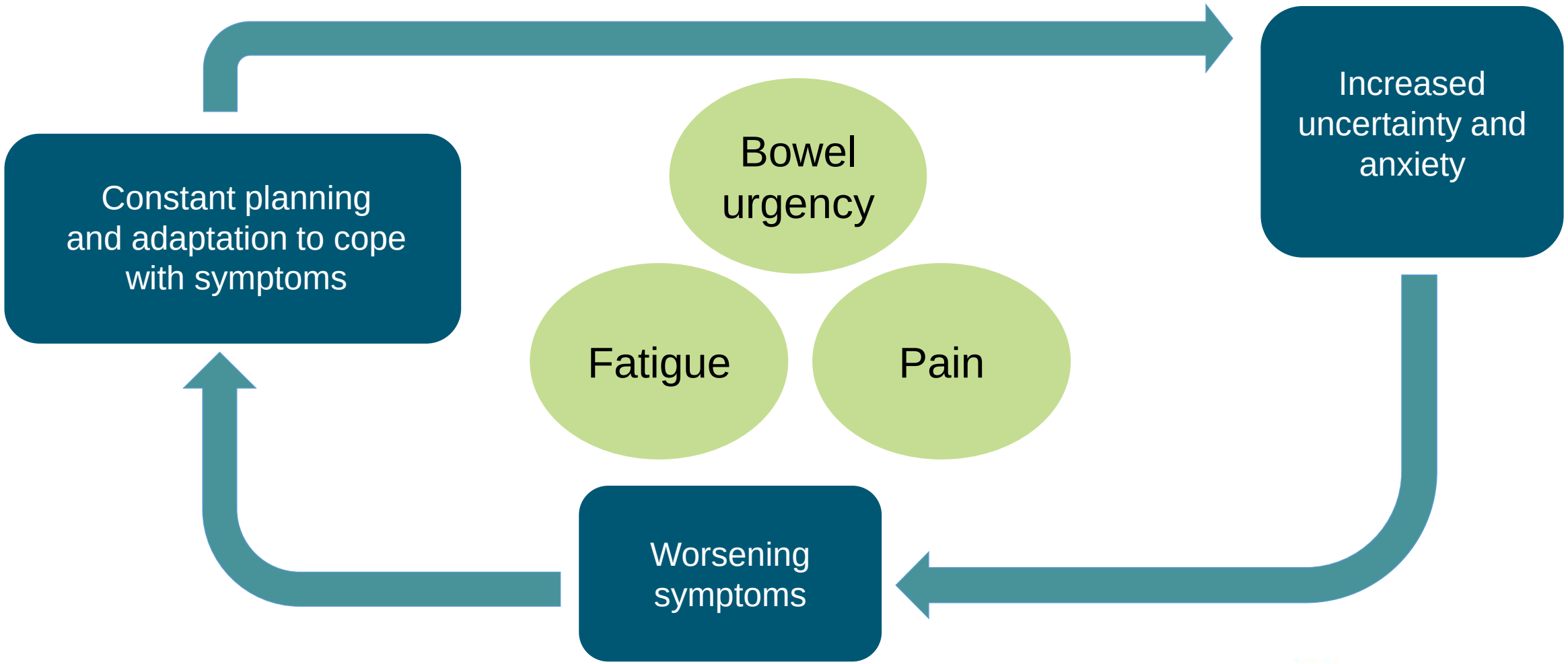
The Cycle of Adaptation to a “New Normal”



Adapted from Dibley L, et al. *Dig Dis Sci*. 2021;66(10):3330-3342.

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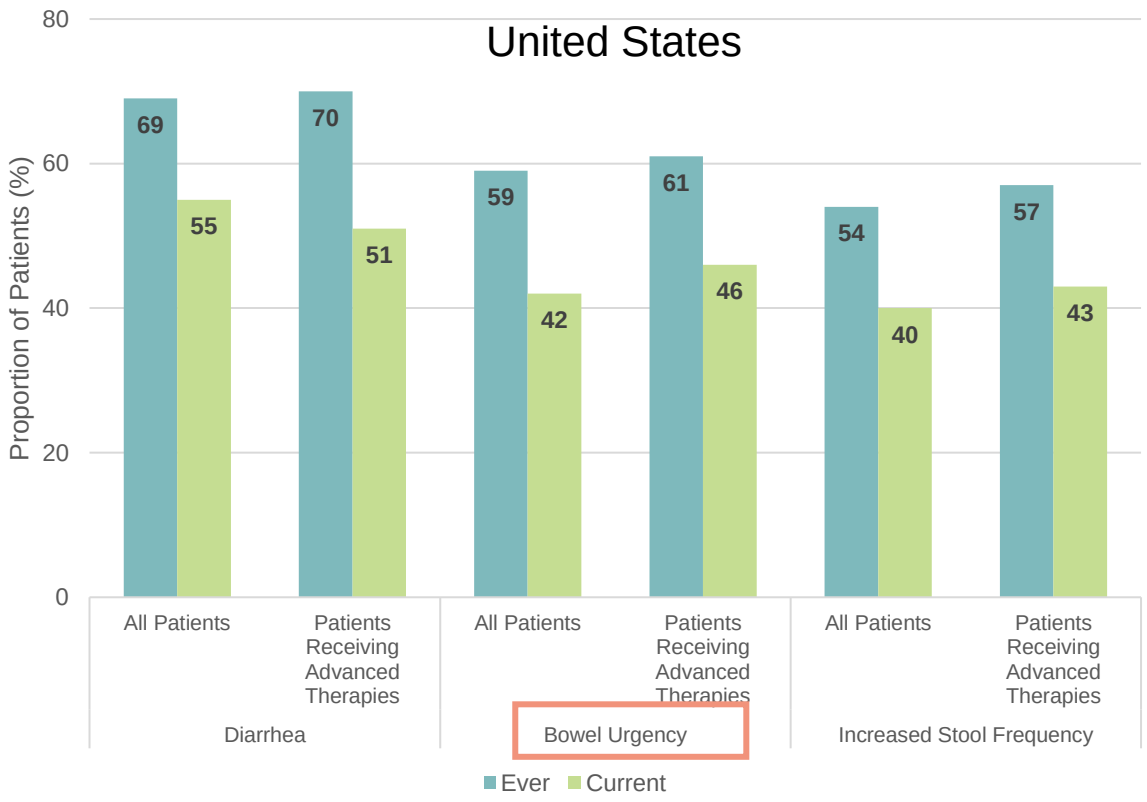
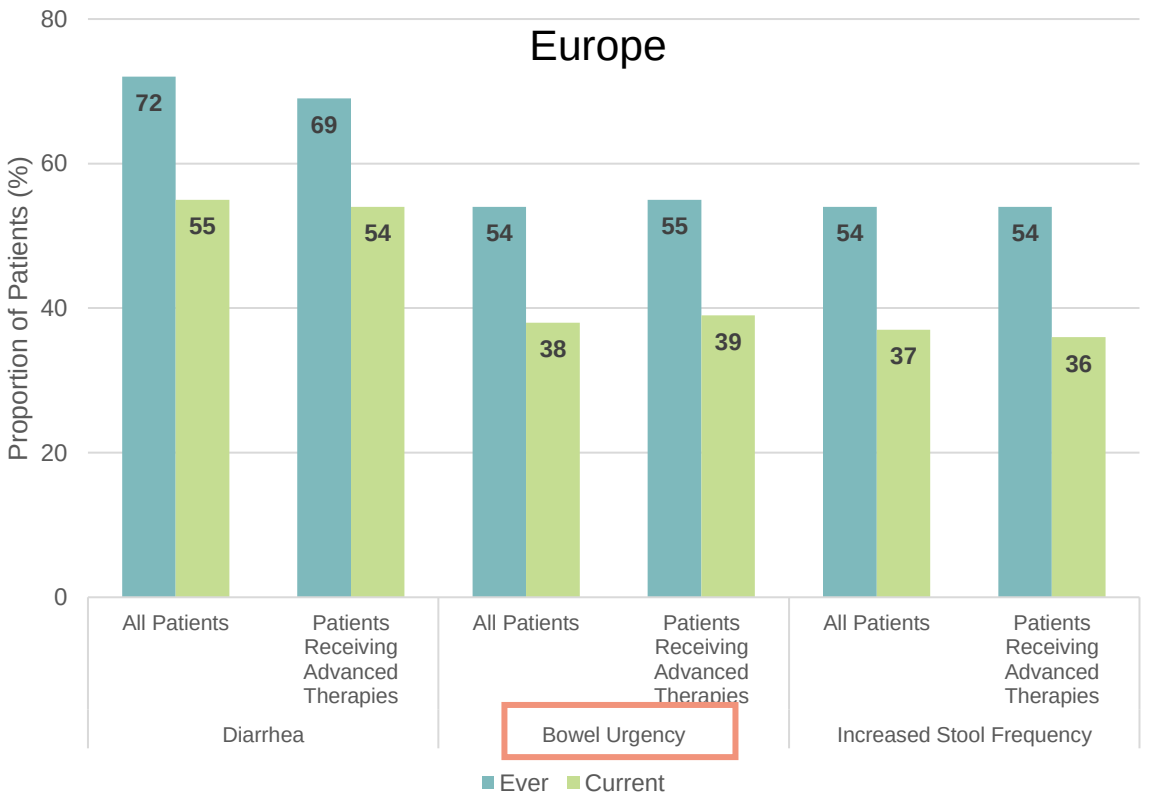
CONFIDE Survey: Diarrhea, Bowel Urgency, Frequency

Bowel urgency was among the top 3 most frequently reported CD symptoms





CONFIDE = Communicating Needs and Features of IBD Experiences.
Schreiber S, et al. *Am J Gastroenterol*. 2023;118(10S):S815.

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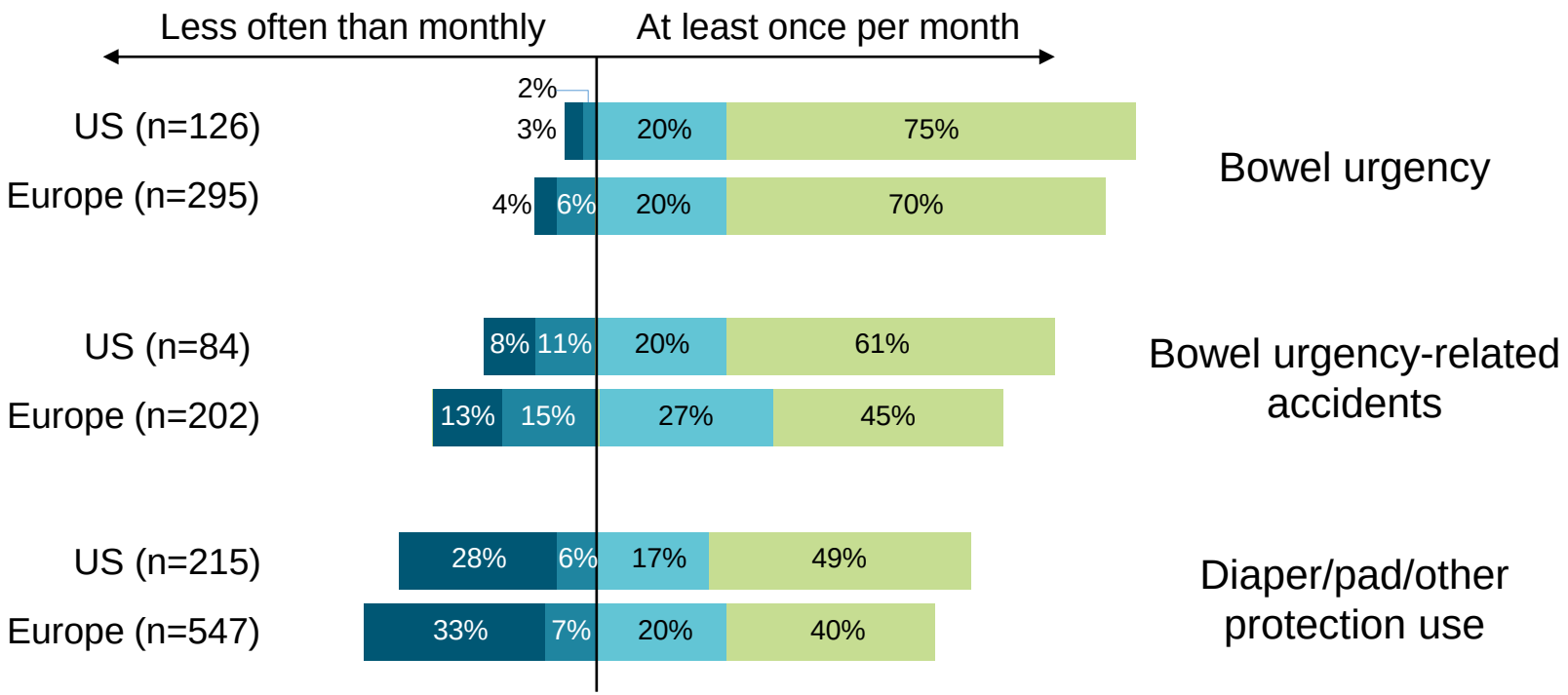
CONFIDE Survey

Patients with CD



Bowel urgency is just as much of an issue in CD as it is in UC

Schreiber S, et al. *Am J Gastroenterol*. 2023;118(10S):S815.

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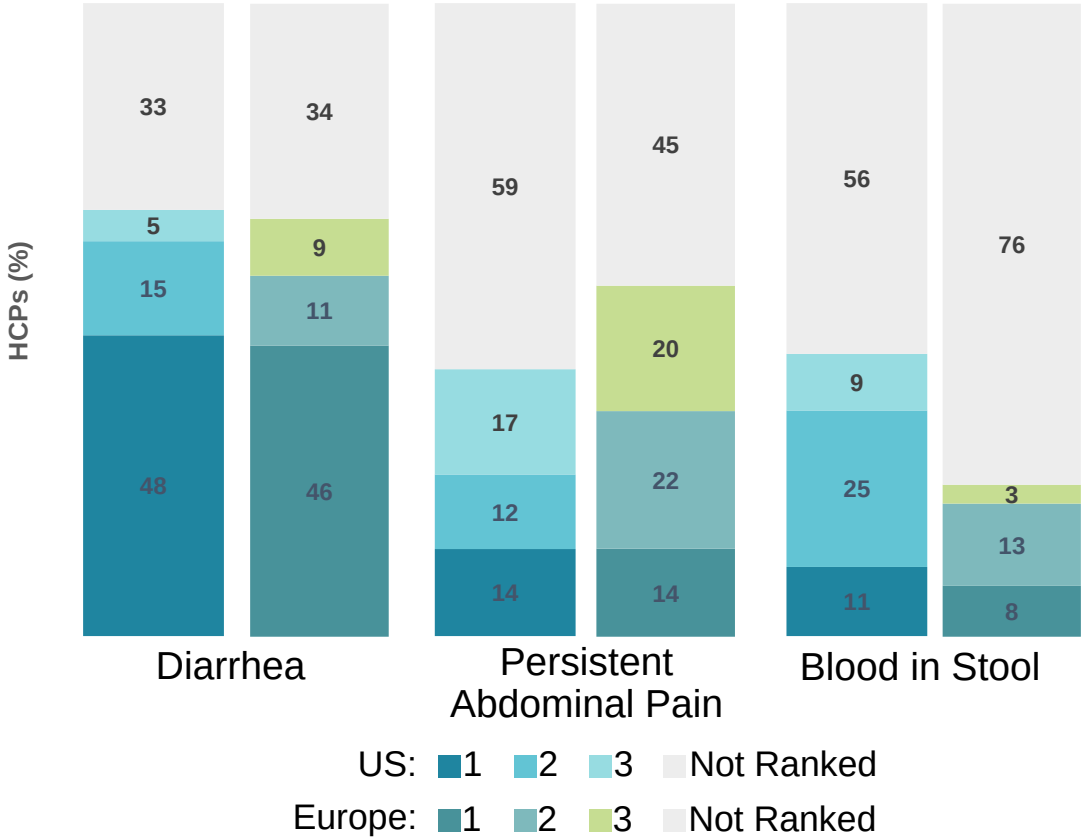
CONFIDE Survey Results

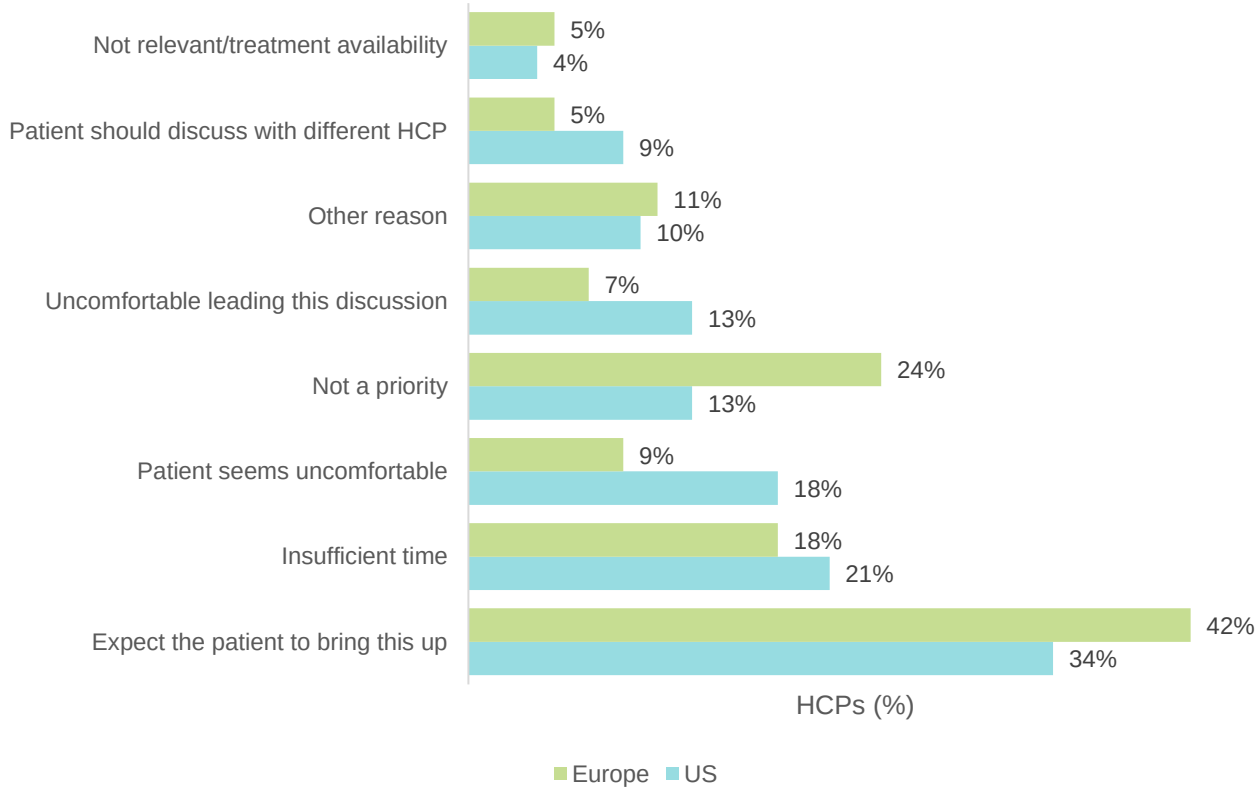
81% of US and 85% of European HCPs did not rank bowel urgency among the symptoms most reported by patients

Ranking of HCP-perceived top 3 CD symptoms reported by patients



HCPs do not proactively discuss bowel urgency and bowel urgency-related accidents with patients

HCP-reported reasons for not proactively discussing bowel urgency



HCPs = health care professionals.

