North Carolina Society of Gastroenterology
2026 Annual Meeting

Small Molecule Therapies

Edward L. Barnes, MD, MPH
Associate Professor of Medicine
Director, Gastroenterology and Hepatology Fellowship
Co-Director, Multidisciplinary Inflammatory Bowel Diseases Center
University of North Carolina at Chapel Hill

Joint Providership

ASGE
American Society for
Gastrointestinal Endoscopy

Disclosures

Consultant for: AbbVie, Boomerang, Eli Lilly, Johnson & Johnson, Pfizer, Pharmassetx, Sanofi, Takeda, and Target RWE.

Research Support from: Eli Lilly, Bausch Health/Salix.

NCSG
North Carolina Society of Gastroenterology

Objectives

As a result of this presentation, physicians/APPs will be able to:

1. **Identify the mechanism of action of small molecule therapies in inflammatory bowel disease**
2. **Discuss rationale for use of small molecule therapies in inflammatory bowel disease**
3. **Discuss strategies for identifying appropriate patients for treatment with small molecule therapies**

NCSG
North Carolina Society of Gastroenterology

Advanced Therapy Options

Class	Biologic Agents	CD	UC
TNF inhibitors	Adalimumab	✓	✓
	Certolizumab	✓	
	Golimumab		✓
	Infliximab	✓	✓
α4β7 integrin inhibitors	Natalizumab	✓	
	Vedolizumab	✓	✓
IL-12/23 inhibitor	Ustekinumab	✓	✓
IL-23 inhibitor	Risankizumab	✓	✓
	Mirikizumab	✓	✓
	Guselkumab	✓	✓
Small Molecule Agents			
S1P receptor modulator	Ozanimod		✓
	Etrasimod		✓
JAK inhibitors	Tofacitinib		✓
	Upadacitinib	✓	✓

NCSG
North Carolina Society of Gastroenterology

What Makes a Small Molecule a Small Molecule

Small Molecules	Biologics
Made by chemical synthesis in a lab	Produced from living cells
Small (under 1000 Daltons) with clear chemical structure	Large, complex proteins or antibody structures
Stable, often orally administered pills	Typically given via injection or infusion

Potential advantages of small molecules:

- Rapid onset of action
- Short half-life
- More predictable pharmacokinetics
- Lack of immunogenicity

NCSG
North Carolina Society of Gastroenterology

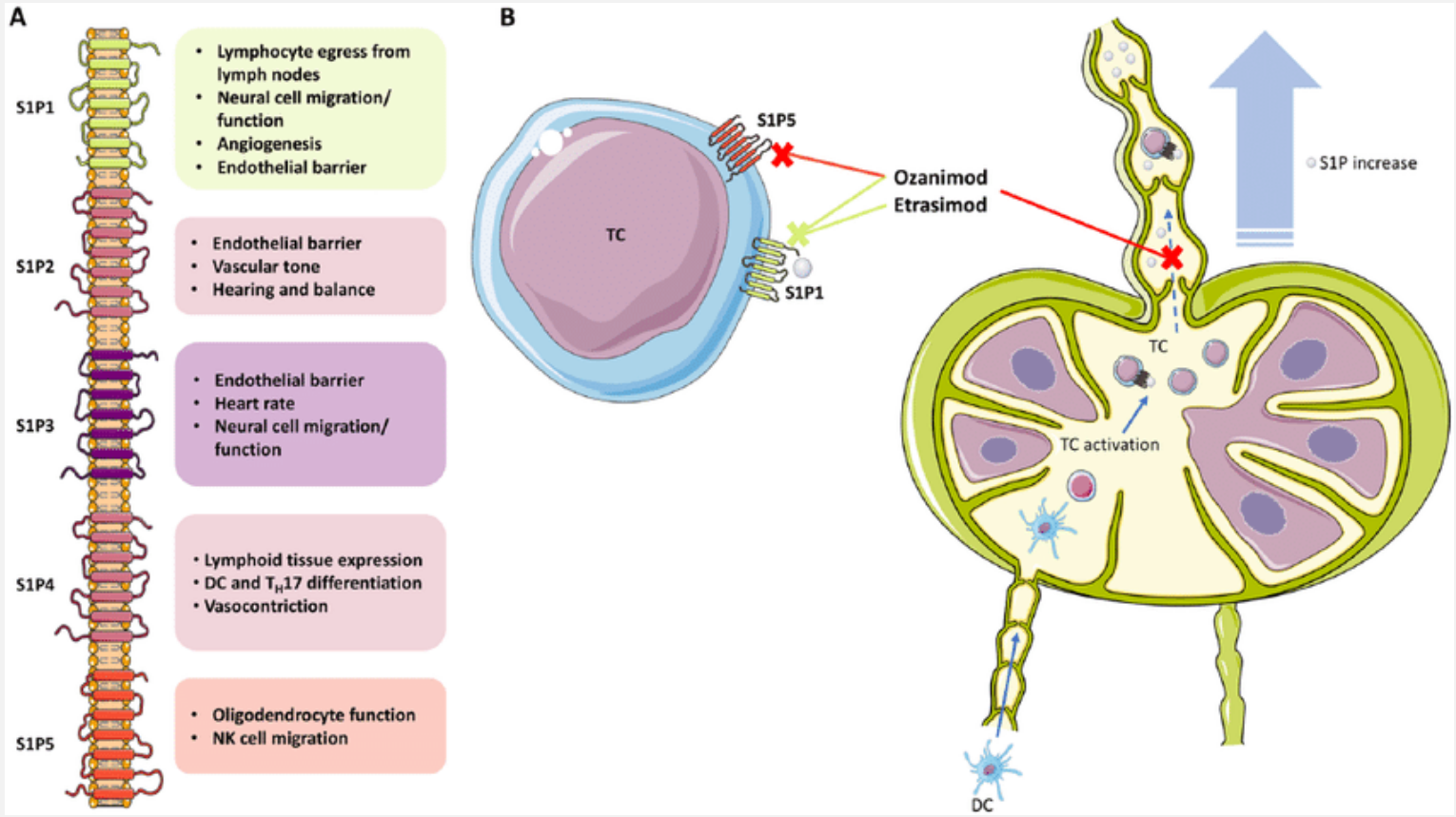
Gisbert JP and Chaparro M. Inflamm Bowel Dis. 2026, in press.

Sphingosine-1-Phosphate Receptor Modulators

In patients with IBD, there are higher levels of S1P in the inflamed gut

Interaction between S1P and S1PR promotes the egress of activated T-cells from lymph nodes following the S1P gradient

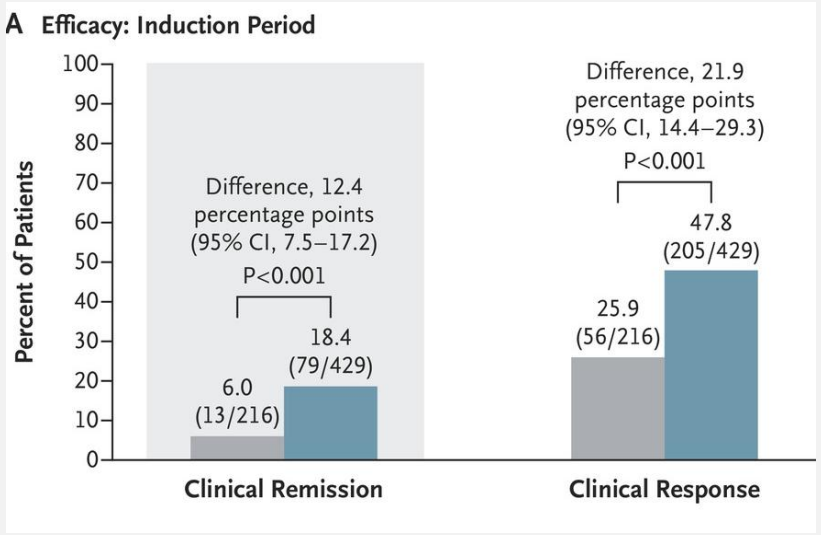
S1P1 receptor agonists block the migration of lymphocytes from lymphoid organs to sites of inflammation

