1

- **Visit gi.org/research-awards** to learn more about the 8 grant categories & apply
- **New! Grant Writing Resources -** gi.org/grant-writing-resources
  - for grant tips, videos, and written resources

2

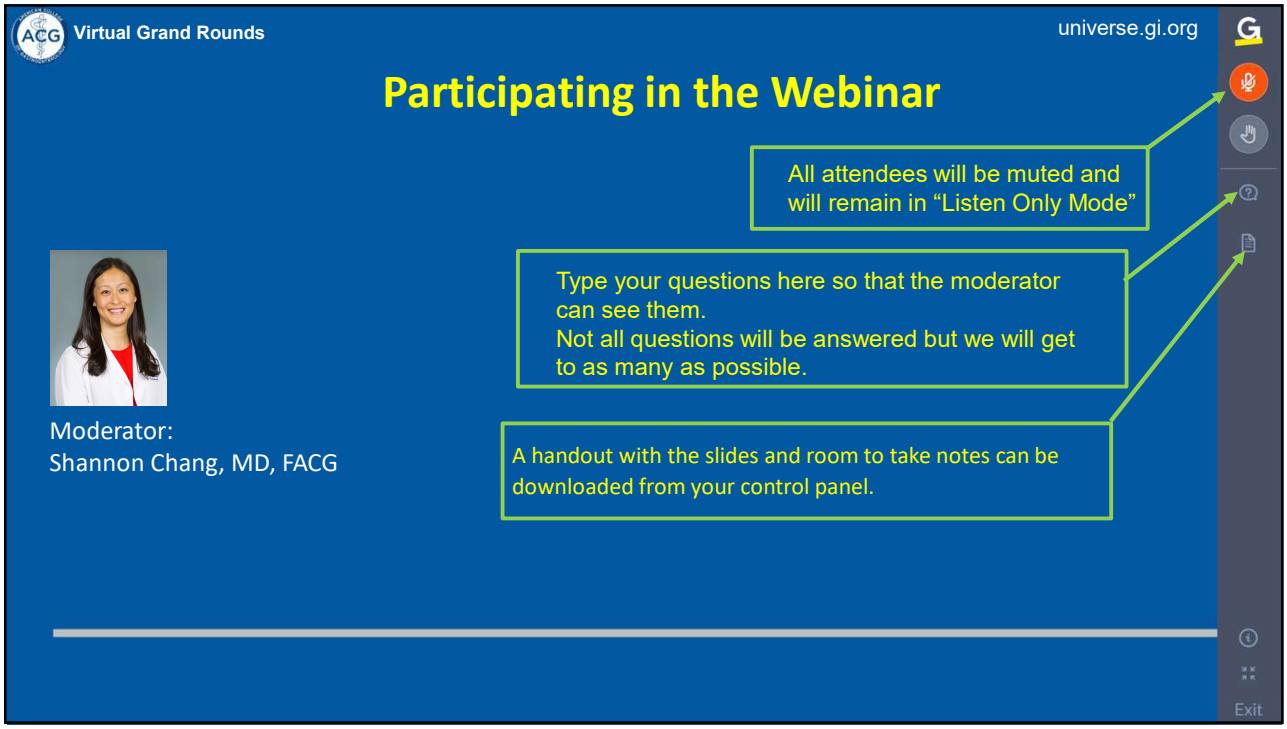
New Extended Deadline: September 15, 2025

3

4


2025
ACG'S HEPATOLOGY SCHOOL & SOUTHERN
REGIONAL POSTGRADUATE COURSE
DECEMBER 5-7, 2025 | RENAISSANCE HOTEL, NASHVILLE, TN
Register online: meetings.gi.org

5


Virtual Grand Rounds
universe.gi.org
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.
Moderator:
Shannon Chang, MD, FACG
Exit

6

Virtual Grand Rounds

universe.gi.org

ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!

