
JANUARY 30 – FEBRUARY 1, 2026
2026
ACG'S IBD SCHOOL &
ACG BOARD OF GOVERNORS /
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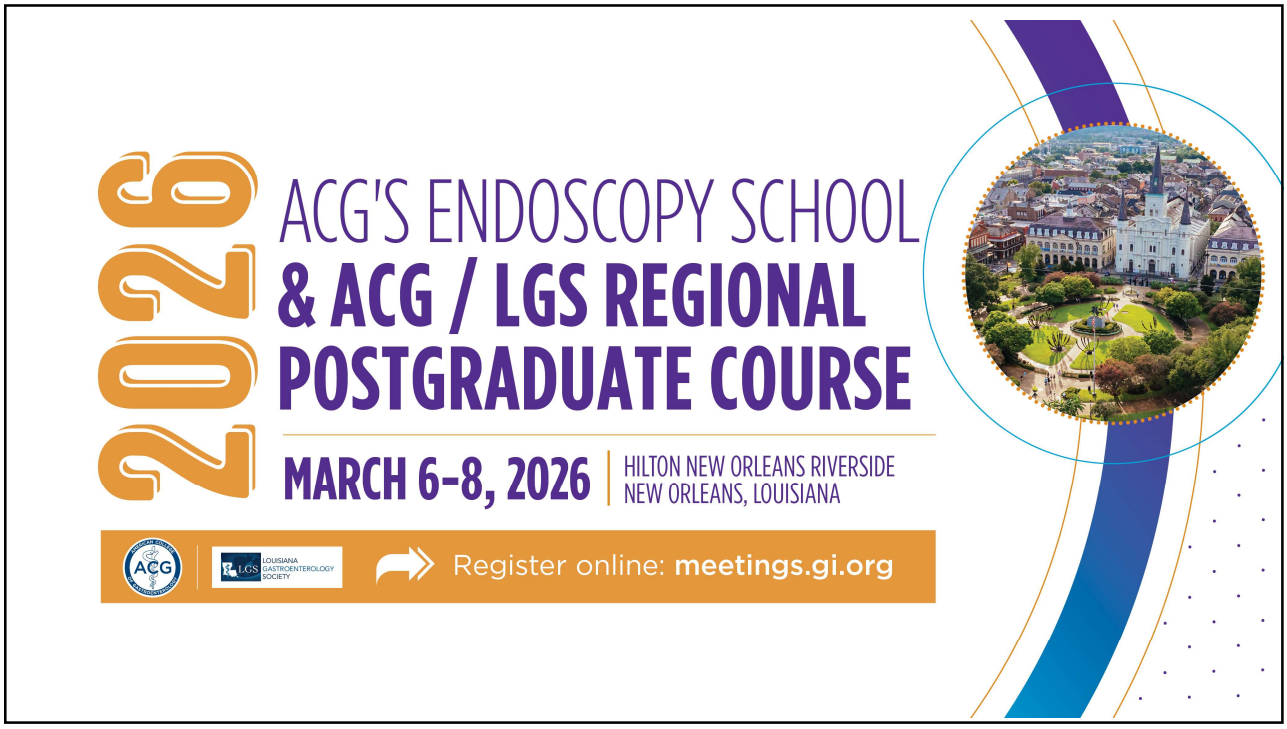
2026
ACG'S ENDOSCOPY SCHOOL
& ACG / LGS REGIONAL
POSTGRADUATE COURSE
MARCH 6-8, 2026
HILTON NEW ORLEANS RIVERSIDE
NEW ORLEANS, LOUISIANA
ACG
LGS LOUISIANA GASTROENTEROLOGY SOCIETY
Register online: meetings.gi.org

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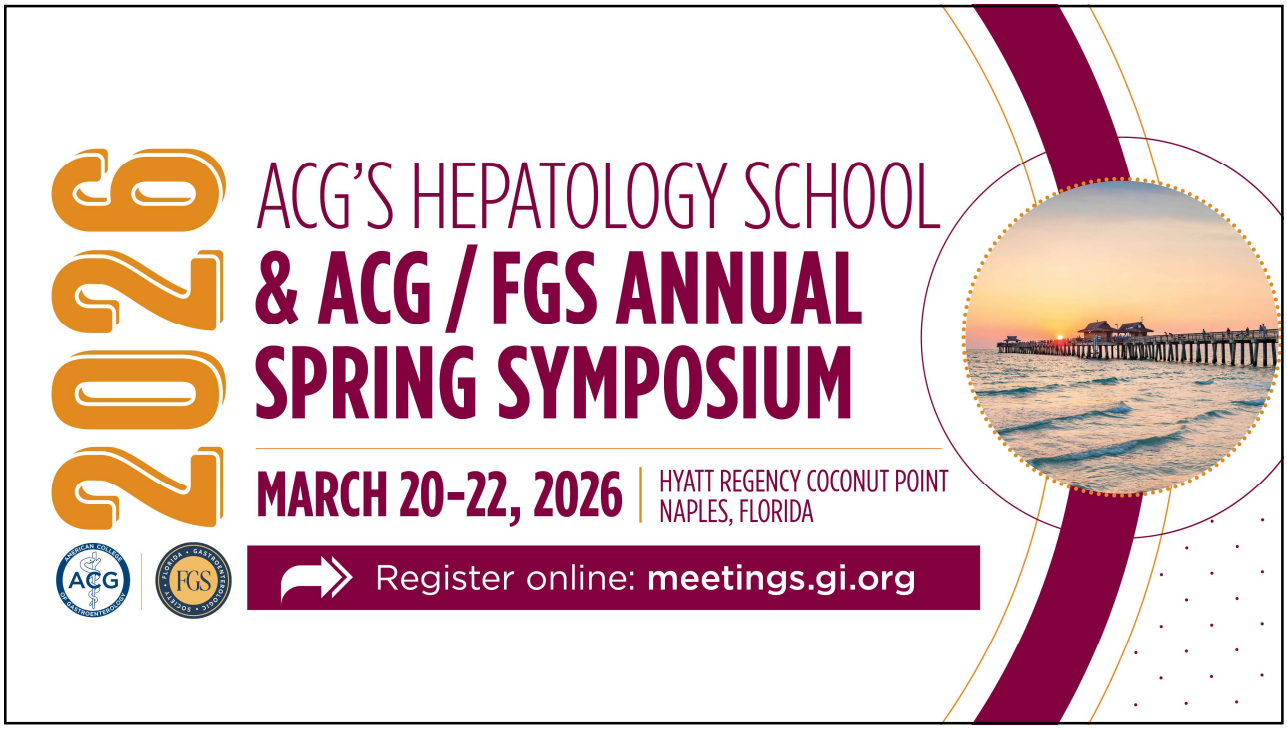
2026
ACG'S HEPATOLOGY SCHOOL
& ACG / FGS ANNUAL
SPRING SYMPOSIUM
MARCH 20-22, 2026
HYATT REGENCY COCONUT POINT
NAPLES, FLORIDA
Register online: meetings.gi.org

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ACG VIRTUAL GRAND ROUNDS
Thursday, January 22 at Noon & 8 pm ET
TNFα Inhibitors for the Treatment of IBD: Therapeutic Advances and Innovative Delivery Methods
David T. Rubin, MD, FACG &
Gil Y. Melmed, MD, MS, FACG
Offered in collaboration with HMP
gi.org/ACGVGR

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Virtual Grand Rounds

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Participating in the Webinar

All attendees will be muted and will remain in "Listen Only Mode"

Type your questions here so that the moderator can see them.
Not all questions will be answered but we will get to as many as possible.

A handout with the slides and room to take notes can be downloaded from your control panel.

Moderators:
Gil Y. Melmed, MD, MS, FACG

HMP Global

Exit

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ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!



Week 05 Internation – Tuesday, January 27, 2026
ACG Guidelines: Eosinophilic Esophagitis
Faculty: Evan S. Dellon, MD, MPH, FACG, and Edoardo Savarino, MD, PhD
Moderator: Edoardo Giovanni Giannini, MD, PhD, FACG
At Noon Eastern


Week 05 – Thursday, January 29, 2026
Alpha-gal Syndrome: How to Detect and Manage GI's Newest Diagnosis
Faculty: Sarah K. McGill, MC, MSc, FACG
Moderator: Amit Gupta, MD, MHPE
At Noon and 8pm Eastern


Week 06 Internation – Wednesday, February 4, 2026
The Paradigm Shift from FMT to Live Biotherapeutic Products in the Treatment of Recurrent Clostridioides difficile Infection
Faculty: Paul Feuerstadt, MD, FACG
Moderator: Ronald K. Hsu, MD, FACG
7:00am Eastern

Visit **gi.org/ACGVGR** to Register

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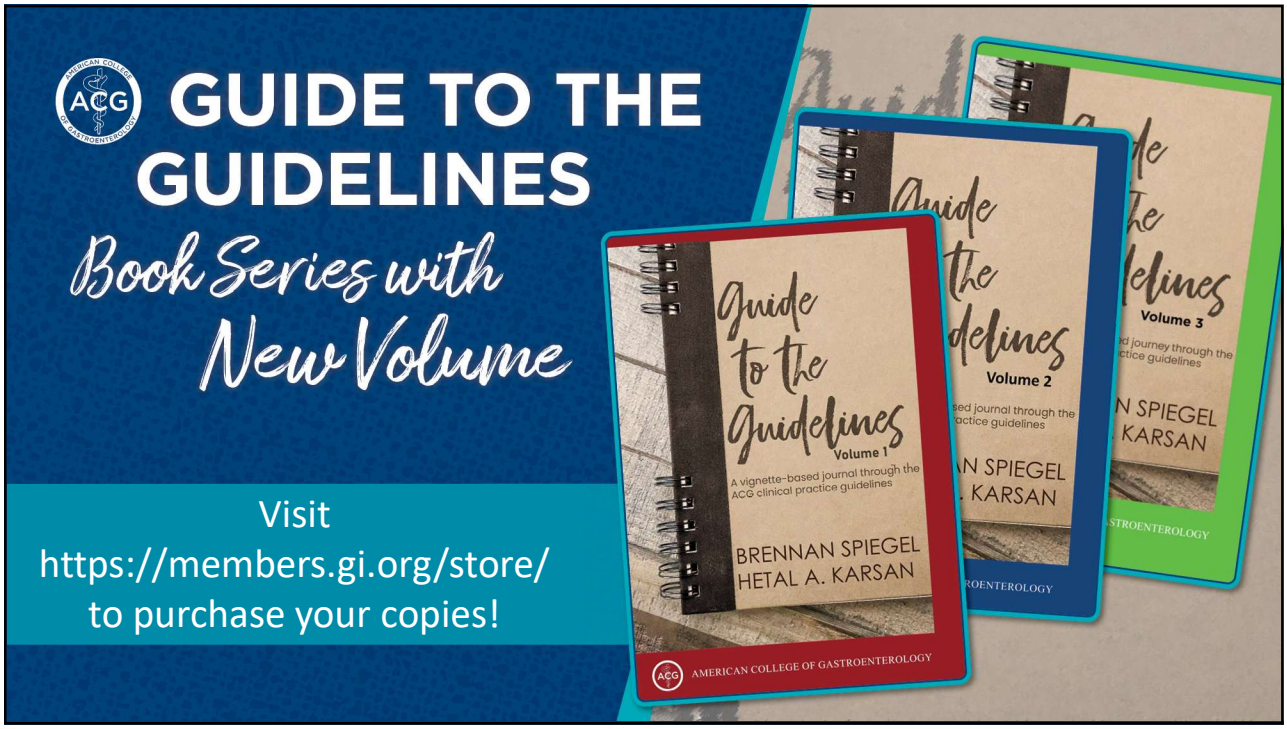

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Disclosures

David T. Rubin, MD, FACG:
AbbVie: Consultant; Abivax: Consultant; Altrubio: Consultant; Athos Therapeutics Inc: Consultant; Avalo Therapeutics: Consult; Bausch Health: Consultant; Bristol-Myers Squibb: Consultant; Buhlmann Diagnostics: Consultant; Celltrion: Consultant; ClostraBio: Consultant; Connect Biopharma: Consultant; Douglas Pharmaceuticals: Consultant; Eli Lilly & Co.: Consultant; Foresee: Consultant; Genentech (Roche) Inc: Consultant; Image Analysis Group: Consultant; InDex Pharmaceuticals: Consultant; Iterative Health: Consultant; Janssen Pharmaceuticals: Consultant; Odyssey Therapeutics: Consultant; Pfizer: Consultant; Sanofi: Consultant; Takeda: Consultant, Grant/Research Support; Throne: Consultant; Vedanta: Consultant; Biosciences: Consultant; Ventyx: Consultant.

