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Participating in the Webinar




Moderator:
Philip S Schoenfeld, MD, MEd, MSCEPI, FACC

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.



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ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!



Week 3 – Thursday, January 18, 2024
 Joy and Wellness in Gastroenterology
 Faculty: Richard S. Bloomfeld, MD FACC
 Moderator: Jonathan A. Leighton, MD, FACC
At Noon and 8pm Eastern



Week 4 – Thursday, January 25, 2024
 Endobariatric Therapies and Pharmacotherapy - When and When Not to Combine
 Faculty: Shelby A. Sullivan, MD, FACC
 Moderator: Mark A. Gromski, MD
At Noon and 8pm Eastern

Visit gi.org/ACGVGR to Register

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Disclosures



Bharati Kochar, MD, MS:
Pfizer, Inc – advisory board – relationship ended



Philip S Schoenfeld, MD, MEd, MSCEPi, FAGC:
AbbVie: Advisory board, Consultant, Speaker Bureau; Ardelyx: Advisory board,
Consultant, Speaker Bureau; Ironwood: Advisory board, Consultant, Speakers
Bureau; Phathom: Advisory board, Speakers Bureau; Salix: Advisory board; Sanofi:
Advisory board.

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

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Evidence-Based GI Highlights: Advances in IBD Therapy



Bharati Kochar, MD, MS
Division of Gastroenterology
Massachusetts General Hospital
Harvard Medical School



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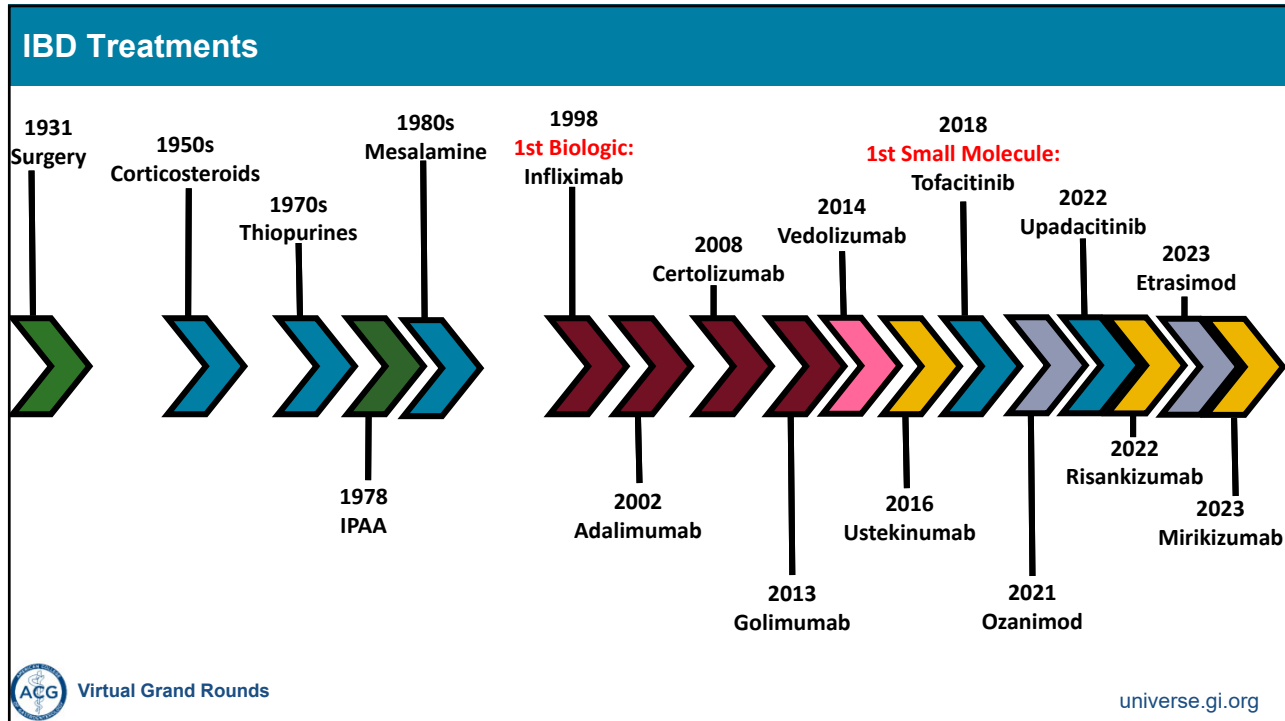
Objectives

- Learn about newer medications for the treatment of IBD
- Understand how to counsel patients about the newer treatment options
- Recognize differential positioning of newer agents



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How can you possibly keep up...?

EVIDENCE-BASED GI | Clinical take-aways and evidence-based summaries of articles in GI, Hepatology & Endoscopy
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Case 1

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Case 1: 64 year old female diagnosed with UC in 2020

March 2022: Presents for a second opinion on ulcerative colitis management

July 2020: Presented for evaluation of bloody diarrhea, last colonoscopy was 3 years prior and it was normal. She had a flex sig and was diagnosed with left-sided UC, treated with mesalamine, don't think she felt better

November 2020: Had a flare and got a course of steroids, all GI symptoms resolved

March 2021: Had another flare, got more prednisone, continued mesalamine

June 2021: Had another flare, got more prednisone, continued mesalamine

August 2021: Had another flare, got more prednisone, continued mesalamine

October 2021: hospitalized for a flare, treated with steroids and started on vedolizumab

January 2022: hospitalized again for a flare, had another flex sig revealed Mayo 3 colitis, discharged with steroids to continue vedolizumab

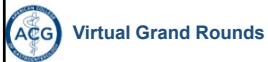
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Review of Systems

All of her joints hurt so much, but especially her knees and hips on both sides and they "feel" swollen even though they never are, but her rings don't fit anymore as well

Notably, she never had arthritis before, but she has friends who told her that is what this feels like

Profound fatigue, which is very uncharacteristic



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Recommendation & Follow-Up

Start infliximab

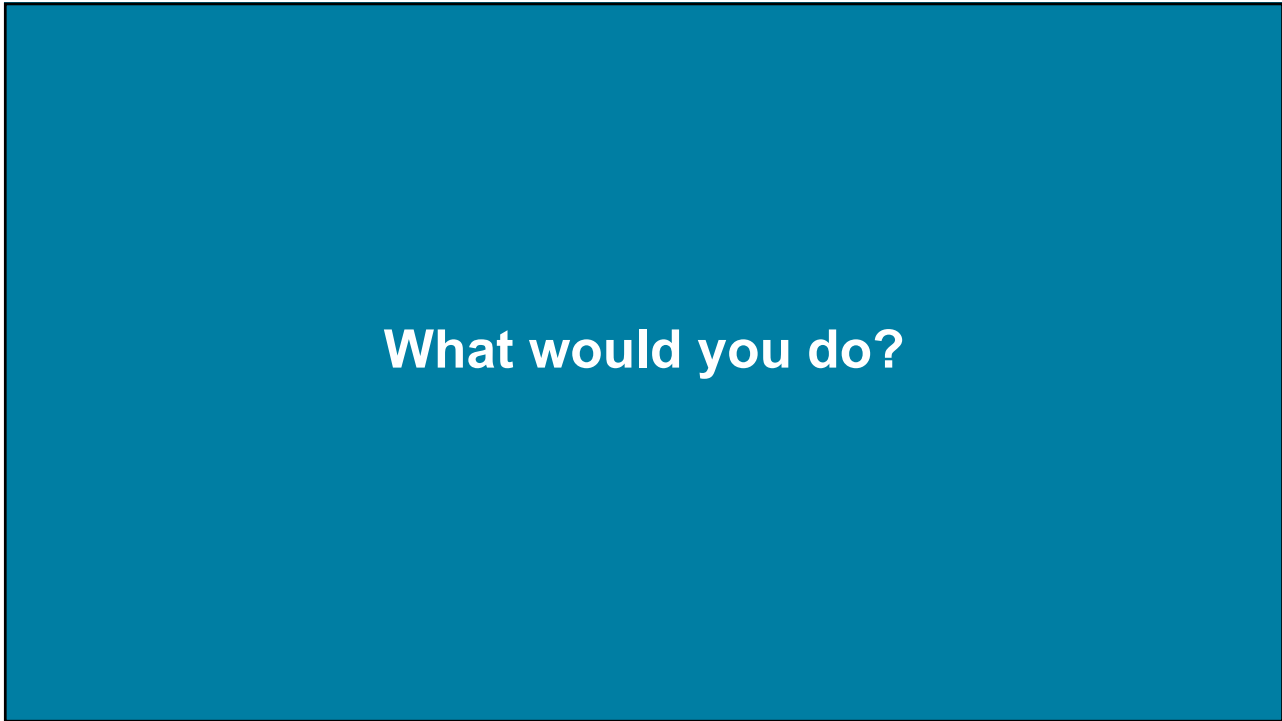
After 2 doses: no improvement, so continued her prednisone