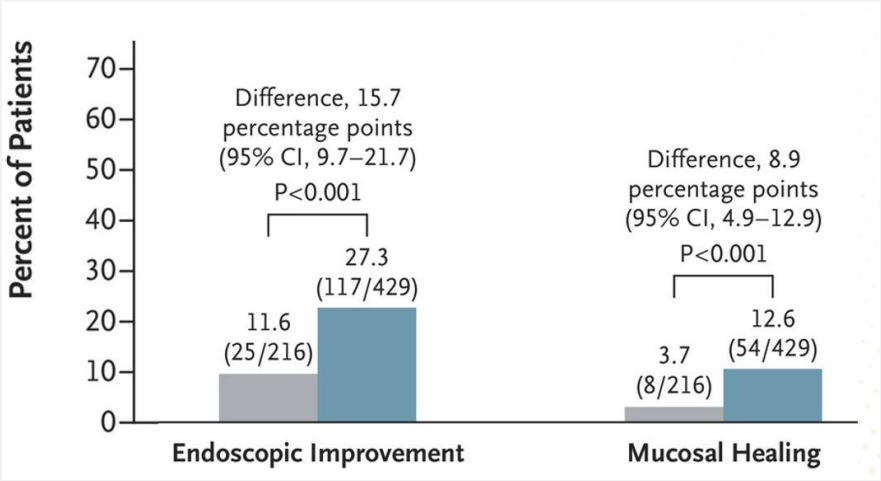


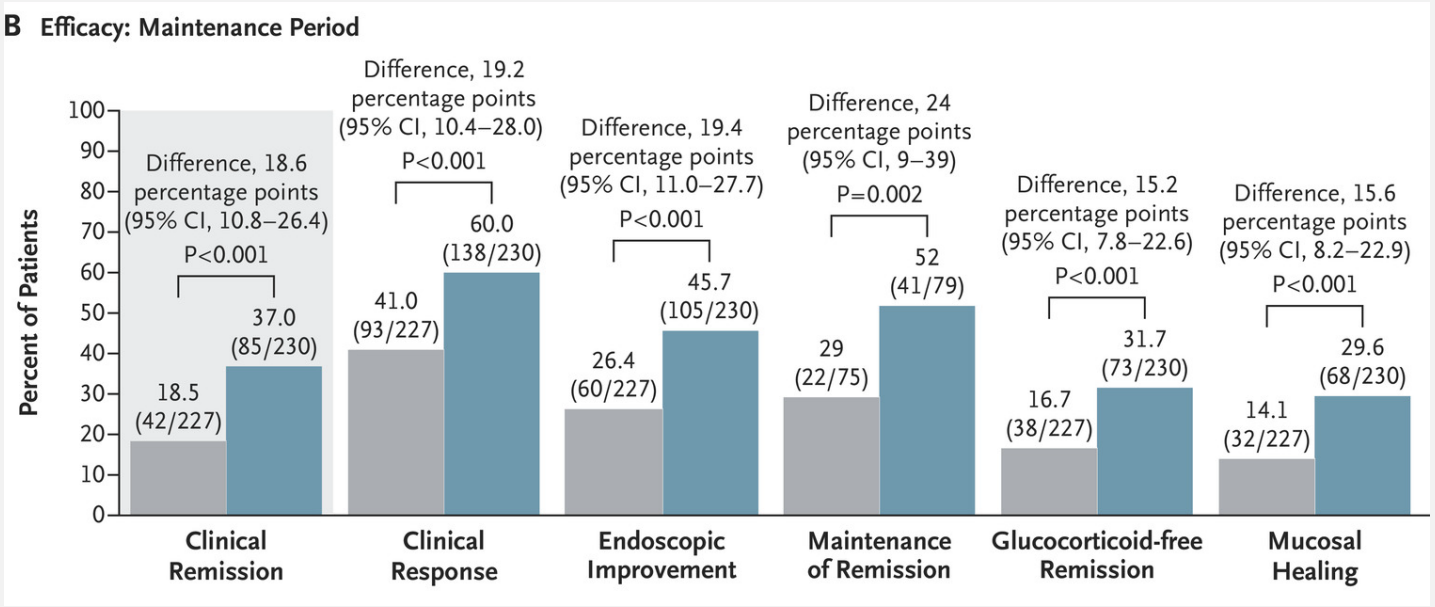
NCSG
North Carolina Society of Gastroenterology

Grossberg LB, et al. Aliment Pharmacol Ther. 2022;55(7):789-804.
Sabino J, et al. Therap Adv Gastroenterol. 2019;12:1756284819853208.

Ozanimod: True North



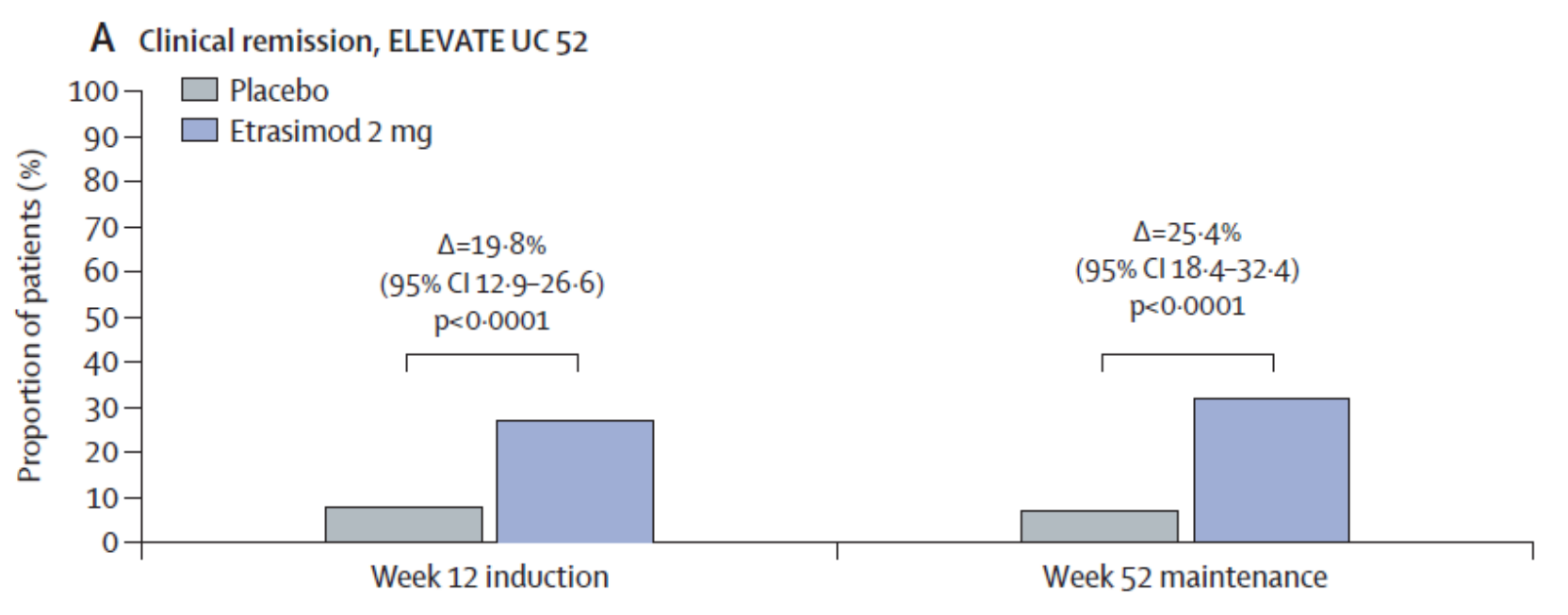


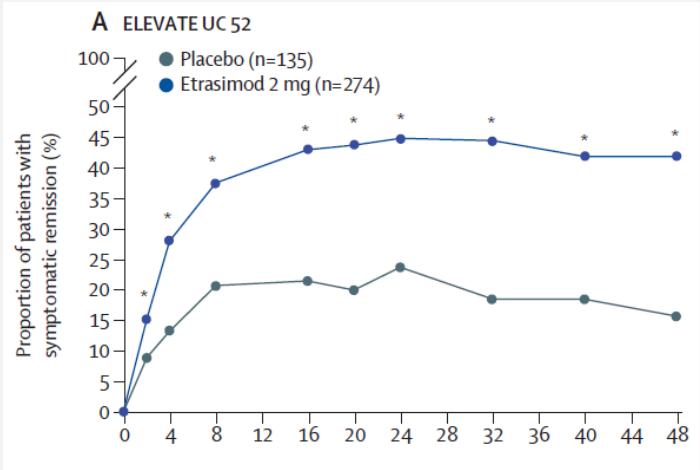


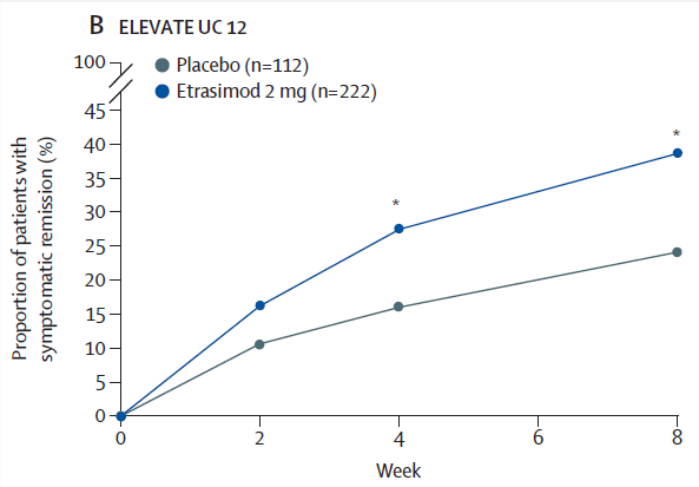
NCSG
North Carolina Society of Gastroenterology

Sandborn WJ, et al. NEJM. 2021;385(14):1280-1291.

Etrasimod: ELEVATE UC 52



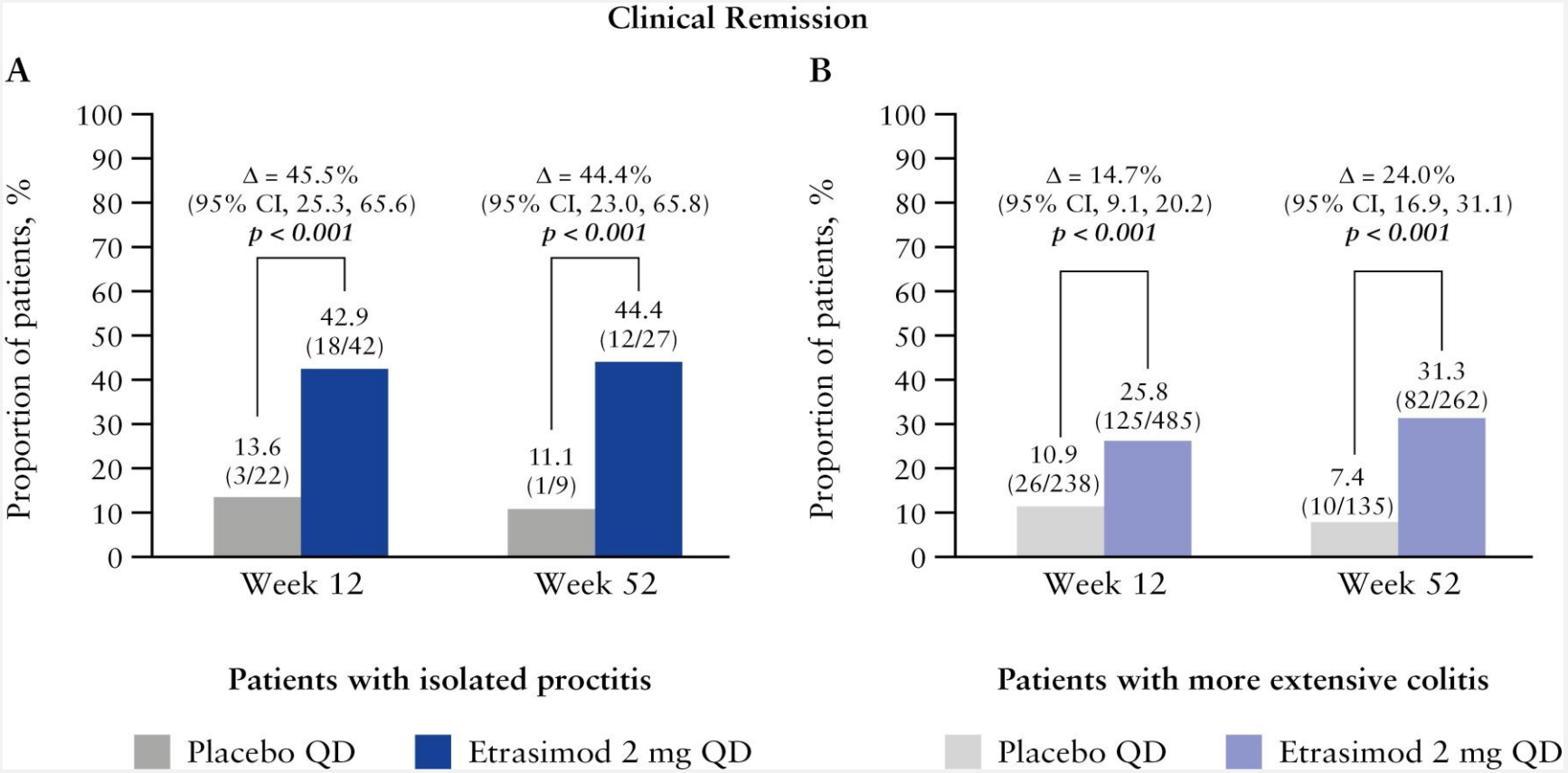




NCSG
North Carolina Society of Gastroenterology

Sandborn WJ, et al. Lancet. 2023;401(10383):1159-1171.