Gil Y. Melmed, MD, MS, FACG:
AbbVie: Consultant, Advisory Board, Speaker's Bureau; Boehringer-Ingelheim: Consultant, Advisory Board, Speaker's Bureau; Bristol Myers Squibb: Consultant, Advisory Board, Speaker's Bureau; Diasorin: Consultant, Advisory Board, Speaker's Bureau; Ferring: Consultant, Advisory Board, Speaker's Bureau; Fresenius Kabi: Consultant, Advisory Board, Speaker's Bureau; Genentech/Roche: Consultant, Advisory Board, Speaker's Bureau; Gilead: Consultant, Advisory Board, Speaker's Bureau; Harp Diagnostics: Consultant, Advisory Board, Speaker's Bureau; Janssen: Consultant, Advisory Board, Speaker's Bureau; Johnson and Johnson: Consultant, Advisory Board, Speaker's Bureau; Lilly: Consultant, Advisory Board, Speaker's Bureau; Merck & Co.: Consultant, Advisory Board, Speaker's Bureau; OptionCare: Consultant, Advisory Board, Speaker's Bureau; Oshi Health: Consultant, Advisory Board, Speaker's Bureau; Pfizer: Consultant, Advisory Board, Speaker's Bureau; Takeda: Consultant, Advisory Board, Speaker's Bureau; Verantos: Consultant, Advisory Board, Speaker's Bureau; Viatris: Consultant, Advisory Board, Speaker's Bureau.

* Supported by an educational grant from Celltrion, Inc.

**All of the relevant financial relationships listed for these individuals have been mitigated*

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TNFα Inhibitors for the Treatment of IBD: Therapeutic Advances and Innovative Delivery Methods

David T. Rubin, MD, FACG
Joseph B. Kirsner Professor of Medicine
Chief, Section of Gastroenterology, Hepatology, and Nutrition
Director, Inflammatory Bowel Disease Center
University of Chicago

Gil Y. Melmed, MD, MS, FACG
Director, IBD Clinical Research, F. Widjadja IBD Institute
Cedars-Sinai Medical Center

Supported by an educational grant from Celltrion, Inc.

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Learning Objectives

- Examine the impact of TNFα inhibitors on mucosal healing and endoscopic remission in patients with IBD
- Evaluate the real-world and clinical data of newer therapies targeting TNFα for the treatment of IBD, including novel formulations and alternative delivery methods
- Implement personalized care plans for patients with IBD that consider clinical evidence, recent real-world data, current guidelines, and patient preferences

TNF = tumor necrosis factor; IBD = inflammatory bowel disease.

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The Biologic Era in Inflammatory Bowel Disease: Why TNF Inhibitors Led the Way

David T. Rubin, MD, FACG

Joseph B. Kirsner Professor of Medicine
Chief, Section of Gastroenterology, Hepatology, and Nutrition
Director, Inflammatory Bowel Disease Center
University of Chicago

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Anti-TNF Therapy in IBD: Tried, Tested, and Still Leading

1. Patient factors that should prompt anti-TNF as first-line advanced therapy
2. Anti-TNF still has the best efficacy
3. Well-known safety profile tempered by efficacy
4. New options for convenient management
5. Anti-TNFs are available and cost-effective

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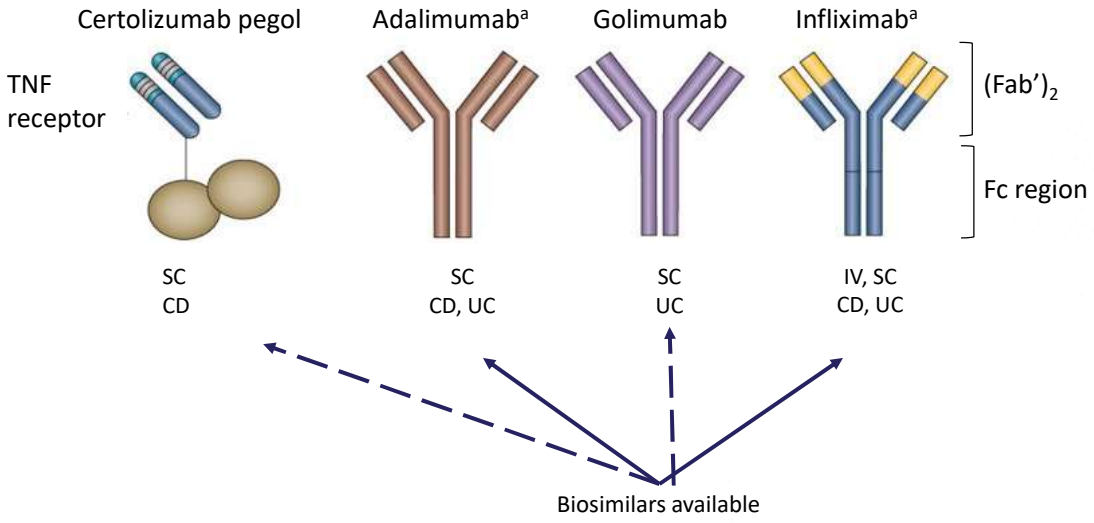
Anti-TNF Therapies in IBD



[a]Approved for pediatric CD and UC.
CD = Crohn's disease; IV = intravenous; SC = subcutaneous; UC = ulcerative colitis.

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We Learned the Most about Anti-TNF Therapies!

- What a biologic therapy is
- Immunogenicity
- The importance of maintenance therapy
- The concept of "top-down" treatment
- Disease modification is possible
- Biosimilar switches are safe and effective
- Immune-based adverse events

- How to design improved clinical trials in IBD
  - — Randomized responders
  - — Ethics of access and need for long-term extension
  - — The role of concomitant steroids
  - — Deeper endpoints

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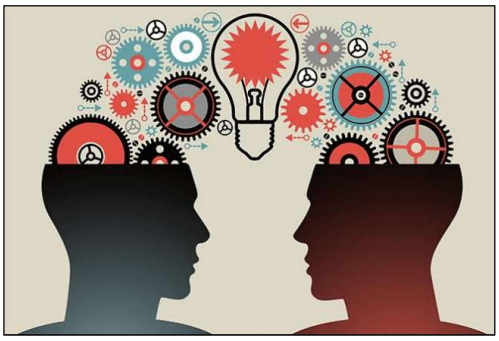
We Know the Most about Patient Selection and Drug Optimization with Anti-TNF

- Patient selection
- Risks of primary non-response and loss of response
- How to interpret loss of response
- How to prevent loss of response (!)
- Serum drug concentration interpretation



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The Right Patient for Anti-TNF: Guideline-Based Recommendations

Moderately-to-severely active UC or CD: Induction and maintenance of remission (adults and pediatrics)

Acute severe UC: Infliximab after IV corticosteroid failure

Perianal fistulizing CD: Induction and maintenance of remission

Post-operative CD to prevent recurrence

Rubin, DT, et al. *Am J Gastroenterol*. 2025;120(6):1187-1224. Hardbord M, et al. *J Crohns Colitis*. 2017;11(7):769-784. Bressler B, et al. *Gastroenterology*. 2015;148(5):1035-1058. Choi CH, et al. *Intest Res*. 2017;15(1):7-37. Wei SC, et al. *Intest Res*. 2017;15(3):266-284. Feuerstein JD, et al. *Gastroenterology*. 2020;158(5):1450-1461. Bitton A, et al. *Am J Gastroenterol*. 2012;107(2):179-194. Brown SR, et al. *Colorectal Dis*. 2018;20(Suppl 8):3-117. Sands BE, et al. *N Engl J Med*. 2004;350(9):876-885. Lichtenstein GR, et al. *Am J Gastroenterol*. 2018;113(4):481-517. Nguyen GC, et al. *Gastroenterology*. 2017;152(1):271-275.

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Optimizing Outcomes with TNF Inhibitors: Challenges and Opportunities for Advancing Clinical Care of Patients with IBD

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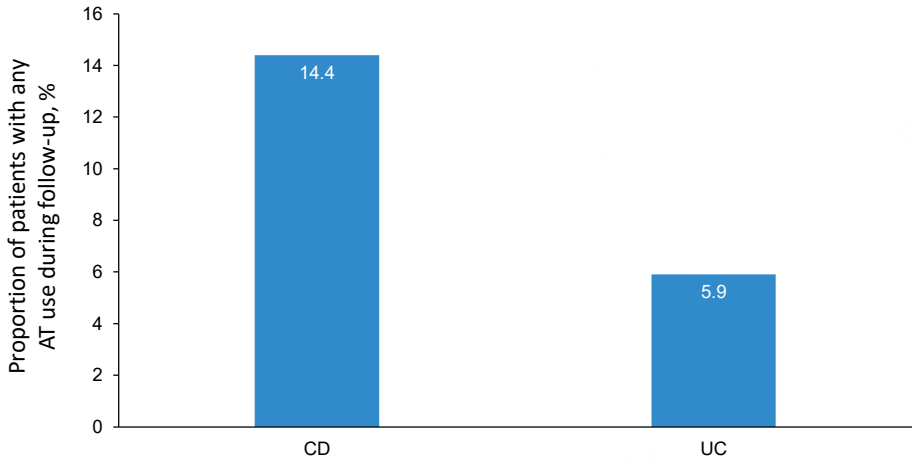
Advanced Treatment Uptake is Low within the First Few Years of IBD Diagnosis



AT = advanced treatment.

Siegel CA, et al. *Crohns Colitis 360*. 2024;6(3):otae040.