Schreiber S, et al. *Am J Gastroenterol*. 2023;118(10S):S815.

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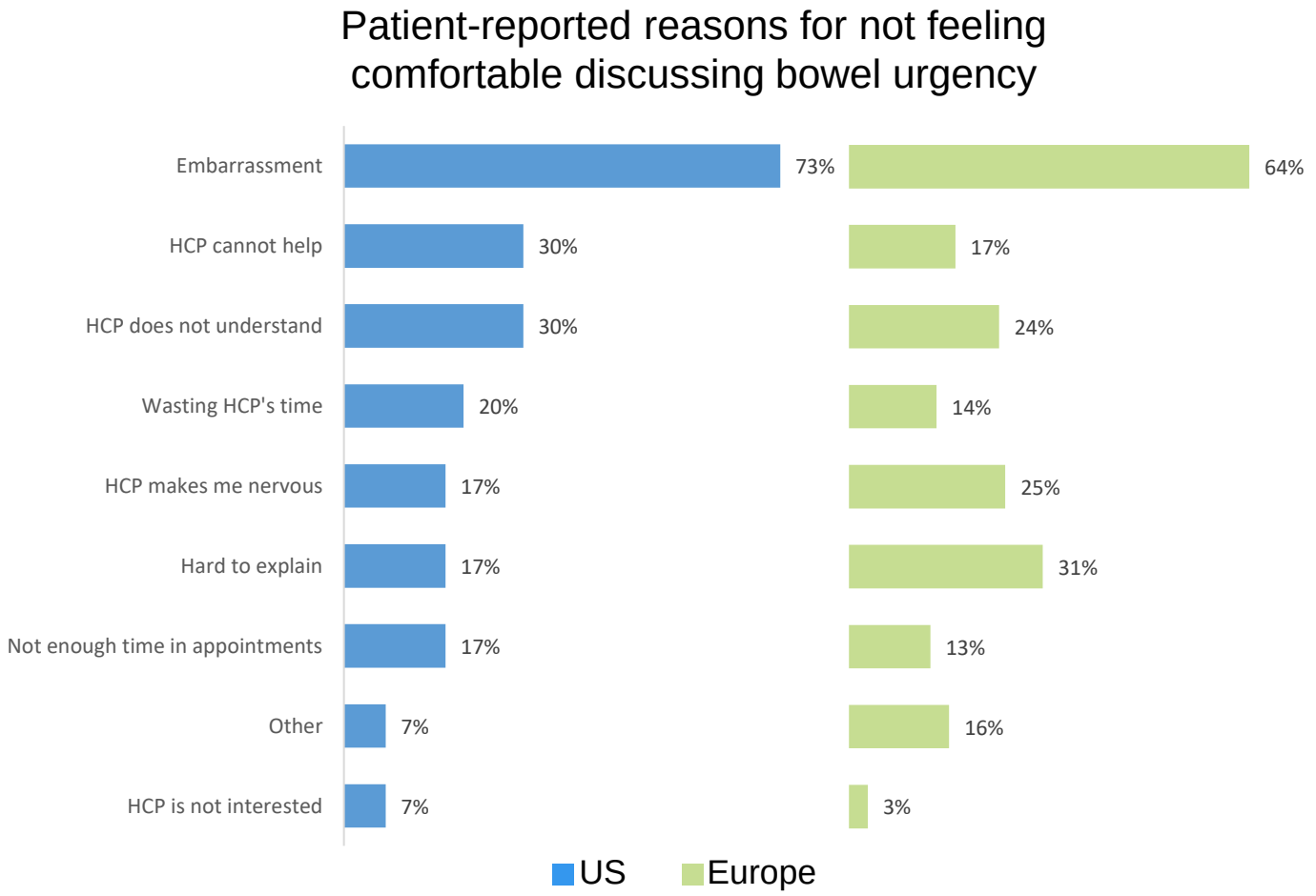
CONFIDE Survey Results

- **Embarrassment was the most common reason** for patient discomfort in discussing bowel urgency and bowel urgency-related accidents with HCPs

- Only **40% of US** and **27% of European patients** were completely comfortable discussing bowel urgency with their HCPs



Schreiber S, et al. *Am J Gastroenterol*. 2023;118(10S):S815.

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CONFIDE Survey Results

Mean severity of urgency before bowel movement by deferral time over the last 3 days among patients with M-S CD experiencing bowel urgency in the past month

Bowel movement deferral time*	Europe (N=208)		US (N=91)	
	Number of patients (n)	Mean Urgency NRS scores** (SD)	Number of patients (n)	Mean Urgency NRS scores** (SD)
I have been able to wait 15 minutes or longer before having a bowel movement	37	6.4 (2.6)	12	6.2 (2.5)
I have needed to get to the bathroom within 5-15 minutes	69	6.5 (1.8)	34	6.9 (1.6)
I have needed to get to the bathroom within 2-5 minutes	67	6.8 (1.7)	29	7.1 (1.5)
I have needed to get to the bathroom in less than 2 minutes	29	7.3 (1.5)	13	7.4 (1.3)
Sometimes I am unable to make it to the bathroom in time	6	8.3 (1.9)	3	9.0 (1.0)

*Bowel movement deferral time question: Over the last three days, how much urgency have you had before bowel movements?
**Urgency NRS is an 11-point horizontal numeric rating scale [0 (No urgency) to 10 (Worst possible urgency)] used to assess the severity of bowel urgency.

Frequency of symptoms and use of diapers/pad/other protection in patients with M-S CD over past 3 months

- **49% of both US** and **European patients** reported bowel movement deferral time of 5 minutes or less

- **49% of US** and **40% of European patients** used diapers at least once a week due to fear/anticipation of bowel urgency-related accidents

Dubinsky MC, et al. *J Crohns Colitis*. 2024;18(Suppl 1):i200-i201.

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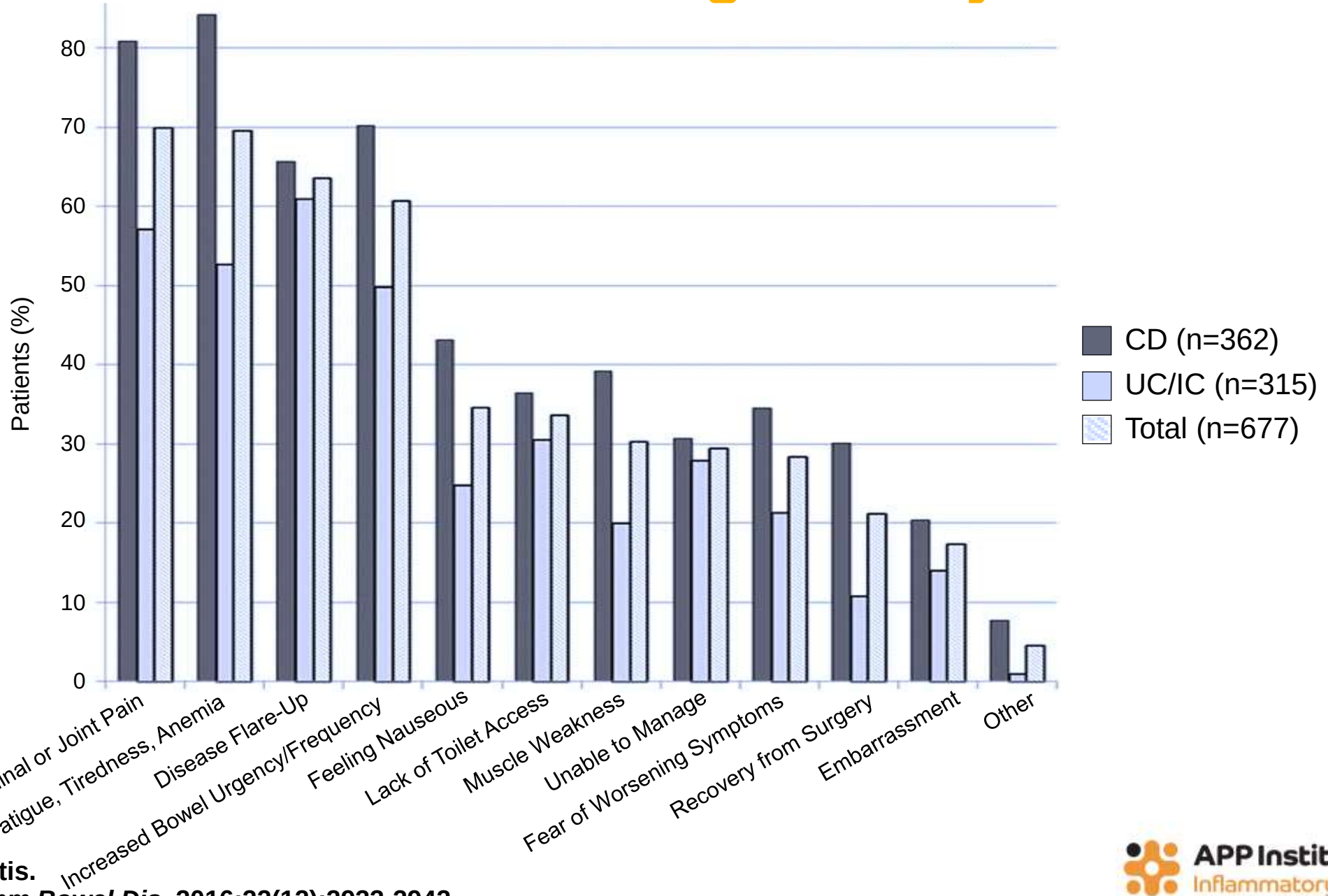
Impact of IBD on Daily Activity

- 79% of patients limited physical activity
- 34% reported *avoiding* running or jogging
- Reasons for limited activity
  - 70% fatigue/tiredness
  - 69% disease flare-ups
  - 61% increased toilet urgency

Tew GA, et al. *Inflamm Bowel Dis*. 2016;22(12):2933-2942.

Reasons for Avoiding Activity in IBD



IC = interstitial cystitis.

Tew GA, et al. *Inflamm Bowel Dis*. 2016;22(12):2933-2942.

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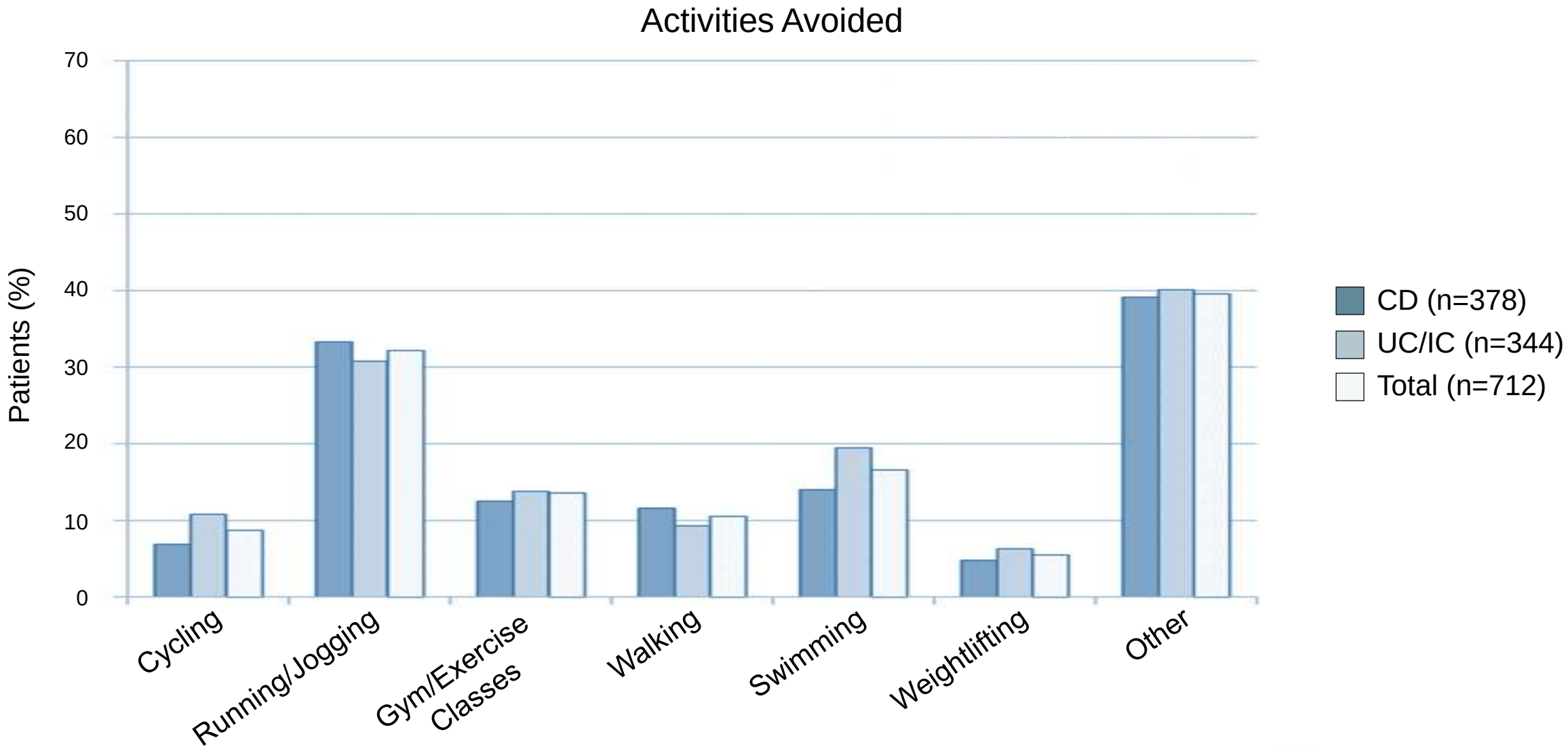
Activity Adaptation in IBD



Tew GA, et al. *Inflamm Bowel Dis*. 2016;22(12):2933-2942.

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IBD and Sexual Health

Sexual functioning, satisfaction, and sexual drive can be negatively impacted by IBD and can impact QoL

Survey of 426 gastroenterologists

70% never or rarely ask patients about sexual dysfunction

75% did not change treatment if a patient reported sexual dysfunction

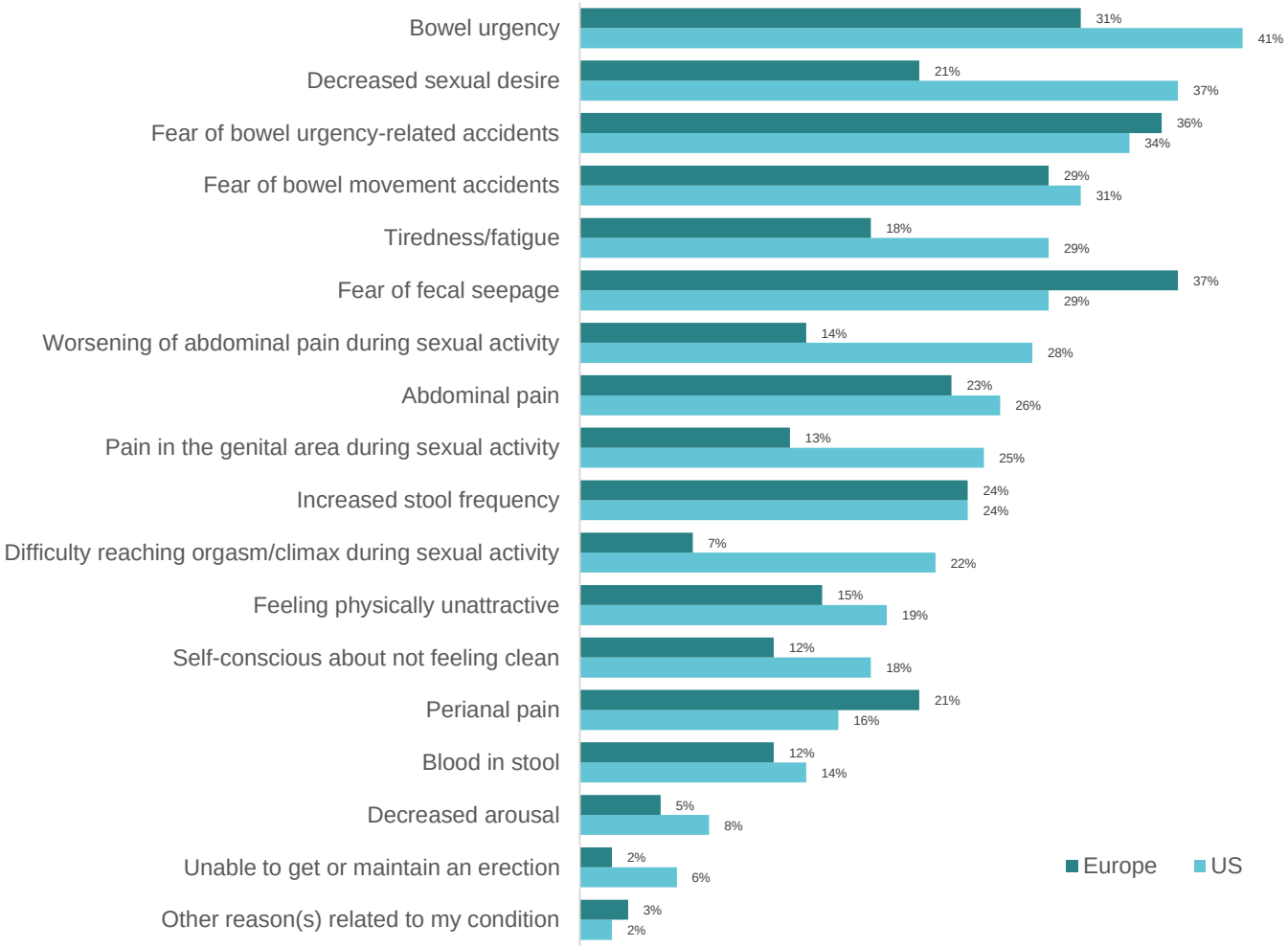
Gastroenterology survey reported barriers to addressing sexual dysfunction during appointments

- Lack of knowledge (80%)
- Lack of experience (58%)
- Lack of time (44%)
- Embarrassment (30%)

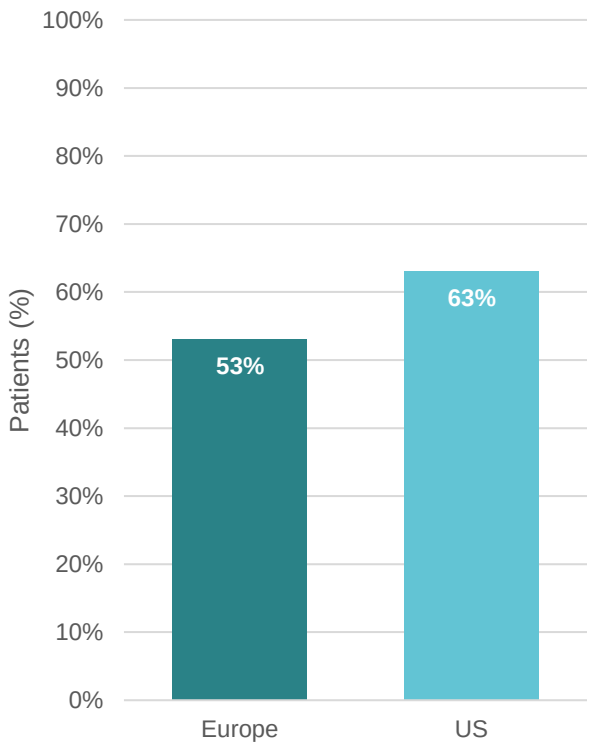
Romano L, et al. *Dig Liver Dis*. 2022;54(11):1494-1501. Mantzouranis G, et al. *J Crohns Colitis*. 2015;9(12):1160-1168.