After 8 weeks: no change at all and joint pain is worsening, not able to get off prednisone

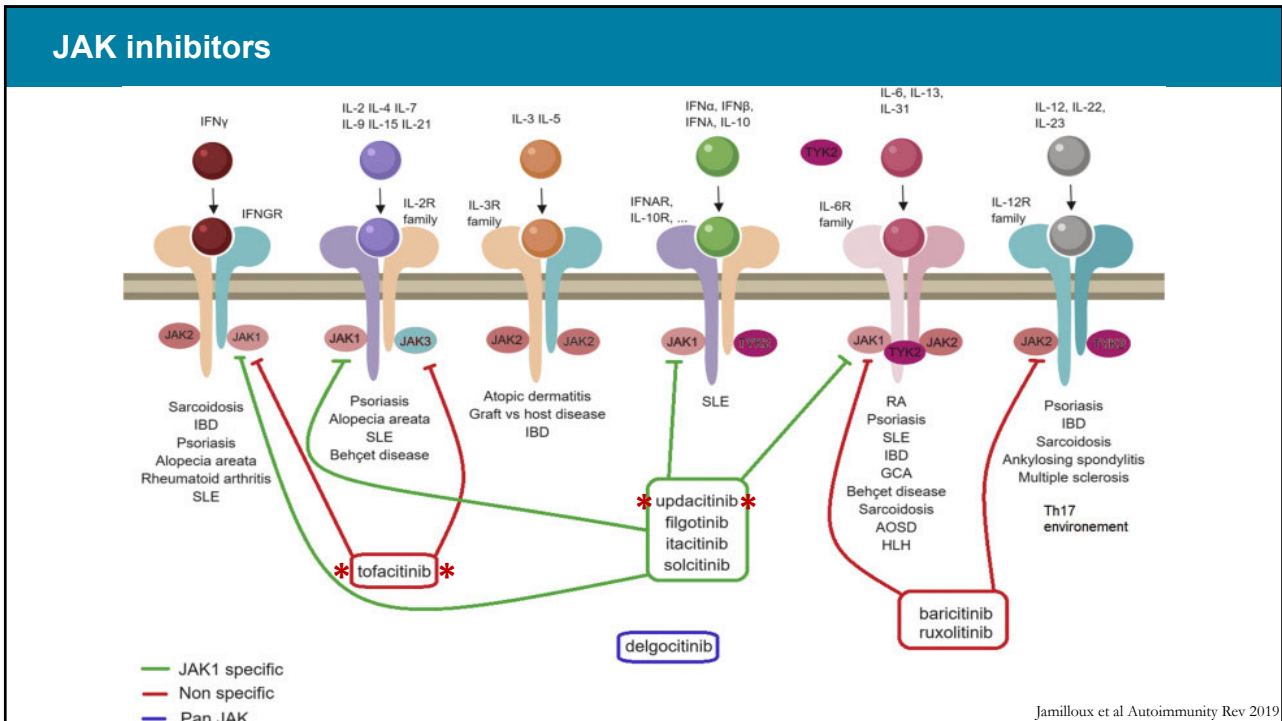


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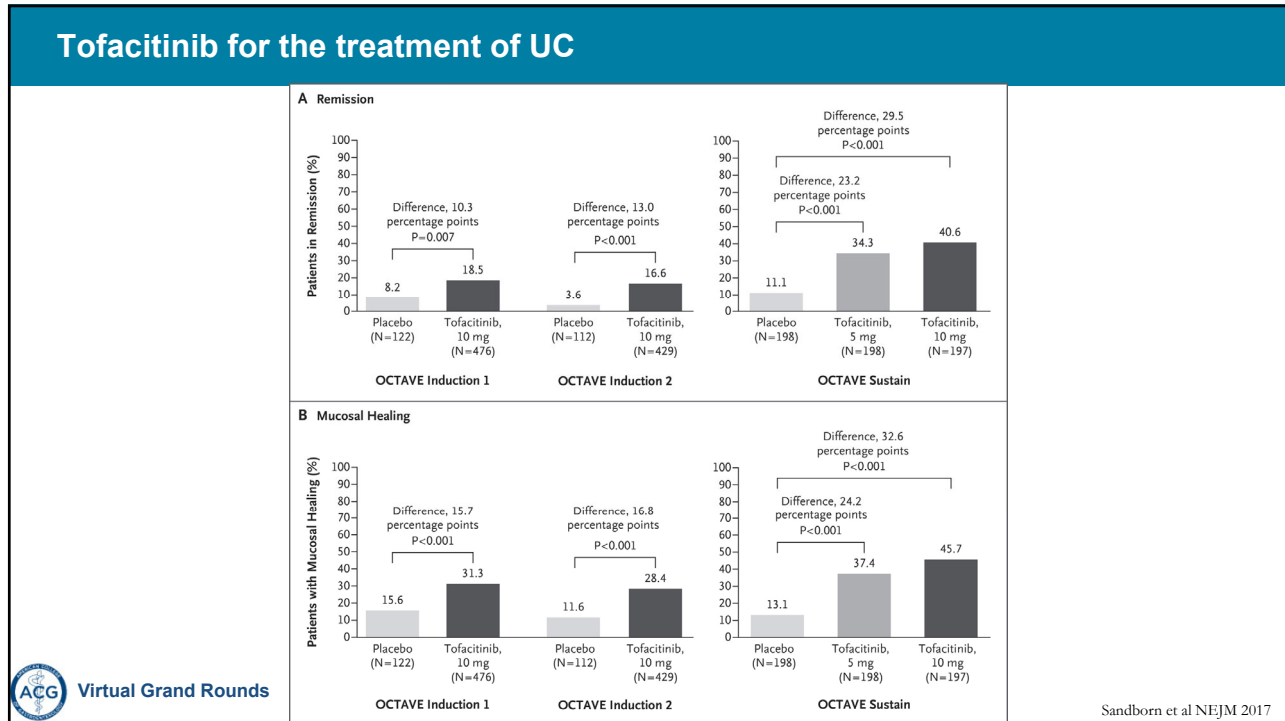
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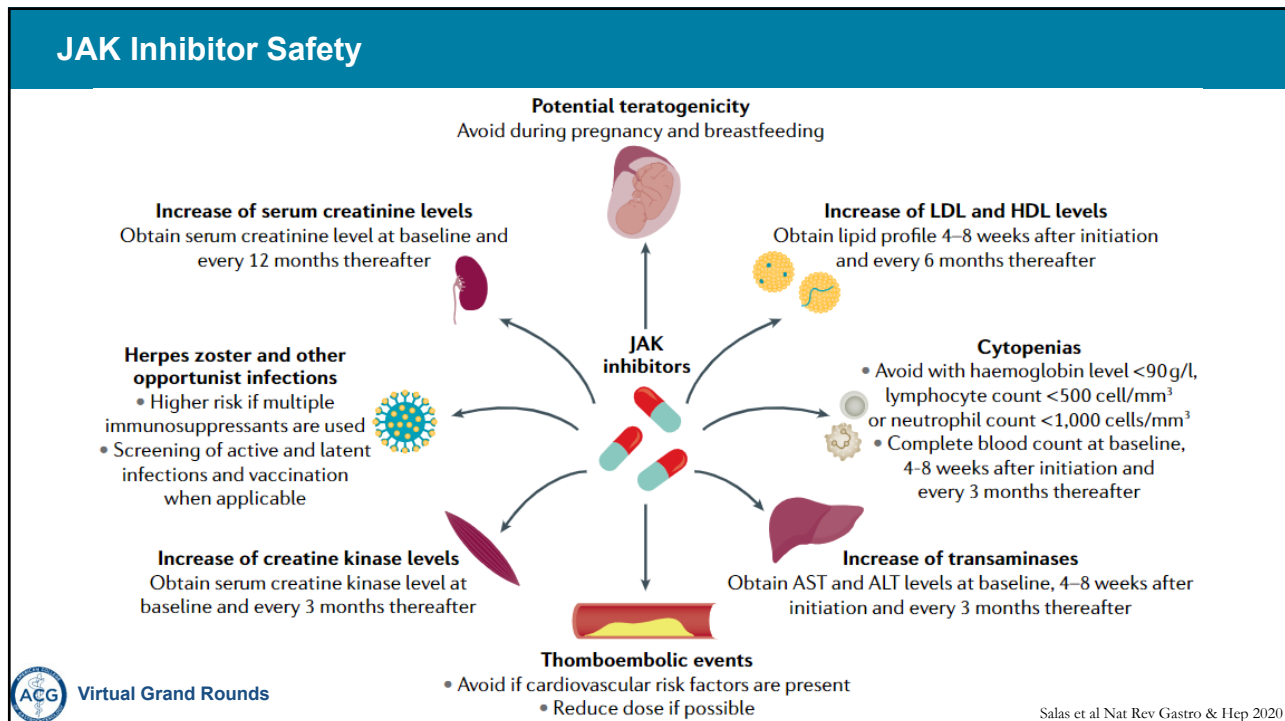