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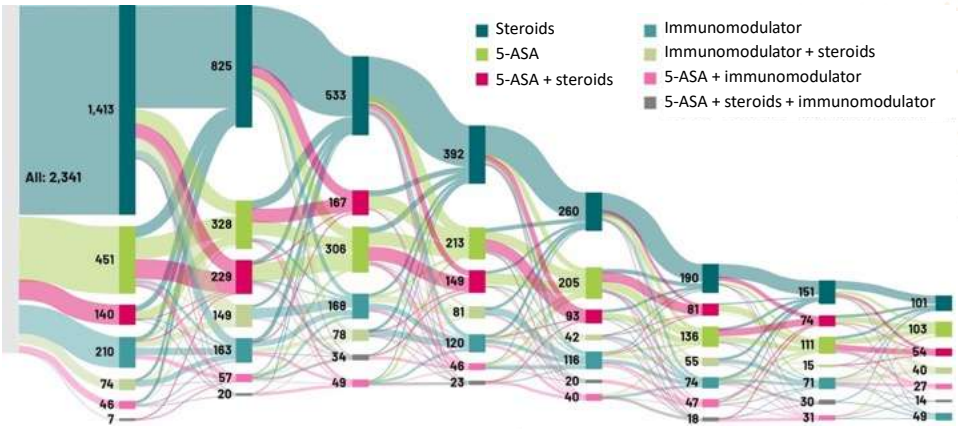
Few Patients with Newly Diagnosed CD Initiated with Advanced Therapy First-Line, Despite Updated Recommendations

- US Merative MarketScan research databases in new CD diagnoses, 2017-2021 (N=1739 patients with CD)

From diagnosis, only 14.4% of patients with CD received any advanced therapy during the mean follow-up period of 2.3 years

13.3% of patients with CD cycled through 3 MoAs before advanced therapy initiation



5-ASA = 5-aminosalicylate; MoAs = mechanisms of action.
Siegel CA, et al. *Crohns Colitis 360*. 2024;6(3):otae040.

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Timing Is Key with Anti-TNF

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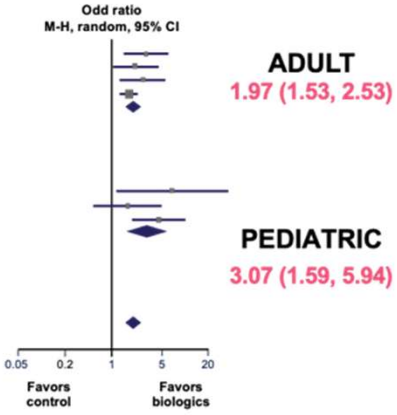
The "Right Time" to Treat is Early in Crohn's Disease!

Study or subgroup	Early treatment biologics Events	Total	Remission rate	Control Events	Total	Remission rate	Weight	Odd ratio M-H, random, 95% CI
1.1.1 Adult								
D'Haens 2008	39	65	60.0%	23	64	35.9%	11.0%	2.67 (1.31, 5.45)
Schreiber 2010	24	39	61.5%	79	176	44.9%	11.1%	1.96 (0.97, 4.00)
Colombel 2015	105	134	78.4%	31	54	57.4%	12.1%	2.69 (1.36, 5.29)
Panaccione 2016	84	174	48.3%	418	1190	35.1%	50.9%	1.72 (1.25, 2.37)
Subtotal (95% CI)	**252**	**412**	**61.2%**	**551**	**1484**	**37.1%**	**85.2%**	1.97 (1.53, 2.53)
Total events	252			551				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.18$, df = 3 ($P = .54$); $I^2=0\%$								
Test for overall effect: $Z = 5.28$ ($P < .00001$)								
1.1.2 Pediatric								
Kim 2011	15	18	83.3%	5	11	45.5%	1.9%	6.00 (1.08, 33.38)
Hyams 2009	16	26	61.5%	13	26	50.0%	4.7%	1.60 (0.53, 4.82)
Walter 2014	58	68	85.3%	41	68	50.3%	8.2%	3.82 (1.67, 8.75)
Subtotal (95% CI)	**89**	**112**	**79.5%**	**59**	**105**	**56.2%**	**14.8%**	3.07 (1.59, 5.94)
Total events	89			59				
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 2.20$, df = 2 ($P = .33$); $I^2=9\%$								
Test for overall effect: $Z = 3.33$ ($P = .00009$)								
Total (95% CI)	**341**	**524**		**610**	**1589**	**38.4%**	**100.0%**	**2.11 (1.66, 2.68)**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 6.12$, df = 6 ($P = .41$); $I^2=2\%$								
Test for overall effect: $Z = 6.13$ ($P < .00001$)								
Test for subgroup differences: $Chi^2 = 1.53$, df = 1 ($P = .22$), $I^2 = 34.7\%$								



Note: Clinical remission was the primary outcome; definitions varied across studies (CDAI <150, PCDAI ≤10, steroid-free remission, and absence of surgery). Adult studies mainly used CDAI-based criteria; pediatric studies relied on PCDAI and longer-term steroid-free remission.
CDAI = CD Activity Index; M-H: Mantel-Haenszel; PCDAI = pediatric CDAI.
Ungaro RC, et al. *Aliment Pharmacol Ther*. 2020;51(9):831-842.

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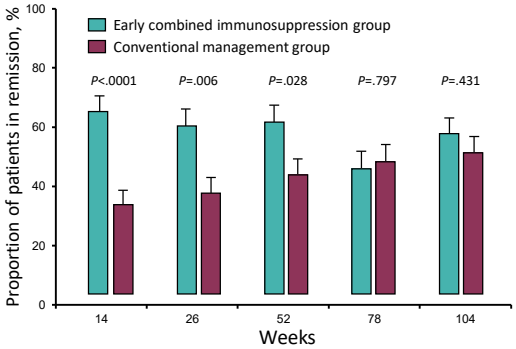
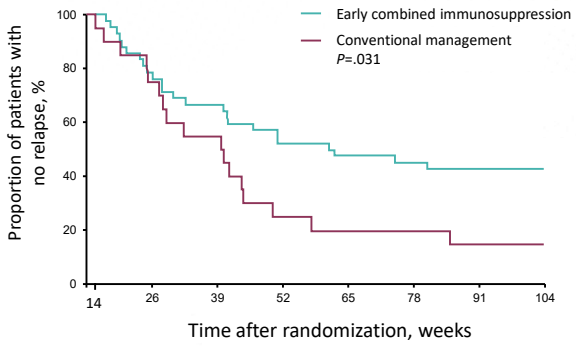
Early Combined Immunosuppression or Conventional Management in Patients with Newly Diagnosed CD (Step-Up/Top-Down)

- Median time from diagnosis to enrollment: 2 and 2.5 weeks
- An open randomized trial





D'Haens G, et al. *Lancet*. 2008;371(9613):660-667.

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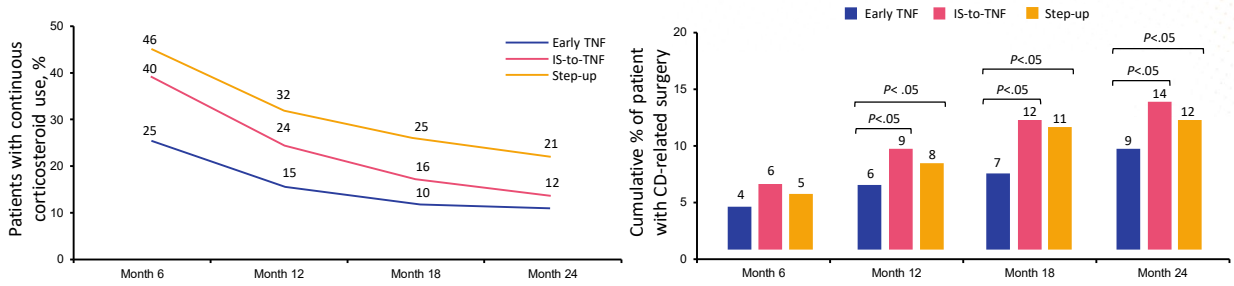
Earlier Use of Anti-TNF Biologic Therapy in CD Has Better Outcomes: Real-World Data

- Claims data assessment
- >3700 patients, all of whom received anti-TNF at some point



IS = immunosuppression.
Rubin DT, et al. *Inflamm Bowel Dis*. 2012;18(12):2225-2231.

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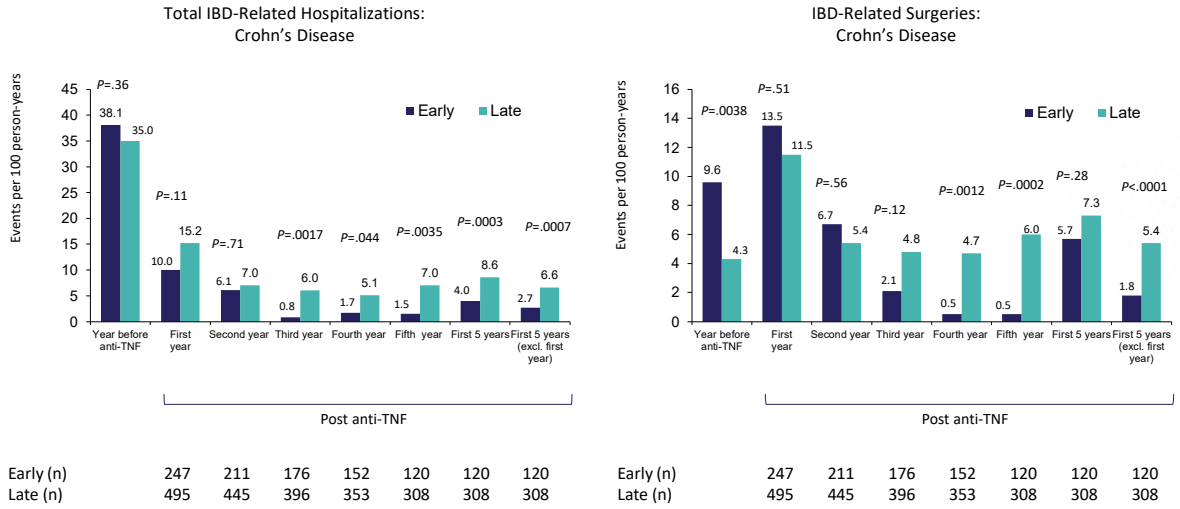
Early Anti-TNF Improves Outcomes



Targownik LE, et al. *Clin Gastroenterol Hepatol*. 2022;20(11):2607-2618.