Impact of Bowel Urgency on Sexual Activity

Patient-provided reasons for avoiding or decreasing sexual activity



Patients who avoided or decreased sexual activity in the last 3 months



Dubinsky MC, et al. Presented at: Digestive Disease Week (DDW); May 6-9, 2023; Chicago, IL. Abstract 1139.

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MUSIC Study: Significant Proportion of Patients with CD Reported Bowel Urgency

Characteristic	Bowel Urgency (UNRS 2-10)* **n=883**	No or Minimal Bowel Urgency (UNRS 0-1)* **n=650**	*P*-Value**
Age (years), mean (SD)	54.1 (15.5)	53.4 (16.1)	.320
Female gender, n (%)	632 (73)	452 (70)	.290
Education (> high school), n (%)	789 (89)	601 (92)	.039
Caucasian (White), n (%)	789 (89)	592 (91)	-
Current smoking (yes), n (%)	29 (3)	11 (2)	.053
Body mass index, mean (SD)	26.8 (6.3)	25.3 (4.9)	<.001
Disease duration (years), mean (SD)	25.7 (14.1)	23.7 (13.7)	.003
Ever GI surgery (yes), n (%)	540 (61)	311 (48)	<.001
Ever GI hospitalization (yes), n (%)	649 (73)	417 (64)	<.001
Number hospitalizations, mean (SD)	3.9 (2.6)	3.1 (2.3)	<.001
Remission (yes), n (%)	544 (62)	599 (92)	<.001

58% of patients reported bowel urgency

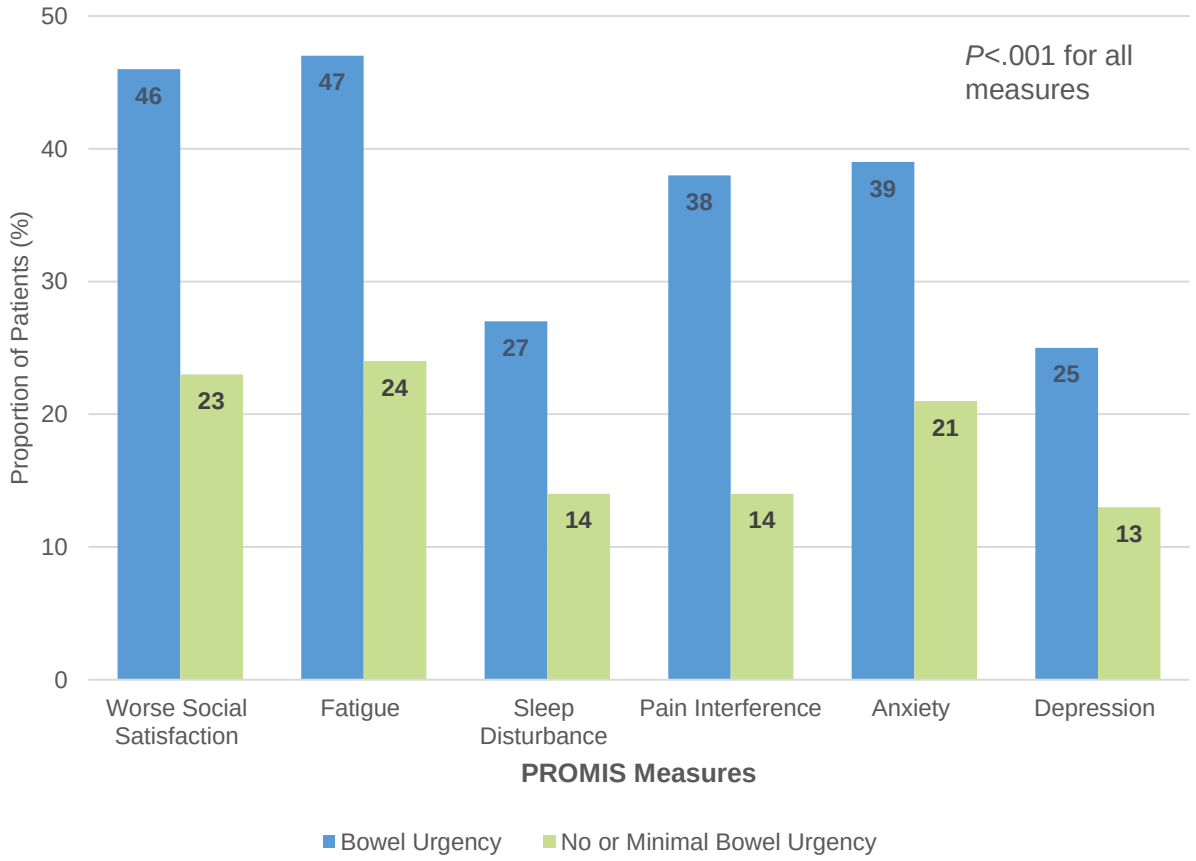
Bowel urgency was higher among patients with active disease as compared to those in remission

(87% vs 48%, *P*<.001)

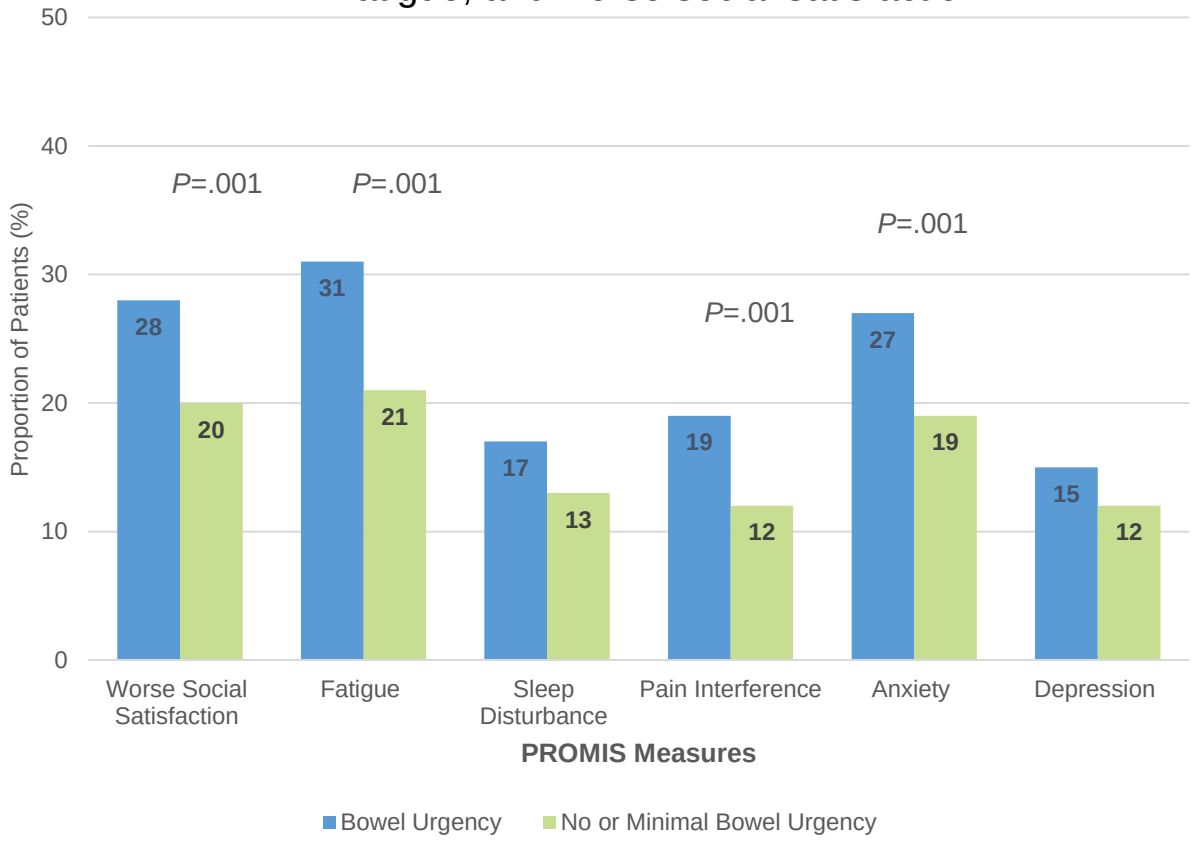
***Urgency was measured using 11-point UNRS: 0-1 = no minimal bowel urgency, 2-10 = bowel urgency;**
****Chi-square test was used to compare no or minimal bowel urgency vs bowel urgency for each of the categorical variables, and t-test was used for continuous variables.**
UNRS = Urgency Numeric Rating Scale; GI = gastrointestinal; SD = standard deviation.
Long MD, et al. Presented at: ACG Annual Scientific Meeting; October 20-25, 2023; Vancouver, Canada. P2155.

MUSIC Study: Bowel Urgency Negatively Impacted Quality of Life in CD

Patients with bowel urgency had significantly worse quality of life



Of those in remission, bowel urgency was significantly associated with anxiety, pain, fatigue, and worse social satisfaction



Long MD, et al. Presented at: ACG Annual Scientific Meeting; October 20-25, 2023; Vancouver, Canada. P2155.

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Defining Bowel Urgency

Definition Used in Study	N
Inability to defer defecation for more than 15 minutes	4
No definition	20
Not making it to the toilet in time	1
Immediate need to defecate	1
Hurry to immediately go to the bathroom/unable to make it in time	1
Simple Clinical Colitis Activity Index (SCCAI) definition	2
Having to rush to the toilet to avoid an accident	1
Sudden and severe urge to defecate	1
Inability to defer defecation for more than 5 minutes after the first call to stool	2
Having to urgently visit the toilet to pass stool	1
Urgency to go to the bathroom	1
An irresistible and urgent desire to defecate	1

Caron B, et al. *Clin Gastroenterol Hepatol*. 2023;21(6):1403-1413.e27.

Barriers to Identifying Bowel Urgency in Patients with CD

Does normal stool frequency mean no bowel urgency?

55% of patients report urgency symptoms with no change in stool frequency

Dibley L, Norton C. *Inflamm Bowel Dis*. 2013;19(7):1450-1462. Dubinsky MC, et al. *Qual Life Res*. 2023;32(12):3403-3415.

Urgency Assessment

Commonly Used CD Indices

- Clinical Disease Activity Index (CDAI)
- Harvey-Bradshaw Index (HBI)
- Inflammatory Bowel Disease Questionnaire (IBDQ)
- Patient-Reported Outcome-2 (PRO-2)

Di Palma JA, Farraye FA. *Gastroenterol Hepatol* (NY). 2011;7(3):163-169.

Commonly Used CD Indices

- Clinical Disease Activity Index (CDAI)
- Harvey-Bradshaw Index (HBI)
- Inflammatory Bowel Disease Questionnaire (IBDQ)
- Patient-Reported Outcome-2 (PRO-2)

None of the commonly used scales capture bowel urgency severity

Di Palma JA, Farraye FA. *Gastroenterol Hepatol* (NY). 2011;7(3):163-169.

Commonly Used UC Indices

- Mayo Score, modified Mayo Score, partial Mayo Score
- Simple Clinical Colitis Activity Index (SCCAI)
- Inflammatory Bowel Disease Questionnaire (IBDQ)
- Patient-Reported Outcome-2 (PRO-2)

Of these, only the SCCAI asks about urgency in an abbreviated fashion

Walsh AJ, et al. *J Crohns Colitis*. 2014;8(4):318-325.

The Urgency Numeric Rating Scale (UNRS): CD and UC

Patients with CD have indicated that it is important to have a bowel urgency scale that distinguishes between different levels of severity instead of just a yes or no

How severe was your urgency (sudden or immediate need) to have a bowel movement in the past 24 hours?

0	1	2	3	4	5	6	7	8	9	10
No urgency										Worst possible urgency

Patients report the severity of their bowel urgency symptoms over the past 24 hours

- Weekly average scores are calculated as mean score over a 7-day period
- Higher scores indicate worse urgency severity (eg, immediacy of need to have a bowel movement)

The UNRS was used in the mirikizumab Phase III studies to assess bowel urgency, whereas the upadacitinib Phase III studies used a yes/no binary scale

Dubinsky MC, et al. *J Patient Rep Outcomes*. 2022;6(1):31. Danese S, et al. *Lancet*. 2022;399(10341):2113-2128. D'Haens G, et al. *N Engl J Med*. 2023;388(26):2444-2455.

Second N-ECCO Consensus Statements in Caring for Patients with IBD

"A major life impact is the **need to be near a toilet**. **Urgency** can be severe, with some patients reporting less than 30 seconds between calls to stool and actual defecations. Fear of losing bowel control is so great that some patients always worry about where the nearest toilet is."

"Recent evidence suggests that, at some point of the disease course, between 31% and 74% of people with IBD experience fecal incontinence, not necessarily related to disease activity.

Despite it being a major concern, incontinence is rarely reported to or addressed by clinicians."

N-ECCO = Nurses European Crohn's and Colitis Organisation.

Kemp K, et al. *J Crohns Colitis*. 2018;12(7):760-776.

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Assessment of Bowel Urgency: Patient-Reported Outcomes

FDA and EMA have recommended that clinical parameters, endoscopic findings, and patient-reported symptoms be separately quantified and reported in IBD trials

PRO tools developed per FDA guidance that include measures of urgency

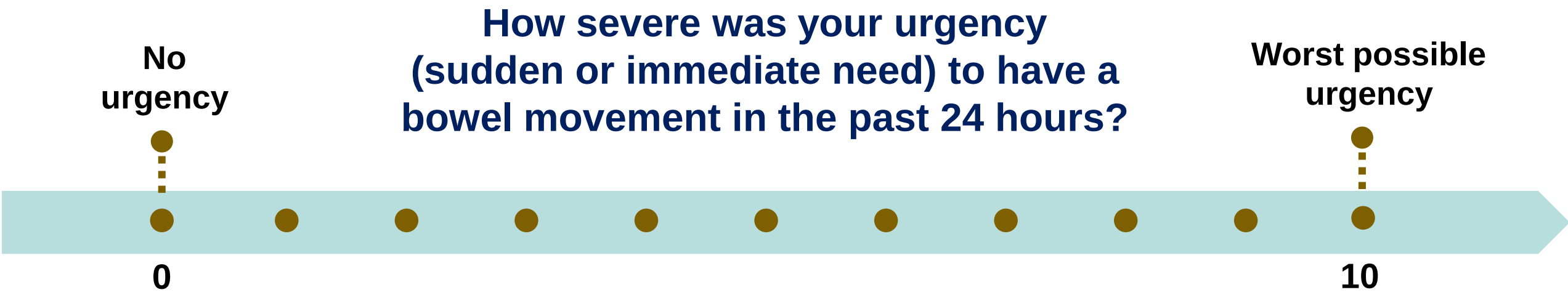
- Symptoms and Impacts Questionnaire for CD (SIQ-CD)
- CD Patient-Reported Outcomes Signs and Symptoms (CD-PRO/SS) diary
- UNRS

Note: *Apart from the UNRS, the other PROs listed include multiple items and measure symptoms assessed by traditionally used scales (eg, SES-CD, CDEIS) and therefore, may be duplicative*

EMA = European Medicines Agency; SES-CD = Simple Endoscopic Score-CD; CDEIS = CD Endoscopic Index of Severity.

FDA. December 2009. Accessed July 23, 2025. www.fda.gov/media/77832/download. Dulai PS, et al. *Aliment Pharmacol Ther*. 2020;51(11):1047-1066. Higgins PDR, et al. *J Patient Rep Outcomes*. 2017;2(2):24. Ghosh S, et al. *J Crohns Colitis*. 2021;15(2):228-237. Dubinsky MC, et al. *Qual Life Res*. 2023;32(12):3403-3415.