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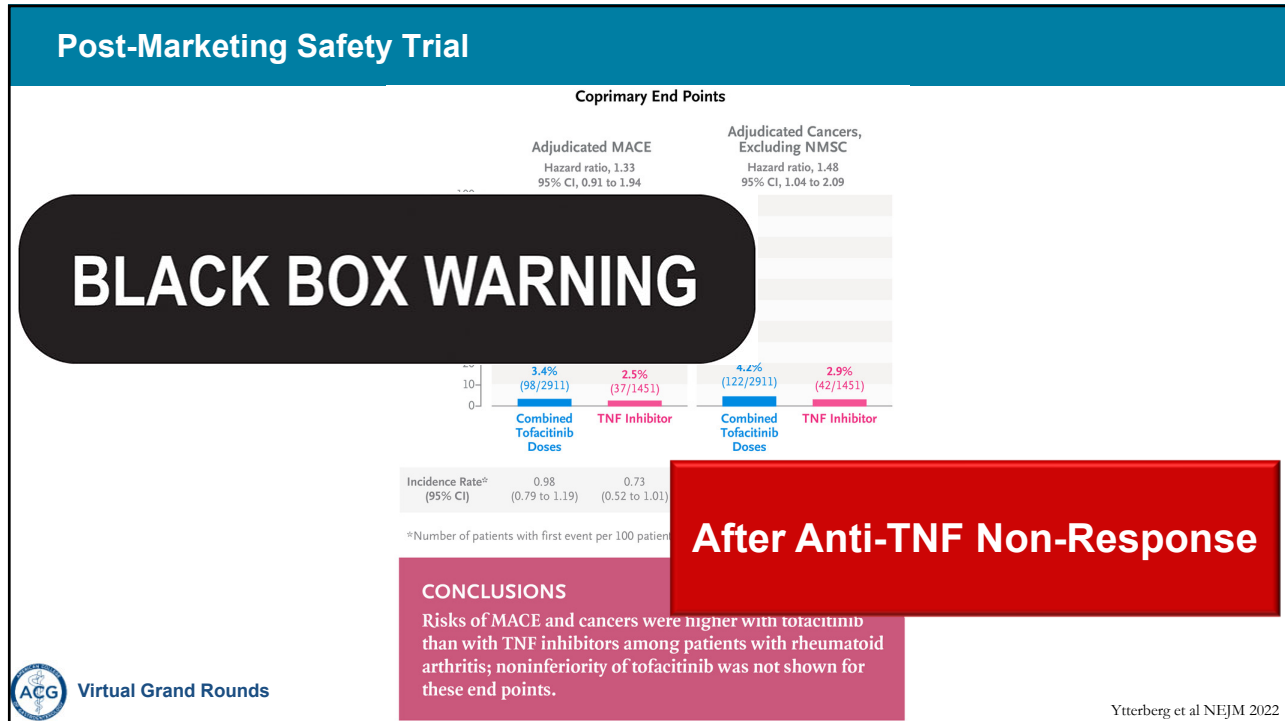
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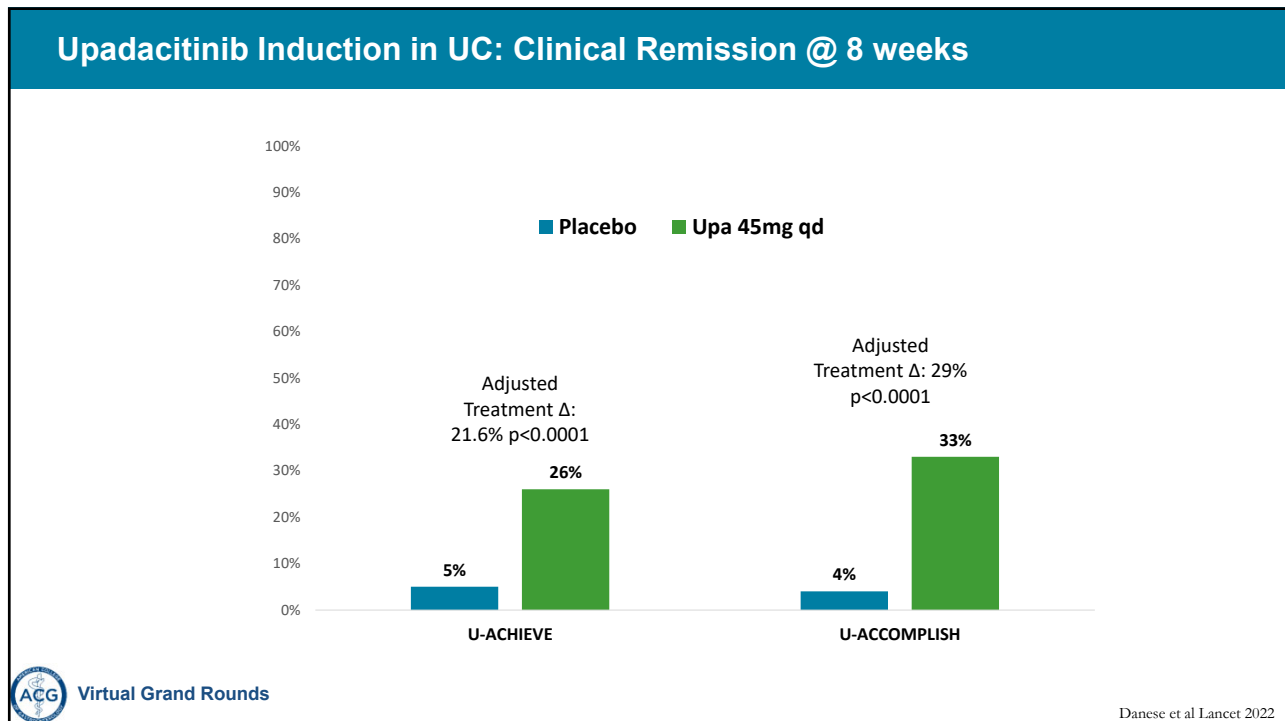
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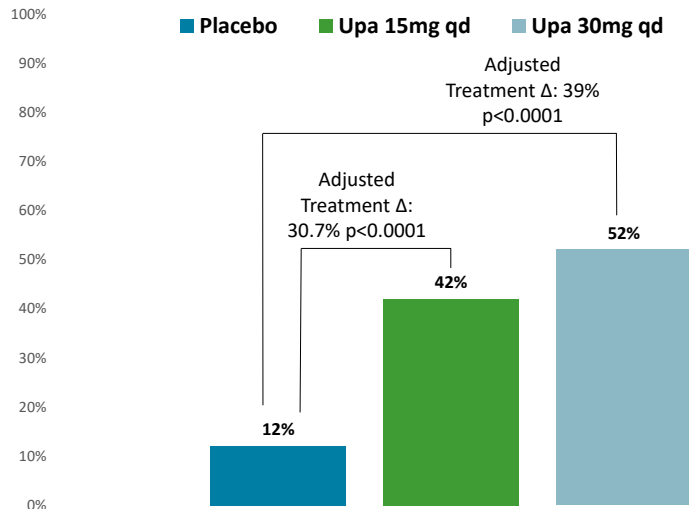