Etrasimod: Isolated Proctitis



NCSG
North Carolina Society of Gastroenterology

Peyrin-Biroulet L, et al. J Crohns Colitis. 2024;18:1270-1282.

Etrasimod: Safety

Adverse reactions in ELEVATE UC 52

Adverse reaction	Etrasimod 2 mg once daily (% of patients, N=289)	Placebo (% of patients, N=144)
Headache	9	5
Elevated liver tests	6	5
Dizziness	5	2
Arthralgia	4	2
Hypertension	3	1
Urinary tract infection	3	2
Nausea	3	1
Hypercholesterolemia	3	0
Herpes viral infection	2	1
Bradycardia	Day 1 = 1% Day 2 = 0.3%	Day 1 = 0% Day 2 = 0%
AV block	0.7	0

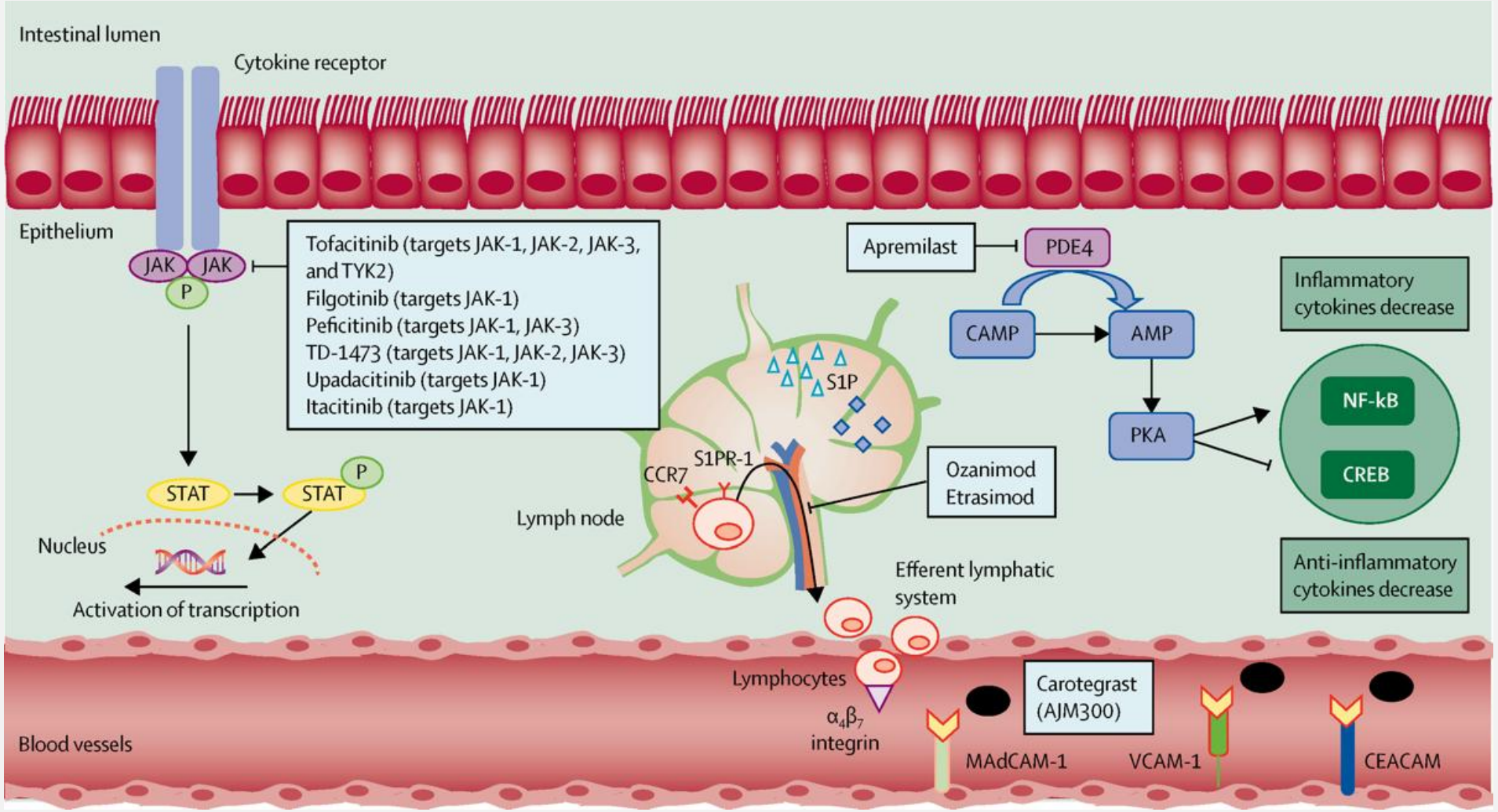
Adverse reactions in ELEVATE UC 12

Adverse reaction	Etrasimod 2 mg once daily (% of patients, N=288)	Placebo (% of patients, N=170)
Headache	6	4
Elevated liver tests	5	<1
Nausea	4	2
Bradycardia	3	0
Urinary tract infection	3	0
Bradycardia	Day 1 = 2.9% Day 2 = 0.3%	Day 1 = 0% Day 2 = 0%
AV block	0.8	0

NCSG
North Carolina Society of Gastroenterology

FDA. Accessed March 12, 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216956s000lbl.pdf.

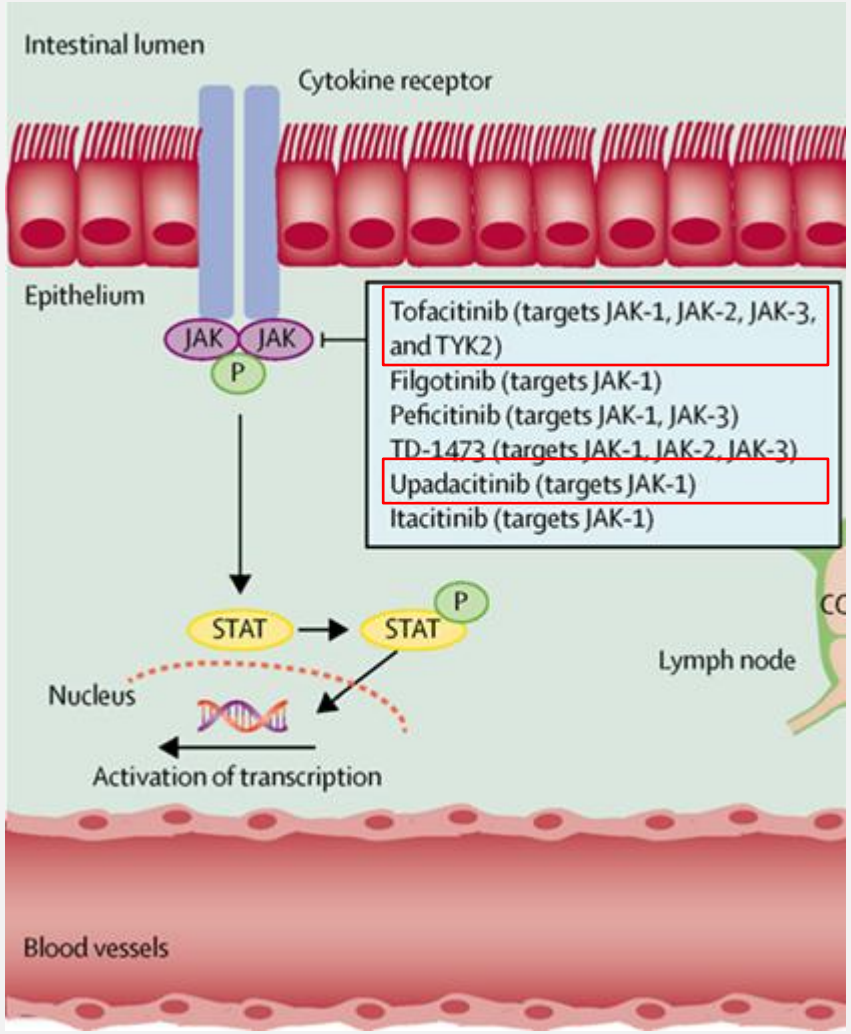
Overview of Jak Inhibitors



NCSG
North Carolina Society of Gastroenterology

Shivaji UN, et al. Lancet Gastroenterol Hepatol. 2020;5(9):850-861.