Week 38 – Thursday September 18, 2025
Inaugural LIVE ENDOSCOPY Event: Diagnostic and Therapeutic UGI Endoscopy: Back to the Basics
Faculty: Aziz Aadam, MD, Gregory B. Haber, MD, Jasmine Sinha, MD, and Srinadh Komanduri, MD
Moderator: Fernando Fluxa, MD, J. Andy Tau, MD, Mohammad Bilal, MD, and Shivangi T. Kothari, MD, FACG
From 12:00 Noon – 2:30 PM ET
There will be no 8pm broadcast

Week 39 – Thursday September 25, 2025
ACG-CGA Joint Webinar- Hereditary Cancer Week- 2025
Faculty: Katherine Germansky, MD, and Pooja Dharwedkar, MD
Moderator: Gautam Naresh Mankaney, MD
At Noon and 8pm Eastern

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

7

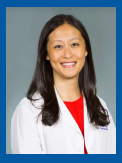
8

Virtual Grand Rounds

universe.gi.org

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.



Shannon Chang, MD, FACG:
AbbVie: Consultant; BMS: Consultant; Janssen: Consultant; Pfizer: Consultant

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

9

Virtual Grand Rounds

universe.gi.org

Update in Ulcerative Colitis and the New American College of Gastroenterology Guidelines

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
Chair, International Organization for the Study of IBD

UChicagoIBD
90 years of Discovery and Innovation

10

Virtual Grand Rounds

universe.gi.org

Why Do We Need Clinical Practice Guidelines?

- **Standardization of Care**
  - Reduces variation in practice and ensures that decisions are not solely based on individual physician preference or habit
- **Evidence Translation**
  - Synthesize the best available research, clinical trials, and expert consensus into practical recommendations
  - Help clinicians stay up-to-date and apply complex evidence in a usable way at the bedside
- **Quality and Safety**
  - Improve patient safety and outcomes by recommending proven diagnostic and therapeutic approaches
  - Avoid ineffective or harmful interventions
  - Promote early recognition of disease and appropriate management
- **Efficiency and Resource Use**
  - Reduce unnecessary testing and treatments, focusing resources on interventions most likely to benefit patients
- **Education and Training**
  - Teaching tools for trainees and clinicians, offering structured learning on standards of care in specific conditions
- **Accountability and Benchmarking**
  - Offers measures quality of care, develops performance metrics, and evaluates compliance
  - Can provide medicolegal protection when physicians follow recognized standards
- **Patient Empowerment**
  - Helps patients understand their treatment options and engage in shared decision-making with their clinicians

11

Virtual Grand Rounds

universe.gi.org

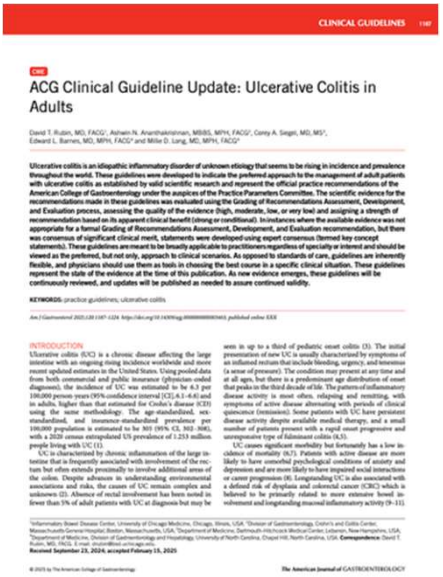
History of the ACG Guidelines for UC 1997 – 2004 – 2010 – 2019 – 2025

- Kornbluth A, Sachar DB. *Ulcerative colitis practice guidelines in adults. American College of Gastroenterology, Practice Parameters Committee.* **Am J Gastroenterol.** 1997;92(2):204-211.
- Kornbluth A, Sachar DB; Practice Parameters Committee of the American College of Gastroenterology. *Ulcerative colitis practice guidelines in adults (update): American College of Gastroenterology, Practice Parameters Committee.* **Am J Gastroenterol.** 2004;99(7):1371-1385.
- Kornbluth A, Sachar DB; Practice Parameters Committee of the American College of Gastroenterology. *Ulcerative Colitis Practice Guidelines in Adults: American College of Gastroenterology, Practice Parameters Committee.* **Am J Gastroenterol.** 2010;105(3):501-523.
- Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. *ACG Clinical Guideline: Ulcerative Colitis in Adults.* **Am J Gastroenterol.** 2019;114(3):384-413.
- Rubin DT, Ananthakrishnan AN, Siegel CA, Barnes EL, Long MD. *ACG Clinical Guideline Update: Ulcerative Colitis in Adults.* **Am J Gastroenterol.** 2025;120(6):1187-1224.

