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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.

Moderator:
Gary R. Lichtenstein, MD, FACG

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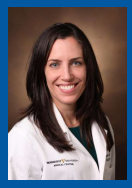

Week 30 – Thursday July 24, 2025
Inpatient Management of the Newly Diagnosed Short Bowel Patient: Consult to Discharge
Faculty: Dawn W. Adams, MD, MS, CNSC
Moderator: Shirley C. Paski, MD
At Noon and 8pm Eastern

Week 31 – Thursday July 31, 2025
Redefining Risk: How Healthcare Transformation is Reshaping Workplace Violence and Patient Behavior
Faculty: Sunanda V. Kane, MD, MSPH, MACG
Moderator: Benjamin J. Houge, MS
At Noon and 8pm Eastern

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

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The IBD Pipeline Explosion: S1Ps, IL23 and Subsequent Medications

Marla Dubinsky, MD

Professor of Pediatrics and Medicine
Chief Pediatric GI and Nutrition
Mount Sinai Kravis Children's Hospital
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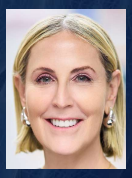
Icahn School of Medicine, Mount Sinai New York



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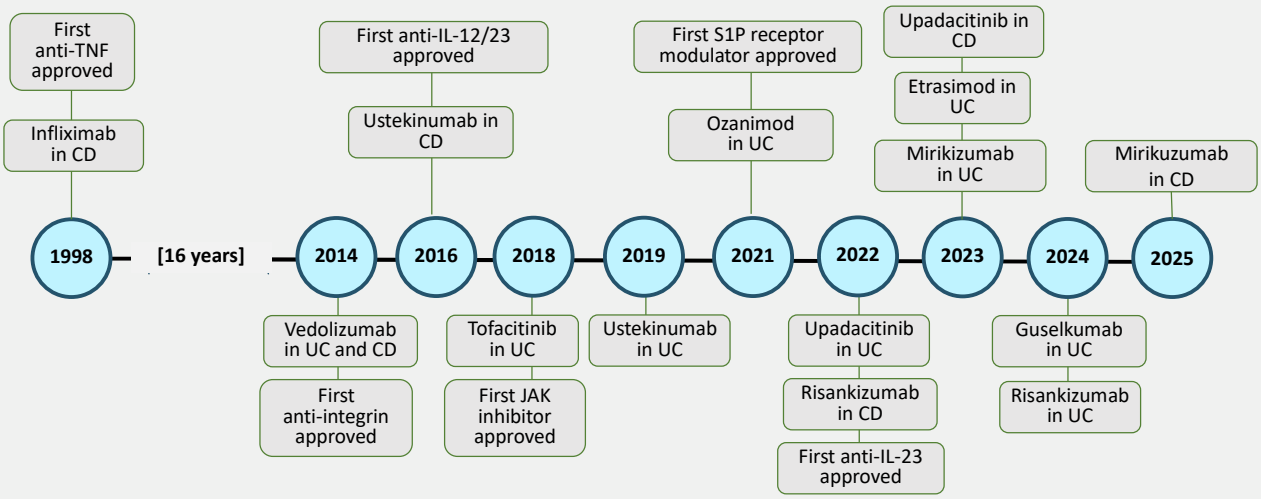
Evolution of the Treatment Landscape for IBD



IL, interleukin; JAK, Janus kinase; S1P, sphingosine-1-phosphate; TNF, tumor necrosis factor.

Modified from Pouillon L, et al. *Nat Rev Gastroenterol Hepatol*. 2021;18(2):143.

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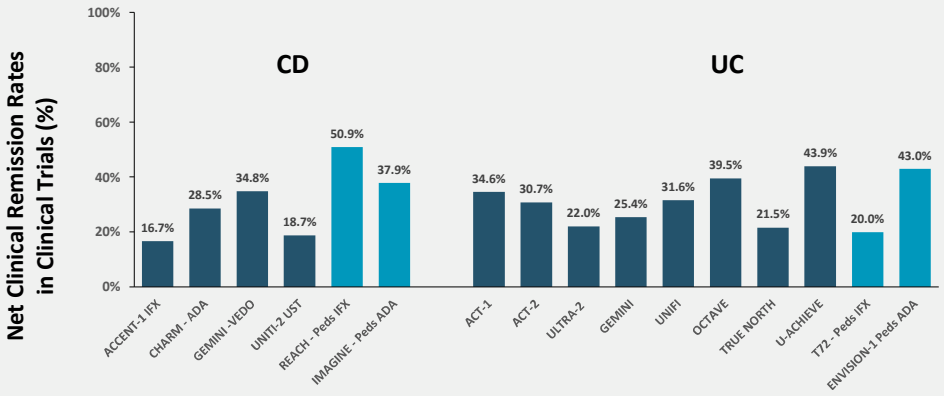
Persistent Unmet Needs in IBD Management Despite Treatment Advances

Significant Room for Improvement



Current tactics for therapy choice led to remission in **less than half** of patients with their first therapeutic choice.

ADA, adalimumab; IFX, infliximab; UST, ustekinumab; VEDO, vedolizumab.

Kayal M, et al. *Clin Gastroenterol Hepatol.* 2022;S1542-3565(22)00201-4; Kayal M, et al. *Clin Gastroenterol Hepatol.* 2023;S1542-3565(23)00035-6.

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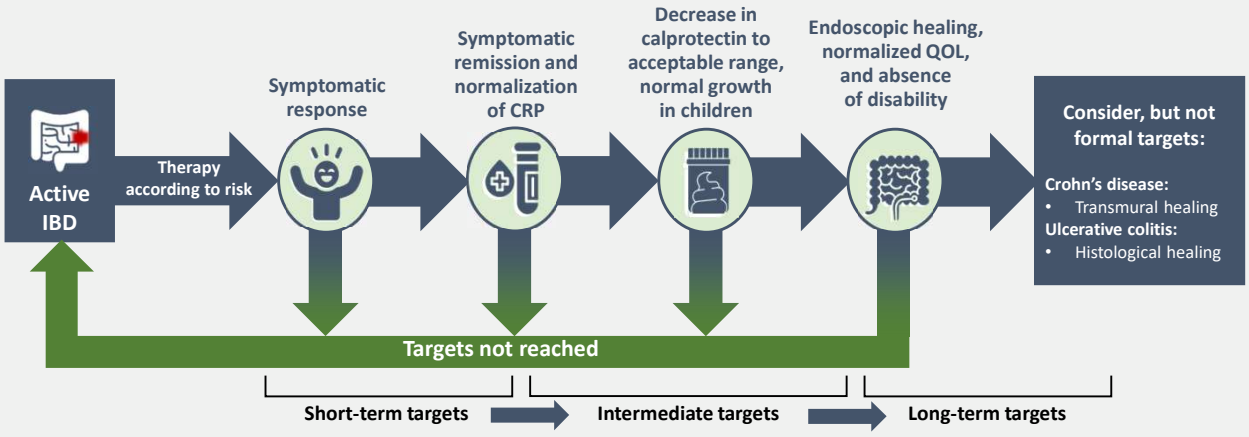
Treatment Targets in CD and UC (STRIDE Recommendations)



QOL, quality of life.

Turner D, et al. *Gastroenterology.* 2021;160(5):1570-1583.

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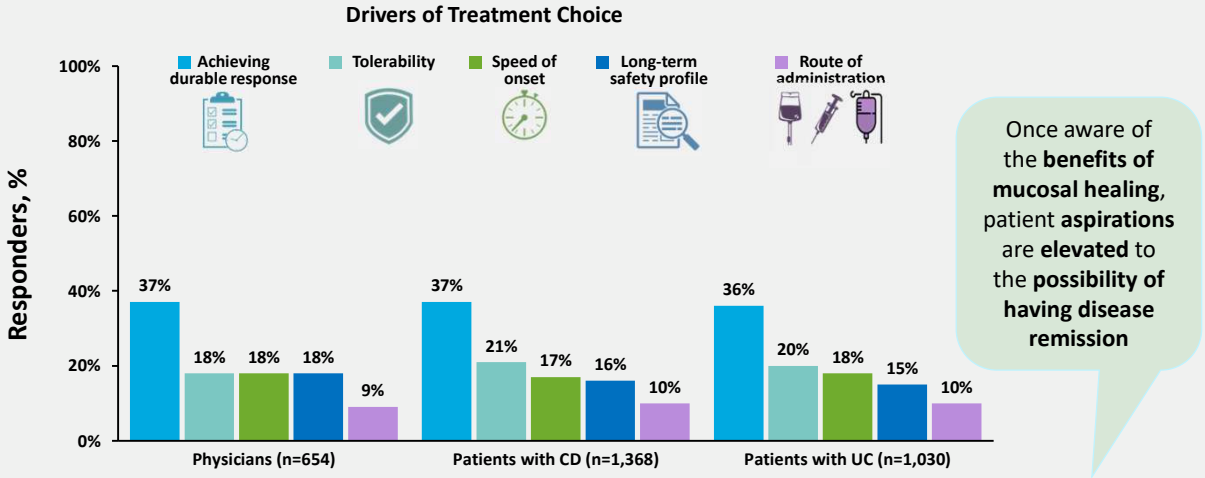
Achieving Immediate Targets Is Rated Highly by Patients With IBD and Clinicians, While Those Aware of Long-term Goals Have Higher Aspirations



Once aware of the **benefits of mucosal healing**, patient **aspirations** are **elevated** to the **possibility of having disease remission**

38% of patients with CD and 36% of those with UC had previously heard of the term 'mucosal healing'

Adapted from Rubin DT, et al. *Inflamm Bowel Dis*. 2021;27:1942–1953.

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Patient Description: 28-Year-Old Female With UC Naive to Advanced Therapy

- **Medical history:**
  - Diagnosed with left-sided UC 18m ago
- **Management since diagnosis:**
  - Mesalamine (4.8 g daily)
  - Rectal therapy (PRN)
- **Current presentation:**
  - New onset rectal bleeding
  - 5-6 loose stools daily
  - Occasional urgency
  - No nocturnal stools
- **Laboratory findings:**
  - Infectious workup – negative
  - C-reactive protein (CRP) 3 mg/L (normal <5 mg/L)
  - Fecal calprotectin (FCP) 690 ug/g (normal <250 ug/g)
- **Patient goals:**
  - To become pregnant in the near future
  - Get symptoms under better control

PRN, as needed.