Overview of Jak Inhibitors

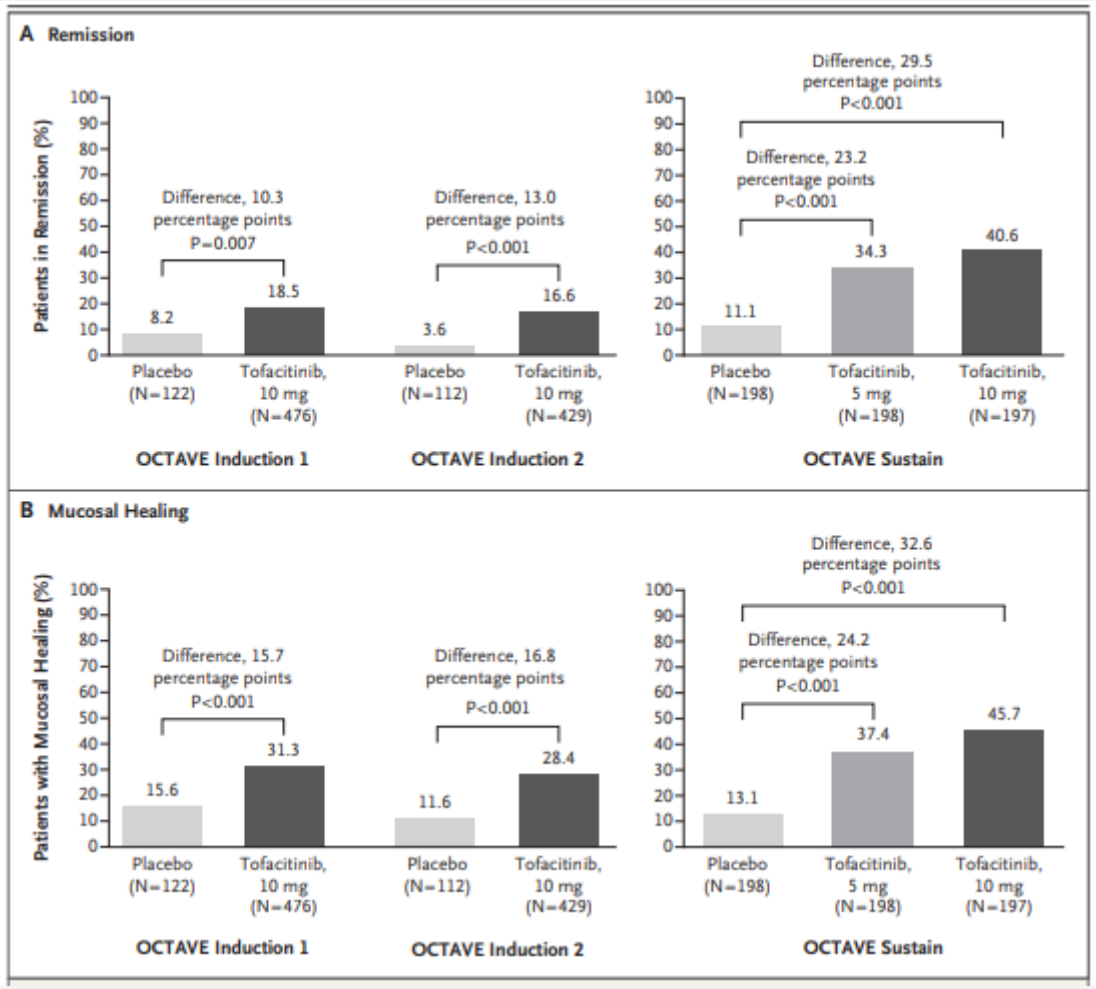


NCSG
North Carolina Society of Gastroenterology

Shivaji UN, et al. Lancet Gastroenterol Hepatol. 2020;5(9):850-861

JAK INHIBITORS ULCERATIVE COLITIS

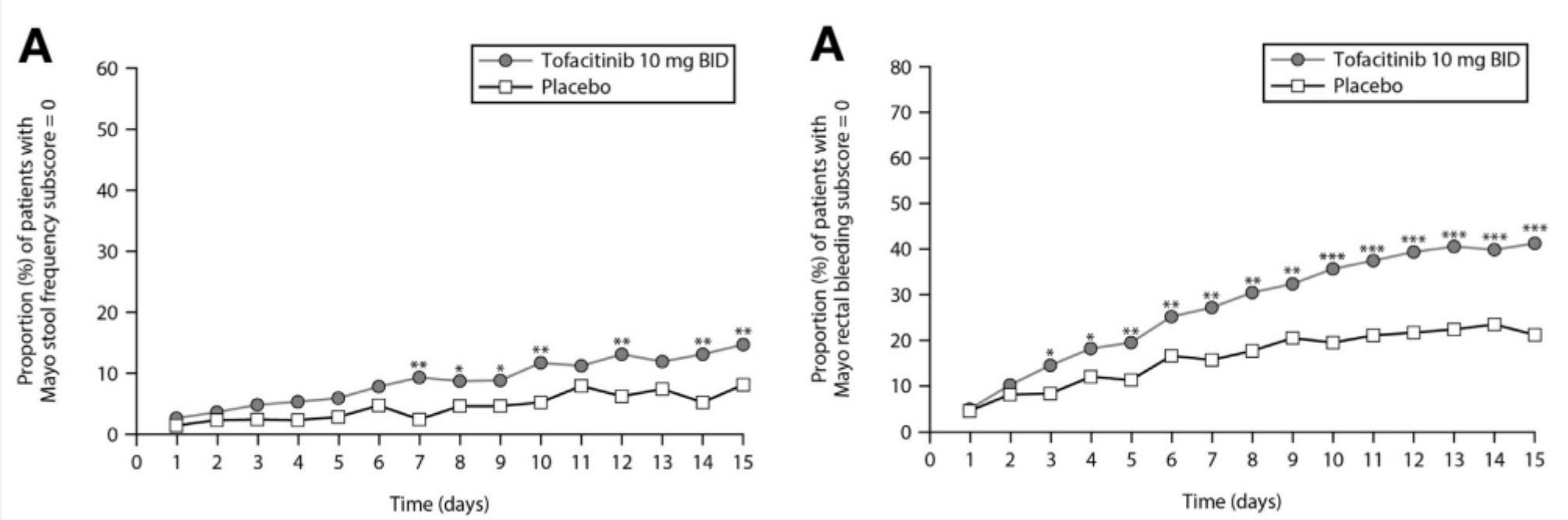
Tofacitinib in Ulcerative Colitis



NCSG
North Carolina Society of Gastroenterology

Sandborn WJ, et al. NEJM. 2017;376:1723-1736.

Tofacitinib in Ulcerative Colitis



NCSG
North Carolina Society of Gastroenterology

Hanauer S, et al. Clin Gastroenterol Hepatol. 2019;17:139-147.

Upadacitinib in Ulcerative Colitis: Induction

	UC1				UC2			
	Placebo (n=154)	Upadacitinib 45 mg once daily (N=319)	Adjusted treatment difference, % (95% CI)	p value	Placebo (N=174)	Upadacitinib 45 mg once daily (N=341)	Adjusted treatment difference, % (95% CI)	p value
Primary endpoint								
Clinical remission (Adapted Mayo)	7 (5%)	83 (26%)	21·6% (15·8–27·4)	<0·0001	7 (4%)	114 (33%)	29·0% (23·2–34·7)	<0·0001
Secondary endpoints								
Endoscopic improvement	11 (7%)	116 (36%)	29·3% (22·6–35·9)	<0·0001	14 (8%)	150 (44%)	35·1% (28·6–41·6)	<0·0001
Endoscopic remission	2 (1%)	44 (14%)	12·7% (8·4–17·0)	<0·0001	3 (2%)	62 (18%)	15·9% (11·4–20·3)	<0·0001
Clinical response (Adapted Mayo)	42 (27%)	232 (73%)	46·3% (38·4–54·2)	<0·0001	44 (25%)	254 (74%)	49·4% (41·7–57·1)	<0·0001
Clinical response (Partial Adapted Mayo) at week 2	42 (27%)	192 (60%)	33·3% (24·8–41·8)	<0·0001	45 (26%)	216 (63%)	37·0% (28·8–45·1)	<0·0001

Clinical remission: 22% and 29% adjusted treatment difference

Endoscopic remission: 13% and 16% adjusted treatment difference

Clinical response: 46% and 49% adjusted treatment difference

NCSG
North Carolina Society of Gastroenterology

Danese S, et al. Lancet 2022; 399: 2113–28

Upadacitinib in Ulcerative Colitis: Maintenance

	Placebo (N=149)	Upadacitinib 15 mg once daily (N=148)	Adjusted treatment difference, % (95% CI)	p value	Upadacitinib 30 mg once daily (N=154)	Adjusted treatment difference, % (95% CI)	p value
Primary endpoint							
Clinical remission (Adapted Mayo)	18 (12%)	63 (42%)	30·7% (21·7–39·8)	<0·0001	80 (52%)	39·0% (29·7–48·2)	<0·0001
Secondary endpoint							
Endoscopic improvement	22 (14%)	72 (49%)	34·4% (25·1–43·7)	<0·0001	95 (62%)	46·3% (36·7–55·8)	<0·0001
Maintenance of clinical remission (Adapted Mayo)	12/54 (22%)	28/47 (59%)	37·4% (20·3–54·6)	<0·0001	40/58 (70%)	47·0% (30·7–63·3)	<0·0001
Corticosteroid-free clinical remission	12/54 (22%)	27/47 (57%)	35·4% (18·2–52·7)	<0·0001	39/58 (68%)	45·1% (28·7–61·6)	<0·0001

Clinical remission:

15mg adjusted treatment difference: 31%

30 mg adjusted treatment difference: 39%

Endoscopic remission:

15mg adjusted treatment difference: 31%

30 mg adjusted treatment difference: 39%

Clinical response:

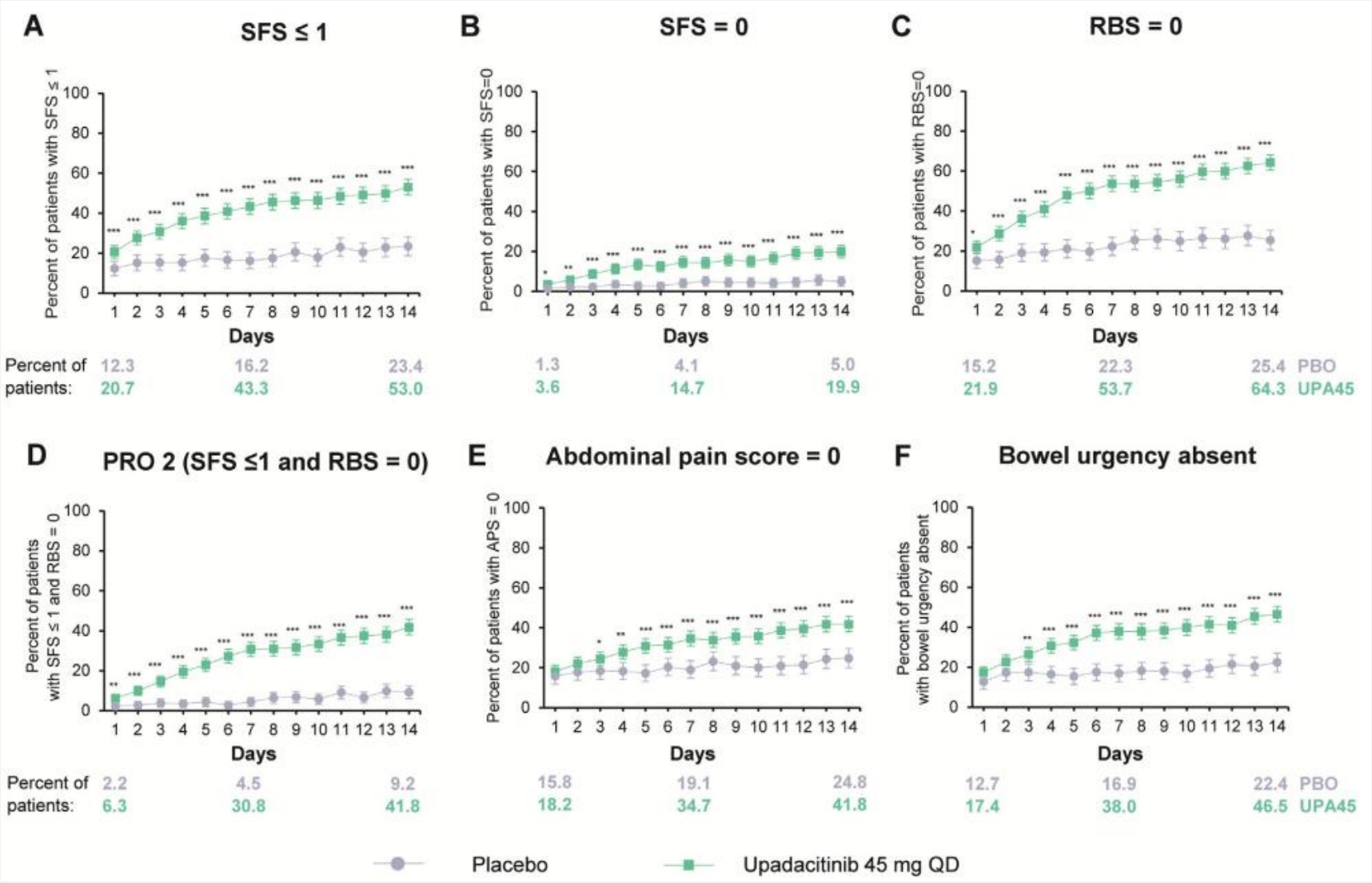
15mg adjusted treatment difference: 31%

30 mg adjusted treatment difference: 39%

NCSG
North Carolina Society of Gastroenterology

Danese S, et al. Lancet 2022; 399: 2113–28

Upadacitinib in Ulcerative Colitis



NCSG
North Carolina Society of Gastroenterology

Loftus E, et al. Clin Gastroenterol Hepatol. 2023;21:2347-2358.

Tofacitinib in Acute Severe Ulcerative Colitis (TACOS)

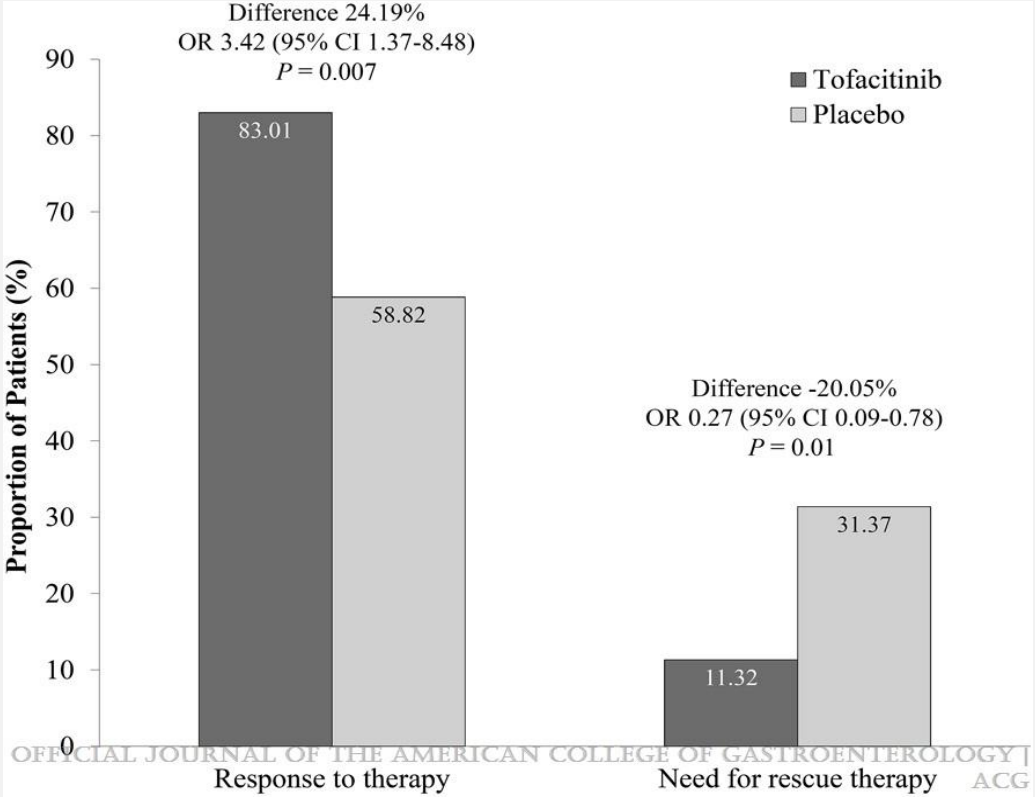
Single-center, double-blind, randomized placebo-controlled trial

Tofacitinib 10 mg po tid vs. placebo

All patients received IV corticosteroids

Primary endpoint was response by day 7

Key secondary outcome was cumulative probability of requiring infliximab or undergoing colectomy within 90 days of randomization



NCSG
North Carolina Society of Gastroenterology

Singh A, et al. Am J Gastroenterol. 202419(7):1365-1372.

Upadacitinib in Acute Severe Ulcerative Colitis

Characteristic or Outcome	Overall (n=25)	Anti-TNF Naïve (n=9)	Anti-TNF exposed (n=16)
Inpatient upadacitinib dose			
30 mg twice daily	18/25 (72%)	7/9 (78%)	11/16 (69%)
45 mg once daily	7/25 (28%)	2/8 (22%)	5/16 (31%)
Patients with follow-up fecal calprotectin <250 mg/kg	12/15 (80%)	6/7 (86%)	6/8 (75%)
Corticosteroid-free clinical remission	15/18 (83%)	6/7 (86%)	9/11 (82%)
90-day colectomy rate	6/25 (24%)	2/9 (22%)	4/16 (25%)
Index admission	4/25 (16%)	2/9 (22%)	2/16 (13%)
Post-discharge	2/25 (8%)	0	2/16 (13%)
Successful upadacitinib dose reduction to 30 mg daily	16/19 (84%)	7/7 (100%)	9/12 (75)
Venous thromboembolic event	1/25 (4%)	1/9 (11%)	0

6 patients with missing fecal calprotectin data, 1 patient with missing corticosteroid-free clinical remission; calprotectin and corticosteroid-free remission data in follow up not calculated among patients who underwent colectomy within 90 days

Berinstein J, et al. Am J Gastroenterol. 2024; 119:1421-1425.

JAK INHIBITORS
CROHN'S DISEASE

Upadacitinib Induction Crohn's Disease

45.4% had previous failure of biologic therapy

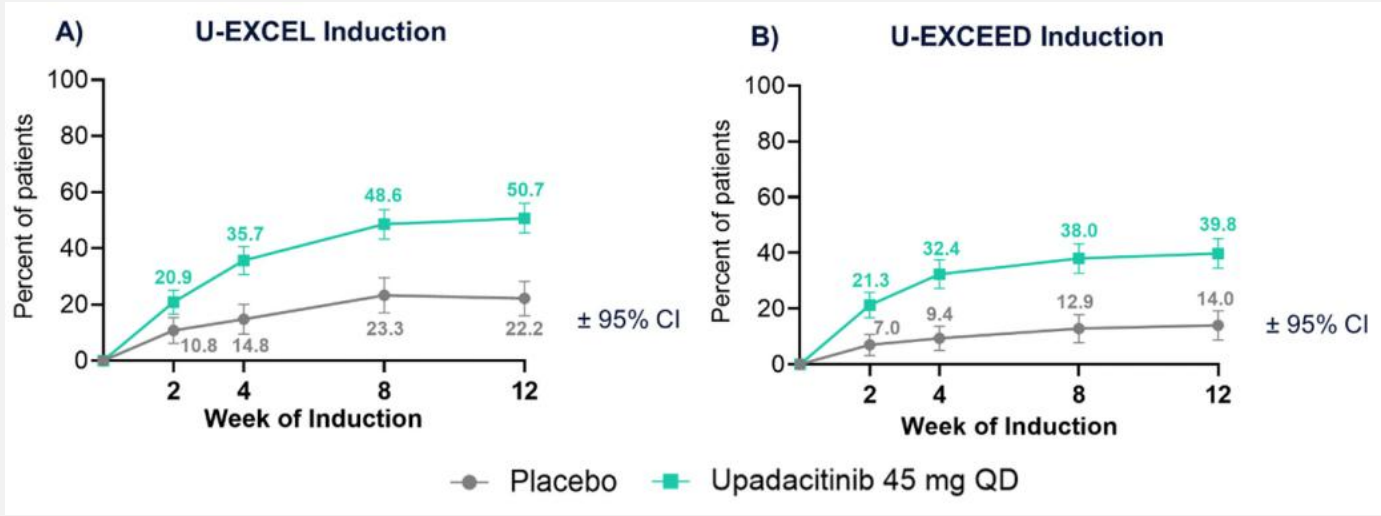
- U-EXCEED all were experienced
- U-ENDURE (maintenance) 75.1% bio-exposed

High rates of endoscopic response

- 45.5% vs 13.1% for U-EXCEL
- 34.6% vs 3.5% for U-EXCEED

Table 2. Primary and Key Secondary End Points under Multiplicity Control for Upadacitinib as Induction Therapy, According to FDA Requirements.*

End Point	U-EXCEL Induction Trial (12 wk)			U-EXCEED Induction Trial (12 wk)		
	Placebo (N=176)	Upadacitinib, 45 mg (N=350)	Adjusted Difference; P Value†	Placebo (N=171)	Upadacitinib, 45 mg (N=324)	Adjusted Difference; P Value†
Primary end points — % (95% CI)						
CDAI clinical remission‡	29.1 (22.4 to 35.8)	49.5 (44.2 to 54.8)	20.8 (12.7 to 28.8); P<0.001	21.1 (14.9 to 27.2)	38.9 (33.6 to 44.2)	17.9 (10.0 to 25.8); P<0.001
Endoscopic response§	13.1 (8.1 to 18.0)	45.5 (40.3 to 50.8)	33.0 (26.2 to 39.9); P<0.001	3.5 (0.8 to 6.3)	34.6 (29.4 to 39.8)	31.2 (25.5 to 37.0); P<0.001
Ranked secondary end points						
SF–APS clinical remission at wk 12 — % (95% CI)¶	22.2 (16.0 to 28.3)	50.7 (45.5 to 56.0)	28.7 (20.9 to 36.4); P<0.001	14.0 (8.8 to 19.2)	39.8 (34.5 to 45.1)	25.9 (18.7 to 33.1); P<0.001
Endoscopic remission at wk 12 — % (95% CI)‖	7.4 (3.5 to 11.3)	28.9 (24.2 to 33.7)	21.8 (15.8 to 27.8); P<0.001	2.3 (0.1 to 4.6)	19.1 (14.9 to 23.4)	16.8 (12.0 to 21.6); P<0.001
Glucocorticoid-free CDAI clinical remission at wk 12**						
No. of patients evaluated	64	126	—	60	108	—
Percent (95% CI)	15.7 (6.8 to 24.7)	42.9 (34.2 to 51.5)	27.7 (15.7 to 39.8); P<0.001	11.7 (3.5 to 19.8)	34.3 (25.3 to 43.2)	22.5 (11.1 to 34.0); P<0.001



NCSG
North Carolina Society of Gastroenterology

Loftus E, et al. N Engl J Med. 2023;388:1966.