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Upadacitinib Maintenance in UC: Clinical Remission @ 52 weeks



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Danese et al Lancet 2022

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Posted on October 18, 2022

Upadacitinib, a Selective JAK1 Inhibitor, for Moderate-Severe Ulcerative Colitis: Adjusting the Top-Down Treatment Algorithm for Ulcerative Colitis



Jami Kinnucan, MD¹ and Philip Schoenfeld, MD, MEd, MSc (Epi)²

¹Senior Associate Consultant, Mayo Clinic, Jacksonville, FL

²Chief (Emeritus), Gastroenterology Section, John D. Dingell VA Medical Center, Detroit, MI

This summary reviews: Danese S, Vermeire S, Zhou W, et al. Upadacitinib as Induction and Maintenance Therapy for Moderately to Severely Active Ulcerative Colitis: Results from Three Phase 3, Multicentre, Double-Blind, Randomised Trials. Lancet 2022; 399: 2113-28. doi: 10.1016/S0140-6736(22)00581-5

Correspondence to Phillip Schoenfeld, MD, MEd, MSc (Epi), Editor-in-Chief. Email: EBGI@gi.org

Access the article through PubMed

Listen to the audio summary

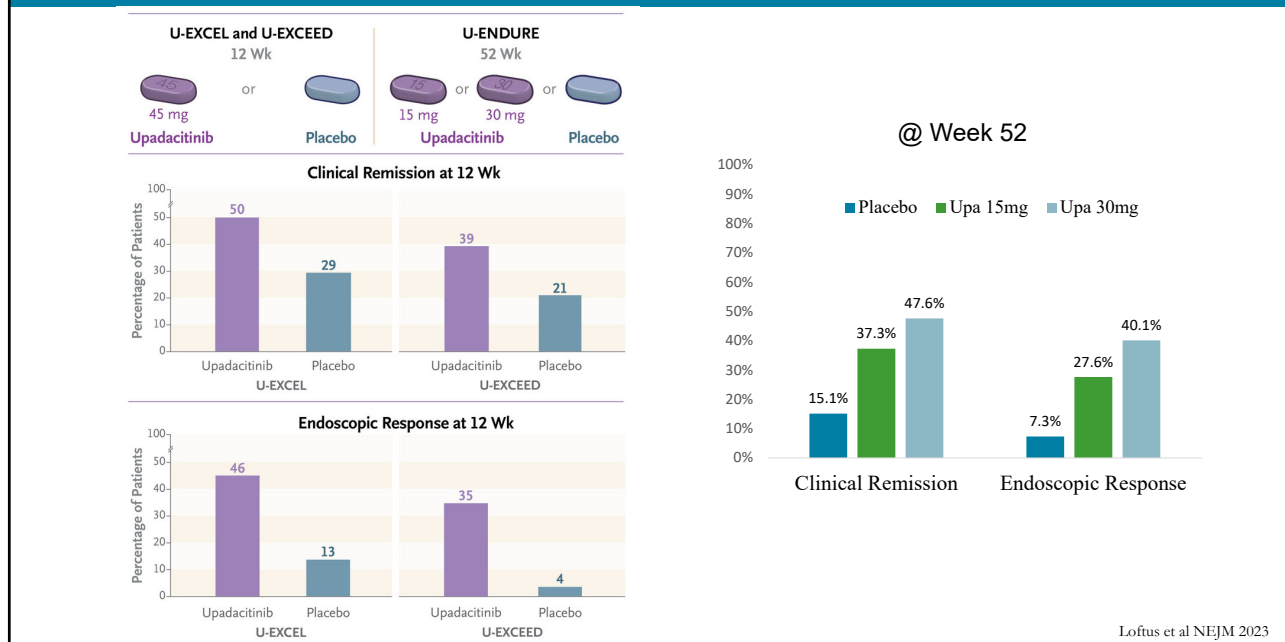


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Side Bar: Upa is the JAK approved for CD in 2023



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Posted on July 12, 2023

Upadacitinib Is Effective for the Induction and Maintenance of Moderate-to-Severe Crohn's Disease

Rahul S. Dalal, MD, MPH¹ and Jessica R. Allegretti, MD, MPH, FACP²

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² Medical Director, Crohn's and Colitis Center, Division of Gastroenterology, Hepatology and Endoscopy, Department of Medicine, Brigham and Women's Hospital; Associate Professor of Medicine, Harvard Medical School, Boston, MA

This summary reviews Loftus EV Jr, Panés J, Lacerda AP, Peyrin-Biroulet L, et al. Upadacitinib Induction and Maintenance Therapy for Crohn's Disease. N Engl J Med 2023 May 25;388(21):1966-1980.

[Access the article on PubMed](#)

[Listen the Audio Summary](#)

Correspondence to Jessica Allegretti, MD, MPH. Associate Editor. Email: EBGI@gi.org

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Back to the Patient

May 2022: Start upadacitinib

Follow Up:

Day 1: She felt better the next day

Day 3: Able to get out of bed without a problem for the first in many months

Day 14: Felt "disease-free"

8 weeks later: Felt very well, lipids went up, flex sig week prior revealed endoscopic remission, decrease dose to 30mg daily



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Case 2

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Case 2: 58 yo M with inflammatory ileal Crohn's disease

58 yo M with a history notable for asthma, hypertension, hyperlipidemia, psoriasis, psoriatic arthritis and most recently inflammatory ileal Crohn's disease who presents for a second opinion on IBD management.

September 2022: he went to his PCP to discuss abdominal pain, he was found to be newly anemic; he had a normal screening colon when he was 50 years old. He went back to the GI, had an EGD and colonoscopy and was found to have some ulceration in the TI with no other abnormalities and pathology report said "ileitis with features of chronicity, clinical correlation recommended"

His medication list includes an inhaler, a beta-blocker, a statin, methotrexate, hydroxychloroquine and more recently pentasa. His anemia is persistent, but his abdominal pain is slightly better, he only feels bloated now, but he can live with that since he modified his diet. He is tired of being on so many medications and wants to know if he can get off Pentasa



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What would you do?

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Biologics are 1st line medical therapy for Crohn's disease