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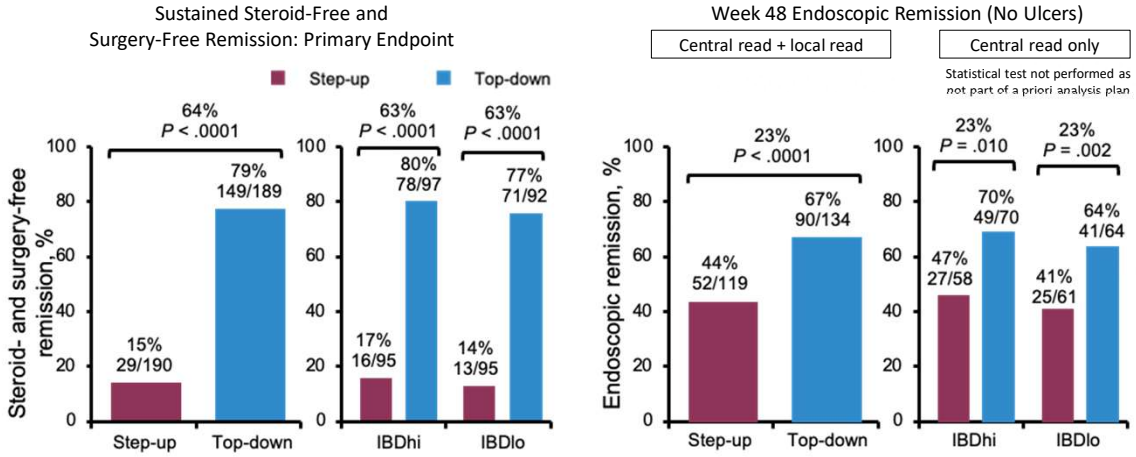
PROFILE Study: Early Therapy Improves Outcomes

- Median time from diagnosis to enrolment (days; min-max): Step-up group (14; 0-191); top-down group (9; 0-168)



Early infliximab/IMM treatment achieves nearly 80% remission rate

IMM = immunomodulator.
Noor NM, et al. *Lancet Gastroenterol Hepatol*. 2024;9(5):415-427.

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PROFILE Study: Safety

- Patients newly diagnosed with Crohn's disease

Adverse Events	Step-Up (n=193)	Top-Down (n=193)
Crohn's flare	225	30
Infection	20	23
Surgery	10[a]	1[b]

[a]Indication for surgery was CD; [b]Indication for surgery was gallstone ileus.
Noor NM, et al. *Lancet Gastroenterol Hepatol*. 2024;9(5):415-427.

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ECCO 2024 CD Guideline: Critical Importance of Early Effective Therapy

ECCO 2020 CD Treatment Guideline	ECCO 2024 CD Treatment Guideline
Monoclonal antibodies Recommendation 1.5. ECCO CD Treatment GL [2020]	3.10.2. The role of 'treat-to-target' and early treatment in the management of CD
"We recommend the use of TNF inhibitors [infliximab, adalimumab, and certolizumab pegol] to induce remission in patients with moderate-to-severe CD who have not responded to conventional therapy [strong recommendation, moderate-quality evidence]." … "Furthermore, anti-TNF agents might be more effective if introduced earlier [in the first 2 years] in the disease course, although these results are based on post-hoc analyses from clinical trials."	"Regardless of the monitoring strategy chosen, it is increasingly clear that early effective treatment should be a focus of management in CD, with emphasis on avoidance of diagnostic delays and any delays in initiation of treatment." … "Previous trials have hinted at the effectiveness of such an approach, and the recently reported UK PROFILE trial provides important evidence in favor of early aggressive treatment of CD."

GL = guideline.

Torres J, et al. *J Crohns Colitis*. 2020;14(1):4-22. Gordon H, et al. *J Crohns Colitis*. 2024;18(10):1531-1555.

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Dosing Is Essential with Anti-TNF

Gil Melmed, MD, MS, FACG, AGAF
Director, IBD Clinical Research, F. Widjadja IBD Institute
Cedars-Sinai Medical Center

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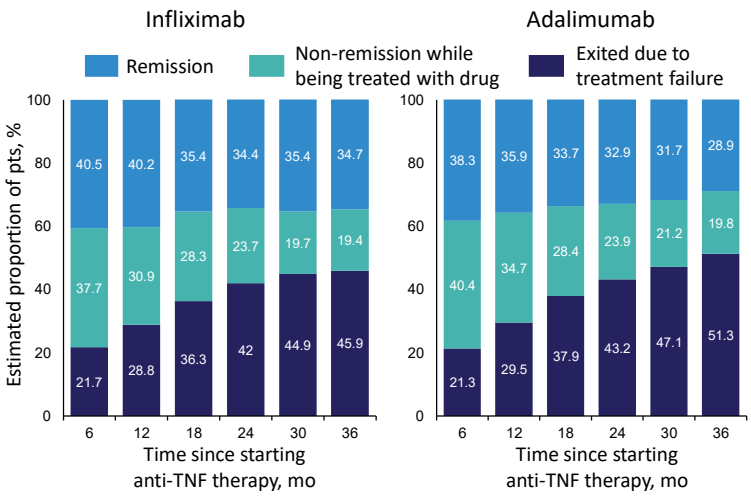
PANTS: 3-Year Follow-Up – Only Around 1/3 of Patients Were in Remission at the End of 3 Years (after Excluding PNR)



- Most LOR in first year
- Higher drug concentrations in first year of treatment may lead to better long-term outcomes
  - Early TDM
  - Combination IMM

LOR = loss of response; PNR = primary non-response; TDM = therapeutic drug monitoring.
Chanchlani N, et al. *Lancet Gastroenterol Hepatol*. 2024;9(6):521-538.

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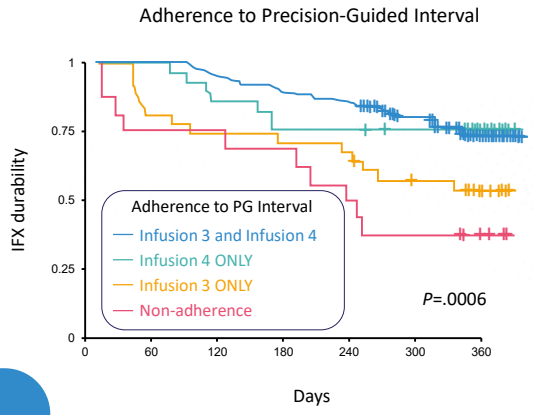
Impact of Early Proactive Precision-Guided Dosing

Week 52 outcomes, PRECISION IFX (adult and pediatric patients with IBD)

- 68% of protocol patients were still on IFX
- 97% were in CS-free remission
- Only 4% received standard maintenance dosing when continuing to target 10 µg/mL

Standard IFX dosing: 5 mg/kg x Q8W



Timing infusion 4 to achieve ≥10 µg/mL is key to long-term outcomes

CS = corticosteroid; IFX = infliximab; PG = precision-guided.
Dubinsky MC, et al. *Inflamm Bowel Dis*. 2022;28(9):1375-1385.

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Meta-Analysis: Proactive TDM vs SOC or Reactive TDM

Proactive TDM is better than SOC

- Treatment failure: RR 0.64 (95% CI 0.48-0.85, *P*<.01)
- Clinical remission: RR 1.07 (0.97-1.26)
- Endoscopic remission: RR 1.19 (0.93-1.53)
- Need for hospitalization: RR 0.64 (0.4-1.0)
- Surgical intervention: RR 0.51 (0.25-1.02)

Proactive TDM is better than reactive TDM

- Treatment failure: RR 0.46 (0.21-0.98, *P*=.04)
- Need for hospitalization: RR 0.33 (0.21-0.54, *P*<.01)

RR = relative risk; SOC = standard of care.
Sethi S, et al. *Aliment Pharmacol Ther*. 2023;57(12):1362-1374.

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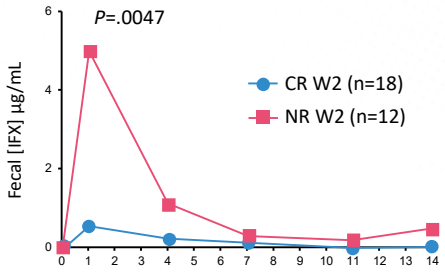
Understand the Pharmacokinetics and Pharmacodynamics of Monoclonal Antibodies

	Drug Levels (Exposure)
Drug-related	↑↓
Presence of ADAs	↓
Concomitant use of immunomodulators	↑
High-baseline TNF-α	↓
Low albumin	↓
High-baseline CRP	↓
Increased BMI	↓
Male sex	↓

Loss of Infliximab into Feces Is Associated with Lack of Response to Therapy in Patients with Severe UC



Maintaining stable therapeutic serum levels of anti-TNFα during maintenance therapy minimizes the risk of ADAs and enhances long-term treatment efficacy

ADAs = anti-drug antibodies; BMI = body mass index; CR = clinical response; CRP = C-reactive protein; NR = non-response.
Ordas I, et al. *Clin Pharmacol Ther*. 2012;91(4):635-646. Brandse JF, et al. *Gastroenterology*. 2015;149(2):350-355.e2. Brandse JF, et al. *Clin Gastroenterol Hepatol*. 2016;14(2):251-258.e1-e2.

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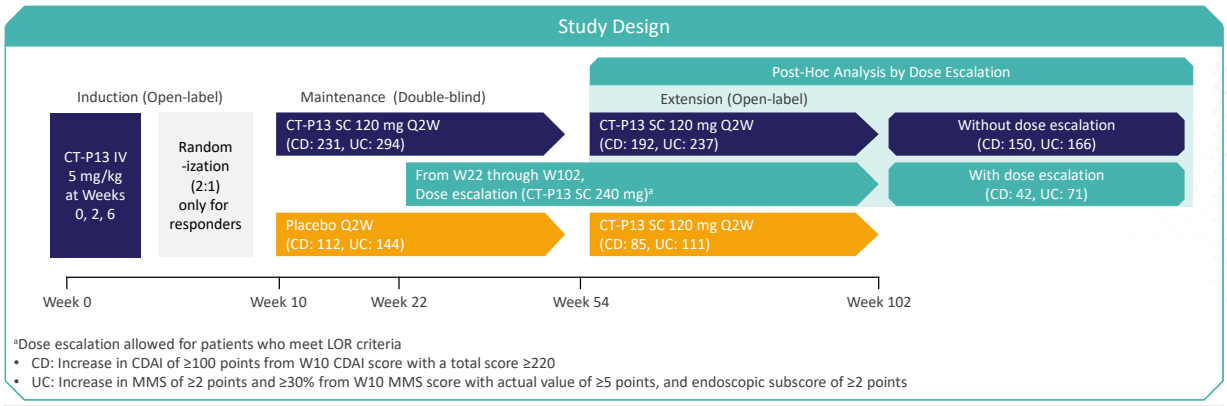
LIBERTY (IFX SC) Study Design



Dose Escalation Summary	CD (n=192)	UC (n=237)
Proportion of Patients with DE prior to Week 102, n (%)	42 (21.9%)	71 (30.0%)

DE = dose escalation; MMS = modified Mayo score.
Hanauer SB, et al. *Gastroenterology*. 2024;167(5):919-933.