Recent Innovations: Urgency Score for Adults with IBD

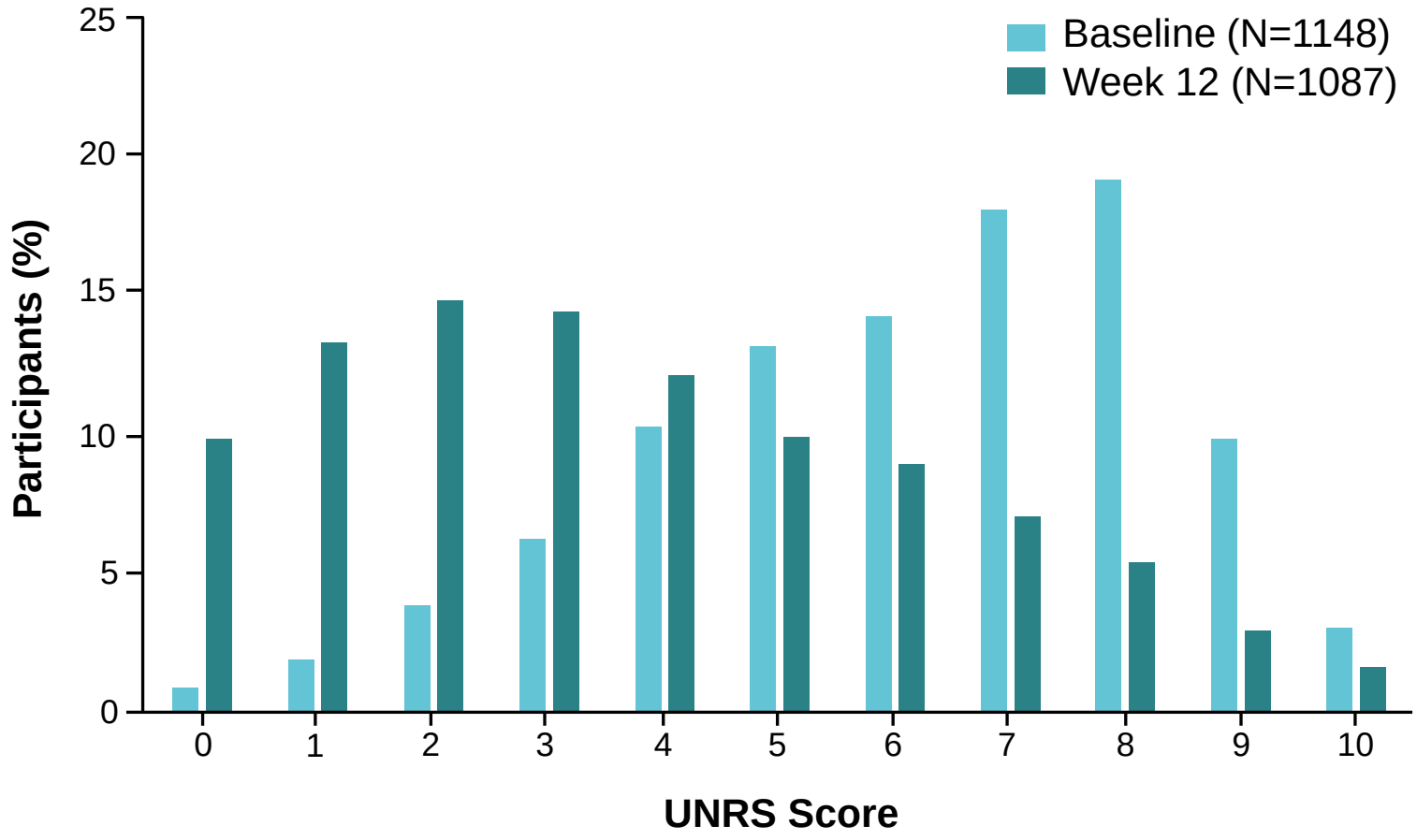


- Bowel urgency is a distinct symptom of CD
- Urgency score is highly correlated with patient global rating of severity scores

Dubinsky MC, et al. *Qual Life Res*. 2023;32(12):3403-3415.

Psychometric Evaluation of Urgency Numeric Rating Scale: UNRS Score Distributions

- Participants registered full range of weekly average UNRS scores (0-10) at baseline and at week 12
- Mean UNRS score was higher (worse) at baseline than at week 12 (6.2 vs 3.7)
- Weekly averages were appropriate to summarize daily UNRS scores



Dubinsky MC, et al. *J Patient Rep Outcomes*. 2022;6(1):114.

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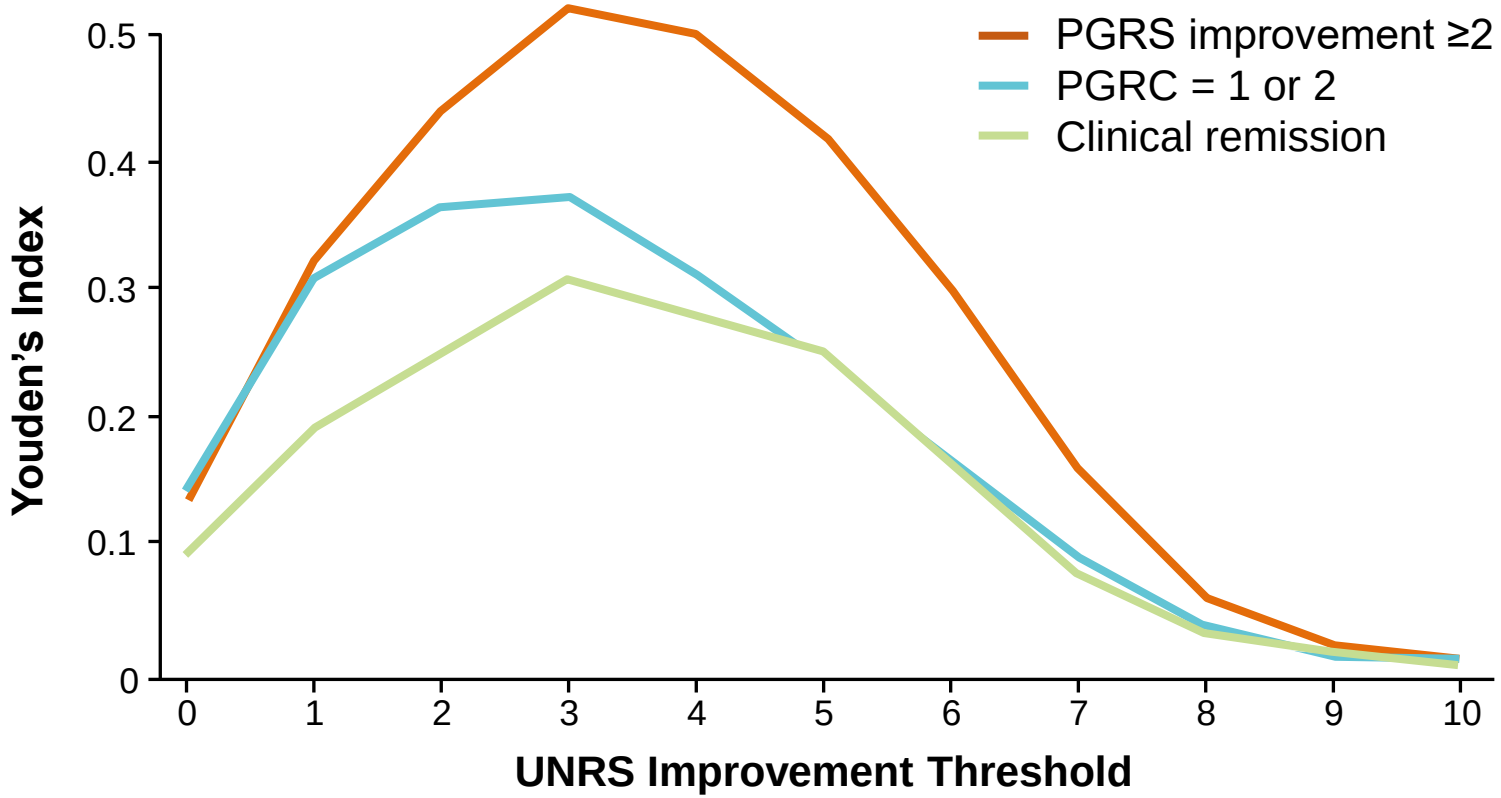
Psychometric Evaluation of UNRS: Patient Improvement from Baseline



≥3-point improvement on UNRS yields best balance between sensitivity and specificity of any UNRS threshold at identifying large improvement in overall symptom severity

Youden's Index from an anchor-based analysis of improvement in UNRS from baseline to week 12.
Clinical remission was defined as Mayo stool frequency subscore of 0, or 1 with a ≥1-point decrease from baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopic subscore of 0 or 1 (excluding friability).
≥3-point improvement on UNRS yields best balance between sensitivity and specificity of any UNRS threshold at identifying large improvement in overall symptom severity.
PGRS = Patient Global Rating of Severity; PGRC = Patient Global Rating of Change.
Dubinsky MC, et al. *J Patient Rep Outcomes*. 2022;6(1):114.

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Why Bowel Urgency Matters: Summary

Bowel urgency is one of the most important symptoms for patients and has a significant impact on patient quality of life and psychosocial function.

HCPs are not always routinely assessing bowel urgency in clinical practice, and there is a communication gap between HCPs and their patients.

Bowel urgency is being increasingly recognized in guideline recommendations and consensus statements as a key component of CD.

The UNRS moves beyond yes/no data and assesses severity over time; it has utility in both clinical trials and clinical practice.

Dubinsky MC, et al. *Qual Life Res*. 2023;32(12):3403-3415. Petryszyn PW, Paradowski L. *Adv Clin Exp Med*. 2018;27(6):813-818. Rubin DT, et al. *Inflamm Bowel Dis*. 2021;27(12):1942-1953. Ueno F, et al. *J Gastroenterol*. 2017;52(5):555-567. Ananthakrishnan AN, et al. *Gastroenterology*. 2021;160(1):445-451. Bernstein CN, et al. *J Clin Gastroenterol*. 2016;50(10):803-818. Kemp K, et al. *J Crohns Colitis*. 2018;12(7):760-776. Lamb CA, et al. *Gut*. 2019;68(Suppl 3):s1-s106. Surti B, et al. *Dig Dis Sci*. 2013;58(5):1313-1321.

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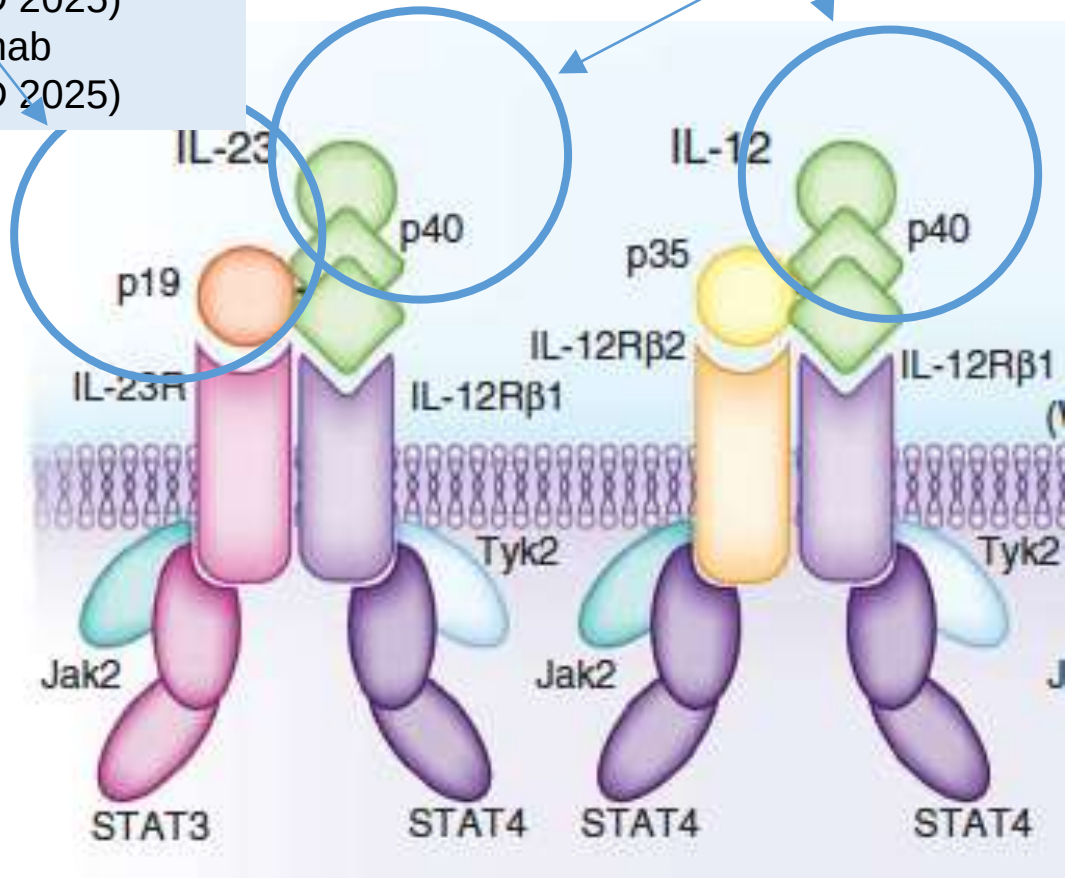
Focus on IL-23 Agents

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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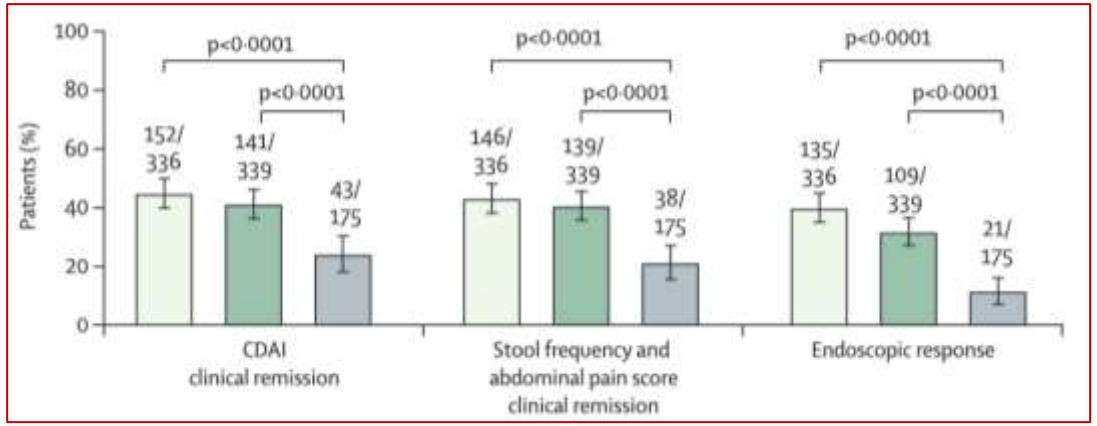
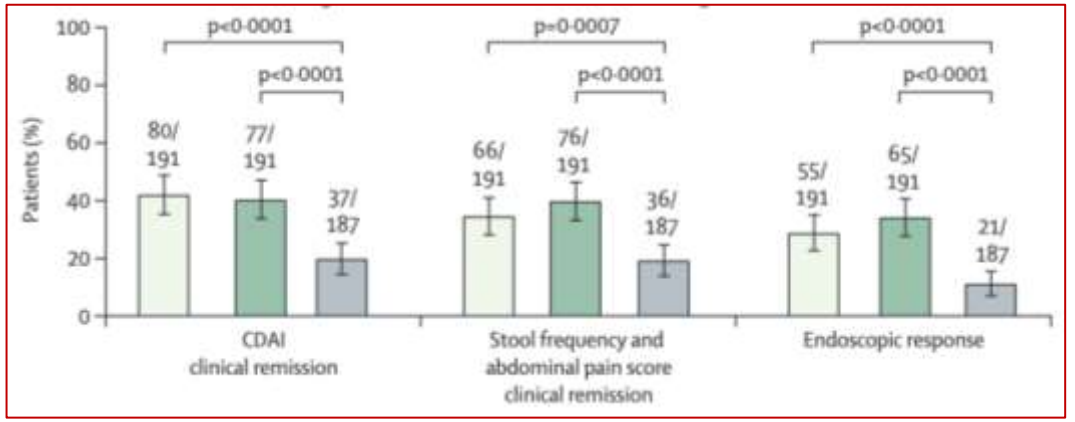
ADVANCE and MOTIVATE: Risankizumab Induction in CD

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

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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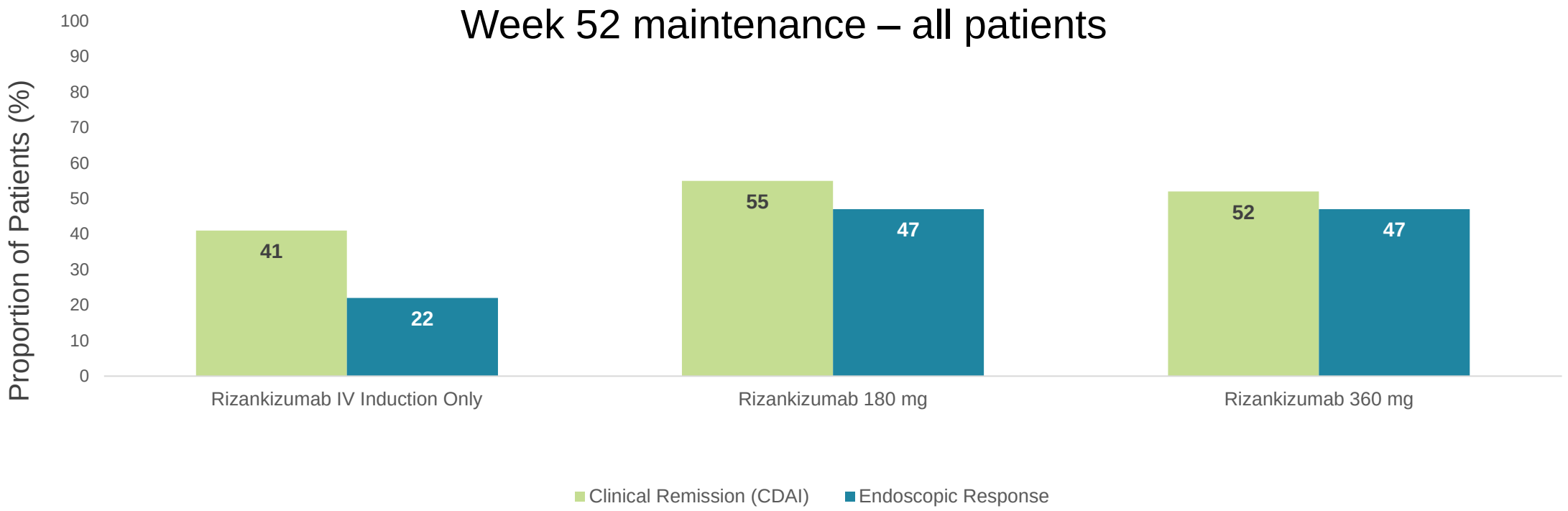
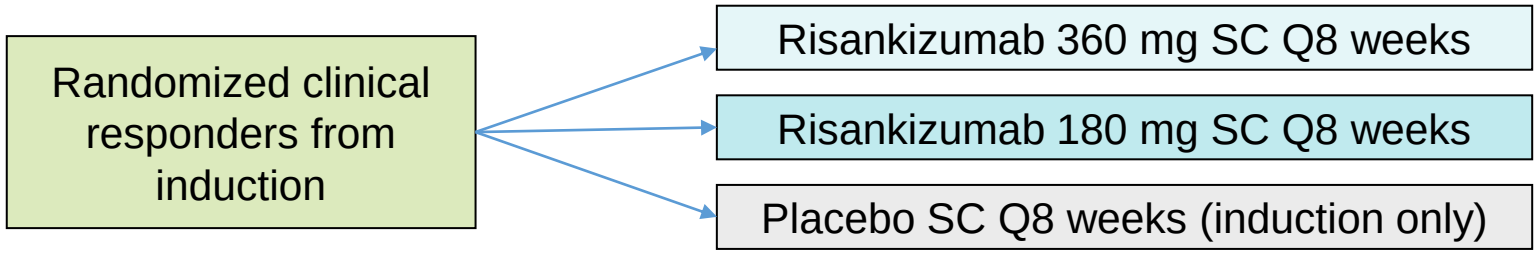
FORTIFY: Risankizumab Maintenance in CD