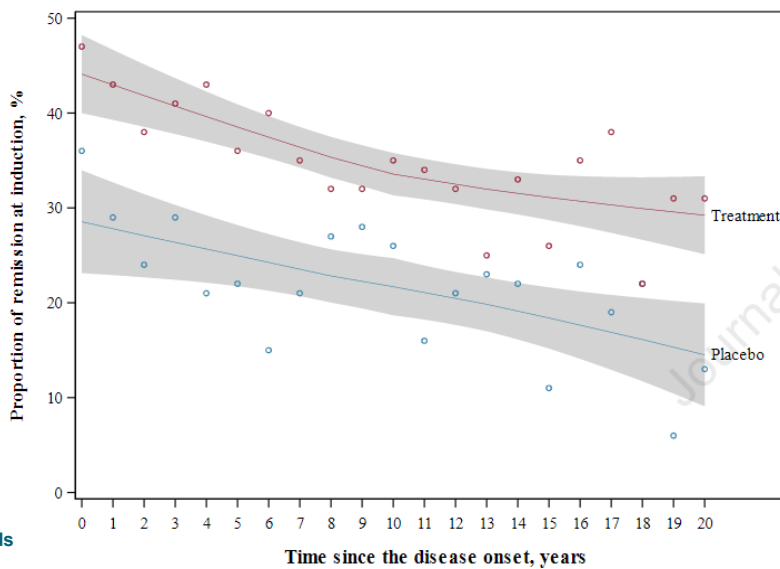
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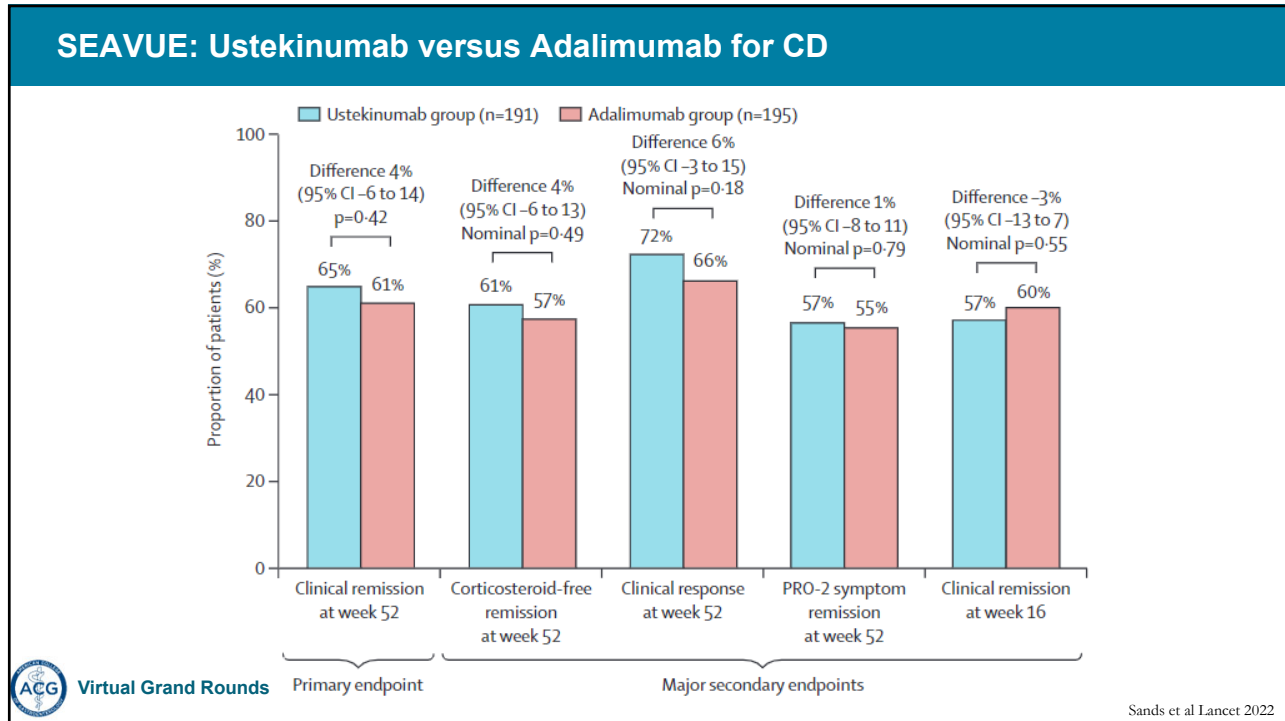
Biologics are more successful at inducing remission when started earlier for Crohn's disease

CD trials



Ben-Horin et al Gastro 2022

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Posted on April 19, 2023

SEAVUE: A Sea of Change in Biologic Positioning for Crohn's Disease

Bharati Kochar, MD, MS

Division of Gastroenterology, Massachusetts General Hospital Investigator, The Mongan Institute, Assistant Professor of Medicine, Harvard Medical School, Boston, MA

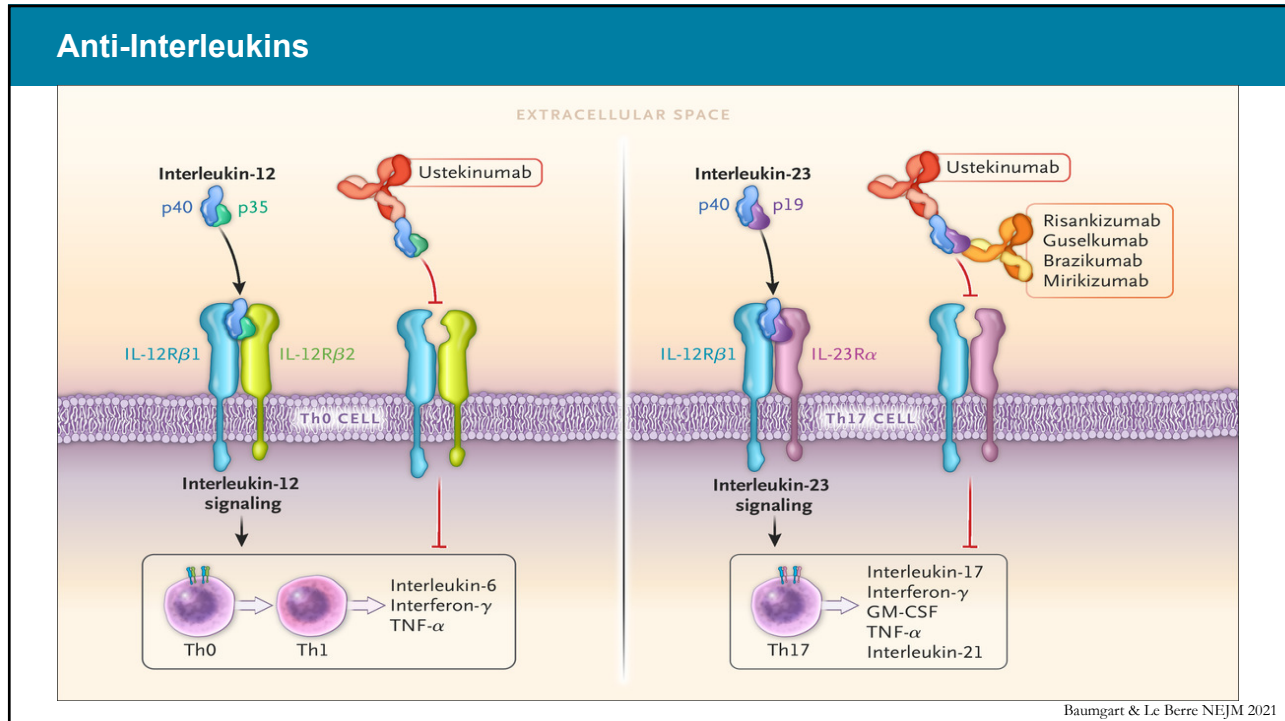
This summary reviews Sands BE, Irving PM, Hoops T, et al. Ustekinumab versus adalimumab for induction and maintenance therapy in biologic-naïve patients with moderately to severely active Crohn's disease: a multicentre, randomised, double-blind, parallel-group, phase 3b trial. *Lancet* 2022;399(10342):2200-2211. doi: 10.1016/S0140-6736(22)00688-2.

[Access the article through PubMed](#)

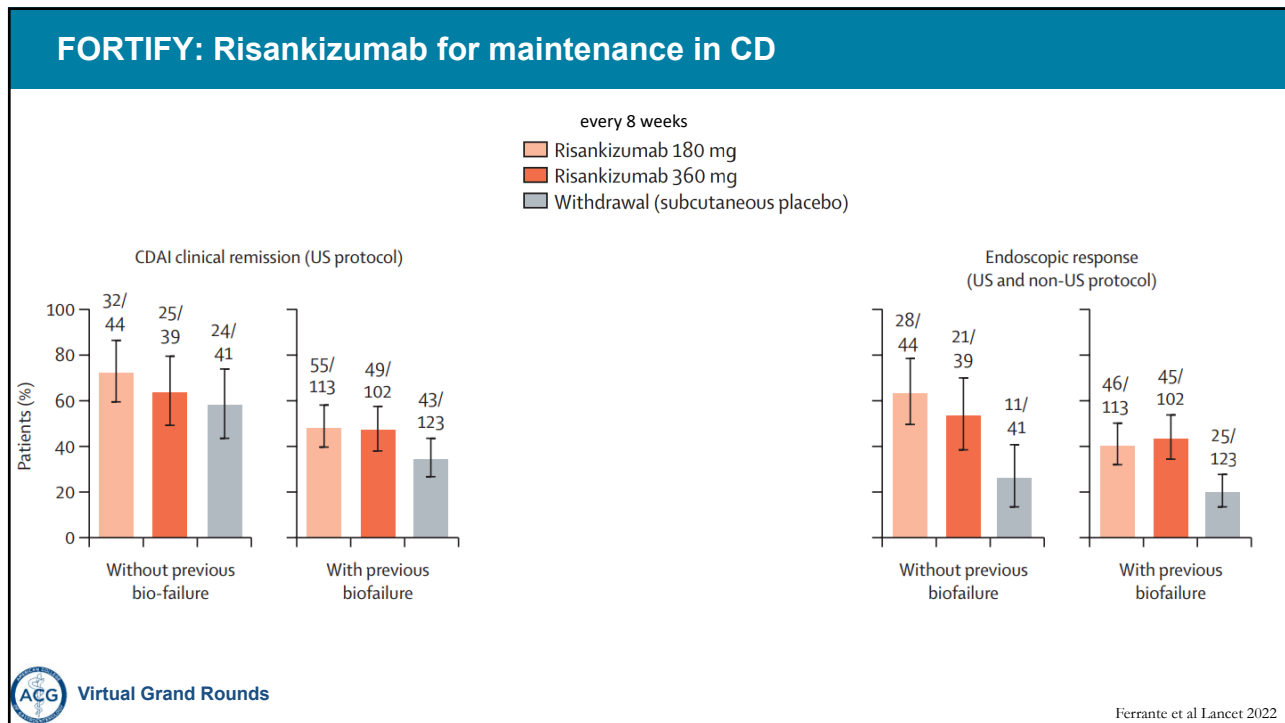
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Posted on January 25, 2023