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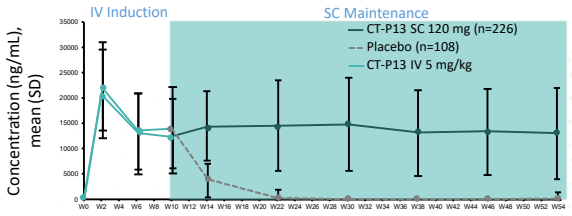
SC Infliximab for Maintenance Is Effective in UC and CD: LIBERTY-CD and LIBERTY-UC

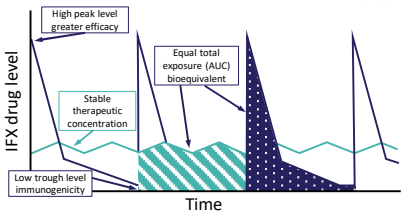
W54 efficacy in CD, n (%)	SC IFX CD n=231	Placebo CD n=112	*P*-value
Clinical remission	144 (62.3%)	32 (32.1%)	<.0001
Endoscopic response	118 (51.1%)	20 (17.9%)	<.0001
Endoscopic remission	80 (34.6%)	12 (10.7%)	<.0001
Corticosteroid-free remission	39/98 (39.8%)	10/44 (22.7%)	.0434

W54 efficacy in UC, n (%)	SC IFX UC n=294	Placebo UC n=144	*P*-value
Clinical remission	127 (43.2%)	30 (20.8%)	<.0001
Clinical response	158 (53.7%)	45 (31.3%)	<.0001
Endoscopic-histologic mucosal improvement	105 (35.7%)	24 (16.7%)	<.0001
Corticosteroid-free remission	44/120 (36.7%)	11/61 (18%)	.0127

Will this PK/PD model have less immunogenicity and loss of response?



Proposed Theoretical Pharmacokinetic Advantages and Disadvantages between IV and SC Infliximab



AUC = area under the curve; PD = pharmacodynamics; PK = pharmacokinetics; SD = standard deviation.
Hanauer SB, et al. *Gastroenterology*. 2024;167(5):919-933. Little RD, et al. *J Clin Med*. 2022;11(20):6173.

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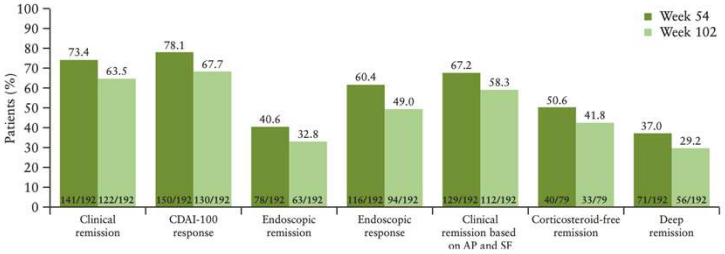
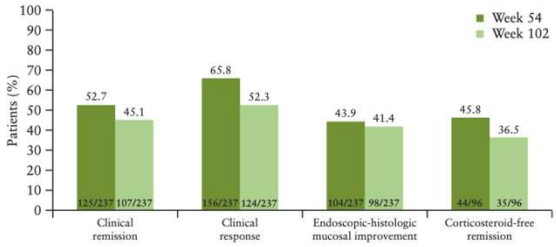
LIBERTY-CD and LIBERTY-UC: 2-Year Efficacy Data

LIBERTY-CD: Proportion of Patients Achieving Efficacy Endpoints



LIBERTY-UC: Proportion of Patients Achieving Efficacy Endpoints



SES-CD = simple endoscopic score for CD.
Colombel JF, et al. *J Crohns Colitis*. 2025;19(6):jjaf060.

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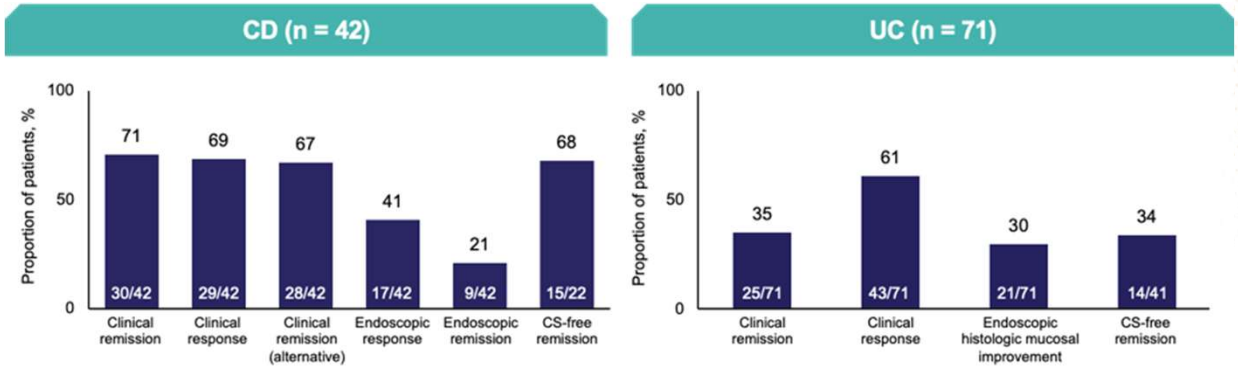
35

LIBERTY (IFX SC): Efficacy at Week 102 in Patients with Dose Escalation



SC infliximab maintained clinical remission rates up to 2 years, and patients who required dose escalation regained response

CS = corticosteroid.
Schreiber S, et al. Presented at: UEGW; 2024. OP149. Hanauer SB, et al. *Inflamm Bowel Dis*. 2025;31(Suppl 1):S13.

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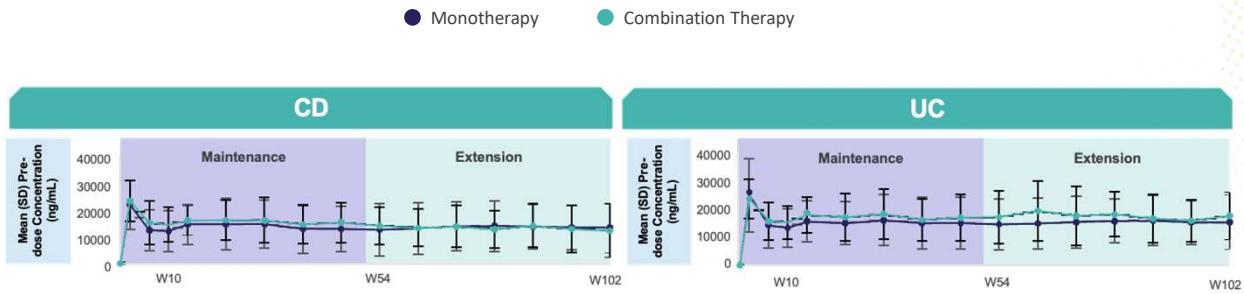
36

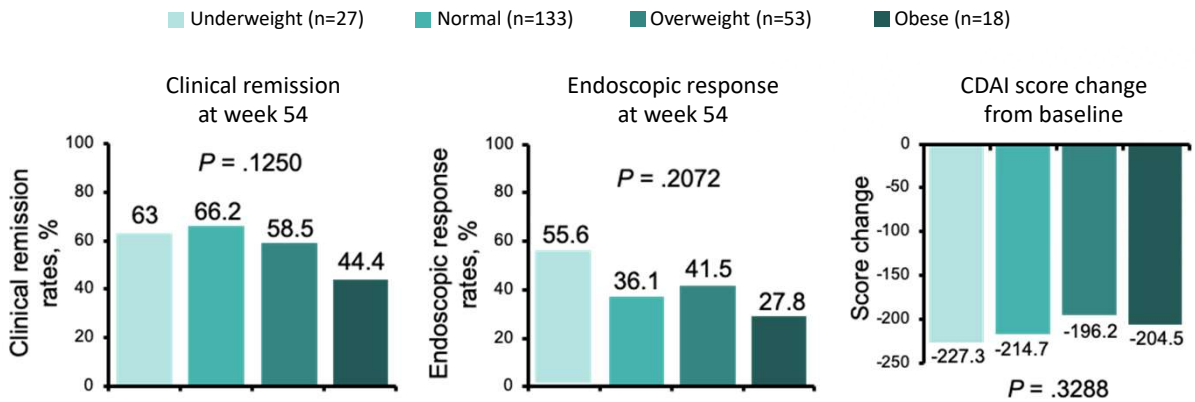
Immunosuppressant Use Post-Hoc Analysis of LIBERTY (IFX SC): Pharmacokinetics



Schreiber S, et al. *Inflamm Bowel Dis*. 2025:izaf038.

37

LIBERTY-CD Post-Hoc Analysis: Impact of BMI on Clinical Outcomes and Drug Levels with Maintenance SC IFX



IQR = interquartile range; TLI = trough level of infliximab.
Yarur A, et al. Presented at: DDW; 2024. Su1755.

38

REMSWITCH: Prediction of Long-Term Relapse after Switching from IV to SC IFX

No impact on the risk of relapse

- Weight/BMI
- Montreal classification
- Clinical activity at baseline
- CRP at baseline
- Concomitant immunosuppressive therapy

- Switching from IV to SC IFX appears to be feasible, safe, and effective
- Would avoid switching patients on 10 mg/kg Q6W or more
- Monitor closely

Parameters	*P*-values	OR	95% CI
Fecal calprotectin level >250 µg/g at baseline	.097	3.31	0.803-13.660
IV maintenance regimen 10 mg/kg/4 weeks	<.0001	61.032	6.137-606.957
IV maintenance regimen 10 mg/kg/6 weeks	.039	4.684	1.085-20.216
IV maintenance regimen 10 mg/kg/8 weeks	.55	1.507	0.392-5.791
IV maintenance regimen 5 mg/kg/8 weeks	Ref	Ref	Ref

OR = odds ratio; CI = confidence interval; Ref = reference.
Buisson A, et al. *Clin Gastroenterol Hepatol*. 2023;21(9):2338-2346.e3.

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Real-World SC IFX Effective at Inducing and Maintaining Remission in Patients with Perianal CD, Similar to IV IFX

Methods

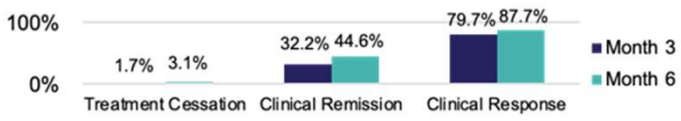
- Multicenter retrospective cohort from GETAID
- Group 1 = active perianal CD in the 6 months prior to SC switch
- Group 2 = inactive perianal CD for >6 months at time of switch but history of seton
- Clinical remission at 6 months = absence of anal ulcers and absence of draining fistula

Results: Group 1

- Active perianal CD (n=66)
- Median f/u: 50.4 weeks
- 44.6% clinical remission at 6M; 86.9% response
- 20% dose optimized (IFX >20 µg/mL)
- 72.4% MRI response; 26.5% seton removed
- Remission inversely linked to BMI, drainage, prior biologic use

Results: Group 2

- Quiescent perianal CD (n=117)
- Median f/u: 53.4 weeks
- Recurrence-free survival: 98% (3M), 92% (12M)
- 20% dose-optimized; no ADA
- 7 recurrences; 4 needed surgery



Conclusions

- SC infliximab is effective and safe for the management of active perianal CD and for maintaining remission in inactive perianal disease
- Comparable outcomes with IV infliximab

Vuitton S, et al. Presented at: DDW; 2024. 1176.