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

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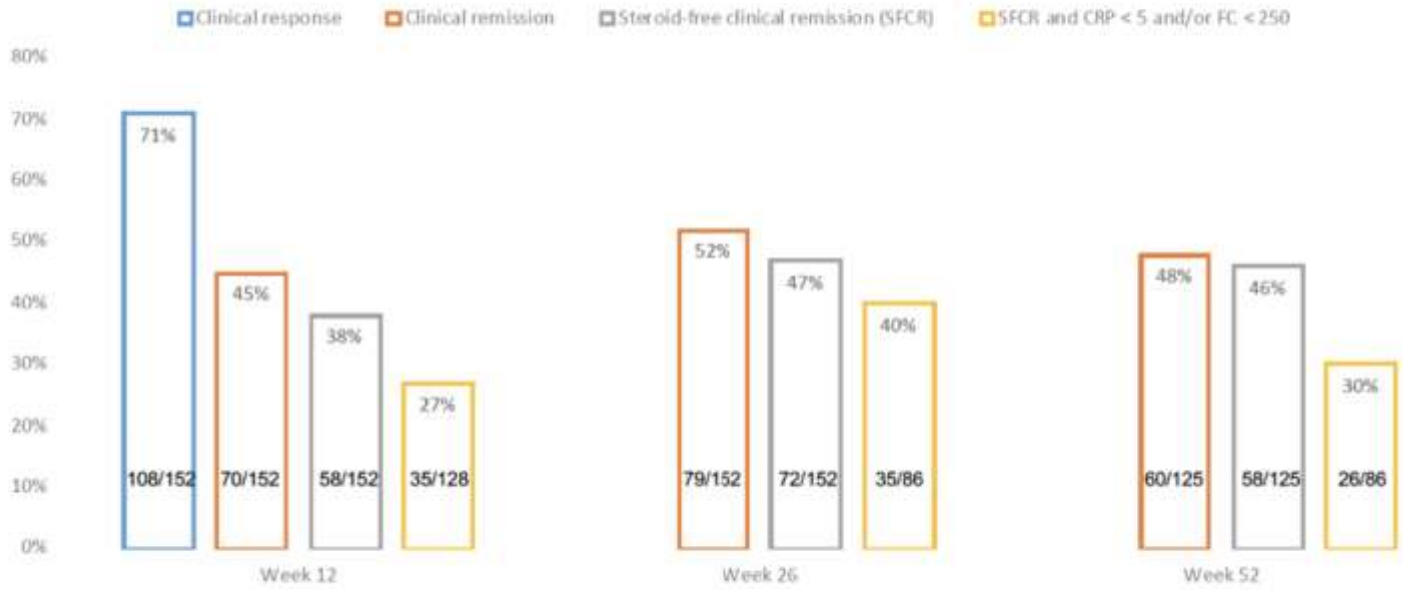
Risankizumab: Real-World Experience (GETAID)

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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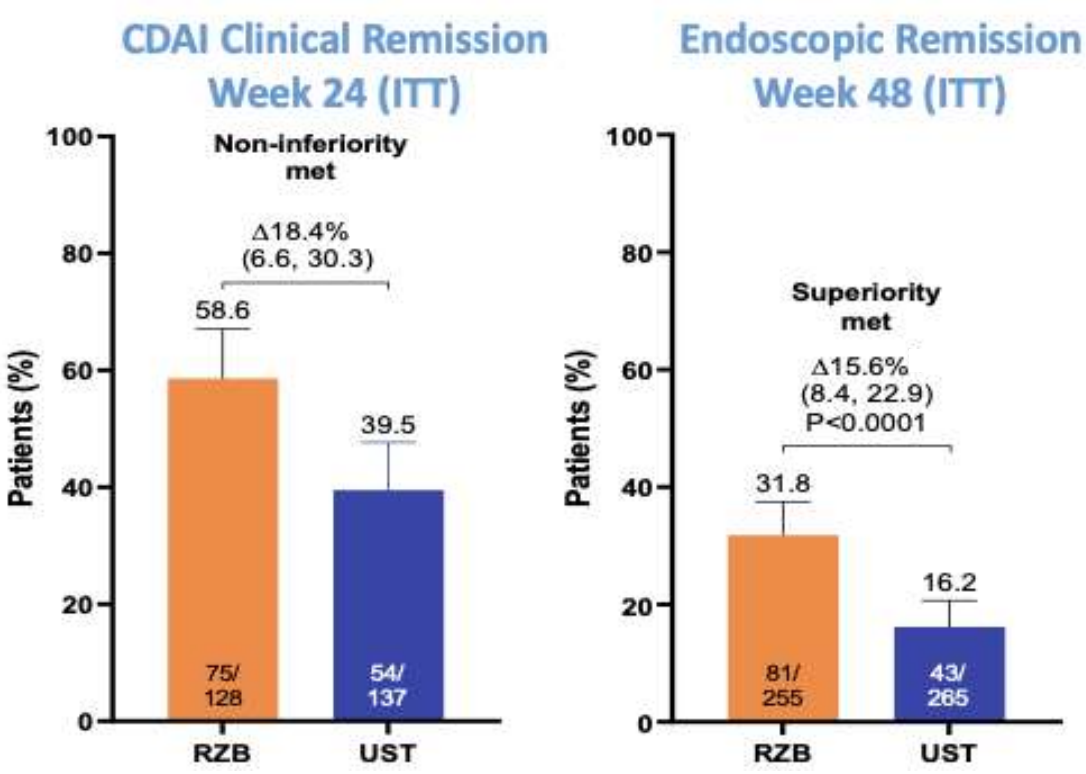
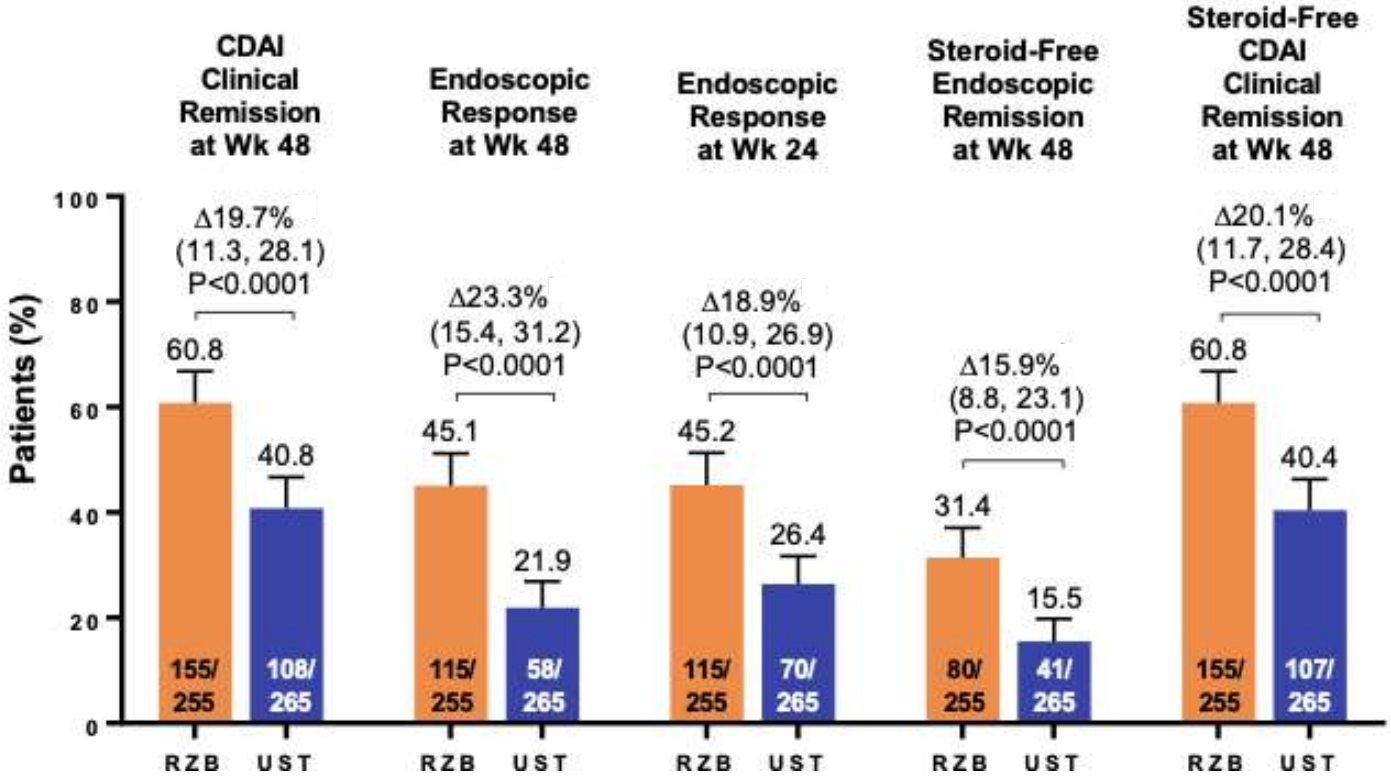
SEQUENCE: Risa vs Uste in TNF-Exposed CD

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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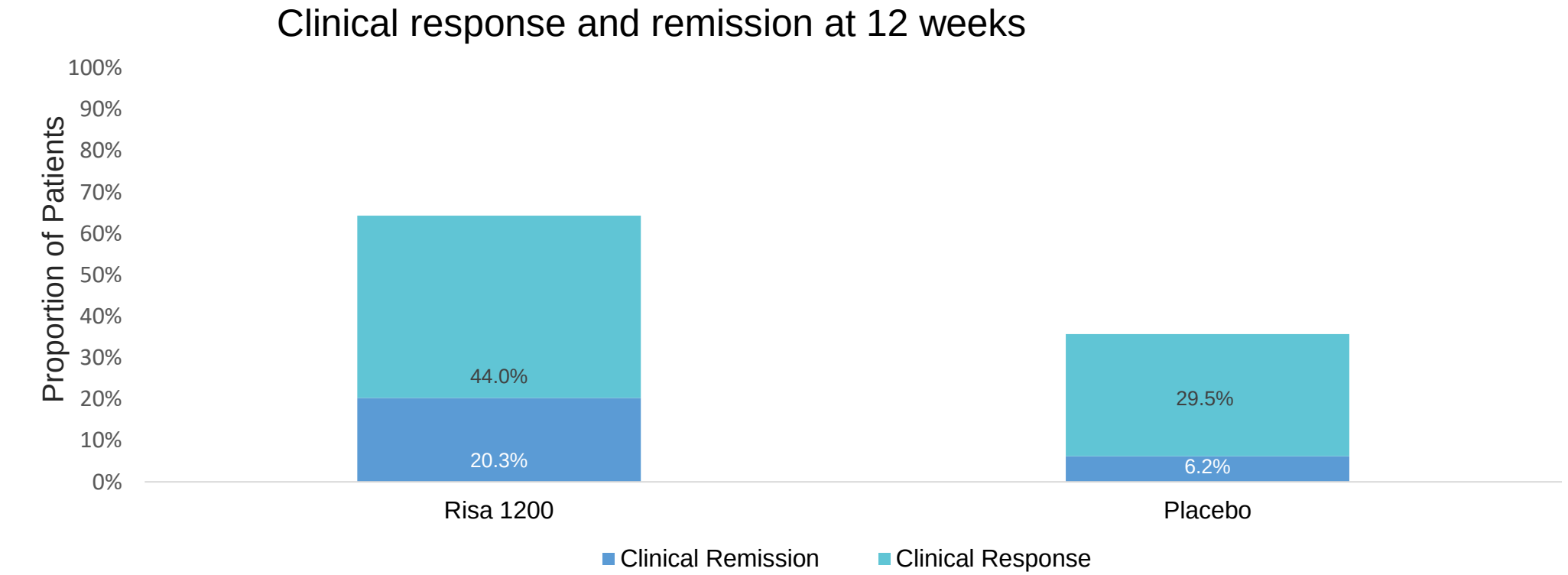
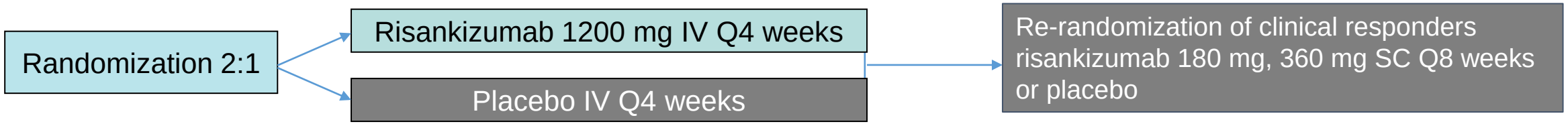
INSPIRE: Risankizumab Induction in UC





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

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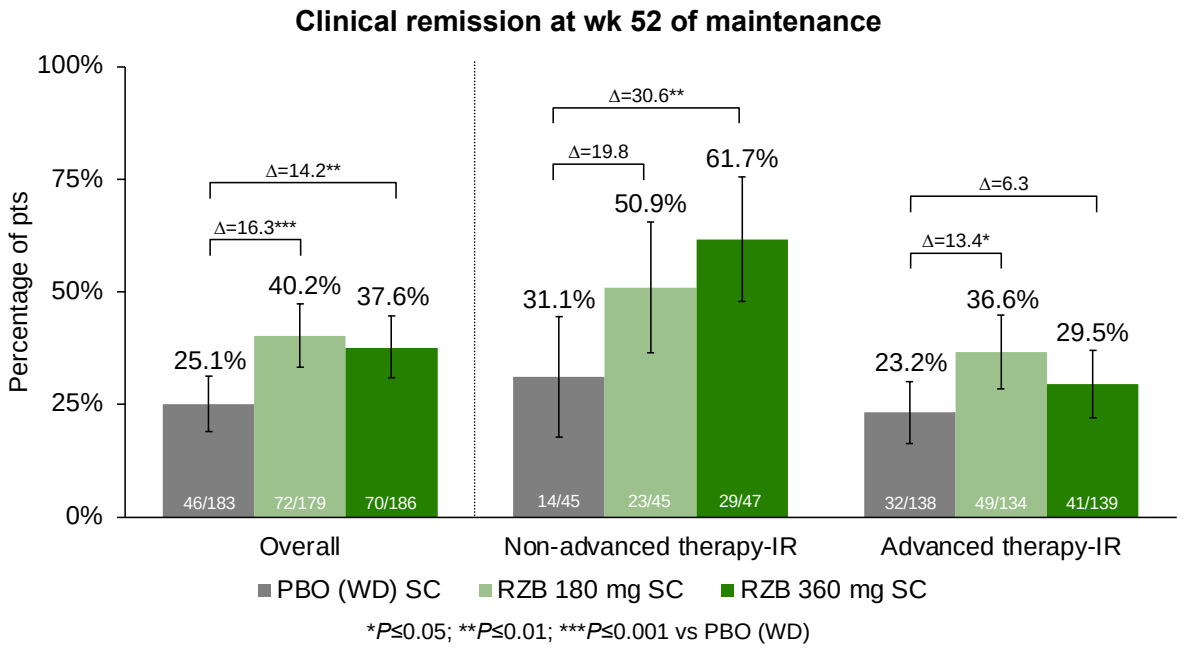
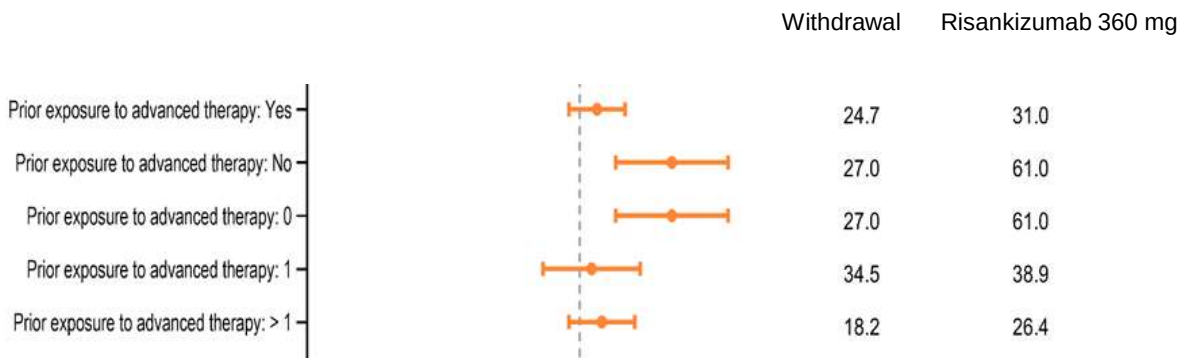
COMMAND: Efficacy and Safety of Risankizumab Maintenance Therapy in Moderate-to-Severe UC