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ACG 2025 Guidelines for the Treatment of Moderate-to-Severe UC

- **Treatment Goal:** Target endoscopic improvement (Mayo 0–1) to support sustained steroid-free remission and prevent hospitalization/surgery
- **Monitoring:** Use FC to guide response, detect relapse, and monitor during maintenance
- **Induction:**
  - First-line: Budesonide MMX (moderate UC), systemic corticosteroids
  - Preferred ATs*: S1P modulators, IL-12/23, IL-23 inhibitors, vedolizumab, anti-TNFs, JAK inhibitors
  - Avoid thiopurine/methotrexate monotherapy for induction
- **Maintenance:**
  - Continue effective induction biologic/JAK/S1P therapy
  - Avoid steroids; thiopurines can be used for steroid-induced remission
  - Avoid methotrexate
- **Positioning:** Vedolizumab preferred over adalimumab; check drug levels for anti-TNF loss of response

*S1P modulators (ozanimod, etrasimod), IL-12/23 (ustekinumab), IL-23 inhibitors (guselkumab, mirikizumab, risankizumab), vedolizumab, anti-TNFs (infliximab, adalimumab, golimumab), JAK inhibitors (tofacitinib, upadacitinib)
AT, advanced therapies; FC, fecal calprotectin.
Rubin et al. Am J Gastroenterol| ACG (2025) 120(6):p 1187-1224.

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AGA Guideline on Pharmacological Management of Adult Outpatients With Moderate-to-Severe UC*

- **SUGGEST** early use of ATs and/or IMM therapy over gradual step up after 5-ASA failure *(conditional recommendation, very low certainty of evidence)*
- **RECOMMEND** any of the following over no treatment: IFX, GOL, VEDO, TOF, UPA, UST, RIS, GUS, OZ, ETR *(strong recommendation, moderate certainty of evidence)*
- **SUGGEST** any of the following over no treatment: ADA, MIRI, FIL *(conditional recommendation, moderate certainty of evidence)*

Consider:
- Biosimilars of IFX, ADA, UST as equivalent in efficacy to originator
- Subcutaneous IFX and VEDO as alternatives to respective IV maintenance doses for most patients
- Extended induction or dose escalation of ATs for some patients with severe disease

AT-Naive (first-line therapy)

- **SUGGEST** HIGHER or INTERMEDIATE over LOWER efficacy medication *(conditional recommendation, low certainty of evidence)*

Efficacy:
- **HIGHER – IFX, VEDO, OZ, ETR, UPA, RIS, GUS**
- **INTERMEDIATE – GOL, UST, TOF, FIL, MIRI**
- **LOWER – ADA**

Prior Exposure to ≥1 AT (particularly anti-TNF)

- **SUGGEST** HIGHER or INTERMEDIATE over LOWER efficacy medication *(conditional recommendation, low certainty of evidence)*

Efficacy:
- **HIGHER – TOF, UPA, UST**
- **INTERMEDIATE – FIL, MIRI, RIS, GUS**
- **LOWER – ADA, VEDO, OZ, ETR**

*Patients with: 1) moderate-to-severe symptoms with Mayo endoscopy sub-score 2 or 3; 2) mild symptoms, with high burden of inflammation or poor prognostic features; 3) patients with corticosteroid-dependence, or refractory to oral corticosteroids.
AT, advanced therapy; ETR, etrasimod; FIL, filgotinib; GOL, golimumab; GUS, guselkumab; IMM, immunomodulator; IV, intravenous; MIRI, mirikizumab; OZ, ozanimod; RIS, risankizumab; TOF, tofacitinib; UPA, upadacitinib.
Singh S, et al. *Gastroenterology.* 2024;167:1307-1343.

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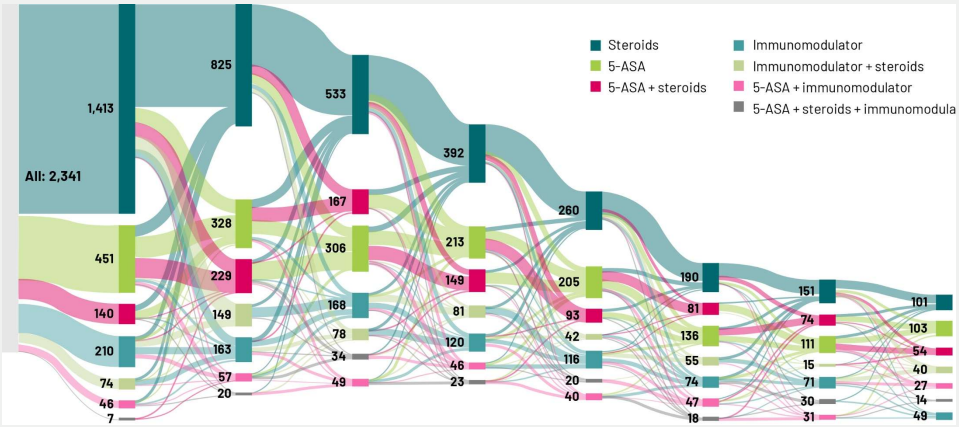
Despite updated recommendations, few patients with newly diagnosed CD were initiated with advanced therapy as first–line treatment

US Merative MarketScan Research databases in new CD diagnoses, 2017-2021 (N=1,739 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



Siegel CA, et al. Crohn's & Colitis 360, 2024;6;otae040, https://doi.org/10.1093/crocol/otae040

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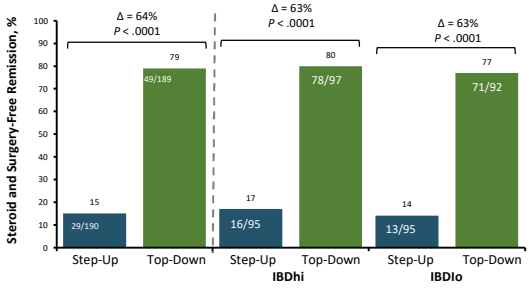
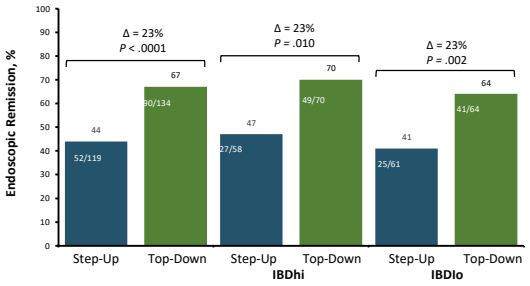
PROFILE: Early Advanced Therapy Improves CD Outcomes[1]

- Top-down treatment with infliximab/immunomodulator combination vs accelerated step-up therapy over 48 weeks

Primary Endpoint



Secondary Endpoint



Lower AEs, serious AEs, infections, disease flares, and complications requiring abdominal surgery in the top-down approach compared with step-up therapy

1. Noor NM et al. *Lancet Gastroenterol Hepatol*. 2024;9:415-427.

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Advanced Therapies for UC

Therapeutic Class	Therapy	Approval Year	Route of Administration
Anti-TNFα	Infliximab	2005*	IV
	Infliximab-dyyb	2016 (IV); 2023 (SC)	IV (induction); IV or SC (maintenance)
	Adalimumab	2012*	SC
	Golimumab	2013	SC
Anti-integrin α4β7	Vedolizumab	2014	IV (induction); IV or SC (maintenance)
Anti-IL-12/IL-23	Ustekinumab	2019	IV (induction); SC (maintenance)
JAK inhibitor	Tofacitinib	2018	Oral
	Upadacitinib	2022	Oral (Approved for after TNF Failure)
S1P Receptor Modulator	Ozanimod	2021	Oral
	Etrasimod	2023	Oral
Anti-IL-23p19	Mirikizumab	2023	IV (induction); SC (maintenance)
	Risankizumab	2024	IV (induction); SC (maintenance)
	Guselkumab	2024	IV (induction); SC (maintenance)

***Subsequently approved for pediatric UC.** SC, subcutaneous.

Entyvio (vedolizumab). Prescribing information. Janssen Biotech, Inc; 2023. Humira (adalimumab). Prescribing information. Janssen Biotech, Inc; 2023. Inflectra (infliximab-dyyb). Prescribing information. Celltrion Inc; 2023. Omvoh (mirikizumab). Prescribing information. Janssen Biotech, Inc; 2023. Remicade (infliximab). Prescribing information. Celltrion Inc; 2016. Simponi (golimumab). Prescribing information. Pfizer Inc; 2023. Skyrizi (risankizumab). Prescribing information. Eli Lilly and Company; 2025. Stelara (ustekinumab). Prescribing information. AbbVie Inc; 2023. Tremfya (guselkumab). Prescribing information. Janssen Biotech, Inc; 2023. Velsipity (etrasimod). Prescribing information. Takeda Pharmaceuticals America, Inc; 2023. Xeljanz (tofacitinib). Prescribing information; Bristol Myers Squibb. 2023. Zeposia (ozanimod). Prescribing information. Pfizer Inc; 2024. Zymfentra (infliximab-dyyb). Prescribing information. AbbVie Inc; 2023.

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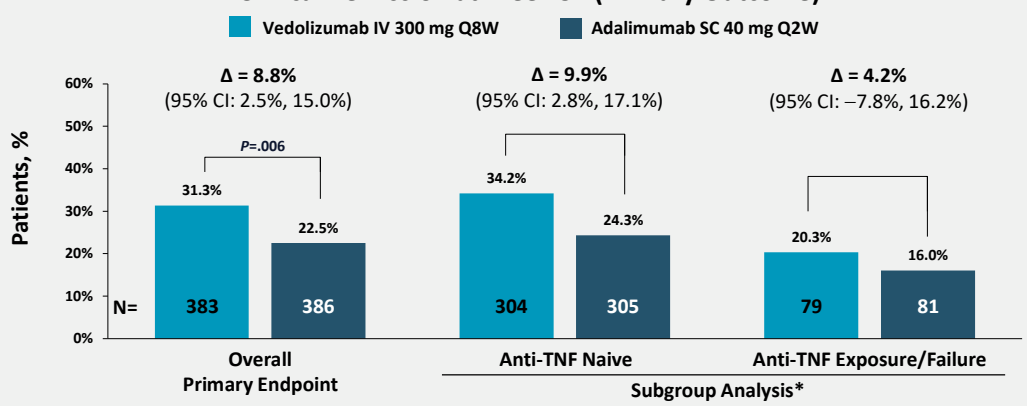
VARSITY: Only Head-to-Head for Moderate-to-Severe UC
Vedolizumab > Adalimumab

Clinical Remission at Week 52 (Primary Outcome)



Clinical remission: Total score of ≤2 on the Mayo scale and no individual subscore >1

*Anti-TNF subgroup analysis was prespecified and produced nominal *P* values.
Data from full analysis set, which includes all randomized patients who received at least 1 dose of study drug.
CI, confidence interval; Q2W, every 2 weeks; Q8W, every 8 weeks.