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Evidence-Based Clinical and Patient Considerations When Deciding on a Strategy

41

Fundamental Principles in the Approach to Positioning and Sequencing of IBD Therapies

- Naïve vs exposed
- Type of treatment comparisons
- Within class vs out of class
- Need for speed
- Disease location
- Disease duration
- It's all about the biology
- Thinking outside the gut

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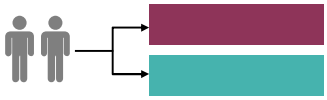
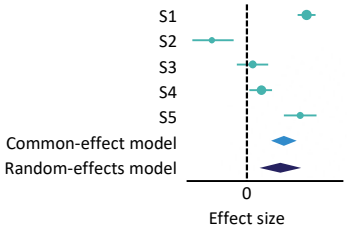
Types of Evidence

Head-to-Head Trial



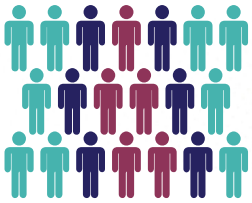
Gold standard: Designed and powered to allow formal comparison between different active therapies

Meta-Analysis



Integrates findings from many individual studies (often RCTs), applying objective statistical formulas

Real-World Data



Routinely collects data on patient health status from many sources (eg, registries), often using propensity score-matched analysis for adequate comparisons

RCT = randomized controlled trial.

Gurevitch J, et al. *Nature*. 2018;555(7695):175-182. Corrigan-Curay J, et al. *JAMA*. 2018;320(9):867-868. Peyrin-Biroulet L, et al. *J Crohns Colitis*. 2017;11(Suppl 2):S567-S575. Favalli EG, et al. *Biomed Res Int*. 2014;2014:831603.

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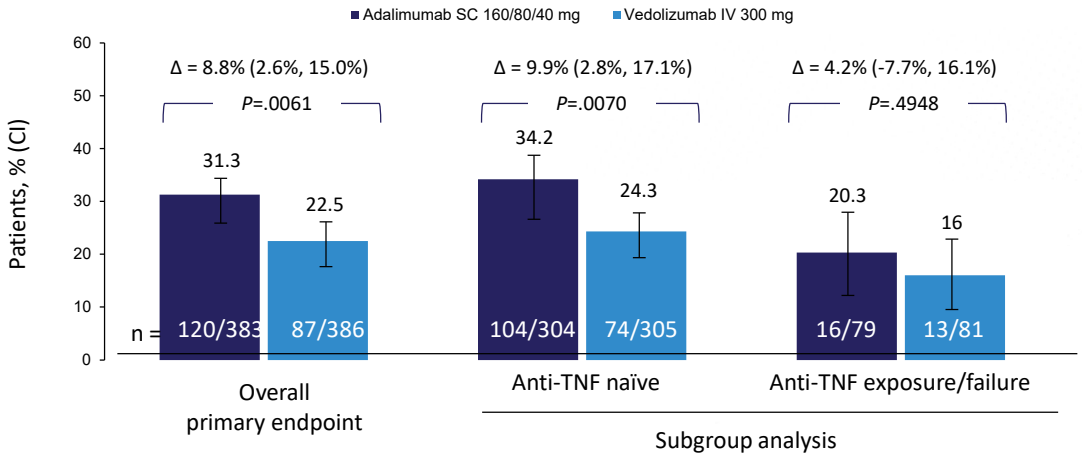
Moderate-to-Severe UC: Vedolizumab > Adalimumab (VARSITY)

Clinical Remission and Mucosal Healing at Week 52

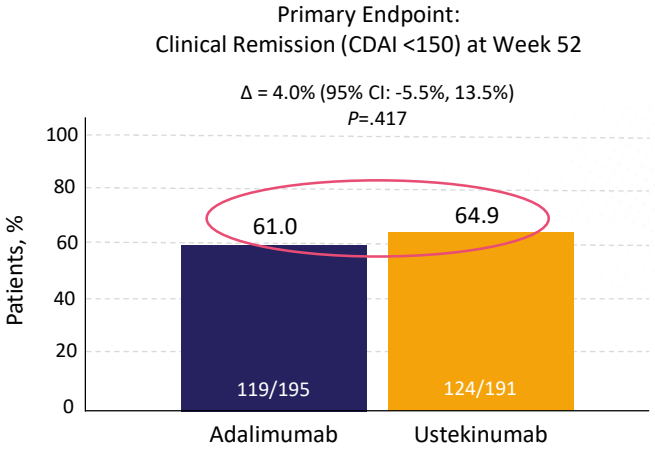


Sands BE, et al. *N Engl J Med*. 2019;381(13):1215-1226.

44

CD First-Line: Ustekinumab = Adalimumab (SEAVUE)

- Randomized, double-blinded, parallel-group, active-controlled study
- Biologic-naïve patients
- N=386; UST=191, ADA=195
- Mean disease duration
  - Ustekinumab arm: 6.8 years (SD 7.8)
  - Adalimumab arm: 6.6 years (SD 7.2)



ADA = adalimumab; UST = ustekinumab.
Sands BE, et al. *Lancet*. 2022;399:2200-2211.

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Comparative Risk of Serious Infections with Biologic Agents: A Systematic Review and Meta-Analysis

Risk of serious infections with advanced therapies for IBD

Meta-analysis of 20 head-to-head studies

Ustekinumab vs TNFα antagonists (5 cohorts; 23,232 patients)	Vedolizumab vs TNFα antagonists (17 cohorts; 51,596 patients)	Ustekinumab vs vedolizumab (5 cohorts; 1420 patients)
• CD: 51% lower risk of serious infections with ustekinumab • UC: Knowledge gap	• CD: No difference in risk of serious infections (OR, 1.03) • UC: 32% lower risk of serious infections with vedolizumab	• CD: 60% lower risk of serious infections with ustekinumab • UC: Knowledge gap

Safety profile of advanced therapies for IBD varies and is influenced by treatment effectiveness and intrinsic immune suppression

Solitano V, et al. *Clin Gastroenterol Hepatol*. 2023;21(4):907-921.e2.

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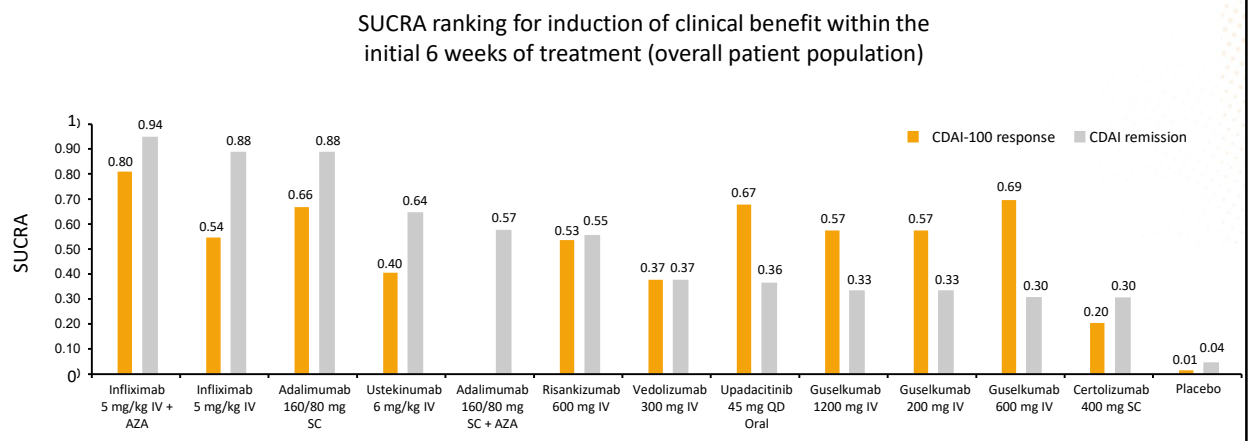
Comparative Onset of Early Effect of Biologics and Small Molecules in Moderately to Severely Active Luminal CD



AZA = azathioprine; SUCRA = surface under the cumulative ranking curve.
Attauabi M, et al. *Aliment Pharmacol Ther*. 2024;60(2):124-143.

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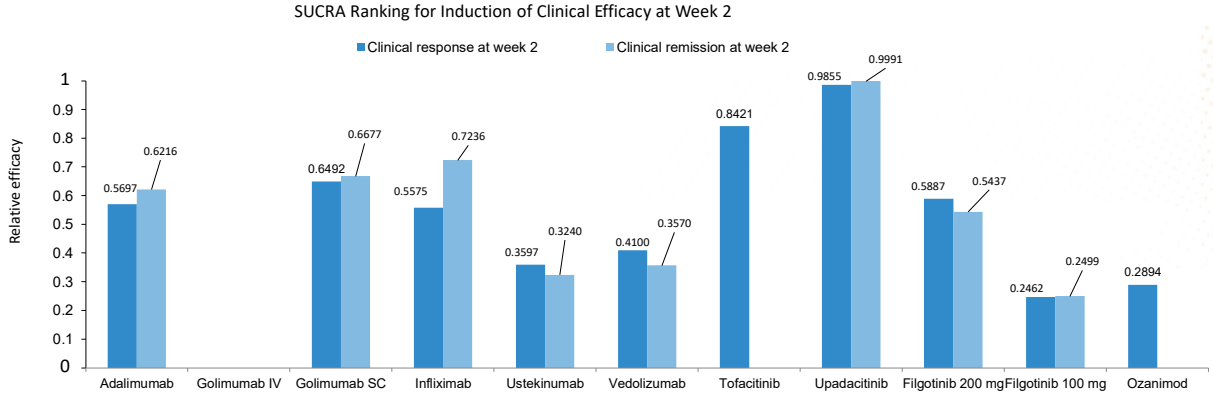
Comparative Onset of Effect of Biologics and Small Molecules in Moderately to Severely Active UC



Attauabi M, et al. *EClinicalMedicine*. 2023;57:101866.

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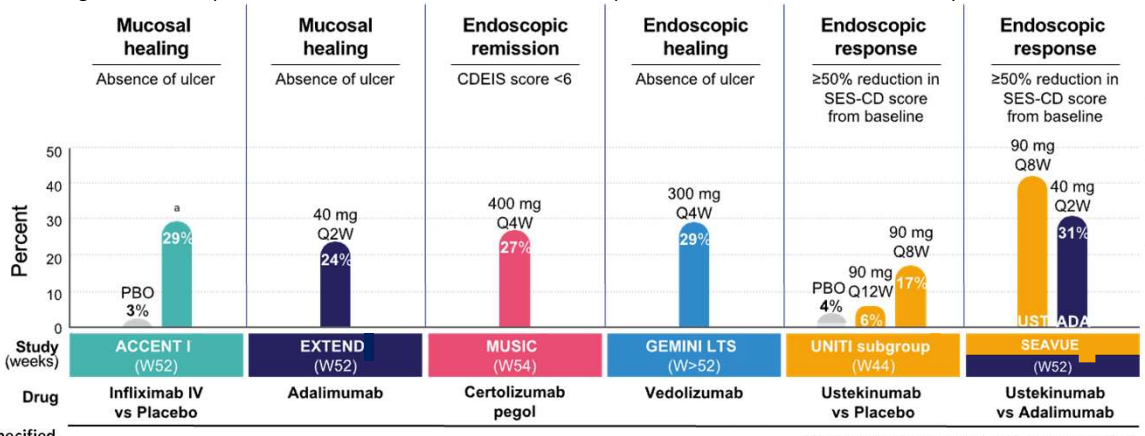
Endoscopic Outcomes by CD Therapeutics: 1-Year Maintenance Data from Clinical Trials

- Endoscopic outcomes were collected during registrational clinical trials but used different endpoints
- Registration trials prior to 2020s either did not evaluate endoscopic outcomes or evaluated as secondary outcomes



[a]Not specified.