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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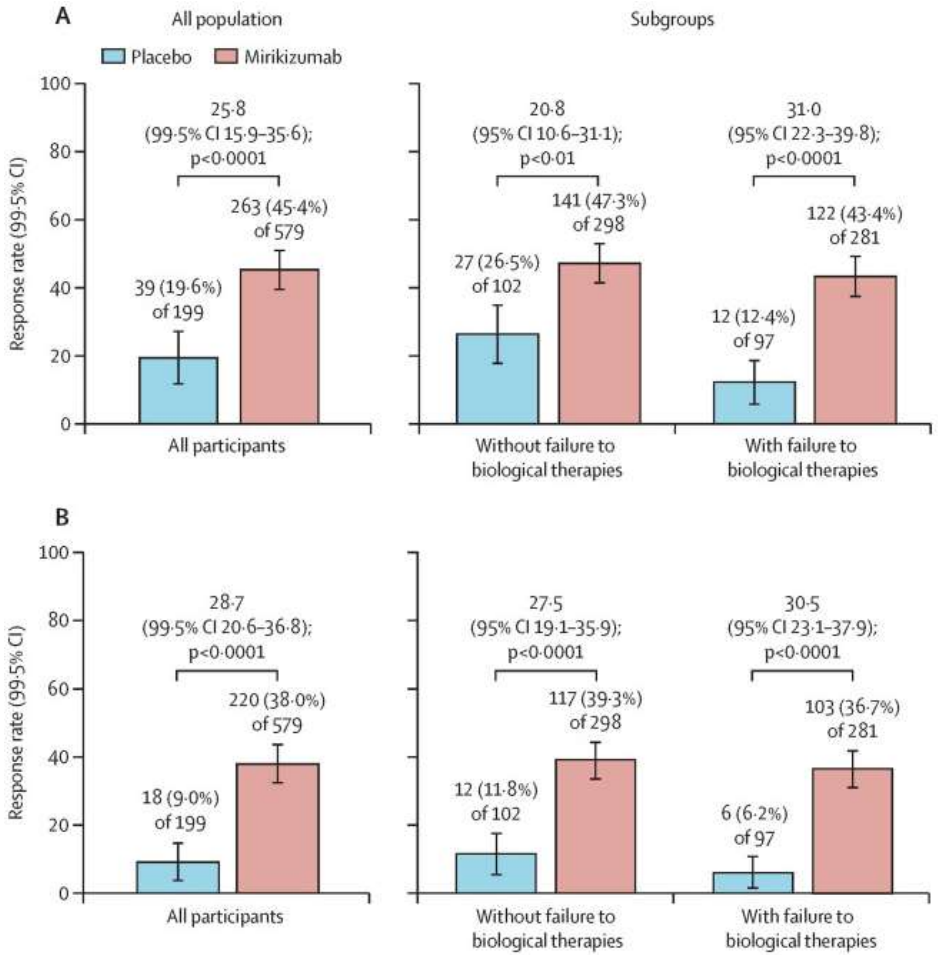
VIVID-1 – Mirikizumab in CD: Treat-Through Design

- 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



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

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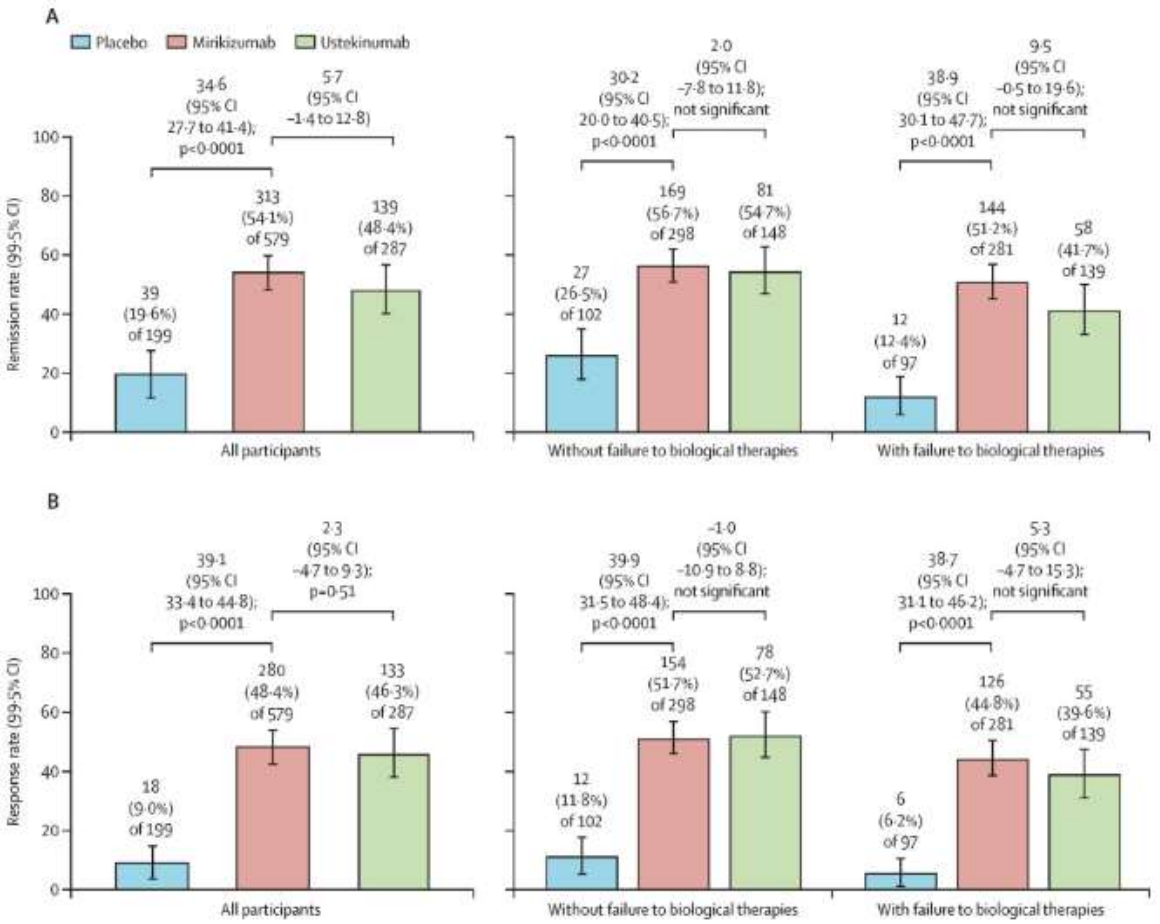
VIVID-1 – Mirikizumab in CD: Treat-Through Design

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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VIVID-2 – Mirikizumab in CD: Long-Term Efficacy (OLE)

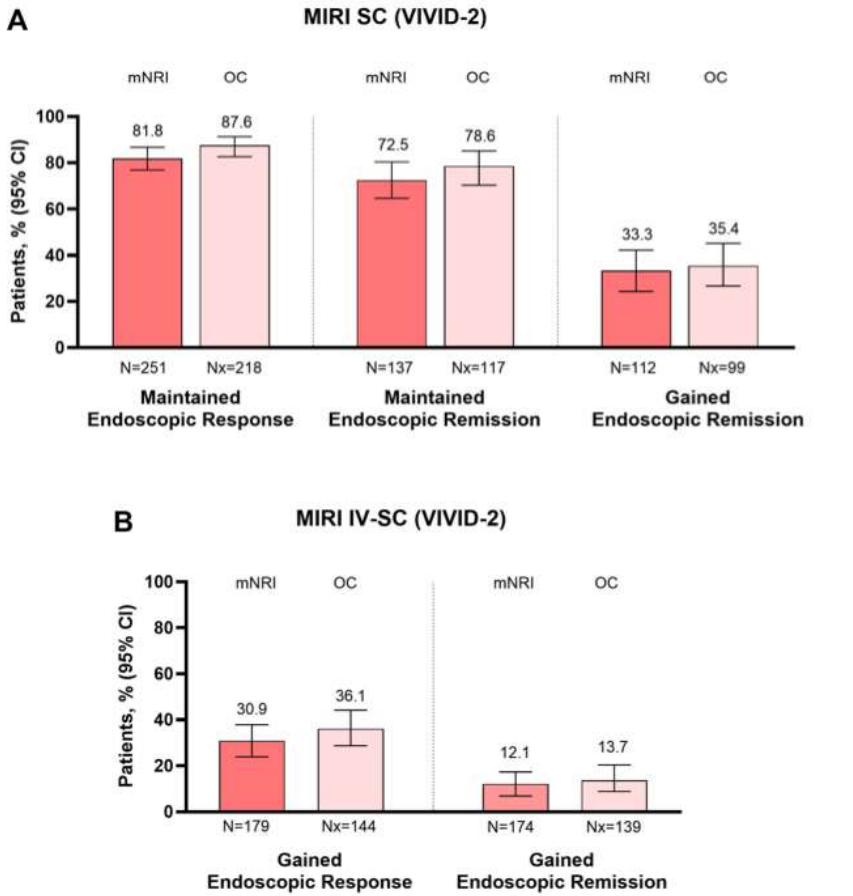


Figure 1. Endoscopic response and remission rates at W104 of continuous MIRI treatment in (A) endoscopic responders at W52 who continued MIRI SC in VIVID-2, and (B) endoscopic nonresponders at W52 who received reinduction with MIRI IV followed by SC maintenance in VIVID-2.

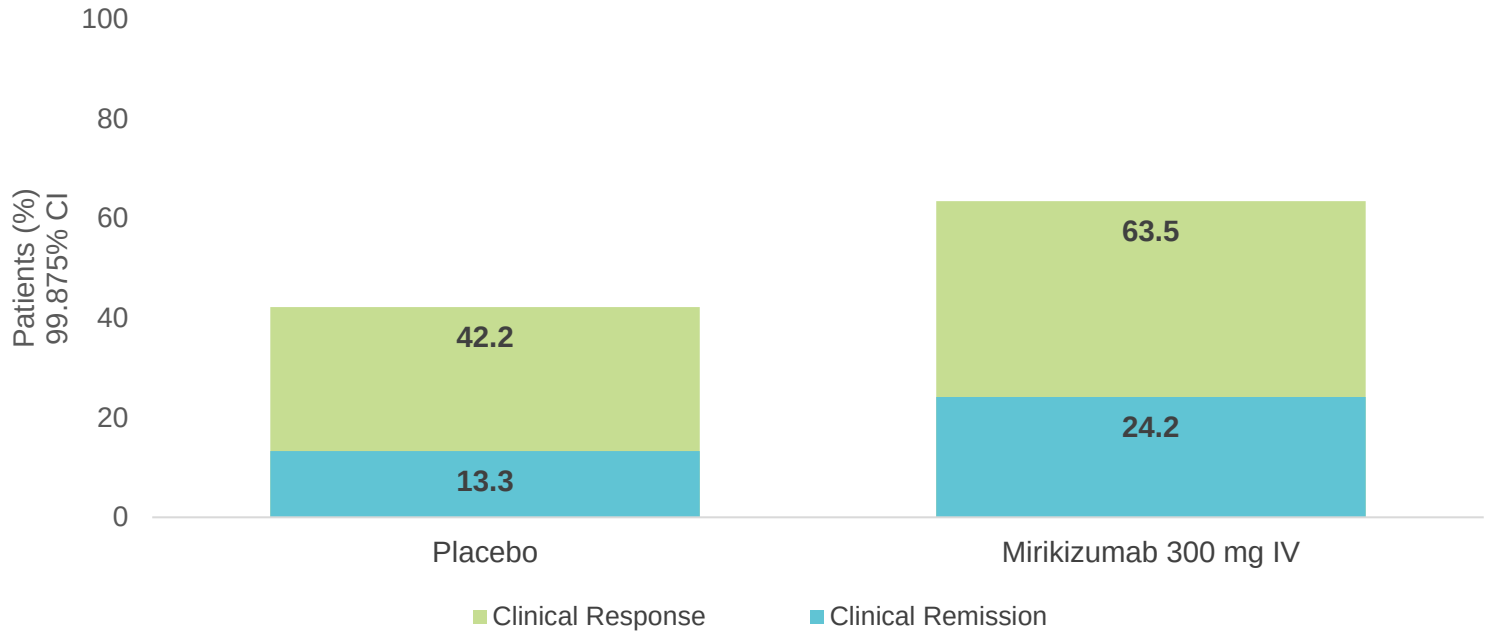
The majority of study participants who achieved endoscopic response and remission at 1 year sustained their response, with additional patients achieving remission during the 2nd year of treatment

OLE = open-label extension; mNRI = modified non-responder imputation; OC = observed case.

Vermeire S, et al. *J Crohns Colitis*. 2025;19(Suppl 1):i91-i93.

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

CI = confidence interval.

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

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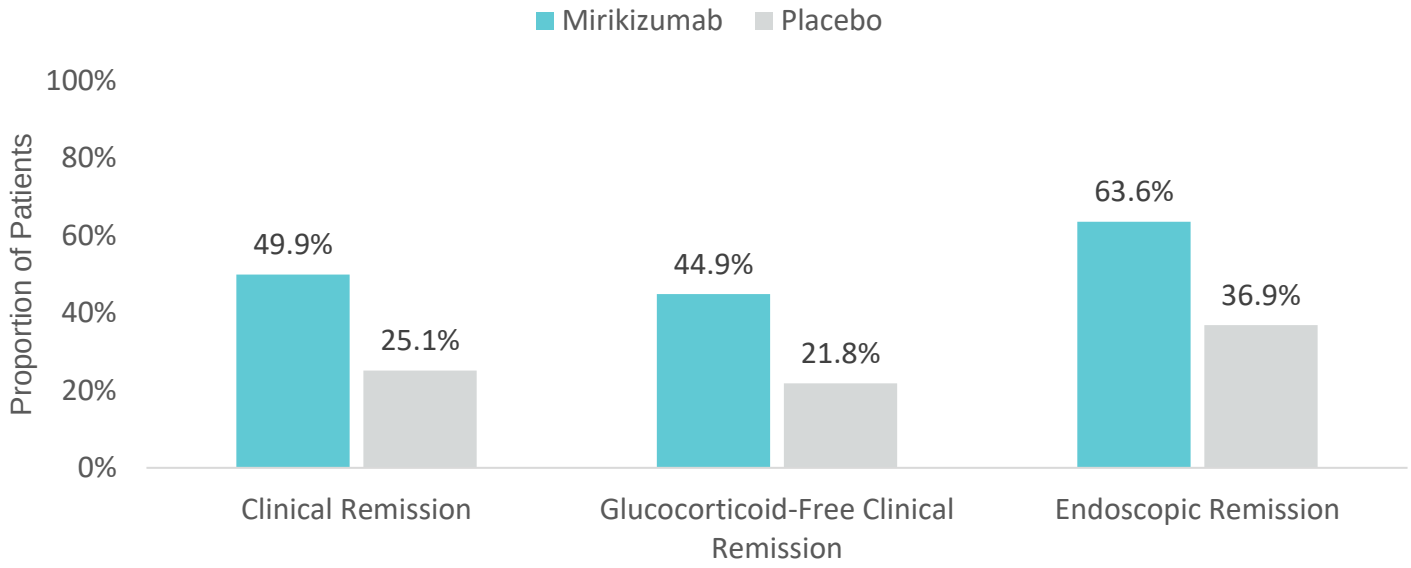
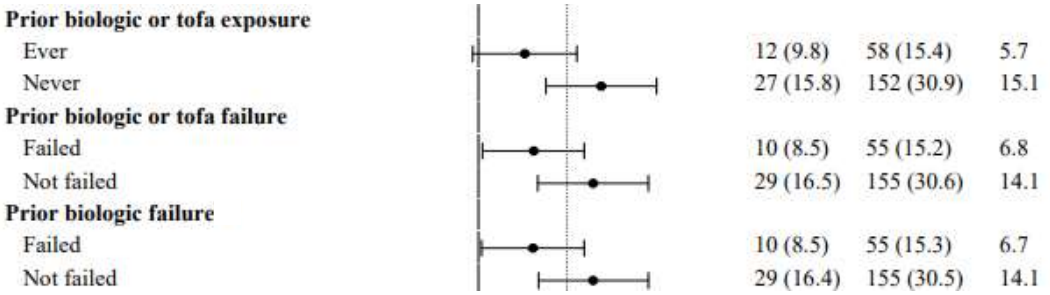
LUCENT-2: Mirikizumab Maintenance in UC

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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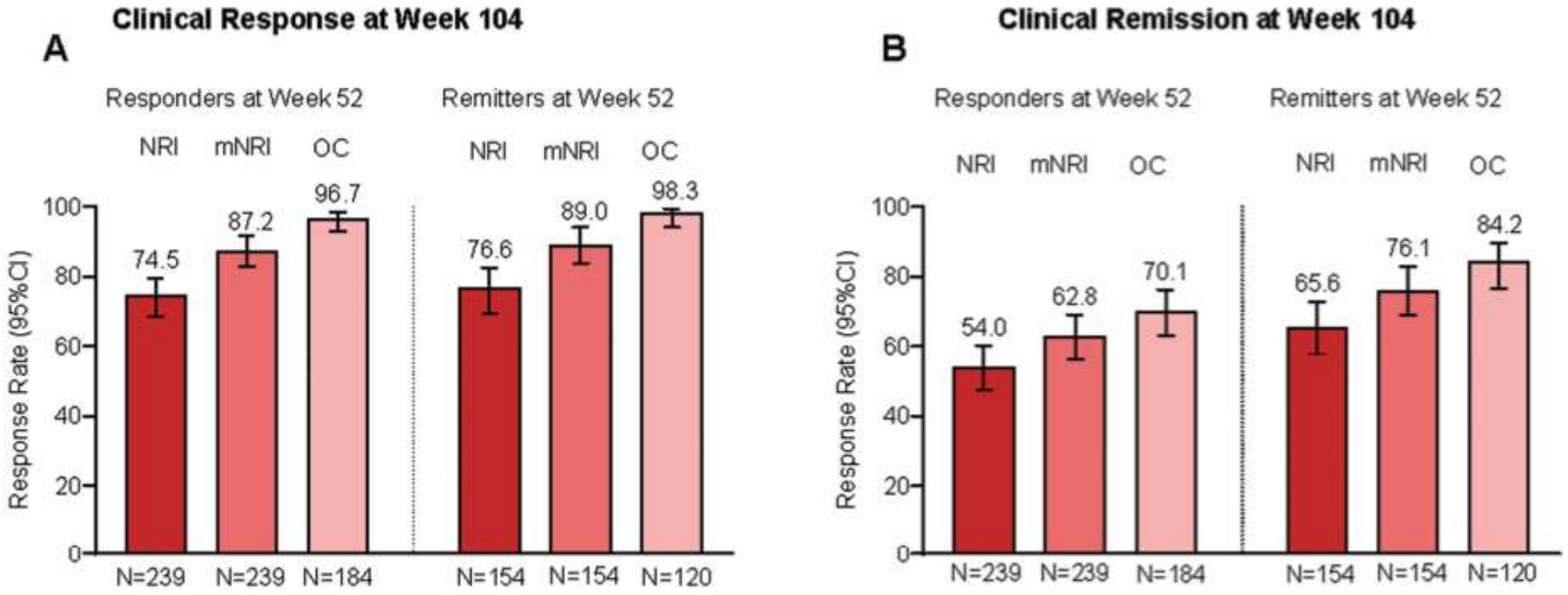
LUCENT-3: Mirikizumab 2-Year Efficacy in UC