Sands BE, et al. *N Engl J Med*. 2019;381:1215-26.725.

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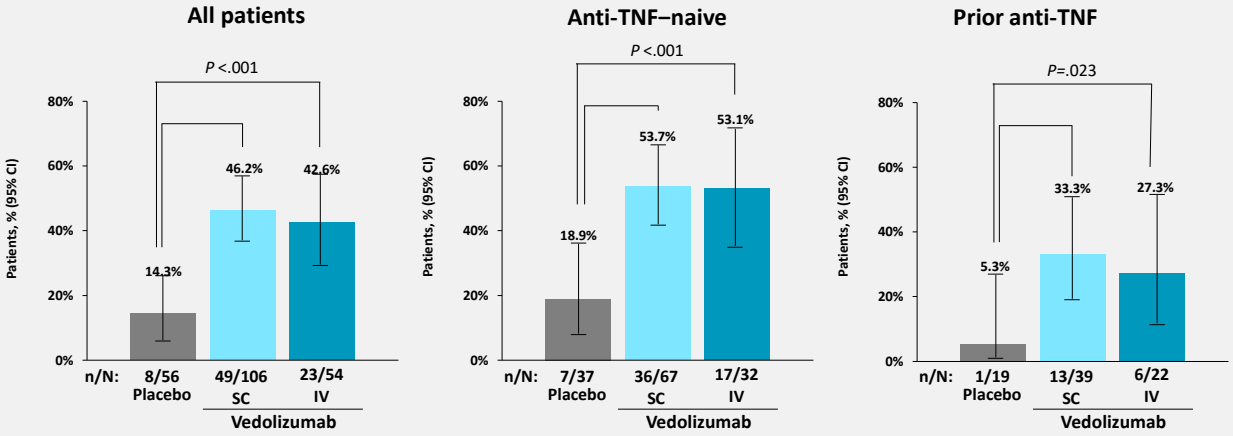
VISIBLE 1: Efficacy of a Subcutaneous Formulation of Vedolizumab in Moderate-to-Severe UC

Clinical Remission at Week 52 (Primary Outcome)



Clinical remission: Total score of ≤2 on the Mayo scale and no subscore >1

Sandborn WJ, et al. *Gastroenterology* 2020;158:562-572.e12.

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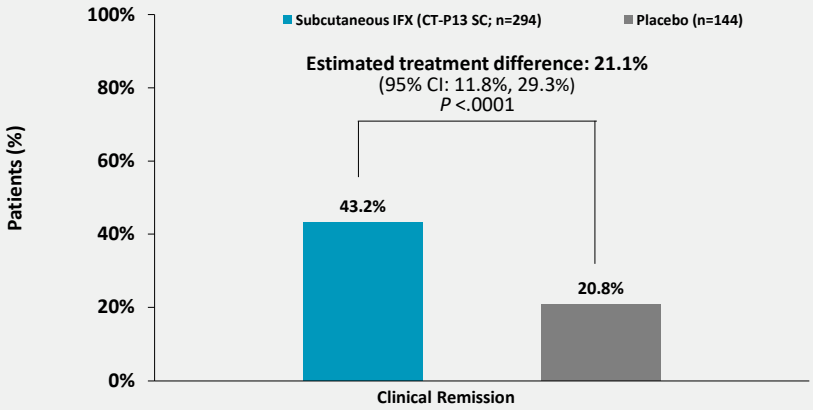
LIBERTY-UC: Subcutaneous Infliximab Maintenance Therapy for UC

Clinical Remission at Week 54 (Primary Outcome)



Clinical remission: Modified Mayo score (ie, SFS and ES of ≤1 and RBS=0)

ES, endoscopic score; RBS, rectal bleeding subscore; SFS, stool frequency.

Hanauer SB, et al. *Gastroenterology.* 2024;167:919-933.

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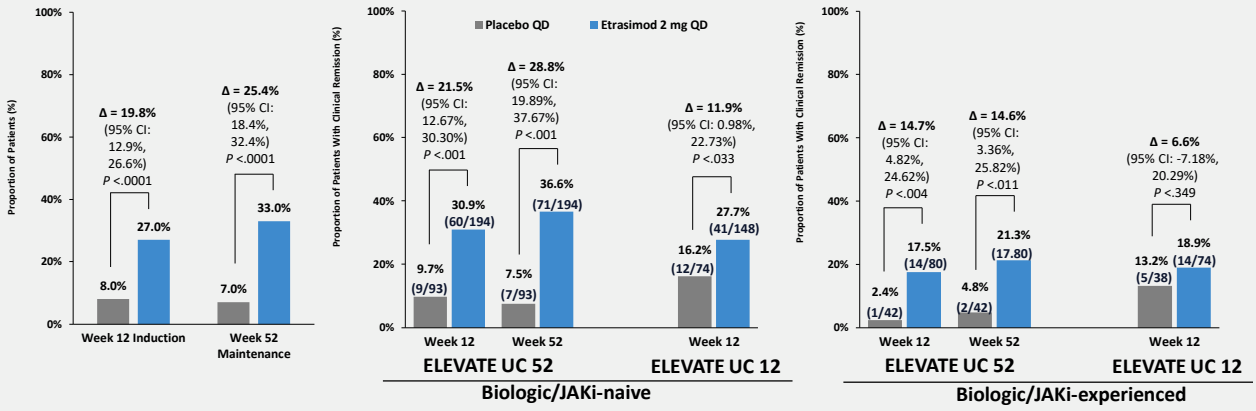
ELEVATE UC 52: Efficacy Stratified by Prior Exposure to Advanced Therapy

Clinical Remission at Weeks 12 and 52 (Primary Outcome)



Clinical remission: SFS=0 (or =1 with a ≥1-point decrease from baseline), RBS=0, and ES of ≤1 (excluding friability)

QD, once daily.

Sandborn WJ, et al. *Lancet*, 2023;401(10383):1159-1171; Vermeire S, et al. *J Crohn's Colitis.* 2024;18(11):1780-1794.

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Safety of S1P Receptor Modulators

- Lab monitoring before and during treatment
  - CBC with differential
  - CMP
- Monitor BP during treatment
- Baseline ECG
- Baseline (or shortly after starting) skin exam
- Baseline (or shortly after starting) ophthalmic exam
- Spirometry if clinically indicated

- BP, blood pressure; CBC, complete blood count; CMP, comprehensive metabolic panel; ECG, electrocardiogram.
- Velsipity (etrasimod). Prescribing information. Takeda Pharmaceuticals America, Inc; 2023.
- Zeposia (ozanimod). Prescribing information. Pfizer Inc; 2024.

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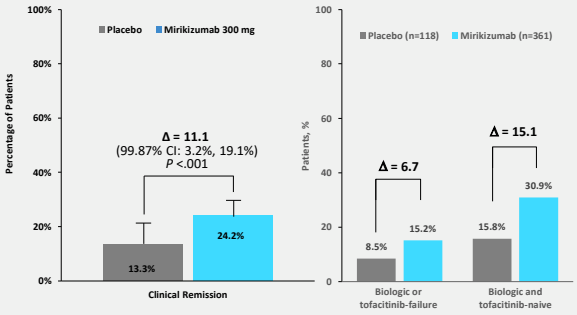
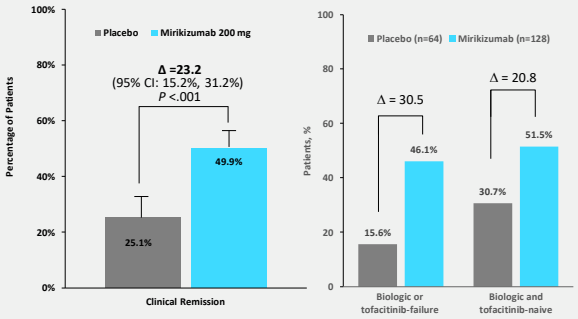
Mirikizumab Efficacy by Prior Biologic/JAK Inhibitor Exposure in LUCENT-1 and LUCENT-2 Trials

Clinical Remission (Primary Endpoint)

Week 12



Week 40



Clinical remission: Modified Mayo SFS=0 or SFS=1 with a decrease of ≥1 point from baseline, RBS=0, and ES of 0 or 1 (excluding friability)

D'Haens G, et al. *N Engl J Med.* 2023;S(59).

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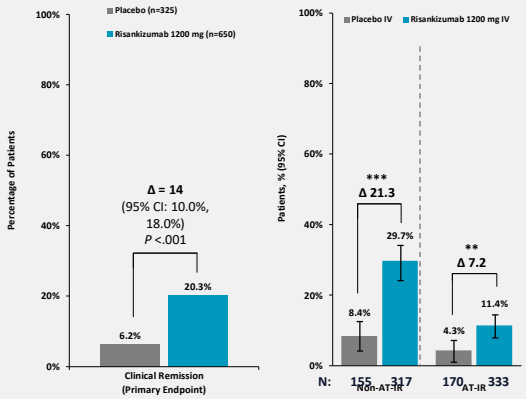
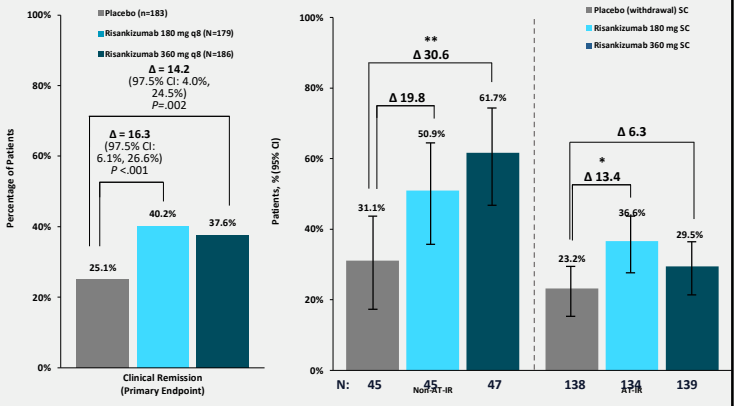
Risankizumab Efficacy by Prior Biologic/JAK Inhibitor Exposure in INSPIRE and COMMAND Trials

INSPIRE Induction Study, Week 12



COMMAND Maintenance Study, Week 52



Clinical remission: SFS ≤1 and not greater than baseline, RBS=0, and ES ≤1 (without friability)

AT-IR, inadequate response or intolerance to advanced therapy. *$P \leq .05$, **$P \leq .01$, ***$P \leq .001$.