Upadacitinib Maintenance Crohn's Disease

Table 3. Primary and Secondary End Points under Multiplicity Control for Upadacitinib as Maintenance Therapy, According to FDA Requirements.*

End Point, Wk 52	Placebo (N=165)	Upadacitinib, 15 mg (N=169)	Adjusted Difference vs. Placebo; P Value†‡	Upadacitinib, 30 mg (N=168)	Adjusted Difference vs. Placebo; P Value†‡
Primary end points — % (95% CI)					
CDAI clinical remission‡	15.1 (9.6 to 20.6)	37.3 (30.0 to 44.6)	23.7 (15.2 to 32.1); P<0.001	47.6 (40.1 to 55.2)	32.8 (23.9 to 41.6); P<0.001
Endoscopic response§	7.3 (3.3 to 11.2)	27.6 (20.8 to 34.4)	21.0 (13.6 to 28.4); P<0.001	40.1 (32.7 to 47.6)	33.7 (26.0 to 41.3); P<0.001
Ranked secondary end points¶					
SF–APS clinical remission — % (95% CI)‖	14.4 (9.0 to 19.8)	35.5 (28.3 to 42.7)	21.9 (13.7 to 30.0); P<0.001	46.4 (38.9 to 54.0)	31.8 (23.2 to 40.3); P<0.001
Clinical response — % (95% CI)**	15.2 (9.7 to 20.6)	41.4 (34.0 to 48.8)	27.1 (18.3 to 35.8); P<0.001	51.2 (43.6 to 58.7)	36.4 (27.5 to 45.2); P<0.001
Endoscopic remission — % (95% CI)††	5.5 (2.0 to 9.0)	19.1 (13.1 to 25.0)	14.4 (7.7 to 21.0); P<0.001	28.6 (21.8 to 35.5)	23.6 (16.1 to 31.0); P<0.001
Glucocorticoid-free CDAI clinical remission among all patients — % (95% CI)‡‡	14.5 (9.1 to 19.9)	36.7 (29.4 to 44.0)	23.8 (15.5 to 32.1); P<0.001	46.4 (38.9 to 54.0)	32.2 (23.4 to 40.9); P<0.001
Deep remission — % (95% CI)§§	3.7 (0.8 to 6.5)	14.8 (9.5 to 20.2)	12.2 (6.3 to 18.1); P<0.001	23.2 (16.8 to 29.6)	19.8 (13.0 to 26.6); P<0.001

Clinical remission: 24% (15mg) and 33% (30mg) adjusted treatment difference

Endoscopic response: 21% and 34% adjusted treatment difference

Clinical response: 27% and 36% adjusted treatment difference

Endoscopic remission: 14% and 24% adjusted treatment difference

NCSG
North Carolina Society of Gastroenterology

Loftus E, et al. N Engl J Med. 2023;388:1966.

Upadacitinib in Perianal Crohn's Disease

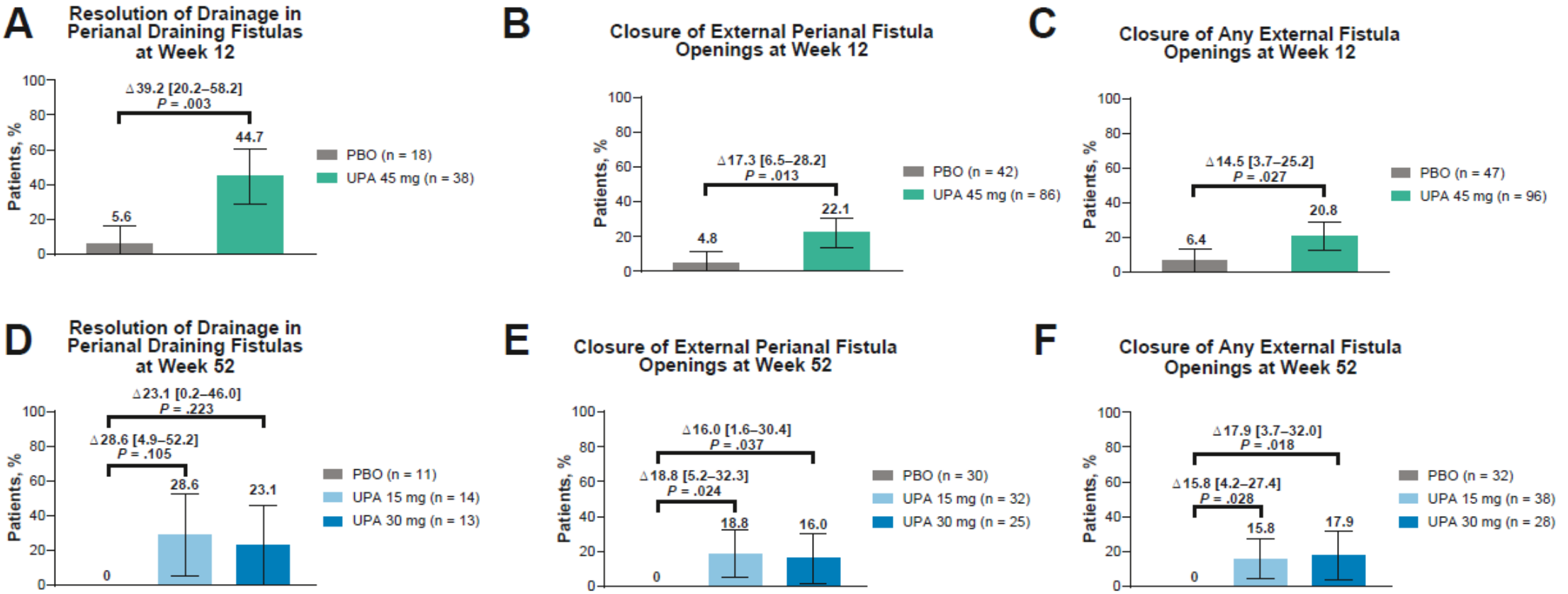


Figure 1. Resolution of drainage in perianal draining fistulas, closure of external perianal fistula openings, and closure of external openings for any fistula at week 12 of the induction trials and week 52 of the maintenance trial. Error bars represent 95% CI. Δ indicates percent difference (95% CI) vs placebo (PBO). CI, confidence intervals; UPA, upadacitinib.

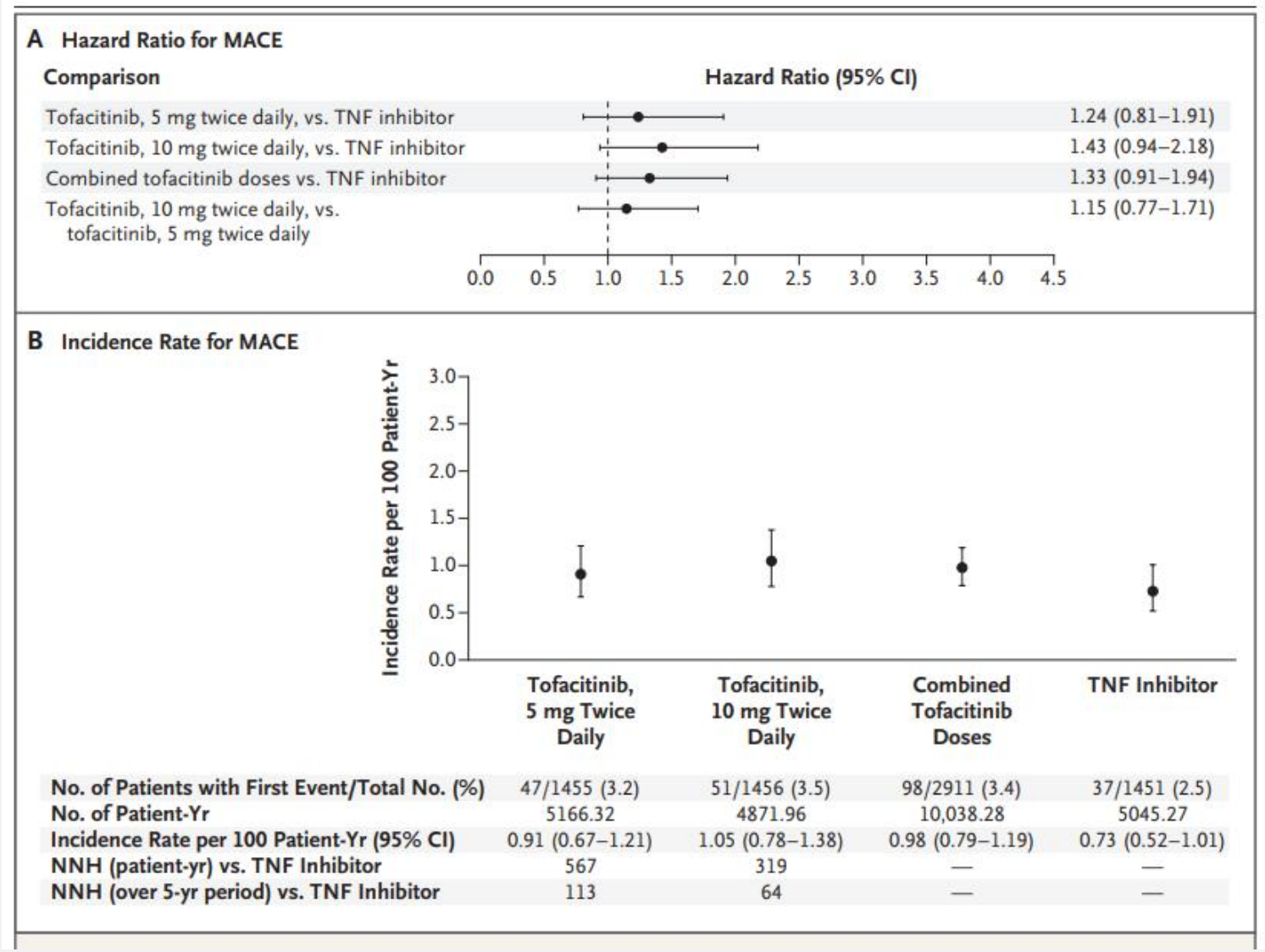
NCSG
North Carolina Society of Gastroenterology

Colombel J-F, et al. Clin Gastroenterol Hepatol. 2025;23:1019-1029.