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

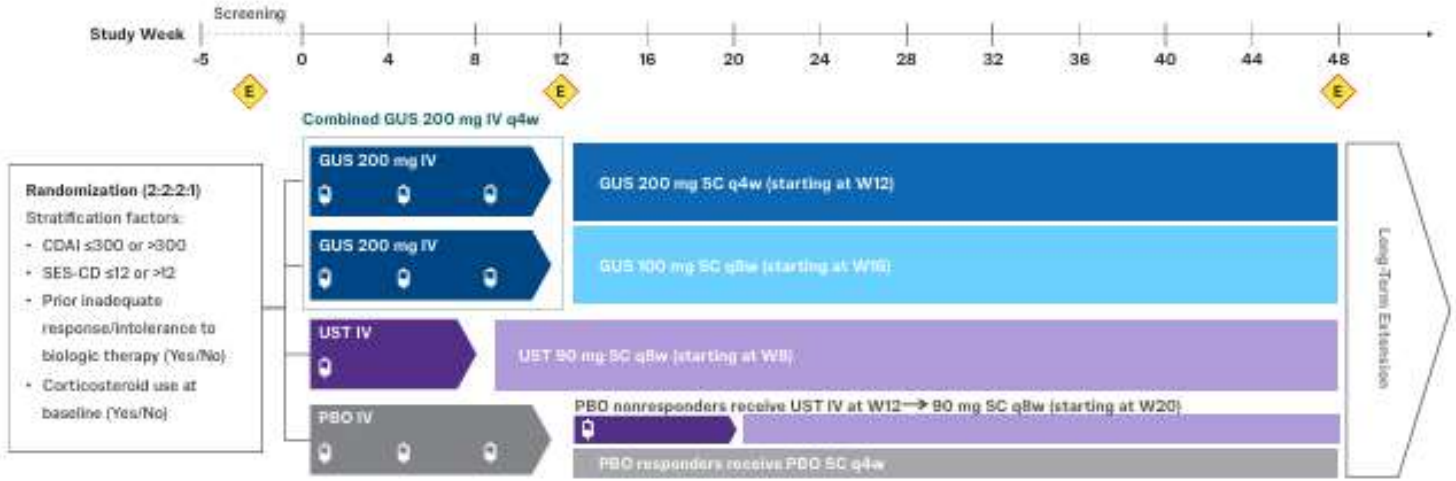
Double-Blind, Treat-Through Design: GALAXI 2 & 3

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



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

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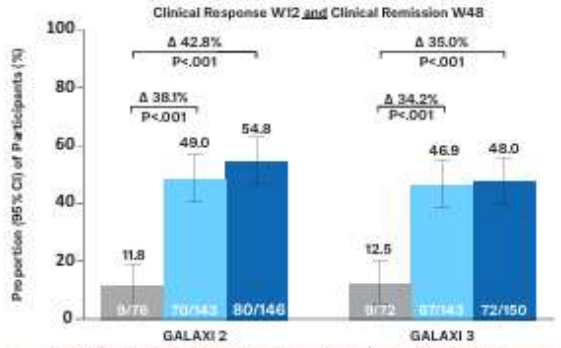
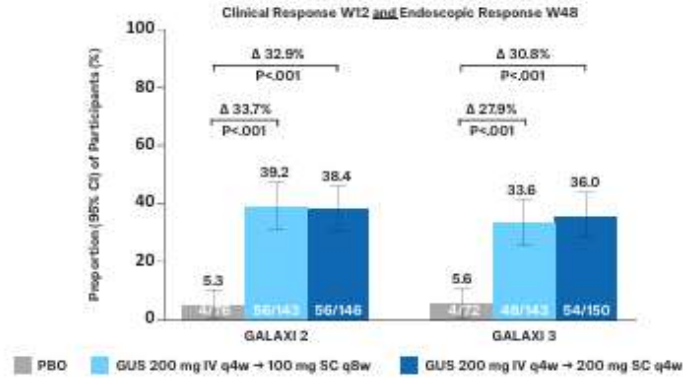
GALAXI 2/3 – Guselkumab for CD: Treat-Through Design

Composite Co-primary Endpoints

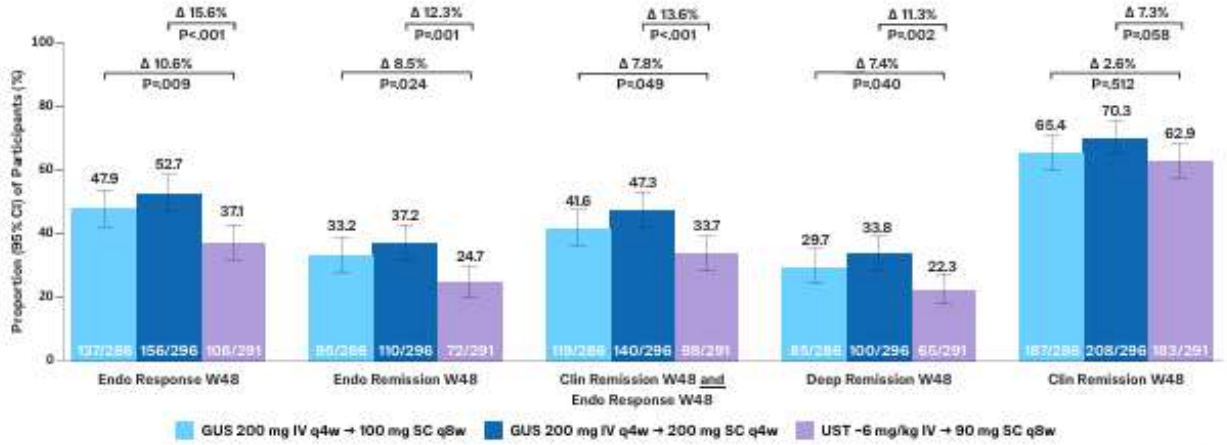


93–97% of GUS participants who achieved the endpoint were corticosteroid-free for ≥90 days before W48



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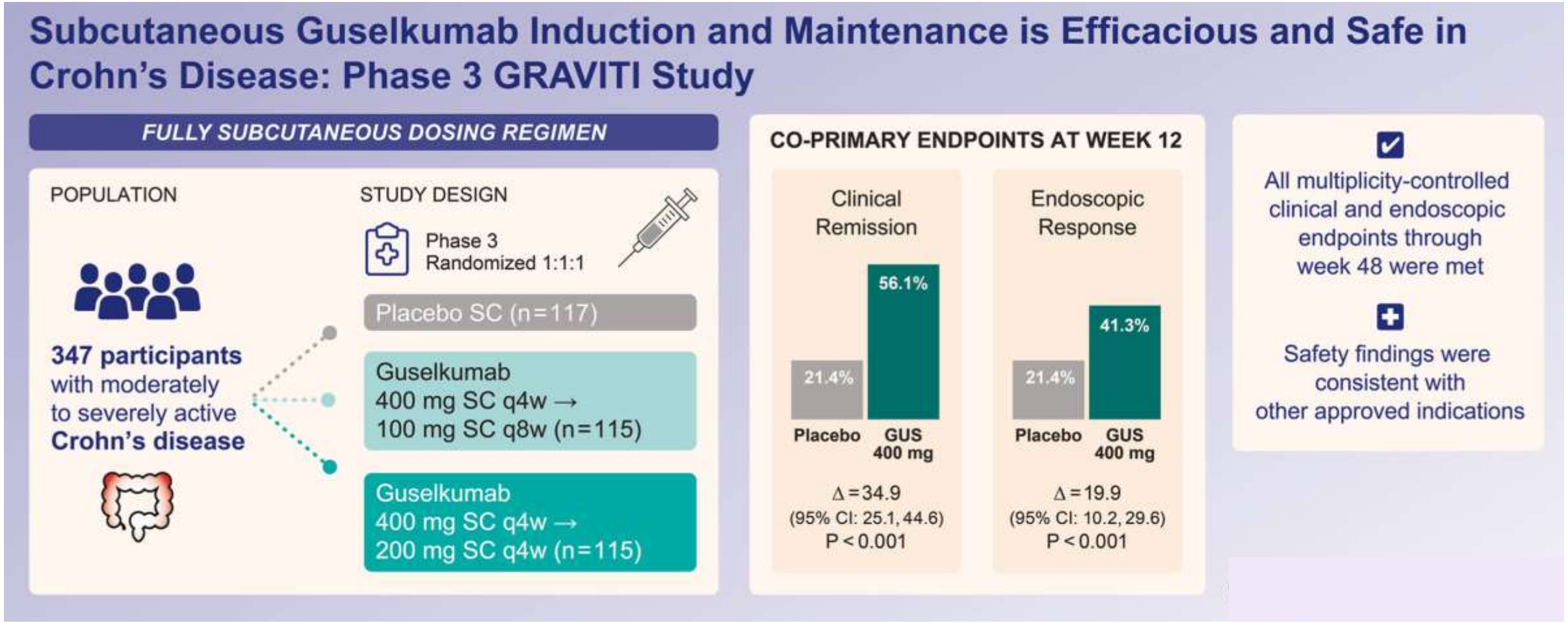
GRAVITI: Phase 3 Study of SC Induction and Maintenance in CD



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

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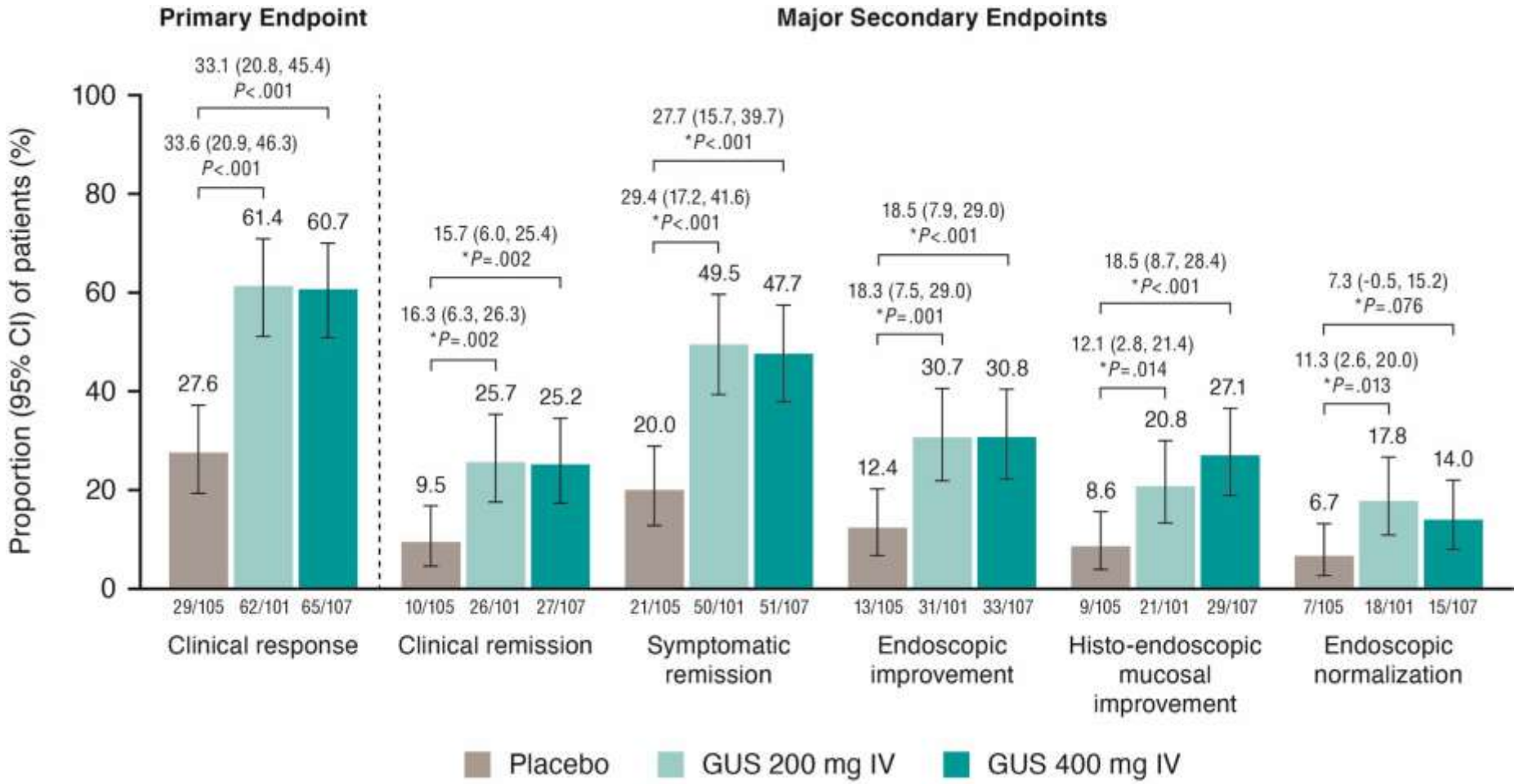
QUASAR: Guselkumab Induction in UC



*Denotes nominal *P*-values.

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

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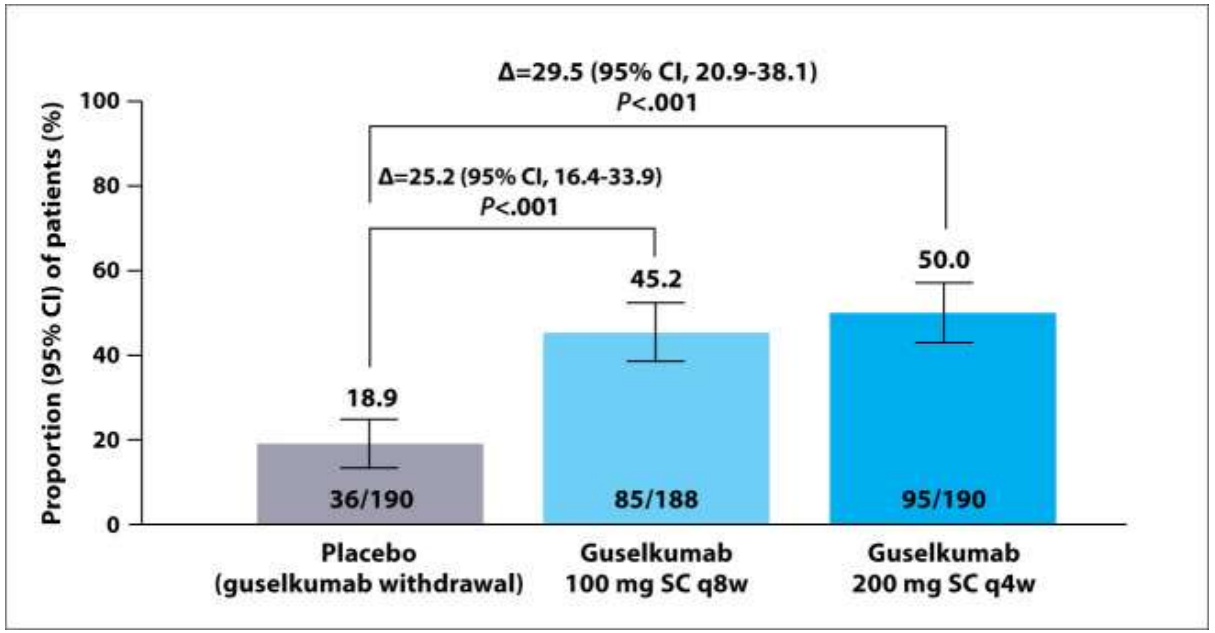
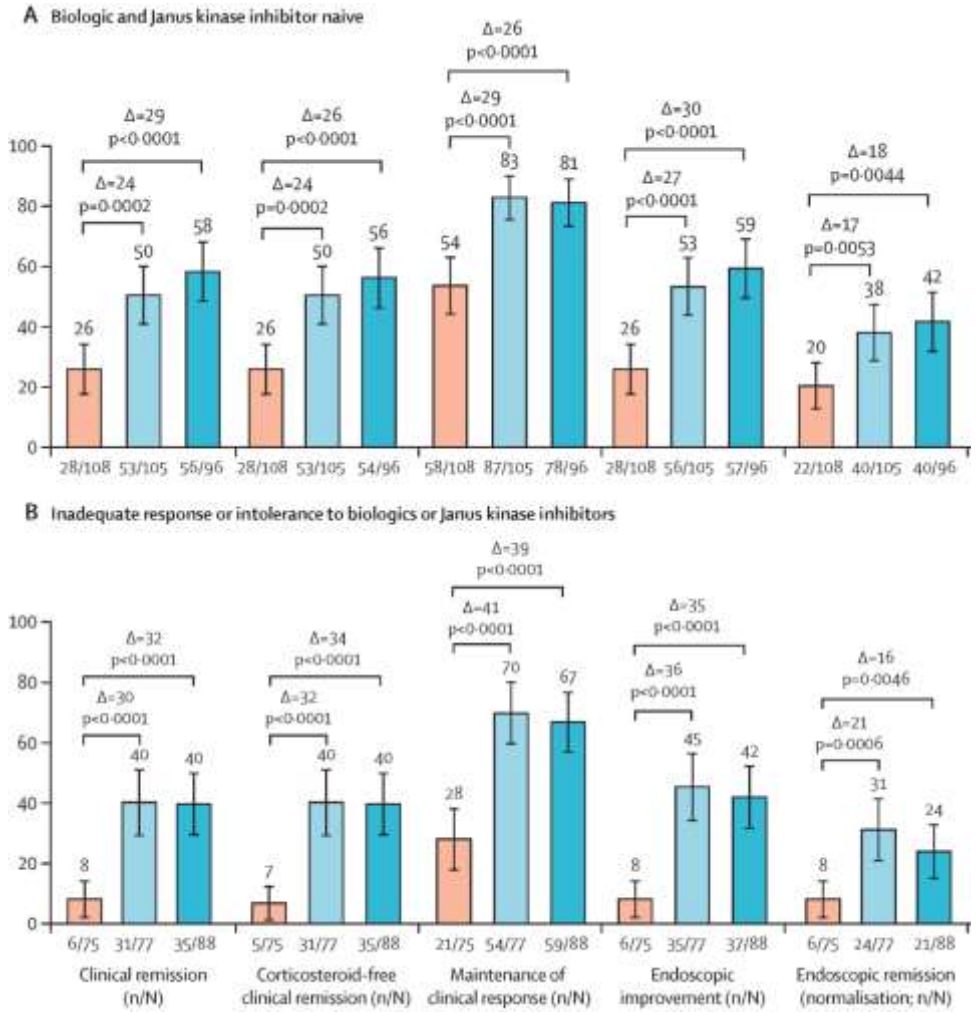
QUASAR: UC Maintenance Outcomes at Week 44