Risankizumab, an Interleukin-23 Inhibitor, for Moderate-Severe Crohn’s Disease: Advancing Care Beyond Anti-TNF Therapy



Bharati Kochar, MD, MS

Division of Gastroenterology, Massachusetts General Hospital Investigator, The Mongan Institute, Assistant Professor of Medicine, Harvard Medical School, Boston, MA

This summary reviews D’Haens G, Panaccione R, Baert F, et al. Risankizumab as Induction Therapy for Crohn’s Disease: Results from the Phase 3 ADVANCE and MOTIVATE Induction Trials. *Lancet* 2022;399(10340):2015-30.

[Access the article through PubMed](#)

[Listen to the audio summary](#)

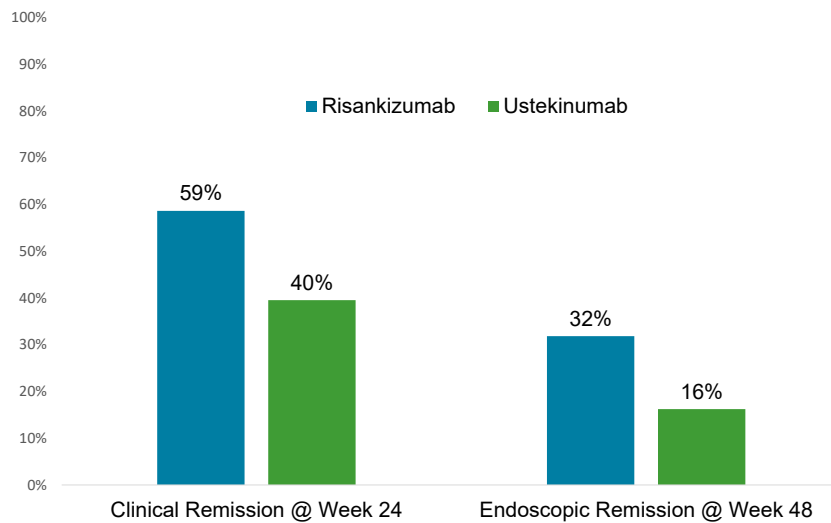
Correspondence to Bharati Kochar, MD, MS, Associate Editor. Email: EBG@gi.org



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SEQUENCE: Risankizumab vs Ustekinumab for CD



No data posted on ClinTrials.gov, so data are from a UEGW 2023 Abstract

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Back to the Patient

Started Risankizumab

His skin cleared for the first time in 10 years

His joints feel better

He is able to eat everything he used to eat better

He is no longer anemic

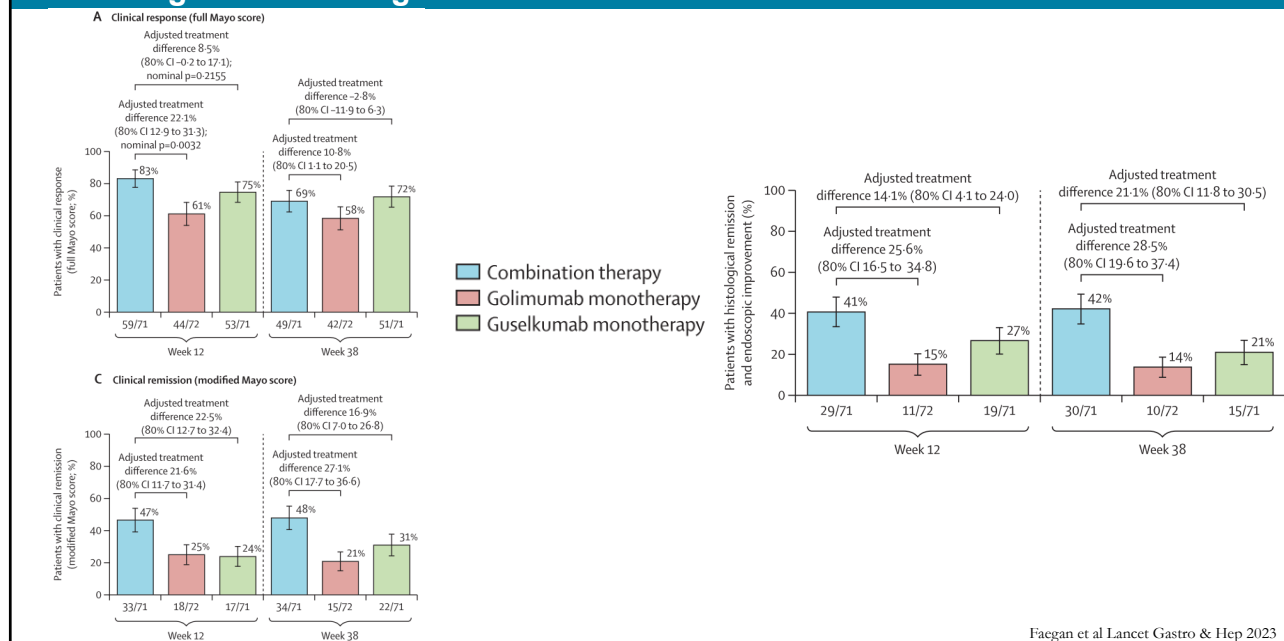
Risankizumab > methotrexate + hydroxychloroquine + pentasa



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Side Bar: Phase II Proof-of-Concept Trial VEGA: guselkumab + golimumab



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Posted on October 17, 2023

The New Frontier of Combination Therapy for IBD: The VEGA RCT



Tarun Chhibba, MD¹ and Bharati Kochar, MD, MS²

¹Advanced Fellow in Inflammatory Bowel Diseases, Division of Gastroenterology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

²Assistant Professor of Medicine, Division of Gastroenterology, Massachusetts General Hospital, Investigator, The Mongan Institute, Harvard Medical School, Boston, MA

This summary reviews Feagan BG, Sands BE, Sandborn WJ, et al. Guselkumab plus golimumab combination therapy versus guselkumab or golimumab monotherapy in patients with ulcerative colitis (VEGA): a randomised, double-blind, controlled, phase 2, proof-of-concept trial. *Lancet Gastroenterol Hepatol* 2023; 8: 307-20 .