Panaccione et al. *J Crohn's Colitis* (2025) 19:(1):jjaf005.

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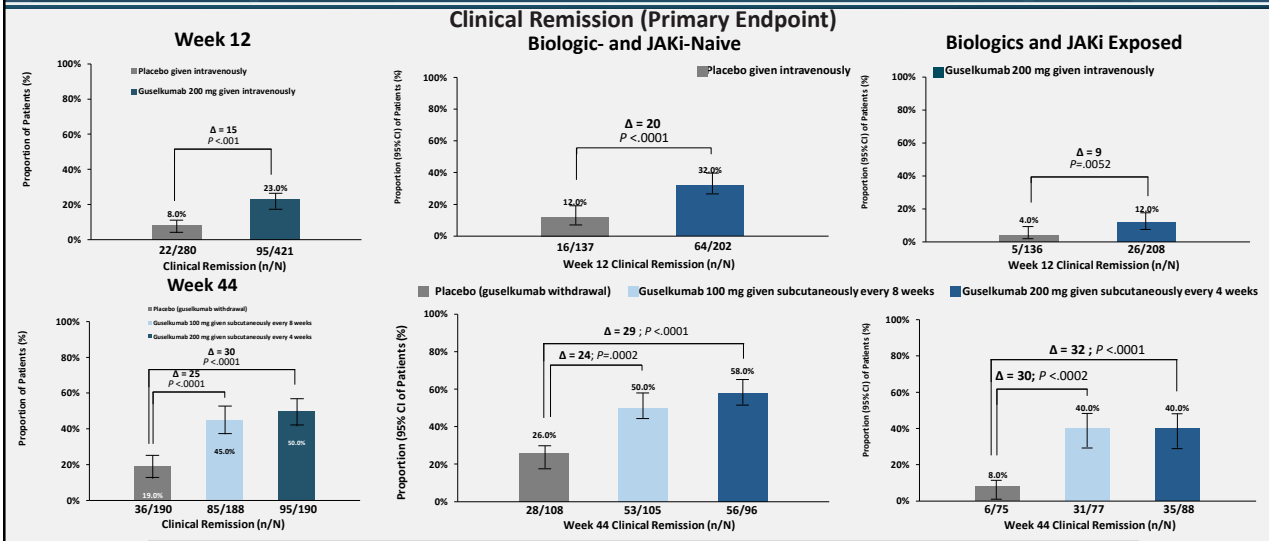
QUASAR: Guselkumab as Induction and Maintenance Therapy for Moderate-to-Severe UC



Clinical remission: SFS ≤1 and not greater than baseline, RBS=0, and ES of ≤1 (no friability)

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

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Safety Overview for Anti-IL-23s

- **Contraindications**
  - Serious hypersensitivity to the drug or its excipients
- **Infection Risk**
  - May increase risk
  - Do not initiate during active infections
  - Discontinue if serious infection develops
- **Tuberculosis (TB)**
  - Screen prior to initiation
  - Treat latent TB before starting therapy
- **Vaccinations**
  - Avoid use of live vaccines
- **Common Adverse Reactions**
  - Upper respiratory infections, headache, injection site reactions, arthralgia, tinea infections, fatigue
- **Liver Function Testing**
  - Routine monitoring (ie, liver enzymes and bilirubin) is recommended, particularly during induction and periodically thereafter
    - By week 12 risankizumab
    - By week 14 guselkumab
    - By week 24 mirikizumab

Omvoh (mirikizumab). Prescribing information. Janssen Biotech, Inc; 2023; Skyrizi (risankizumab). Prescribing information. Eli Lilly and Company; 2025; Tremfya (guselkumab). Prescribing information. Janssen Biotech, Inc; 2023.

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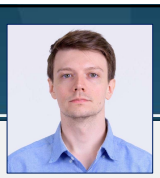
Patient Description: 33-Year-Old Male With CD Failing Anti-TNF Therapy



- **Medical history:**
  - 5-year history of CD
- **Current management:**
  - IFX 5 mg/kg every 6 weeks
  - Recent IFX level of 12 µg/mL
- **Current presentation:**
  - Worsening symptoms over the past 3 months
  - Increased abdominal pain
  - 5-lb weight loss
  - 2-3 loose stools daily
  - Fatigue
- **Laboratory findings:**
  - CRP 12 mg/L (normal <5 mg/L)
  - Fecal calprotectin 430 ug/g (normal <250 ug/g)
- **Colonoscopy results:**
  - Linear circumferential ulcers in the last 12 cm of the terminal ileum
  - Aphthous ulcerations in the cecum and ascending colon
  - SES-CD score – 9
- **Patient concerns:**
  - Increased anxiety and fatigue
  - Worsening pain

SES-CD, Simple Endoscopic Score for Crohn's Disease.

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ACG 2025 Guidelines for the Management of CD

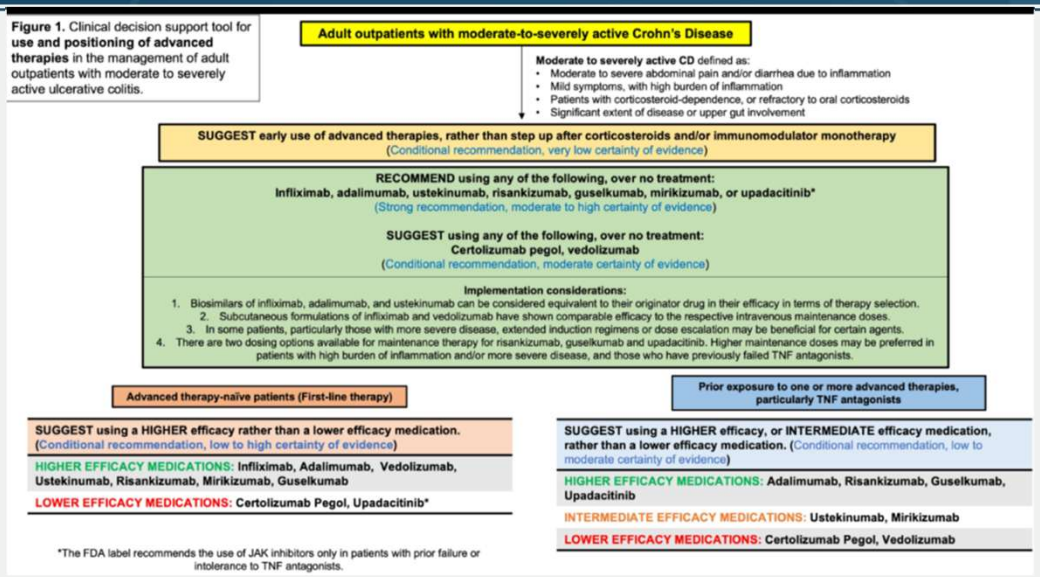
EARLY initiation of advanced therapy is KEY for optimal outcomes in CD

		Induction	Maintenance	Comments	
Mild to moderate disease	**Oral mesalamine**	⊘	⊘		Sulfasalazine should be considered only for those with symptomatic mild colonic Crohn's disease
	Ileal release budesonide	✓	⊘		
Moderate to severe	**Oral corticosteroids** (Prednisone 40 mg daily for 1-2 weeks, with subsequent tapering)	✓	⊘	Think early advanced therapy for these patients	
	Thiopurines (Azathioprine 2-2.5 mg/kg/day, Mercaptopurine 1-1.5 mg/kg/day)	⊘	✓	• TPMT testing before start • Given the adverse effect profile of thiopurine monotherapy (eg, lymphoma, skin cancer), consider newer, safer agents for maintenance	IV IFX + thiopurines >> immunomodulators or IV IFX alone in those whoa are naïve to those agents
	Methotrexate (up to 25 mg 1×/week IM/SC)	⊘	✓	• ↓ to 15 mg/wk @ 4 mo if steroid-free remission	
	Anti-TNF agents (IV infliximab; SC adalimumab; SC certolizumab pegol)	✓	✓	• SC infliximab for maintenance only • Check TB, hepatitis B testing pre-treatment	**Remember to address disease modifiers!** • NSAID use • Cigarette smoking • Management of stress, depression, and anxiety • Diet
	IV vedolizumab	✓	✓	SC vedolizumab for maintenance only	
	Anti-IL 12/23 agents (Ustekinumab)	✓	✓	• RISA>> UST for anti-TNF experienced pt • GUS → SC or IV induction • MIRI, RISA, UST → IV induction	
	Anti-IL 23 agents (Guselkumab; Mirikizumab; Risankizumab)	✓	✓		
	Upadacitinib	✓	✓	Use limited to anti-TNF-experienced patients in the US	

Lichtenstein et al. Am J Gastroenterol | ACG (2025) 120(6):p 1225-1264,

30

AGA 2025 CD Guidelines out for Comments



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Advanced Treatment Options for CD

Therapeutic Class	Therapy	Approval Year	Route of Administration
Anti-TNFα	Infliximab	1998*	IV
	Infliximab-dyyb	2016 (IV); 2023 (SC)	IV (induction); IV or SC (maintenance)
	Adalimumab	2007*	SC
	Certolizumab pegol	2008	SC
Anti-integrin α4β7	Vedolizumab	2014	IV (induction); IV or SC (maintenance)
Anti-IL-12/IL-23	Ustekinumab	2016	IV (induction); SC (maintenance)
JAK inhibitor	Upadacitinib	2023	Oral
Anti-IL-23p19	Risankizumab	2022	IV (induction); SC (maintenance)
	Mirikizumab	2025	IV (induction); SC (maintenance)
	Guselkumab	2025	SC or IV (induction); SC (maintenance)

*Subsequently approved for pediatric CD.