JAK INHIBITORS SAFETY AND OTHER CONSIDERATIONS

Safety of Tofacitinib: ORAL Surveillance

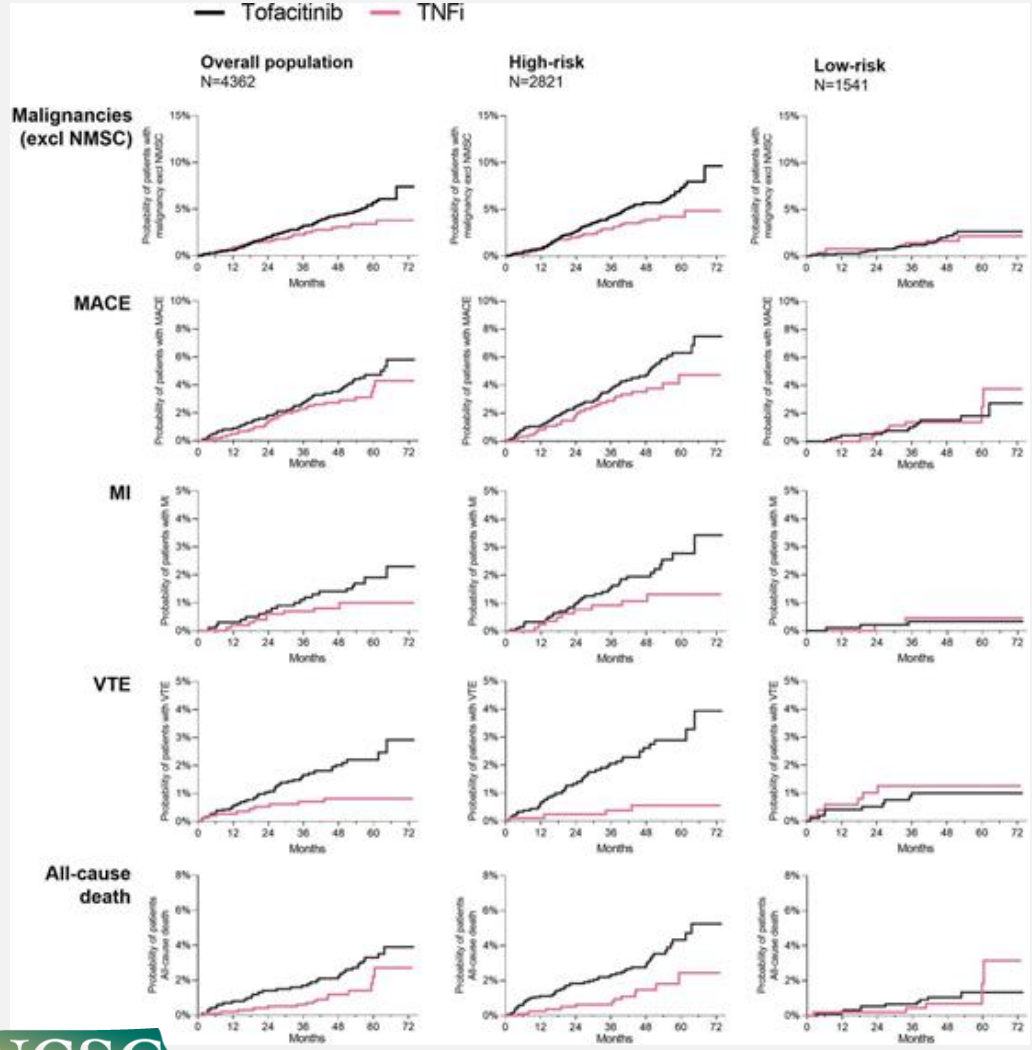
Randomized, open-label, noninferiority, post-authorization, safety end-point trial involving patients with active rheumatoid arthritis despite methotrexate treatment who were 50 years of age or older and had at least one additional cardiovascular risk factor

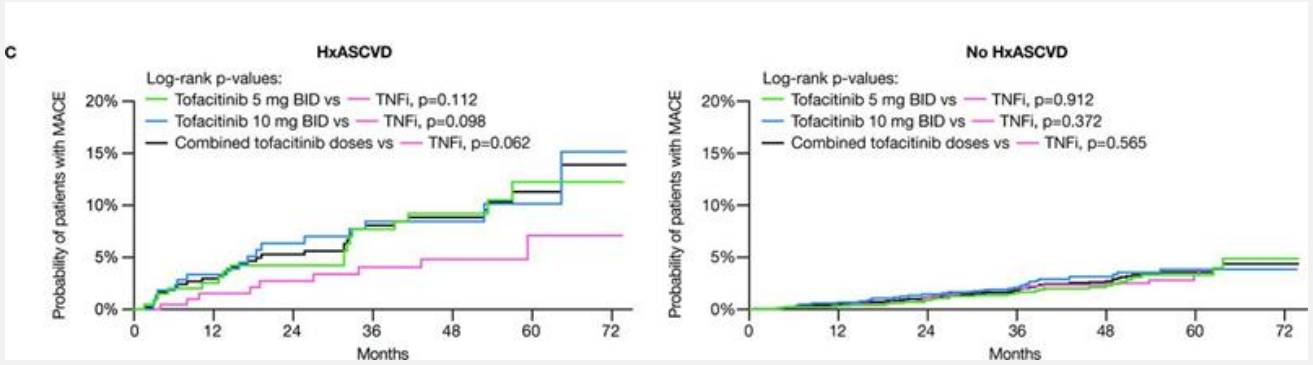


NCSG
North Carolina Society of Gastroenterology

Ytterberg S, et al. NEJM. 2022;386:316-26

Digging into ORAL Surveillance





High-risk patients have easily identifiable risk factors:

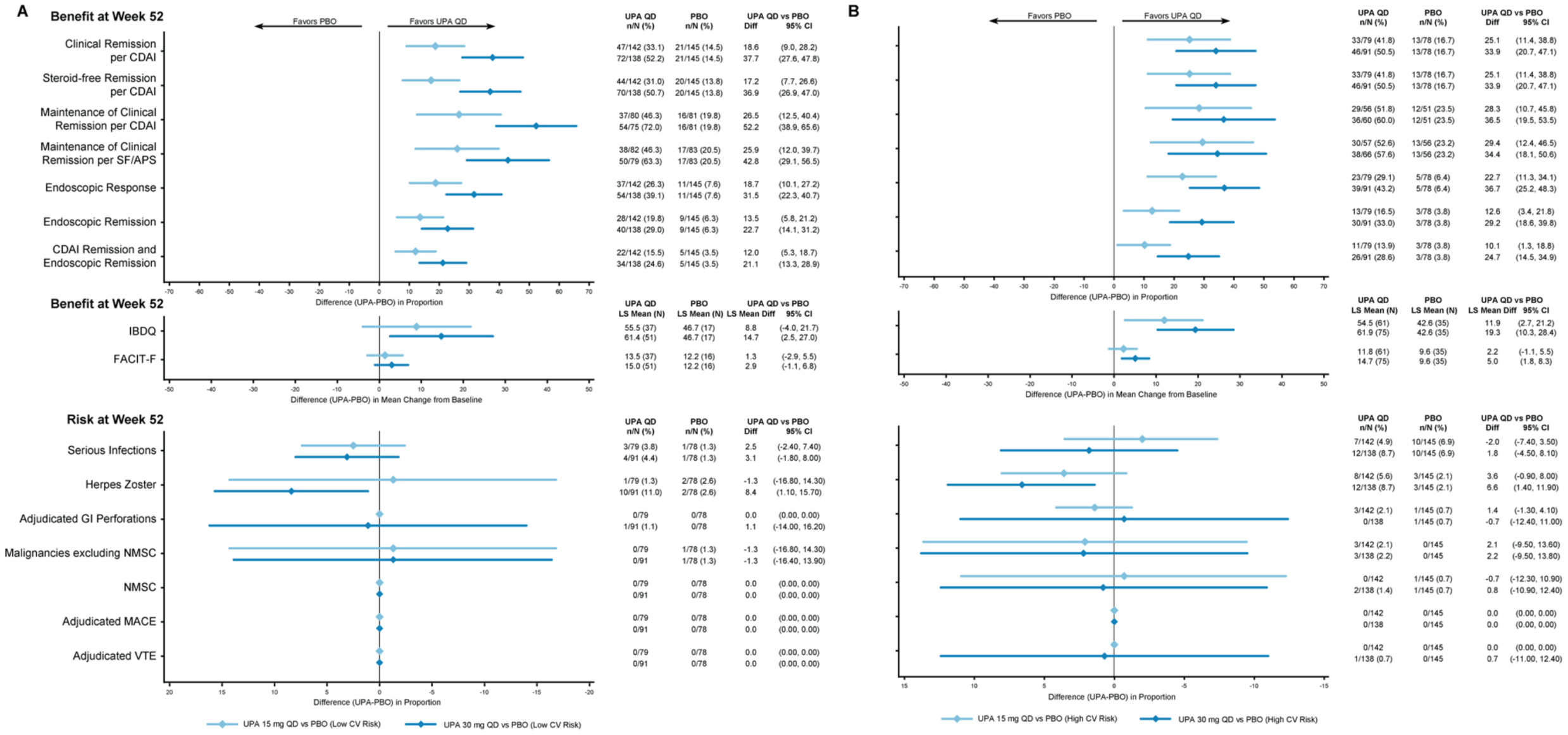
- Age 65 years or older
- Long smoking history (past or current)

Low-risk patients have no detectable risk increase using tofacitinib vs. anti-TNF in up to 6 years of follow-up

NCSG
North Carolina Society of Gastroenterology

Kristensen LE, et al. Ann Rheum Dis. 2023;82:901-910.
Charles-Schoeman C, et al. Ann Rheum Dis. 2023;82:119-129.