By prior advanced therapy exposure



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

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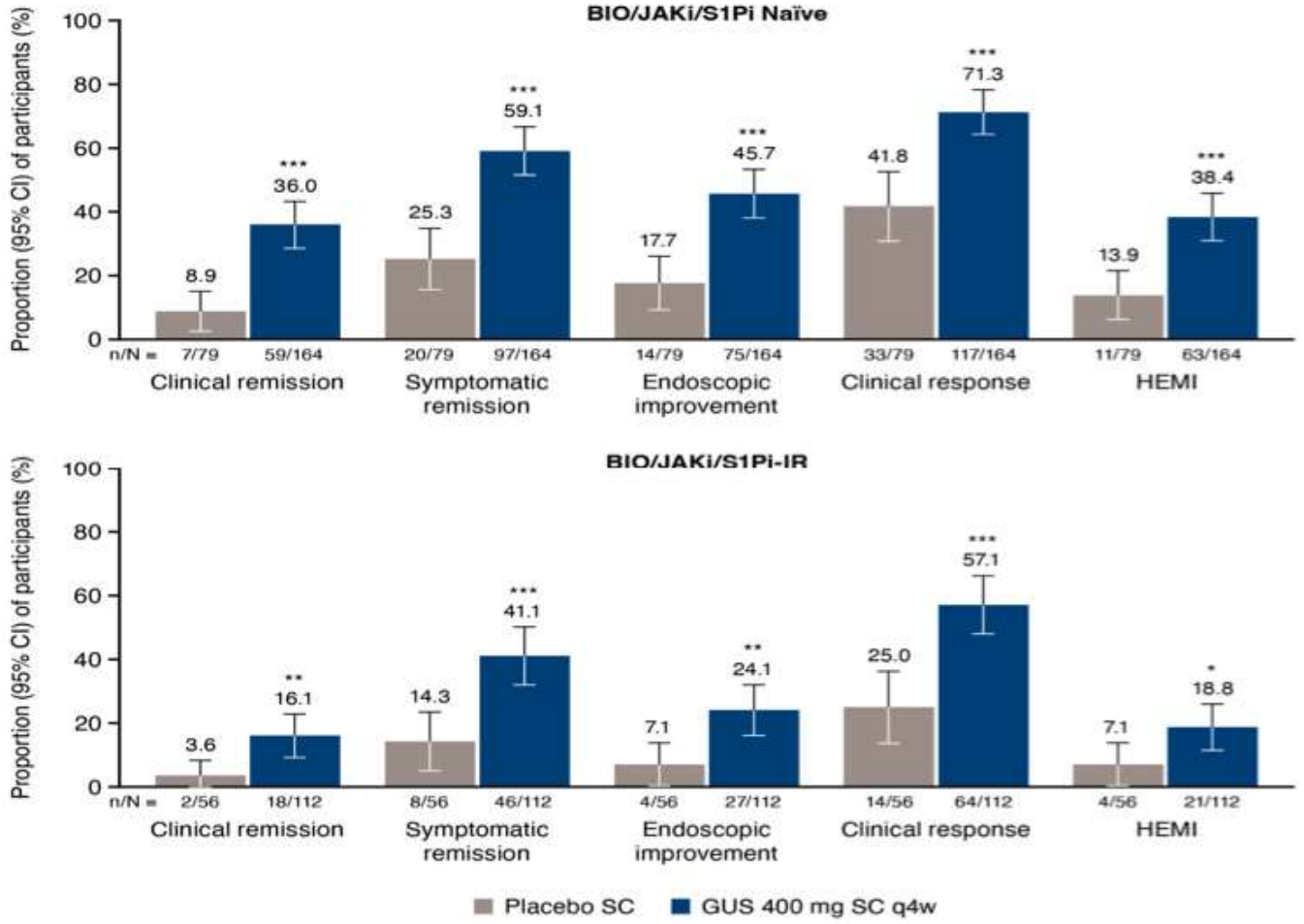
ASTRO: Phase 3 Study of SC Guselkumab Induction in UC

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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Obesity in IBD

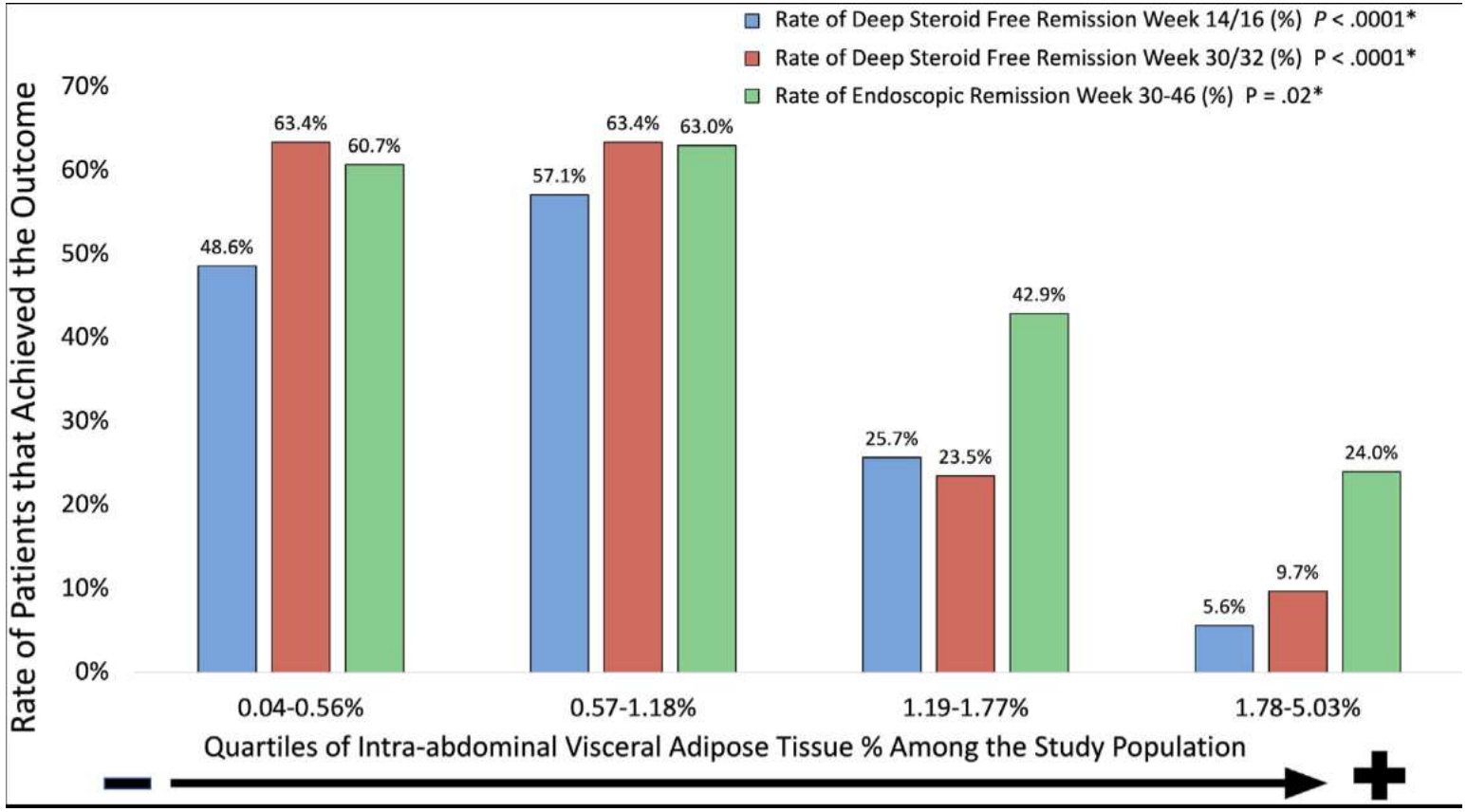
Obesity in IBD

- 15-40% of patients with IBD are obese
- Obesity may affect IBD-related therapy
  - Data from other autoimmune diseases suggest that obesity results in suboptimal response to therapy
  - May promote rapid clearance of biologic agents, leading to low trough concentrations
  - May be a rationale for using weight loss interventions as adjunctive therapy in patients with IBD who are obese
  - Obesity is recognized as a perpetual state of chronic low-grade inflammation
- Obesity makes colorectal surgery technically challenging and might increase the risk of perioperative complications

Singh S, et al. *Nat Rev Gastroenterol Hepatol*. 2017;14(2):110-121.

Role of Adipose Tissue

- Mesenteric VAT has a predominance of pro-inflammatory M1 macrophages that secrete several inflammatory cytokines, including TNF and IL-1
- Higher intra-abdominal visceral adipose tissue mass is associated with lower rates of clinical and endoscopic remission in patients with IBD initiating biologic therapy



VAT = visceral adipose tissue.

Singh S, et al. *Nat Rev Gastroenterol Hepatol*. 2017;14(2):110-121. Yarur AJ, et al. *Gastroenterology*. 2023;165(4):963-975.e5.

Pharmacological, Nutritional, and Lifestyle Considerations for People with IBD and Obesity

- No interventional studies of interventional weight loss in IBD
- Trials of diet and/or lifestyle-induced weight loss in other autoimmune diseases suggest improvement in outcomes with weight loss
- In a meta-analysis of patients with psoriasis who were obese or overweight, those on weight loss intervention were more likely to achieve 75% reduction in Psoriasis Area and Severity Index score (OR 2.92, 95% CI 1.39-6.13)
- In psoriatic arthritis, ≥5% from baseline values is associated with a higher rate of remission in overweight/obese patients who start anti-TNF
- Studies are ongoing assessing the role of pharmacologic intervention for obesity in IBD

OR = odds ratio.

Singh S, et al. *Nat Rev Gastroenterol Hepatol*. 2017;14(2):110-121. Upala S, et al. *Int J Obes* (Lond). 2015;39(8):1197-1202. Di Minno MND, et al. *Ann Rheum Dis*. 2014;73(6):1157-1162.

GLP-1 Receptor Agonists and IBD: Potential Mechanisms?

- In animal models, GLP-1 therapy improves DSS-induced colitis in mice through modulating group 3 innate lymphoid cells (ILC3s), a subset of innate lymphoid cells that regulate intestinal immunity

- GLP-1 receptor agonists affect gut homeostasis in both proximal and distal parts of the gut

GLP-1 = glucagon-like peptide-1; DSS = dextran sodium sulfate.

Sun H, et al. *Immunology*. 2024;172(3):451-468. Bang-Berthelsen CH, et al. *Inflamm Bowel Dis*. 2016;22(9):2078-2097.

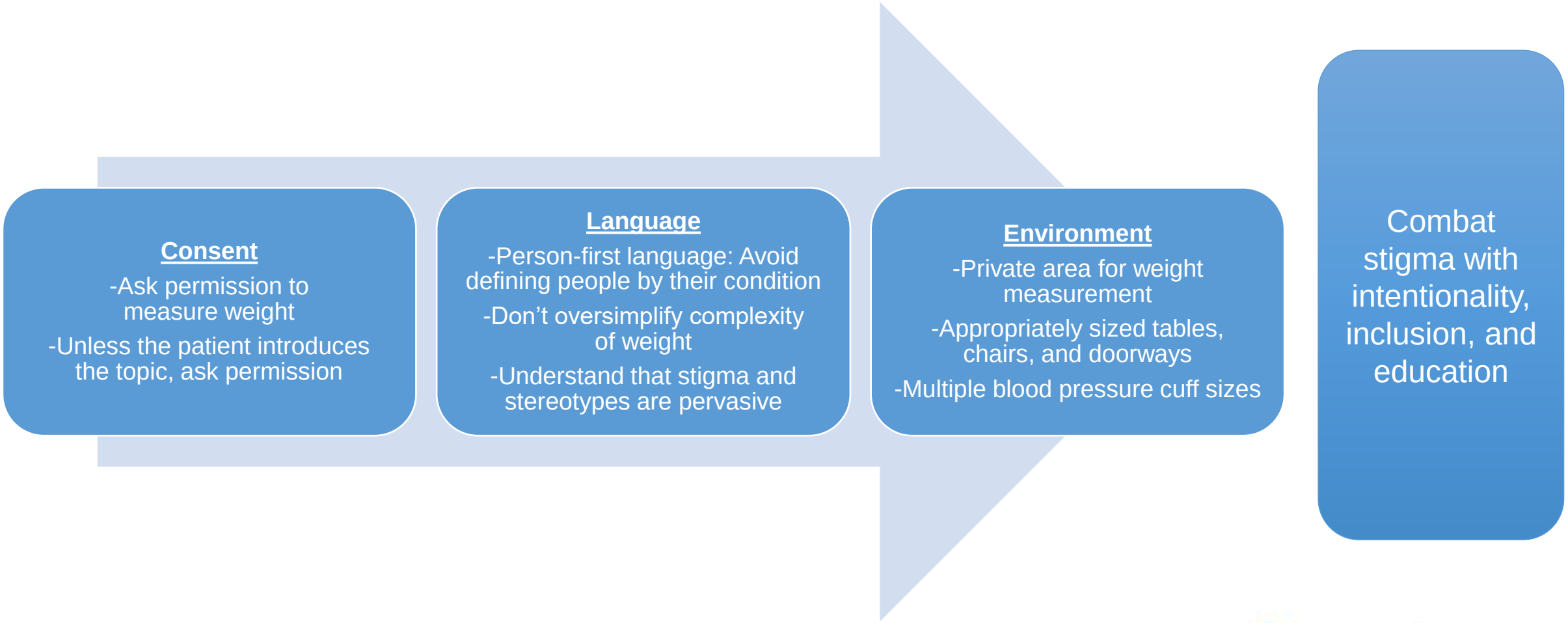
GLP-1 Receptor Agonists and IBD: Safety and Efficacy

- In a cohort of 224 patients with IBD on GLP-1: No increased risk of disease exacerbation, hospitalization, steroids, surgery, med escalation
  - Significant decrease in BMI in the year following GLP-1 receptor agonist initiation (median BMI 33.5 vs 31.6 kg/m^2, *P*<.01)
- Separate cohort of 120 patients: ~11% had GI side effects, significant weight reduction, no differences in hospitalizations or endoscopic scores, and CRP reduced (*P*=.005)
- In a double-blind crossover study of patients with J-pouch and high BM frequency, GLP-1 reduced daily BF by more than 35% (*P*<.03)
- Interventional data with objective inflammatory outcomes are needed

BMI = body mass index; BM = bowel movement; BF = bowel frequency.

Levine I, et al. *Inflamm Bowel Dis*. 2025;31(2):467-475. Anderson SR, et al. *Am J Gastroenterol*. 2025;120(5):1152-1155. Herfarth H, et al. *Am J Gastroenterol*. 2024;119(9):1935-1938.

Enhancing Engagement by Minimizing Stigma



Albury C, et al. *Lancet Diabetes Endocrinol*. 2020;8(5):447-455.

Case

Case

- *35-year-old woman presents to your clinic with a 6-month history of increasing abdominal pain, diarrhea (up to 8 episodes per day), and weight loss of 8 kg*
- *She describes severe urgency affecting her QoL*
- *She has a known diagnosis of moderate-to-severe UC pancolitis, which has been managed with infliximab monotherapy; symptoms indicate loss of response to current therapy*

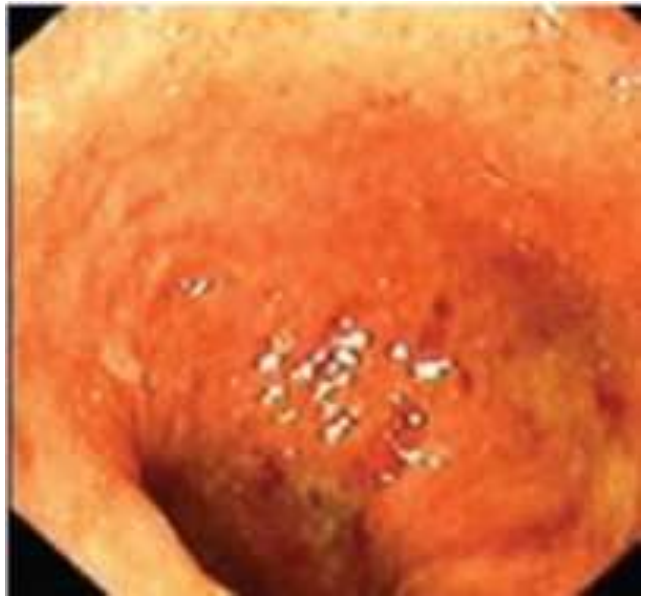
What do you suggest as next steps?

What Further Investigation Is Needed?

- Infectious workup
- Biologic marker workup (calprotectin)
- Colonoscopy or intestinal ultrasound as objective assessment of inflammatory activity
- TNF drug and antibody levels

Further Data

- Infliximab drug level 17 ug/mL, no antibodies
- *C diff* negative
- CRP 35 mg/L
- Calprotectin 456 ug/g
- Colonoscopy: Mayo 2



What therapy do you suggest?

Rapid Fire – Case Modifications: Which Class Would You Choose?

- Extra-intestinal manifestations
  - Psoriasis
  - Ankylosing spondylitis
- Cardiovascular complications
  - History of MI
  - CHF
  - Smoking
- Disease phenotype
  - Perianal disease
- History of prior malignancy
- Obesity

MI = myocardial infarction; CHF = congestive heart failure.

Key Learning Points

- Symptom assessment and biologic/endoscopic assessment necessary in CD and UC
- Bowel urgency has profound effects on QoL; validated UNRS available for assessment
  - Impacts physical activity, social satisfaction, and sexual health
- IL-23 agents are effective in both CD and UC; data on improved efficacy as compared to IL-12/23 in CD
- Obesity is common in IBD and may play a role in IBD outcomes
  - Weight loss therapies may provide an adjunct to improve IBD outcomes
- Comprehensive, holistic care is indicated in patients with IBD