Cimzia (certolizumab pegol). Prescribing information. Takeda Pharmaceuticals America, Inc; 2023. Entyvio (vedolizumab). Prescribing information. Janssen Biotech, Inc; 2023. Humira (adalimumab). Prescribing information. UCB, Inc; 2024. Inflectra (infliximab-dyyb). Prescribing information. Celltrion Inc; 2023. Omvoh (mirikizumab). Prescribing information. Janssen Biotech, Inc; 2023. Remicade (infliximab). Prescribing information. AbbVie Inc; 2023. Rinvoq (upadacitinib). Prescribing information. AbbVie Inc; 2023. Skyrizi (risankizumab). Prescribing information. Eli Lilly and Company; 2025. Stelara (ustekinumab). Prescribing information. AbbVie Inc; 2023. Tremfya (guselkumab). Prescribing information. Janssen Biotech, Inc; 2023. Zymfentra (infliximab-dyyb). Prescribing information. AbbVie Inc; 2023.

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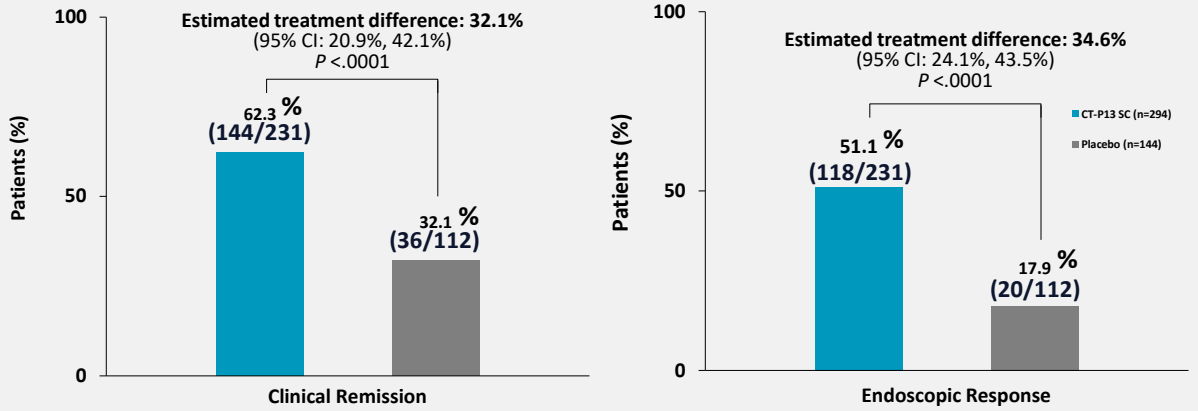
LIBERTY-CD: Subcutaneous Infliximab Maintenance Therapy for CD

Clinical Remission and Endoscopic Response at Week 54 (Co-Primary Endpoints)



Clinical remission: CDAI Score <150; Endoscopic Response (50% Reduction in SES-CD)

CDAI, Crohn's Disease Activity Index.

Hanauer SB, et al. *Gastroenterology.* 2024;167:919-933.

33

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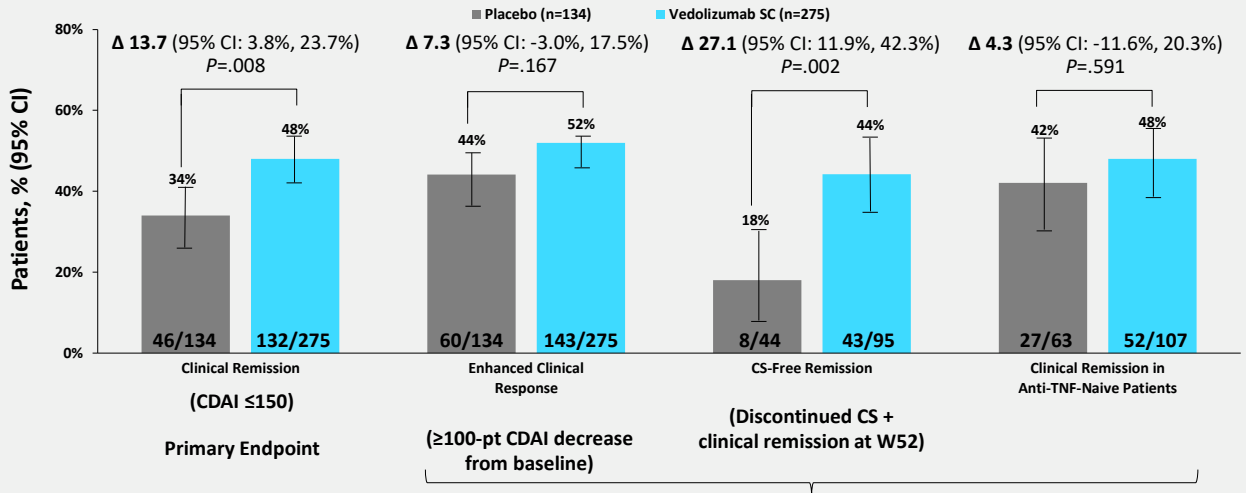
VISIBLE 2: Efficacy of Subcutaneous Vedolizumab as Maintenance Therapy for CD

Clinical Remission at Week 52 (Primary Outcome)



CS, corticosteroid.

Vermeire S, et al. *J Crohn's Colitis*. 2022;16:27-38.

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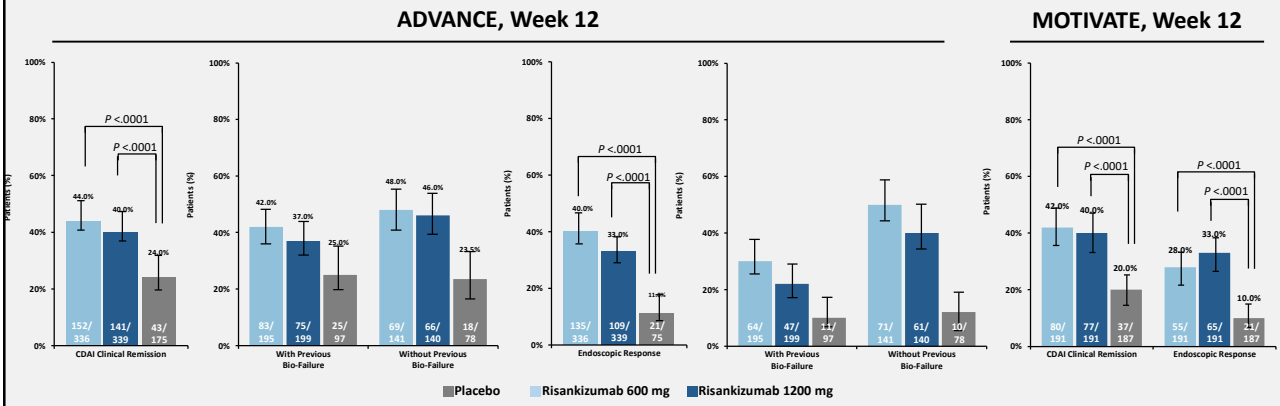
Risankizumab Efficacy for Moderately to Severely Active CD: ADVANCE and MOTIVATE Induction Trials

Clinical Remission and Endoscopic Response at Week 12 (Co-Primary Endpoints)



Clinical remission (US protocol): CDAI <150; Clinical remission (non-US protocol): SF/APS (average daily very soft/liquid SF ≤2.8 and average daily APS ≤1.0 and both not worse than baseline) or CDAI 50% from baseline (or for SES-CD of 4 at baseline, ≥2-point reduction); Endoscopic response: >50% decrease in SES-CD (or for isolated ileal disease and a baseline SES-CD of 4, ≥2-point reduction)

APS, abdominal pain score; SF, stool frequency.

D'Haens G, et al. *Lancet*. 2022;399:2015-2030;

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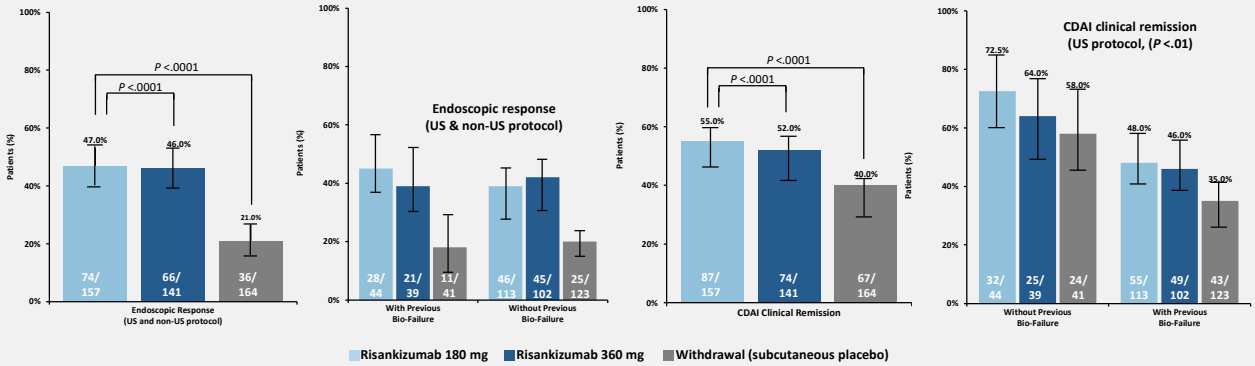
FORTIFY: Risankizumab as Maintenance Therapy For Moderately-to-Severe CD

Endoscopic Response (Primary Endpoint) and Clinical Remission

FORTIFY, Week 52



Clinical remission (US protocol): CDAI <150; Clinical remission (non-US protocol): SF/APS (average daily very soft/liquid SF ≤2.8 and average daily APS ≤1.0 and both not worse than baseline) or CDAI 50% from baseline (or for SES-CD of 4 at baseline, ≥2-point reduction); Endoscopic response: >50% decrease in SES-CD (or for isolated ileal disease and a baseline SES-CD of 4, ≥2-point reduction)