Upadacitinib: Cardiovascular Risk



North Carolina Society of Gastroenterology

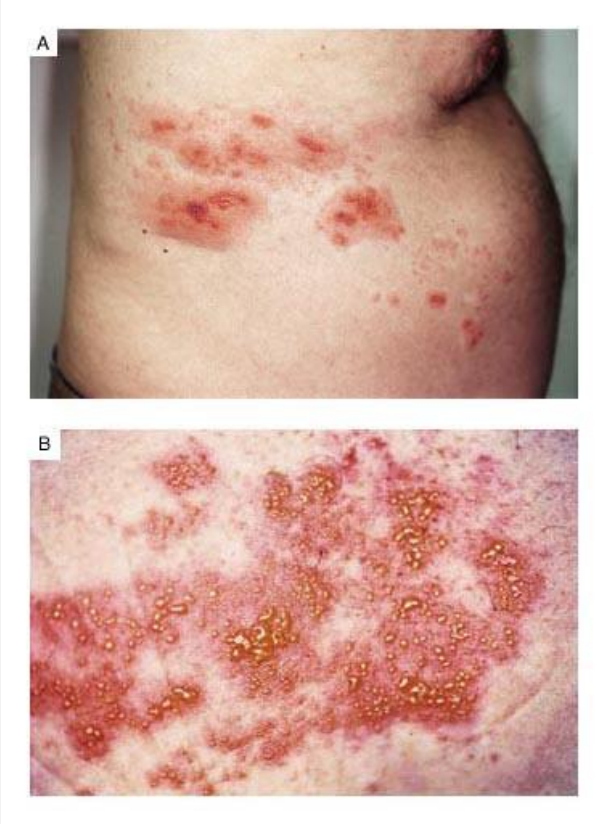
Vermeire S, et al. JCC. 2026; epublished Jan 9.

Upadacitinib: Zoster and Acne

Herpes zoster rates in induction trials

CD (45 mg):
- U-EXCEL: 2.9%
- U-EXCEED: 1.5%

UC (45 mg)
- UC1: <1%
- UC2: 1%



Acne

In Clinical Trials
- UC: 8%
- CD: 7%

Real World Cohort from University of Chicago
- 35/119 (29%) patients developed acne on upadacitinib 45 mg po daily
- Median time from initiation of upadacitinib to occurrence of acne was 32 days (IQR 18-49)
- Acne incidence associated with younger age and female sex

NCSG
North Carolina Society of Gastroenterology

Loftus E, et al. N Engl J Med. 2023;388:1966.
Danese S, et al. Lancet 2022;399:2113-28.
Gnann JW and Whitley RJ. N Engl J Med. 2022;347:340-346.
Choi D, et al. Inflamm Bowel Dis. 2025;31:2311-2314.

Requirements Prior to Therapy

Before First Dose	S1PR Modulator (Ozanimod, Etrasimod)	Anti-TNF (Infliximab, Adalimumab, Certolizumab, Golimumab)	Vedolizumab	Anti-IL-12/23, IL-23 (Ustekinumab, Guselkumab, Mirikizumab, Risankizumab)	JAK Inhibitor (Tofacitinib, Upadacitinib)
Pregnancy test	Negative test				Negative test
Vaccinations	VZV	HBV	HBV	HBV	VZV, HBV
Infections	Monitoring for infections	Monitoring for infections	Monitoring for infections	Monitoring for infections	Monitoring for infections
Blood test	CBC, LFTs	CBC, LFTs	CBC, LFTs	CBC, LFTs	CBC, LFTs, lipids
ECG	Heart block				
TB screening (skin test, blood test, or X-ray)	(Yes)	Yes	Yes	Yes	Yes
First dose monitoring	In patients with certain cardiac conditions	Infusion reactions and hypersensitivity	Infusion reactions and hypersensitivity	Infusion reactions and hypersensitivity	
Blood pressure					
Eye examination	In patients with uveitis or macular edema; required for etrasimod				
Skin examination	Required for etrasimod	Suggested		Suggested	Suggested

NCSG
North Carolina Society of Gastroenterology

Upadacitinib Label Change

October 13, 2025

U.S. Food and Drug Administration (FDA) Approves Updated Indication Statement for RINVOQ® (upadacitinib) for the Treatment of Inflammatory Bowel Disease

- *Updated indication allows the use of RINVOQ® (upadacitinib) prior to the use of tumor necrosis factor (TNF) blocking agents in patients for whom use of these treatments is clinically inadvisable and who have received at least one approved systemic therapy*

NORTH CHICAGO, Ill., Oct. 13, 2025 /PRNewswire/ -- AbbVie (NYSE: ABBV) today announced the U.S. Food and Drug Administration (FDA) approval of a supplemental new drug application (sNDA) that updates the indication statement for RINVOQ® (upadacitinib) for the treatment of adults with moderately to severely active ulcerative colitis (UC) and moderately to severely active Crohn's disease (CD).

NCSG
North Carolina Society of Gastroenterology

https://news.abbvie.com/2025-10-13-U-S-Food-and-Drug-Administration-FDA-Approves-Updated-Indication-Statement-for-RINVOQ-R-upadacitinib-for-the-Treatment-of-Inflammatory-Bowel-Disease

Making Treatment Decisions

Adult outpatients with moderate to severely active ulcerative colitis

Moderate to severely active UC defined as:
- Moderate to severe symptoms with Mayo endoscopy sub-score 2 or 3
- Mild symptoms, with high burden of inflammation or poor prognostic features
- Patients with corticosteroid-dependence, or refractory to oral corticosteroids

SUGGEST early use of advanced therapies and/or immunomodulator therapy, rather than gradual step up after failure of 5-aminosalicylates

Conditional recommendation, very low certainty of evidence)

RECOMMEND using any of the following, over no treatment:
Infliximab, Golimumab, Vedolizumab, Tofacitinib*, Upadacitinib*, Ustekinumab, Risankizumab, Guselkumab, Ozanimod, and Etrasimod

(Strong recommendation, moderate certainty of evidence)

SUGGEST using any of the following, over no treatment:
Adalimumab, Mirikizumab or Filgotinib*

(Conditional recommendation, moderate certainty of evidence)

Implementation considerations:
- Biosimilars of Infliximab, Adalimumab, and Ustekinumab can be considered equivalent to their originator drug in their efficacy
- Subcutaneous formulations of Infliximab and Vedolizumab can be considered as an alternative to the respective intravenous maintenance doses for most patients
- Extended induction or dose escalation of several advanced therapies can be considered for some patients with severe disease

ADVANCED THERAPY-NAÏVE PATIENTS (FIRST-LINE THERAPY)

SUGGEST using a HIGHER efficacy, or INTERMEDIATE efficacy medication, rather than a lower efficacy medication.

(Conditional recommendation, low certainty of evidence)

HIGHER EFFICACY MEDICATIONS: Infliximab, Vedolizumab, Ozanimod, Etrasimod, Upadacitinib*, Risankizumab, Guselkumab

INTERMEDIATE EFFICACY MEDICATIONS: Golimumab, Ustekinumab, Tofacitinib*, Filgotinib*, Mirikizumab

LOWER EFFICACY MEDICATIONS: Adalimumab

PRIOR EXPOSURE TO ONE OR MORE ADVANCED THERAPIES, PARTICULARLY TNF ANTAGONISTS

SUGGEST using a HIGHER efficacy, or INTERMEDIATE efficacy medication, rather than a lower efficacy medication.

(Conditional recommendation, low certainty of evidence)

HIGHER EFFICACY MEDICATIONS: Tofacitinib, Upadacitinib, Ustekinumab

INTERMEDIATE EFFICACY MEDICATIONS: Filgotinib, Mirikizumab, Risankizumab, Guselkumab

LOWER EFFICACY MEDICATIONS: Adalimumab, Vedolizumab, Ozanimod, Etrasimod

NCSG
North Carolina Society of Gastroenterology

Singh S, et al. Gastroenterology. 2024;167:1307-1343.

Making Treatment Decisions

ADVANCED THERAPY-NAÏVE PATIENTS (FIRST-LINE THERAPY)

SUGGEST using a HIGHER efficacy, or INTERMEDIATE efficacy medication, rather than a lower efficacy medication.

(Conditional recommendation, low certainty of evidence)

HIGHER EFFICACY MEDICATIONS: Infliximab, Vedolizumab, Ozanimod, Etrasimod, Upadacitinib*, Risankizumab, Guselkumab

INTERMEDIATE EFFICACY MEDICATIONS: Golimumab, Ustekinumab, Tofacitinib*, Filgotinib*, Mirikizumab

LOWER EFFICACY MEDICATIONS: Adalimumab

PRIOR EXPOSURE TO ONE OR MORE ADVANCED THERAPIES, PARTICULARLY TNF ANTAGONISTS

SUGGEST using a HIGHER efficacy, or INTERMEDIATE efficacy medication, rather than a lower efficacy medication.

(Conditional recommendation, low certainty of evidence)

HIGHER EFFICACY MEDICATIONS: Tofacitinib, Upadacitinib, Ustekinumab

INTERMEDIATE EFFICACY MEDICATIONS: Filgotinib, Mirikizumab, Risankizumab, Guselkumab

LOWER EFFICACY MEDICATIONS: Adalimumab, Vedolizumab, Ozanimod, Etrasimod

NCSG
North Carolina Society of Gastroenterology

Singh S, et al. Gastroenterology. 2024;167:1307-1343.

Making Treatment Decisions

Efficacy

- Indication
- Rapidity of onset
- Durability
- Pharmacokinetics/TDM
- Combination vs monotherapy

Safety

- Infection
- Cancer
- Specific concerns by agent or mechanism

Individual Characteristics

- Age
- Comorbidities
- Patient values/preferences

Disease Characteristics

- IBD extent
- Disease behavior/complication
- Disease severity
- Early vs late
- EIMs

NCSG
North Carolina Society of Gastroenterology

Summary

Small molecule therapies have an important role in the current management of ulcerative colitis and Crohn's disease (upadacitinib)

Understanding the appropriate patient factors to guide treatment initiation is critical

Continued evaluation of JAK-inhibitors in special populations may further define the role of these therapies in the treatment armamentarium

NCSG
North Carolina Society of Gastroenterology

CME/MOC Question

A 45 year old man with extensive UC, previously in remission on infliximab, now presents with increased frequency, urgency and bleeding. Infliximab trough level testing demonstrates an undetectable infliximab level with high titer antibodies. What is the next best choice of maintenance therapy for this patient?

A. Mesalamine (oral and topical therapy)
B. Shorten the interval between infliximab doses
C. Upadacitinib
D. Vedolizumab

Joint Providership

ASGE
American Society for Gastrointestinal Endoscopy

NCSG
North Carolina Society of Gastroenterology

CME/MOC Answer

C. Upadacitinib

In a patient with secondary loss of response to infliximab due to high-titer antibodies, upadacitinib has been associated with the largest treatment effects of the choices offered. This is also recommended by recent guidelines such as the AGA and ACG Guidelines for the management of ulcerative colitis.

Joint Providership

ASGE
American Society for Gastrointestinal Endoscopy

NCSG
North Carolina Society of Gastroenterology