[Access the article through PubMed](#)

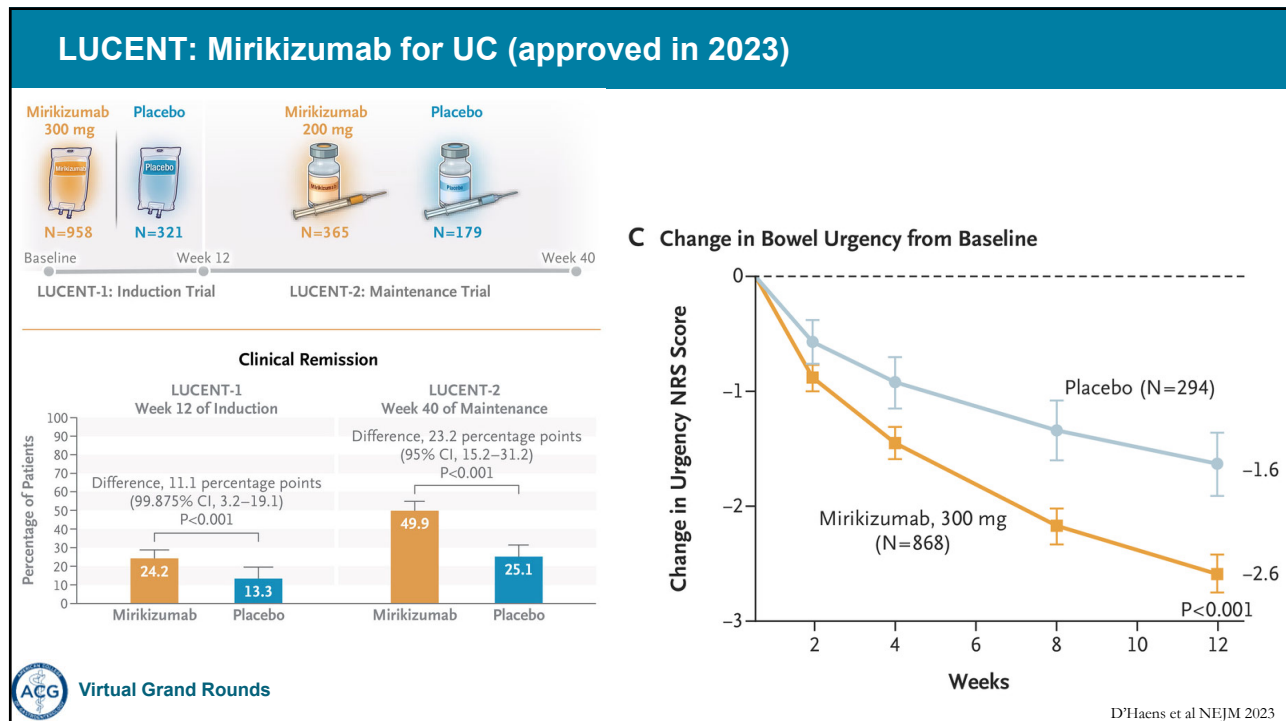
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Case 3

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Case 3: 42 yo F with UC

42 yo F presents for a second opinion on the management of UC

2019: Presented for evaluation of bloody diarrhea, diagnosed by colonoscopy with left sided UC. She was treated with mesalamine and felt well for 2 years.

2021: flare responsive to hydrocortisone enemas.

Jan 2023: flare requiring hospitalization, discharged on budesonide-MMX. Her GI doctor recommended started vedolizumab, but she did not want to be stuck. So her GI doctor ordered adalimumab, but she did not want to stick herself.

March 2023: She read that there are oral options for UC. She is still having 5 BMs daily, the first 3 of the day are bloody. She is not waking up at night and hasn't lost any weight, but doesn't have an appetite anymore

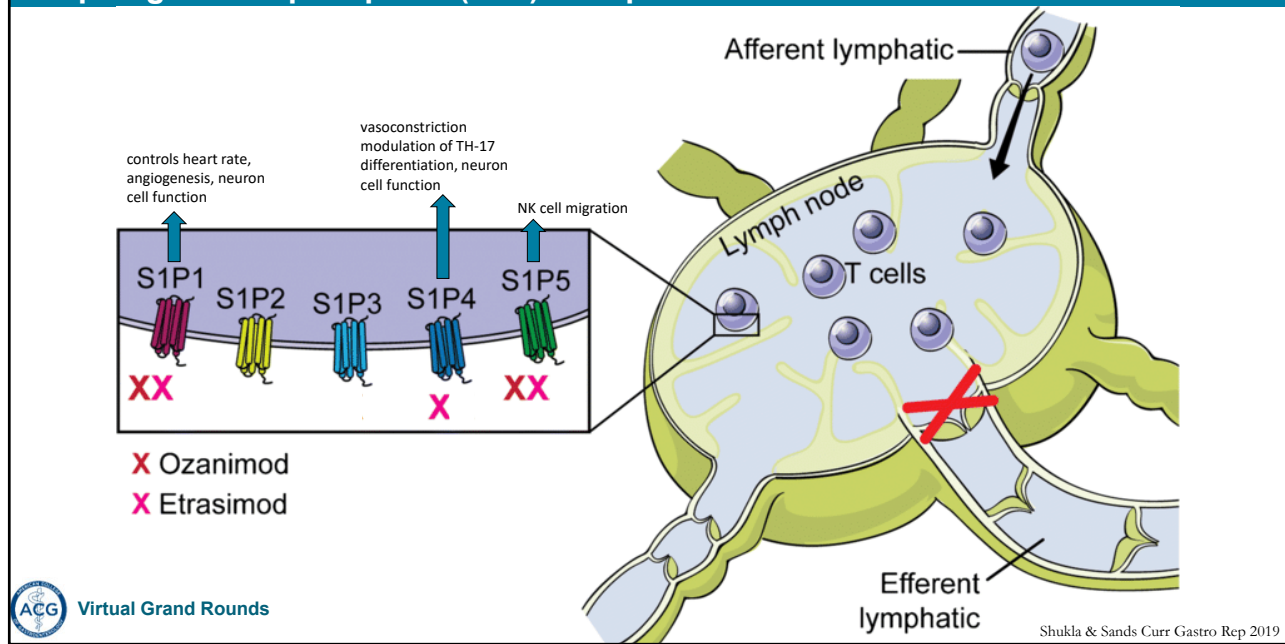


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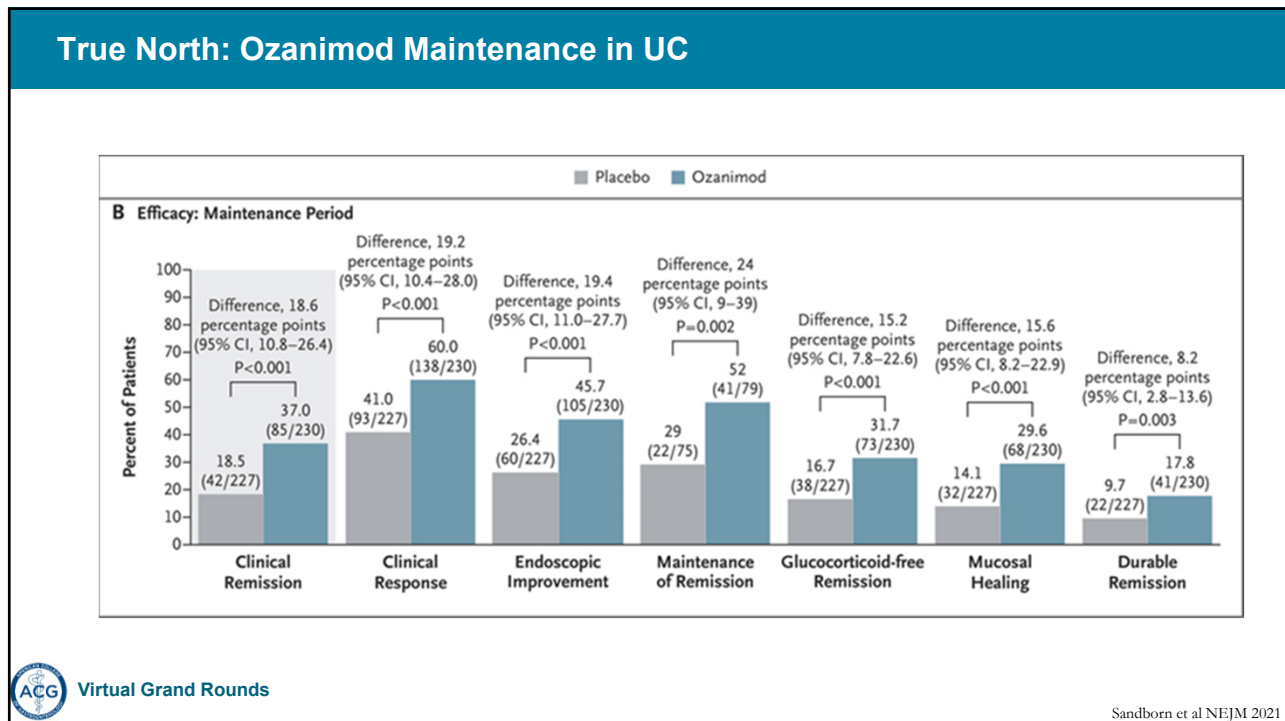
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Anti-Trafficking: Sphingosine-1-phosphate (S1P) Receptor Modulators



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True North: Ozanimod Maintenance in UC



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Posted on December 14, 2022

Ozanimod for Moderate-Severe Ulcerative Colitis: Rethinking the Top-Down Treatment Algorithm

Oriana Damas, MD¹ and Philip Schoenfeld, MD, MEd, MSc (Epi)²



¹Assistant Professor of Medicine, University of Miami School of Medicine, Miami, FL

²Chief (Emeritus), Gastroenterology Section, John D. Dingell VA Medical Center, Detroit, MI.