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

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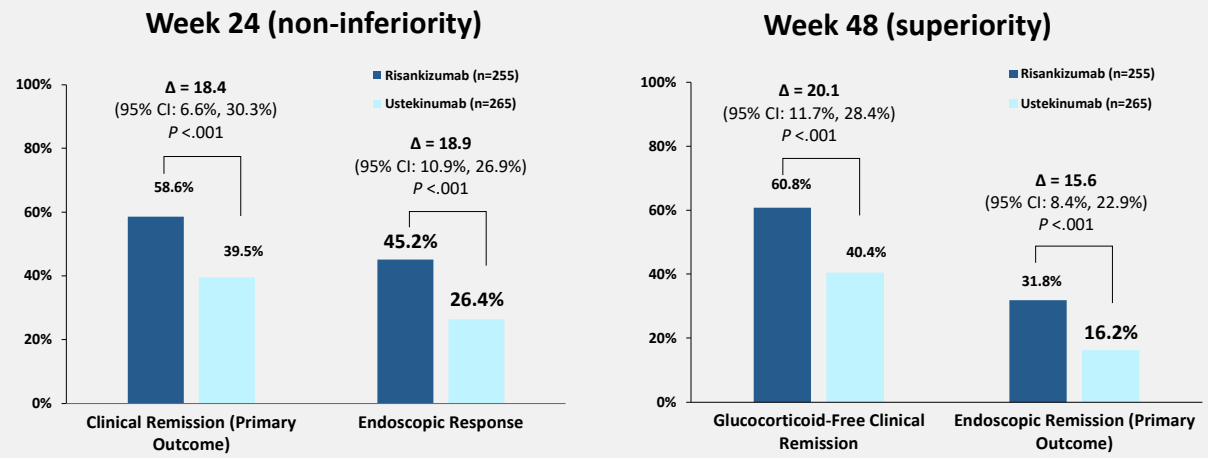
Risankizumab vs Ustekinumab for Moderate to Severe CD Exposed to Anti-TNF: SEQUENCE Head-to-Head, Open-Label Trial



Clinical remission: CDAI <150; Endoscopic remission: SES-CD of ≤4, decrease of ≥2 points from baseline, and no subscore >1 in any individual variable on the SES-CD

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

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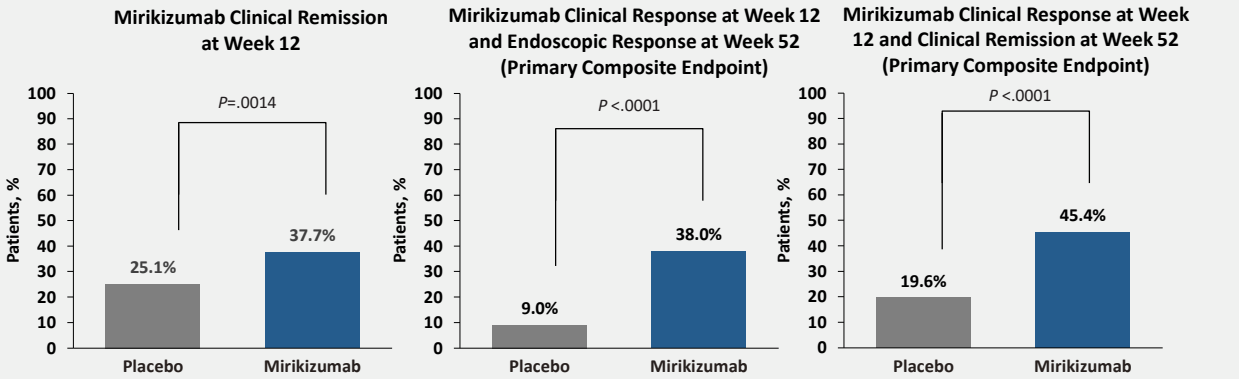
Mirikizumab Efficacy for Moderately to Severely Active CD: VIVID-1 Trial, Week 12 and Week 12 to Week 52



(N=199) Placebo IV or SC Q4W; any participant in the placebo arm who was considered a nonresponder at Week 12 received 900 mg mirikizumab IV Q4W for 3 doses, then 300 mg SC Q4W for the remainder of the study

(N=579) 900 mg mirikizumab IV Q4W for 3 doses, then 300 mg SC Q4W

Clinical remission: CDAI score <150; PRO clinical response: ≥30% decrease in SF or APS, or both, and neither score worse than baseline; Endoscopic response: ≥50% reduction from baseline in SES-CD total score

PRO, patient-reported outcome; Q4W, every 4 weeks.

ClinicalTrials.gov. Accessed April 28, 2025. https://clinicaltrials.gov/study/NCT03926130?tab=results#publications; Ferrante M, et al. *Lancet*. 2024;404:2423-2436.

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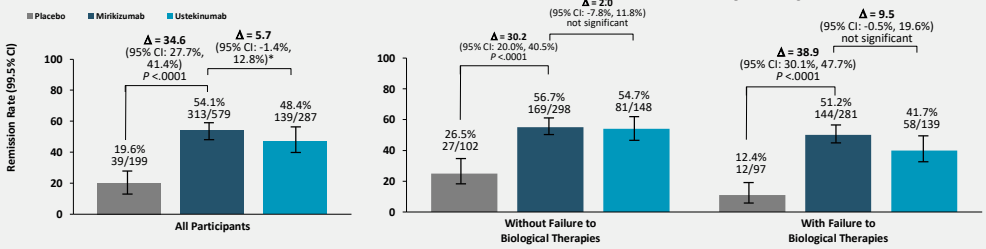
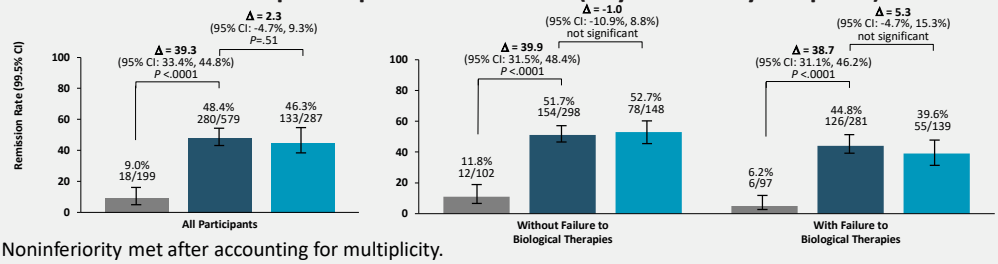
Mirikizumab Efficacy for Moderately to Severely Active CD: VIVID-1 Trial, Week 52 (Ustekinumab Comparator)

Clinical Remission At Week 52 (Key Secondary Endpoint)



Endoscopic Response At Week 52 (Key Secondary Endpoint)



CDAI clinical remission at week 52: CDAI score <150; Endoscopic response: ≥50% reduction from baseline in SES-CD total score

*Noninferiority met after accounting for multiplicity.

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

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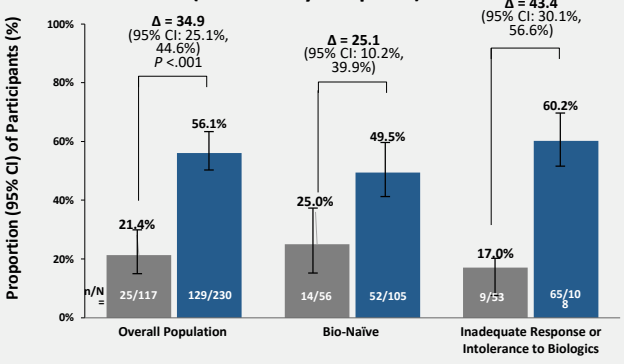
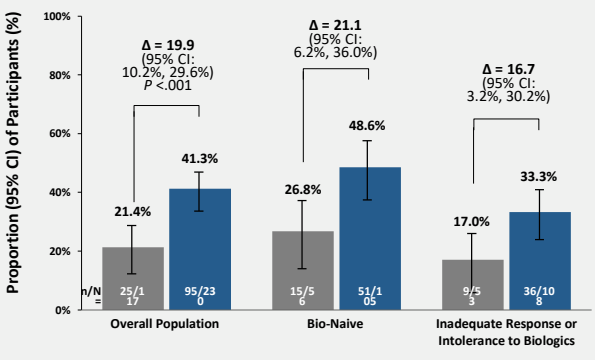
GRAVITI: Subcutaneous Guselkumab as Induction Therapy for Moderate-to-Severe CD

Clinical Remission at Week 12 (Co-Primary Endpoint)



Endoscopic Response at Week 12 (Co-Primary Endpoint)



Placebo

Guselkumab

Clinical remission: CDAI score <15
Endoscopic response: 50% improvement in SES-CD

Hart A, et al. *Gastroenterology*. 2025;18:S0016-5085(25)00522-0.

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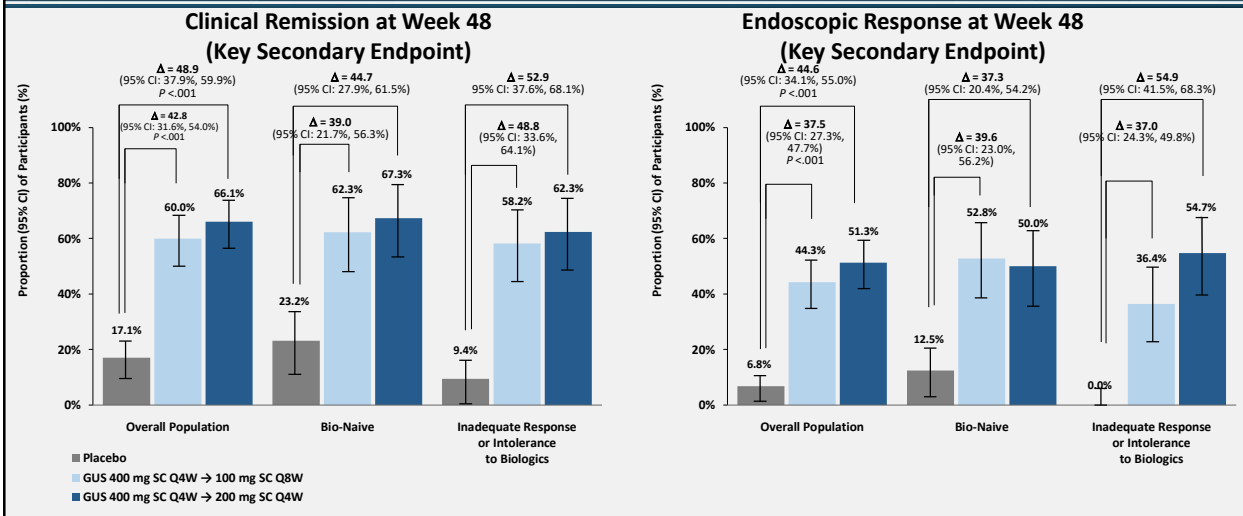
GRAVITI: Subcutaneous Guselkumab as Maintenance Therapy for Moderate-to-Severe CD



Clinical remission: CDAI <150; Endoscopic response: 50% improvement in SES-CD

Hart A, et al. *Gastroenterology*. 2025.18:S0016-5085(25)00522-0.