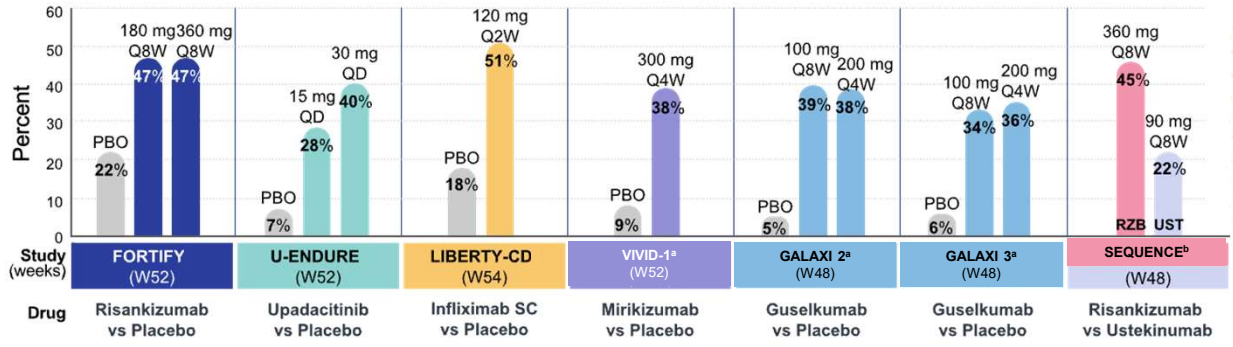
Not intended for head-to-head drug comparison.

CDEIS = CD endoscopic index of severity; LTS = long-term study; PBO = placebo.

Hanauer SB, et al. *Lancet*. 2002;359(9317):1541-1549. Rutgeerts P, et al. *Gastroenterology*. 2012;142(5):1102-1111.e2. Hébuterne X, et al. *Gut*. 2013;62(2):201-208. Noman M, et al. *J Crohns Colitis*. 2017;11(9):1085-1089. Rutgeerts P, et al. *Gastroenterology*. 2018;155(4):1045-1058. Sands BE, et al. *Lancet*. 2022;399(10342):2200-2211. Neurath MF, Vieth M. *Gut*. 2023;72(11):2164-2183.

49

Endoscopic Outcomes by CD Therapeutics: 1-Year Maintenance Data from Clinical Trials (Cont'd)



Not intended for head-to-head drug comparison.

[a]Mirikizumab and guselkumab have been approved by the FDA for the treatment of CD; [b]Endoscopic response was the secondary endpoint for the SEQUENCE study.

FDA = US Food and Drug Administration; RZB = risankizumab.

Ferrante M, et al. *Lancet*. 2022;399(10340):2031-2046. Loftus EV Jr, et al. *N Engl J Med*. 232;388(21):1966-1980. Hanauer SB, et al. *Gastroenterology*. 2024;167(5):919-933. Ferrante M, et al. *J Crohns Colitis*. 2024;18(Suppl 1):i7-i9. Panaccione R, et al. *Gastroenterology*. 2024;166(5):1057b1. Peyrin-Biroulet L, et al. *N Engl J Med*. 2024;391(3):213-223. Neurath MF, Vieth M. *Gut*. 2023;72(11):2164-2183.

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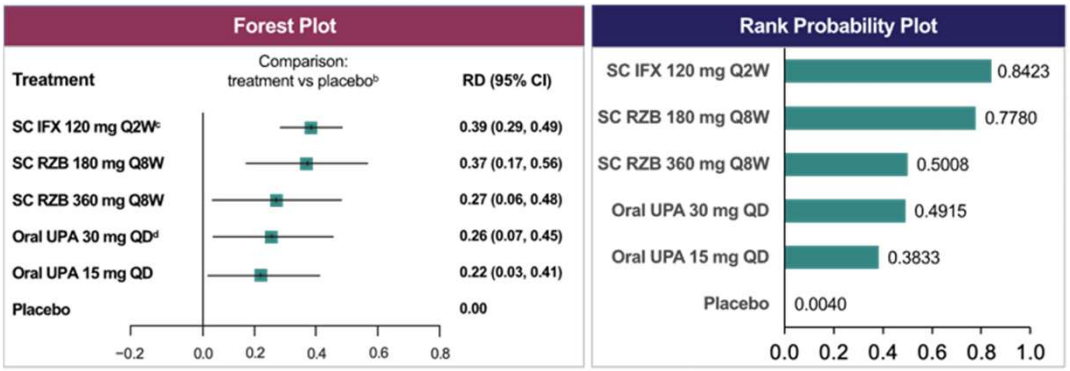
Comparison of Endoscopic Response Rate in First-Line-Use Patients

SC IFX 120 mg Q2W showed the highest risk difference for achieving endoscopic response[a] (0.39 [0.29-0.49]) during the maintenance phase. In terms of rank probability plot, SC IFX 120 mg Q2W demonstrated the highest *P*-score.



Data were synthesized in a frequentist NMA random-effects model that included all evaluated dosing regimens (including dose escalation).
[a]Endoscopic response: ≥50% decrease in SES-CD from baseline; [b]Random-effects model; [c]36 out of 205 patients received dose escalation (240 mg Q2W) upon secondary loss of response; [d]Escalated dose on the US FDA label.
RD = risk difference; UPA = upadacitinib.
Schreiber S, et al. *J Crohns Colitis*. 2024;18(Suppl 1):i1189-i1190. Presented at: ECCO Congress; 2024. P623.

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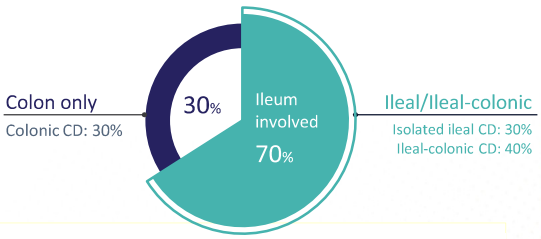
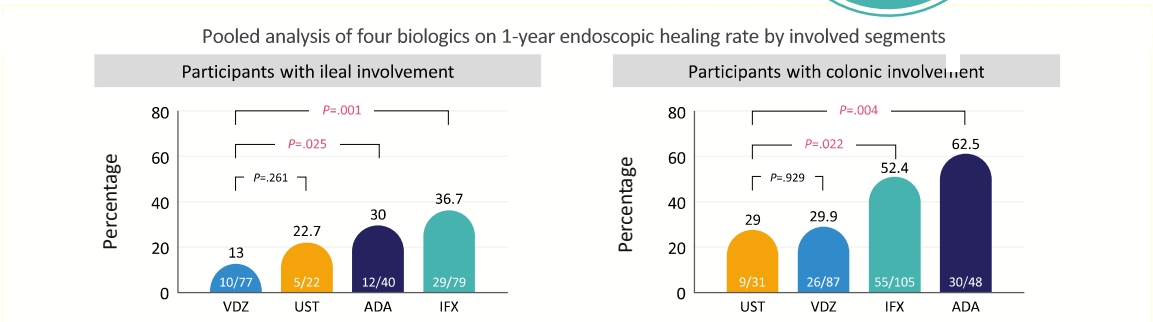
Why Should We Care about Segmental Healing?

- About 70% of patients with CD have ileal involvement (30% with isolated ileal disease), and the terminal ileum is often the most difficult to treat
- While TNF-α inhibitors have been demonstrated to be one of the most effective drugs in achieving endoscopic healing in ileal CD, it is still more challenging than for colonic segments





VDZ = vedolizumab.
Richard N, et al. *World J Gastroenterol*. 2023;29(21):3222-3240. Dulai PS, et al. *Clin Gastroenterol Hepatol*. 2019;17(13):2634-2643. Narula N, et al. *Am J Gastroenterol*. 2022;117(7):1106-1117.

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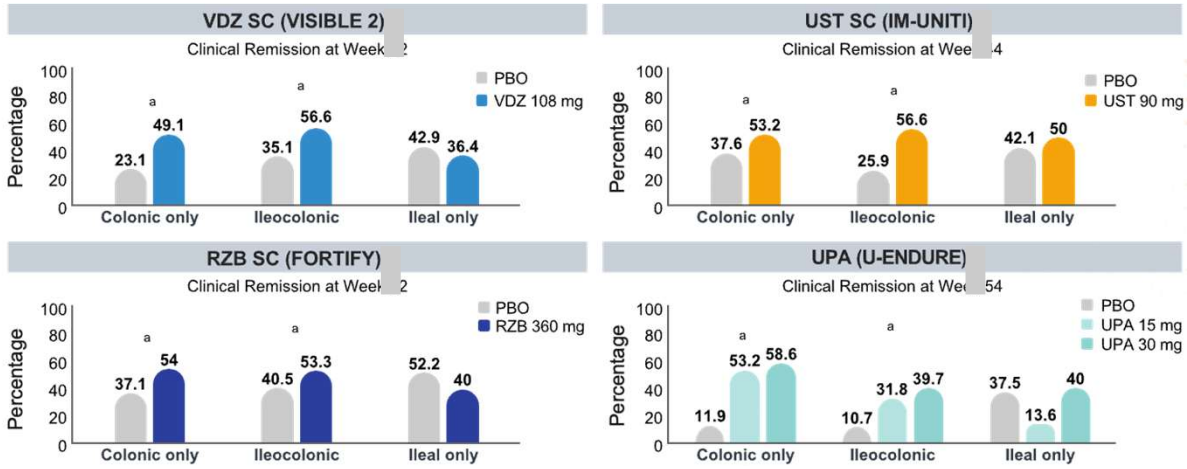
IBD Therapeutics Show Lower Efficacy in Isolated Ileal Disease

Advanced therapies vary in their ability to treat CD affecting different locations



[a]Statistically significant.

Vermeire S, et al. *J Crohns Colitis*. 2022;16(1):27-38. Feagan BG, et al. *N Engl J Med*. 2016;375(20):1946-1960. Ferrante M, et al. *Lancet*. 2022;399(10340):2031-2046. Loftus EV Jr, et al. *N Engl J Med*. 2023;388(21):1966-1980. Atreya R, et al. *Curr Res Pharmacol Drug Discov*. 2022;3:100097.