This summary reviews Sandborn WJ, Feagan BG, D'Haens G, et al. Ozanimod for Induction and Maintenance of Ulcerative Colitis. *N Engl J Med* 2021; 385: 1280-91.

Correspondence to Philip Schoenfeld, MD, MEd, MSc. Editor-in-Chief. Email: EBGI@gi.org

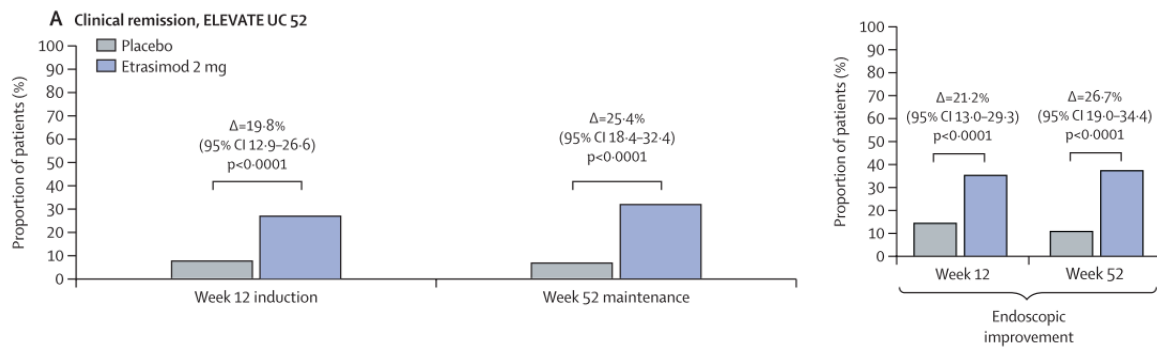


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ELEVATE: Etrasimod for UC (approved in 2023)



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Sandborn et al *Lancet* 2023

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Posted on November 15, 2023

Etrasimod, a Sphingosine 1-Phosphate Receptor Modulator, for Moderate-Severe Ulcerative Colitis: New Options for Oral Therapy



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¹Chief (Emeritus), Gastroenterology Section, John D. Dingell VA Medical Center, Detroit, MI.

²Instructor, Division of Gastroenterology, Hepatology, and Endoscopy, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

This summary reviews Sandborn WJ, Vermeire S, Peyrin-Biroulet L, et al. Etrasimod as induction and maintenance therapy for ulcerative colitis (ELEVATE): Two randomised, double-blind, placebo-controlled, phase 3 studies. Lancet 2023; 401: 1159-71.

[Access the article through PubMed](#)

[Listen to the Audio Summary](#)

Correspondence to Philip Schoenfeld, MD, MEd, MSc. Editor-in-Chief. Email: EBGI@gi.org



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Adverse Events reported in the Clinical Trials

Table 2. Safety Findings through t			Table 2. Safety Findings through †			ELEVATE UC 52		
Variable	Maintenance Period‡		Variable	Maintenance Period‡		Etrasimod group (n=289)	Placebo group (n=144)	
	Placebo (N = 227)	Ozanimod (N = 230)						
Adverse event — no. (%)	83 (36.6)	113 (49.1)	Cancer — no. (%)			206 (71%)	81 (56%)	
Serious adverse event — no. (%)	18 (7.9)	12 (5.2)	Basal-cell carcinoma	0	1 (0.4)	20 (7%)	9 (6%)	
Most frequent adverse events — no. (%):			Rectal adenocarcinoma	0	1 (0.4)	12 (4%)	7 (5%)	
Anemia	4 (1.8)	3 (1.3)	Adenocarcinoma of the colon	1 (0.4)	0	0	0	
Nasopharyngitis	4 (1.8)	7 (3.0)	Breast cancer	1 (0.4)	0	0	0	
Headache	1 (0.4)	8 (3.5)	Adverse events of special interest — no. (%)			0	0	
Alanine aminotransferase increased§	1 (0.4)	11 (4.8)	Bradycardia	0	0	22 (8%)	13 (9%)	
Arthralgia	6 (2.6)	7 (3.0)	Hypertension	3 (1.3)	4 (1.7)	24 (8%)	14 (10%)	
γ-Glutamyltransferase increased§	1 (0.4)	7 (3.0)	Hypertensive crisis	1 (0.4)	1 (0.4)	24 (8%)	7 (5%)	
Infection — no. (%)	27 (11.9)	53 (23.0)	Macular edema	0	1 (0.4)	9 (3%)	2 (1%)	
Serious infection	4 (1.8)	2 (0.9)	Laboratory assessments — no./total no. (%)			20 (7%)	9 (6%)	
Nasopharyngitis	4 (1.8)	7 (3.0)	Alanine aminotransferase			15 (5%)	1 (1%)	
Upper respiratory tract infection	4 (1.8)	2 (0.9)	≥2× ULN	12/227 (5.3)	32/230 (13.9)	14 (5%)	6 (4%)	
Herpes zoster infection¶	1 (0.4)	5 (2.2)	≥3× ULN	4/227 (1.8)	7/230 (3.0)	13 (4%)	3 (2%)	
			≥5× ULN	1/227 (0.4)	2/230 (0.9)	11 (4%)	5 (3%)	
			Absolute lymphocyte count			3 (1%)	5 (3%)	
			<200 cells per mm ³	0/227	5/230 (2.2)	2 (1%)	0	
			<500 cells per mm ³	4/227 (1.8)	100/230 (43.5)	0	0	
						0	0	
						4 (1%)	0	
						1 (<1%)	0	
						1 (<1%)	0	
						1 (<1%)	0	
						1 (<1%)	0	

Sandborn et al NEJM 2021
Sandborn et al Lancet 2023

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S1P-RM Prescribing

- Wash-out**
- SHINGRIX (BEFORE initiation) & birth control for ♀**
- Initial Work-Up:**
 - CBC WITH differential to r/o lymphopenia
 - LFTs
 - EKG to r/o prolonged QT, heart block
 - Eye Exam (*on label for etrasimod*)
 - ?JC virus
- Medication List Check for DDIs:** beta-blockers, CCBs, MAOIs, CYP2C8 drugs, SSRIs, SNRIs
- NO COMBINATION immunosuppression** (even 3mo after)
- Counsel to avoid high volumes of ↑ tyramine foods**
 - *aged cheeses, processed meats, pickled & fermented vegetables, citrus & tropical fruits, fermented EtOH*
- IF SOB, get PFTs**
- IF vision changes, get eye exam**
- IF neuro symptoms, MRI to r/o PRES**



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What would you do?

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Next Steps

Full colonoscopy: the scope is part of the physical exam!

Scope revealed moderate pancolitis, no significant lab abnormalities

Both vedolizumab and S1P-RM are reasonable 1st line advanced therapies for mild to moderate UC not responsive to corticosteroids and mesalamine

She has not yet had a trial of systemic corticosteroids: pred taper + mesalamine, **re-assess in 4 months** if no improvement after getting off steroids, step up to advanced therapy



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Positioning of Advanced Therapies for IBD

Insurance Coverage

Disease-related factors:

- Disease location and behavior
- future risk for more aggressive disease

Patient-related factors:

- EIMs
- Co-existing IMIDs for which there could be unifying treatments
- Risk for infections and other adverse events: co-morbidities, polypharmacy

Pharmacokinetics:

- Altered anatomy
- HLA-DQA1*05 positivity

Lifestyle: preference for route of administration

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Summary

Many new medications approved

Many more medications in the pipeline

But do not cycle through drugs

We still don't have molecular phenotyping of disease and tailored treatments

If you're not sure, just ASK!



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Thank You
Questions?




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Questions



Bharati Kochar, MD, MS



Philip S Schoenfeld, MD, MSeD, MSCEPi, FACG

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CONNECT AND COLLABORATE IN GI



ACG GI Circle
Connect and collaborate within GI



IBD Circle
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