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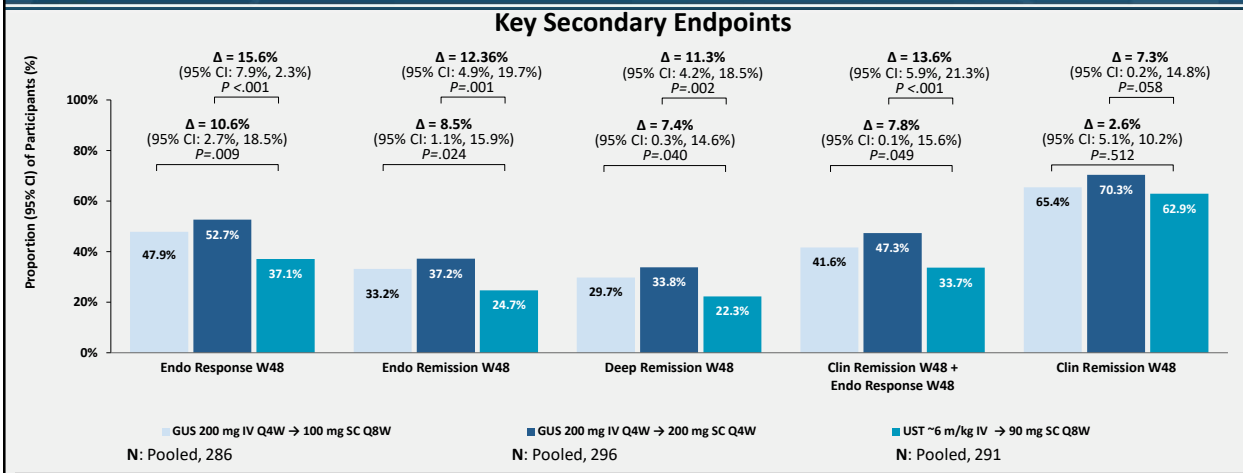
Guselkumab vs Ustekinumab (Pooled GALAXI 2 & GALAXI 3)



N: Pooled, 286 **N**: Pooled, 296 **N**: Pooled, 291

Clinical remission: CDAI <150; Endoscopic response ≥50% improvement in SES-CD or SES-CD ≤2; Endoscopic remission: SES-CD ≤4 and ≥2-point reduction and no subscore >1; Deep remission: Clinical remission AND endoscopic remission

Endo, endoscopic.

Tremfya (guselkumab). Prescribing information. Janssen Biotech, Inc; 2023.

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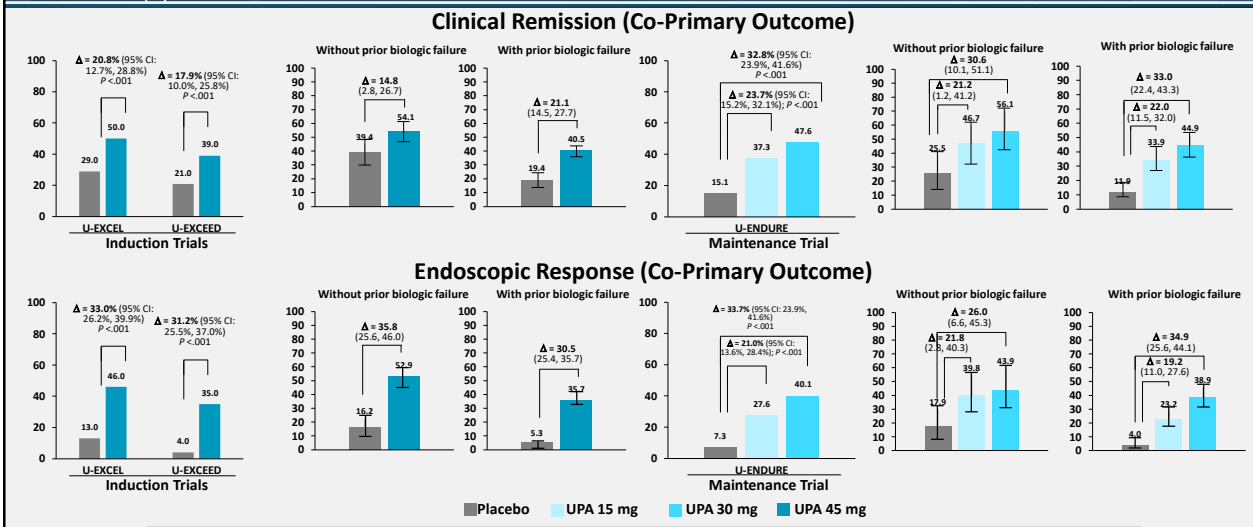
U-EXCEL, U-EXCEED, and U-ENDURE: Upadacitinib Induction and Maintenance Therapy for CD



Clinical remission: CDAI <150
Endoscopic response: SES-CD of >50% (or for patients with an SES-CD of 4 at baseline, a decrease of ≥2 points)

Loftus EV, et al. *N Engl J Med.* 2023;388(21):1966-1980; Peyrin-Biroulet L, et al. *Clin Gastroenterol Hepatol.* 2024;10:2096-2106.

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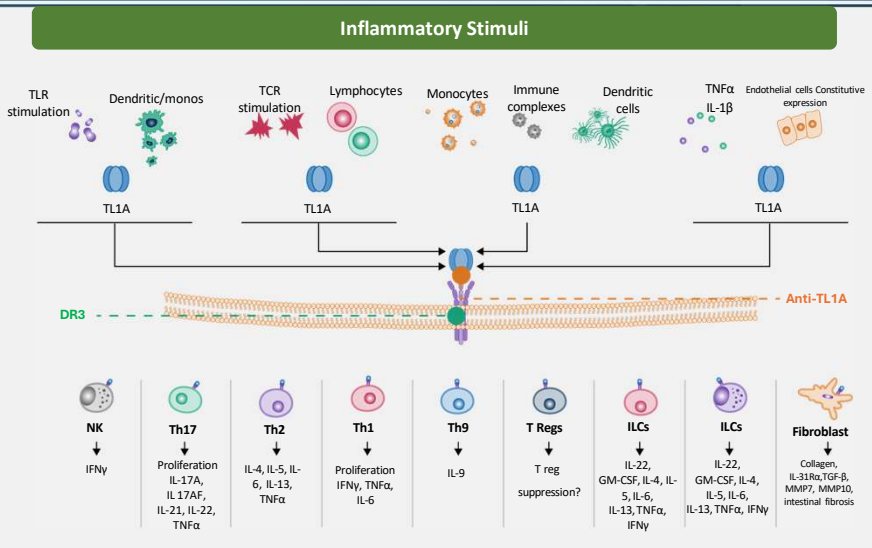
TL1A as a Therapeutic Target for IBD[1]

TL1A and its receptor, DR3, are implicated in immune pathways involved in **IBD pathogenesis and intestinal fibrosis**



1. Bamias G et al. *Gut.* 2025;74:652-668.

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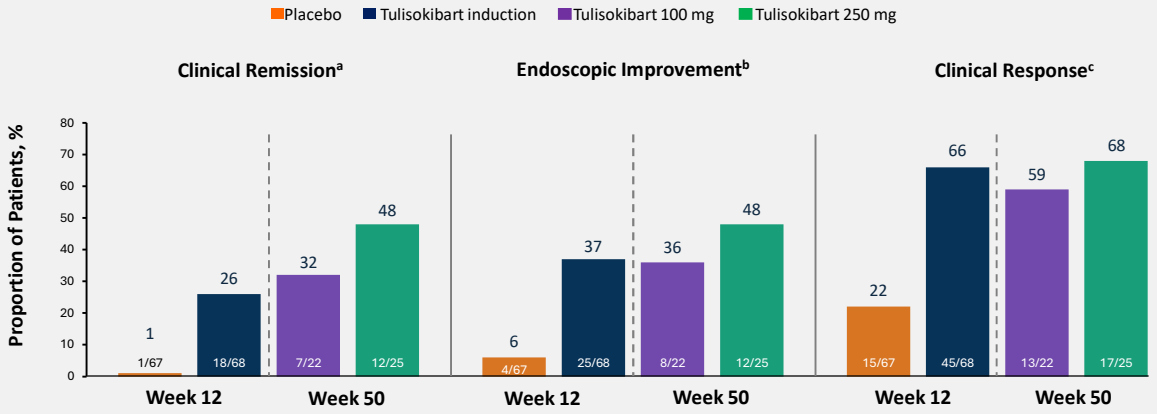
ARTEMIS-UC: Clinical Remission and Endoscopic Response Rates at Week 12 and at Week 50[1]

Primary endpoint: Clinical remission at Week 12



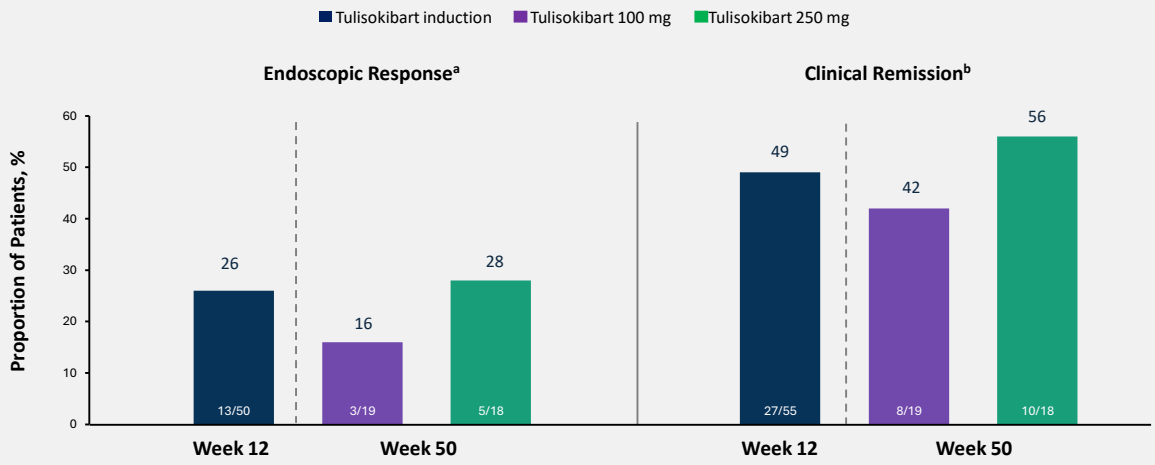
[a] Defined per mMS as endoscopic subscore of 0 or 1, RB subscore of 0, and SF subscore of 0 or 1 and not greater than baseline. [b] Defined as endoscopy subscore ≤1 with no friability. [c] Defined per mMS as reduction from baseline ≥ 2 points and ≥ 30% in mMS, accompanied by a reduction ≥1 in RB subscore or absolute RB subscore ≤1.