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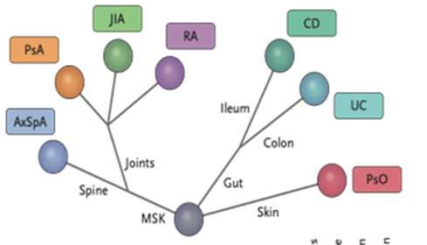
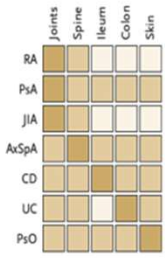
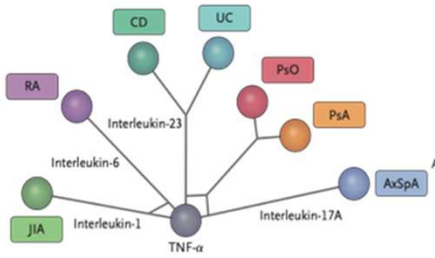
TNF Is an "Upstream" Cytokine

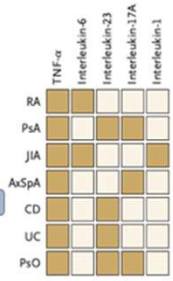
Organ-Based Concept





Signature Cytokine-Based Concept





AxSpA = axial spondyloarthritis; JIA = juvenile idiopathic arthritis; PsA = psoriatic arthritis; PsO = psoriasis; RA = rheumatoid arthritis.

Schett G, et al. *N Engl J Med*. 2021;385(7):628-639.

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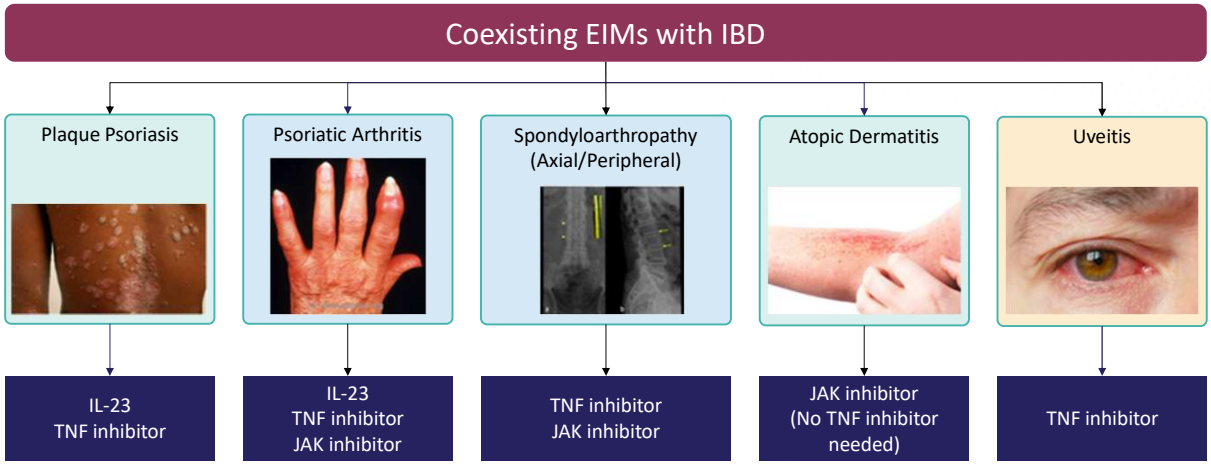
Choosing Advanced Therapies for UC Based on Concomitant Immune Conditions and Extraintestinal Manifestations



EIMs = extraintestinal manifestations; IL = interleukin.
Courtesy of David T. Rubin, MD.

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Summary: TNFα Inhibitors for the Treatment of IBD: Therapeutic Advances and Innovative Delivery Methods

- Use what you know: We know THE MOST about anti-TNFs
- They are EFFECTIVE, especially when used EARLY and FIRST
- They are great for extraintestinal manifestations
- They are safer than inadequate disease control
- Anti-TNF (infliximab) is still primary choice in hospitalized ASUC and for perianal disease
- They are a “gateway to JAK inhibitors” when you need something next
- They are AVAILABLE TO US
- They are (now) AFFORDABLE (relatively speaking!)

ASUC = acute severe ulcerative colitis.

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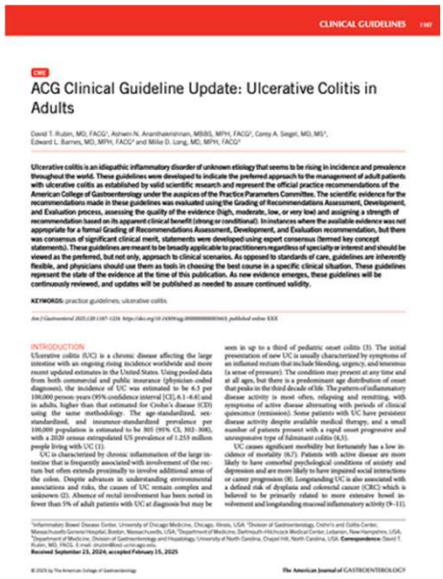
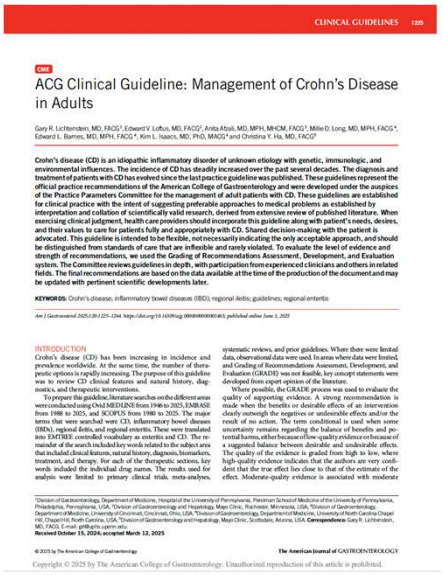


CLINICAL GUIDELINES

ACG Clinical Guideline Update: Ulcerative Colitis in Adults



CLINICAL GUIDELINES

ACG Clinical Guideline: Management of Crohn's Disease in Adults

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Anti-TNF in the ACG Guidelines: UC 1

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Table 2. Summary and strength of GRADED recommendations for the management of ulcerative colitis

Induction of remission in moderately to severely active UC
28. In patients with moderately to severely active UC, we recommend anti-TNF therapy using infliximab for induction of remission (Strong recommendation, high quality of evidence)
29. In patients with moderately to severely active UC, we recommend anti-TNF therapy using adalimumab or golimumab for induction of remission (Strong recommendation, moderate quality of evidence)
33. When infliximab is used as induction therapy for patients with moderately to severely active UC, we recommend combination therapy with a thiopurine (Strong recommendation, moderate quality of evidence for azathioprine)
Maintenance of remission in patients with previously moderately to severely active UC
42. We recommend continuing anti-TNF therapy using adalimumab, golimumab or infliximab (IV or SC dosing) for maintenance of remission after anti-TNF induction in patients with prior moderately to severely active UC (Strong recommendation, moderate quality of evidence)
Positioning considerations for the patient with moderately to severely active UC
44. In patients with moderately to severely active UC who are responders to anti-TNF therapy and now losing response, we suggest measuring serum drug levels and anti-drug antibodies (if there is not sufficient drug present) to assess reason for loss of response (Conditional recommendation, very low quality of evidence)
Management of the hospitalized patient with acute severe UC
51. In patients with ASUC failing to adequately respond to IVCS by 3 d, we recommend medical rescue therapy with infliximab or cyclosporine (Strong recommendation, moderate quality of evidence)
52. In patients with ASUC who achieve remission with infliximab treatment, we recommend maintenance of remission with the same agent (Strong recommendations, moderate quality of evidence)

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

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Anti-TNF in the ACG Guidelines: UC 2

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Table 3. Summary of key concept statements for the management of ulcerative colitis

Induction of remission in moderately to severely active UC
28. The patient with nonresponse or loss of response to anti-TNF therapy should be assessed with trough serum concentrations of drug to identify the reason for lack of response and whether to optimize the existing therapy or select an alternate therapy
29. Patients who are primary nonresponders to an anti-TNF (defined as lack of therapeutic benefit after induction and despite sufficient serum drug concentrations) should be evaluated and considered for alternative mechanisms of disease control (e.g., in a different class of therapy) rather than cycling to another drug within the anti-TNF class
30. Biosimilars to anti-TNF therapies and to ustekinumab are acceptable substitutes for originator therapies. Delays in switching should not occur and patients and clinicians should be notified about such changes
31. Subcutaneous infliximab and vedolizumab are considered equivalent to the standard intravenous maintenance dosing of these agents. The equivalence of the subcutaneous formulations for induction or as substitution for escalated doses of these therapies has not been robustly established
Positioning considerations for the patient with moderately to severely active UC
45. Infliximab is the preferred anti-TNF therapy for patients with moderately to severely active UC
Management of the hospitalized patient with acute severe UC
55. Infliximab and cyclosporine do not increase postoperative complications of colectomy and surgery should not be deferred based on this exposure

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

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Anti-TNF in the ACG Guidelines: Crohn's Disease

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Table 1. Recommendations for Management of Crohn's Disease

12. We recommend anti-tumor necrosis factor (TNF) agents (intravenous infliximab, subcutaneous adalimumab, subcutaneous certolizumab pegol) for induction and maintenance of remission for moderately to severely active CD (strong recommendation, moderate level of evidence)
13. We recommend combination therapy of intravenous infliximab with immunomodulators (thiopurines) as compared with treatment with either immunomodulators alone or intravenous infliximab alone in patients with CD who are naive to those agents (strong recommendation, moderate level of evidence)
14. We recommend subcutaneous infliximab as an option for maintenance of remission in patients with moderately to severely active CD who respond to intravenous induction with infliximab (strong recommendation, moderate level of evidence)
Fistulizing CD
24. We recommend infliximab use for induction of remission of perianal fistulizing CD (strong recommendation, moderate level of evidence)
25. We suggest adalimumab use for induction of remission of perianal fistulizing CD (conditional recommendation, low level of evidence)
26. We suggest the use of antibiotics combined with infliximab or adalimumab to improve clinical response in perianal fistulizing CD (conditional recommendation, very low level of evidence)
Postoperative CD
33. In patients with high-risk CD, we recommend anti-TNF therapy to prevent postoperative endoscopic recurrence (strong recommendation, moderate level of evidence)

Table 2. Key concepts

48. Anti-TNF agents are effective for severely active CD and infliximab may be administered in the inpatient setting for patients with severe to fulminant disease

Lichtenstein GR, et al. *Am J Gastroenterol*. 2025;120:1225–1264.

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Why Anti-TNF, and Why Now?

Indication	Evidence
Small bowel CD	Early anti-TNF linked to better outcomes (SONIC, PROFILE)
EIMs (arthralgia)	Anti-TNF effective across joint, skin, ocular domains
Perianal disease	Infliximab is the only approved therapy for complex perianal CD
Disease progression	Delay = fibrosis, strictures, loss of window of opportunity

Colombel JF, et al. *N Engl J Med*. 2010;362(15):1383-1395; Noor NM, et al. *Lancet Gastroenterol Hepatol*. 2024;9(5):415-427.

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What If … ?

- ? Patient A was planning a pregnancy?
- ? Patient A was a pediatric patient with growth failure?
- ? Patient A had a perianal abscess history?
- ? Patient A was biologic-experienced, with anti-TNF failure?
- ? Patient A had a history of breast cancer?

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Key Learning Points

- This patient is ready for biologics – anti-TNF offers the right match for phenotype and urgency
- Extraintestinal and perianal signs should accelerate treatment plans
- Use TDM, education, and early intervention to optimize outcomes
- Don’t wait for complications to escalate – act early

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Questions

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