1. Ma C et al. UEGW 2024. Abstract OP194.

45

APOLLO-CD: Endoscopic Response and Clinical Remission With Tulisokibart at Week 12 and at Week 50[1]

- Primary endpoint: Endoscopic response at Week 12



[a] Reduction of SES-CD by ≥50% from baseline. Endpoint assessed using per-protocol analysis set (excluding patients with significant protocol deviations) at week 12 and the intention-to-treat analysis set at week 50 (12-week responders). [b] CDAI <150.

1. Siegel C et al. UEGW 2024. Abstract OP078.

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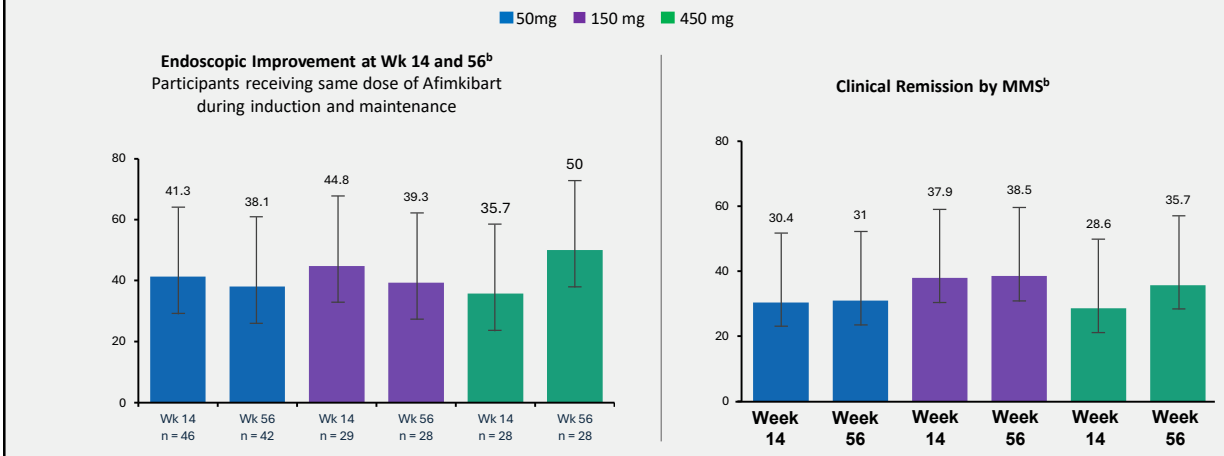
TUSCANY-2: Clinical Remission UC With Afimkibart at Week 14 and at Week 56[1]

- Primary endpoint: Clinical remission at Week 14



[a] Clinical remission by tMS defined as tMS ≤2, with no individual subscore >1. Excluding participants with missing data due to medical or operational complications resulting from COVID-19. [b] Data shown for participants receiving the same afimkibart dose during both the induction and maintenance period of the study (50 mg to 50 mg; 150 mg to 150 mg; 450 mg to 450 mg).

1. Danese S et al. UEGW 2024. Abstract OP079.

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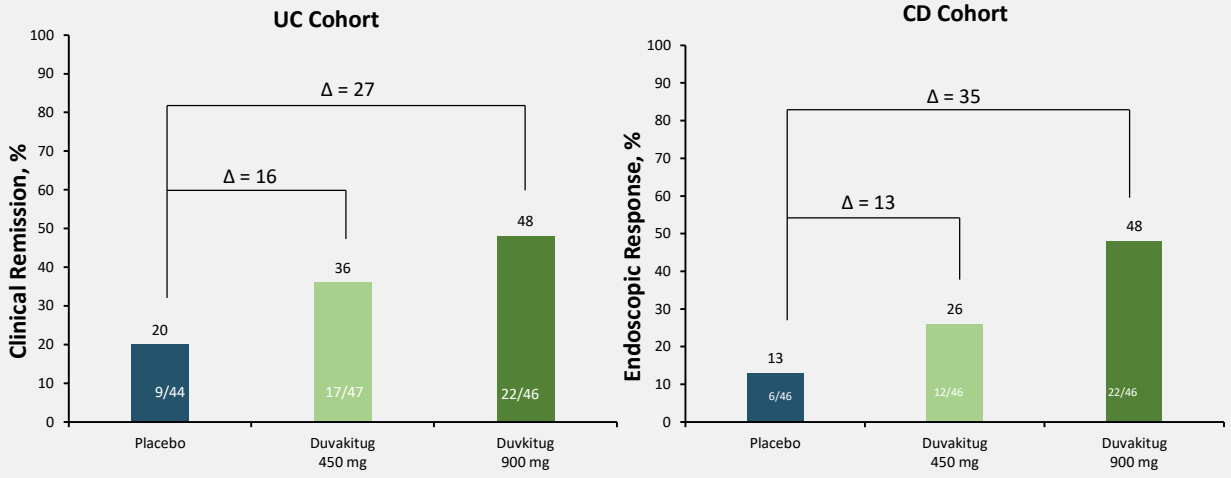
RELIEVE-UCCD: Primary Efficacy Outcomes With Duvakitug at Week 14[1,2]



1. Reinisch W et al. ECCO 2025. Presentation OP40. 2. Jairath V et al. ECCO 2025. Presentation OP41.

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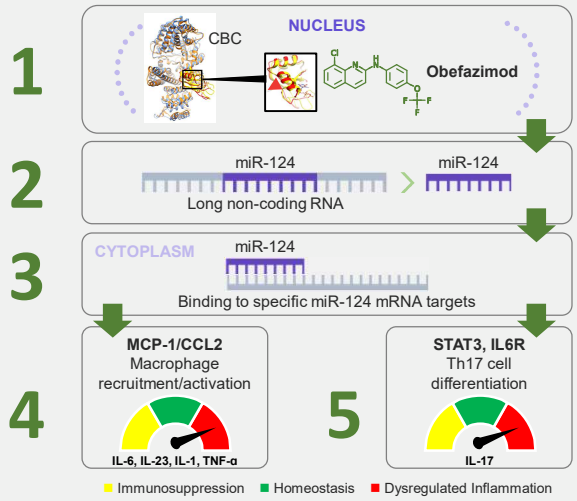
Obefazimod Enhances Expression of miR-124, Resulting in Stabilization of the Dysregulated Inflammatory Response Present in UC[1-3]



1. Obefazimod binds to CBC within the nucleus (demonstrated by cryo-electron microscopy)[a]
2. Induces selective splicing of a single, long, non-coding RNA, leading to enhanced expression of miR-124
3. miR124 binds to its specific mRNA targets in the cytoplasm, reducing translation into their respective proteins
4. Reduced translation of MCP-1/CCL2 stabilizes macrophage activation and recruitment to the gut
5. Reduced translation of STAT3 and IL-6R stabilizes Th17 differentiation and related cytokines

[a]Cryo-electron microscopy is a technique for determining protein structure. CBC, cap binding complex; CCL2, C-C motif chemokine ligand 2; IL, interleukin; MCP-1, monocyte chemoattractant protein-1; miR, microRNA; R, receptor; STAT3, signal transducer and activator of transcription 3; Th, T-helper cell; TNF, tumor necrosis factor; UC, ulcerative colitis.

1. Vermeire S, et al. *Lancet Gastroenterol Hepatol.* 2022;7(11):1024-1034. **2.** Apolit C, et al. *Clin Transl Gastroenterol.* 2023;14:e00560. **3.** Data on file. Abivax.

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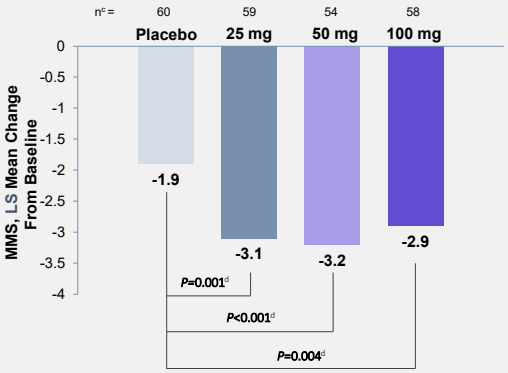
Obefazimod: Results From a Phase 2 Randomized Double-Blind Study

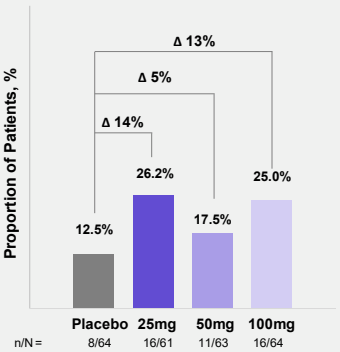
Statistically significant improvements were observed across all doses

- **49% of patients had prior advanced therapy use**
  - Among these patients, 93% had ≥2 prior advanced therapies

Change From Baseline[a] in MMS[b] at Week 8



Clinical Remission[e]



- [a]ANCOVA model for change from baseline MMS at Week 8, which includes baseline MMS as a covariate, treatment and previous exposure to biological drugs or JAK inhibitors as fixed effects, and a random error term. [b]MMS is the sum of assessment scores (0–3) of mucosal appearance on endoscopy, stool frequency, and rectal bleeding. [c]n=number of patients in the category with data available for baseline and Week 8 visit. [d]*P* values are based on nonparametric ANCOVA using ranked data. [e]Clinical remission (per MMS) is defined as SFS of ≤1, RBS of 0, and endoscopic subscore of ≤1.
- ANCOVA, analysis of covariance; JAK, Janus kinase; LS, least squares; MMS, modified Mayo score; RBC, rectal bleeding subscore; SFS, stool frequency subscore.
- Vermeire S, et al. *Lancet Gastroenterol Hepatol.* 2022;7(11):1024-1034.

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Summary of Key Points

- The treatment landscape for IBD has significantly expanded in recent years
- The emergence of personalized medicine enables clinicians to tailor therapy based on patient characteristics, prior treatment history, and personal goals
- Early advanced therapy changes the natural history of IBD
- Treatment choice matters based on prior advance therapy exposure
- An exciting pipeline with novel targets

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Questions

Marla C. Dubinsky, MD

Gary R. Lichtenstein, MD, FACG

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GI Innovation Through Collaboration
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GI
ACG GI Circle
Connect and collaborate within GI
IBD Circle
A Partnership of the American College of Gastroenterology and the Crohn's & Colitis Foundation

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