12

Virtual Grand Rounds

universe.gi.org



CLINICAL GUIDELINES

ACG Clinical Guideline Update: Ulcerative Colitis in Adults

Rubin DT, Ananthakrishnan AN, Siegel CA, Barnes EL, Long MD. *Am J Gastroenterol*. 2025;120(6):1187-1224.

13

Virtual Grand Rounds

universe.gi.org

How Are the Guidelines Made?

- Indicate the ***preferred approach to the management of adult patients with ulcerative colitis*** as established by valid scientific research and represent the official practice recommendations of the ACG under the auspices of the Practice Parameters Committee.
- **Grading of Recommendations Assessment, Development, and Evaluation (GRADE)** process, assessing the quality of the evidence and strength of recommendation based on its apparent clinical benefit (strong or conditional).
- When available evidence was not appropriate for a formal GRADE recommendation, ***but there was consensus of significant clinical merit***, statements were developed using expert consensus (termed key concept statements).
- **Viewed as the preferred, but not only, approach to clinical scenarios.**
- *As opposed to standards of care, guidelines are inherently flexible, and clinicians should* ***use them as tools*** *in choosing the best course in a specific clinical situation.*
- These guidelines represent the state of the evidence at the time of this publication. As new evidence emerges, these guidelines will be continuously reviewed, and updates will be published as needed to assure continued validity.

Rubin DT, Ananthakrishnan AN, Siegel CA, Barnes EL, Long MD. *Am J Gastroenterol*. 2025;120(6):1187-1224.

14

Virtual Grand Rounds

universe.gi.org

STRENGTH OF RECOMMENDATION:

STRONG: *Recommendation is made when the benefits or desirable effects of an intervention clearly outweigh the negatives or undesirable effects and/or the result of no action.*
CONDITIONAL: *Used when some uncertainty remains regarding the balance of benefits and potential harms, either because of low quality evidence or because of a suggested balance between desirable and undesirable effects.*

Patients: Some individuals would want the suggested course of action whereas others may not.
A discussion regarding pros, cons, and available alternatives is appropriate to reach an individualized patient-specific decision

Clinicians: A shared decision-making model through a discussion regarding the available evidence and alternative options is appropriate, taking into consideration the values and preferences of the patient

QUALITY OF EVIDENCE:

HIGH: *The authors are very confident that the true effect lies close to that of the estimate of the effect.*
MODERATE: *Moderate confidence in the effect estimate, although further research would be likely to have an impact on the confidence of the estimate.*
LOW: *Limited confidence in the estimate, and thus, the true effect could differ from the estimate of the effect.*
VERY LOW: *Very little confidence in the effect estimate and that the true effect may be substantially different than the estimate of effect.*

We prioritized **direct evidence** and did not make recommendations for positioning based on network meta-analyses.

15

Virtual Grand Rounds

universe.gi.org

New Ulcerative Colitis Practice Guidelines in Adults 2025

7	Sections
1	NEW section on positioning therapies
9	New therapies discussed
8	Tables
54	GRADEd Recommendations (Table 2)
57	Key Concept Statements (Table 3)
3	Figures

1. Ustekinumab
2. Upadacitinib
3. Ozanimod
4. Etrasimod
5. Mirikizumab
6. Risankizumab
7. Guselkumab
8. Infliximab SC
9. Vedolizumab SC

- Colorectal cancer surveillance removed

Am J Gastroenterol. 2025;120(6):1187-1224.

16

Virtual Grand Rounds

universe.gi.org

Comparison of the AGA and ACG Ulcerative Colitis Guidelines

	AGA Living Guideline (2024)	ACG Clinical Guideline (2025)[2]
Focus	Pharmacologic management for moderate-to-severe UC	Comprehensive management of UC (diagnosis, monitoring, prevention, induction and maintenance of remission, and hospitalized care)
Scope of Patients	Adults with moderate-to-severe UC	Adults with UC of ALL severities, including hospitalized patients
Methodology	GRADE methodology, uses PICO questions	GRADE framework with recommendations and KEY CONCEPTS
Therapies Covered	Immunomodulators, advanced therapies with detailed comparative efficacy discussion	Conventional therapies, advanced therapies, detailed comparative efficacy discussion
Update Cycle	Living guideline designed for continuous updates every 6 months	Planned periodic updates
	***Gastroenterology*. 2024;167(7):1307-1343.**	***Am J Gastroenterol*. 2025;120(6):1187-1224.**

17

Virtual Grand Rounds

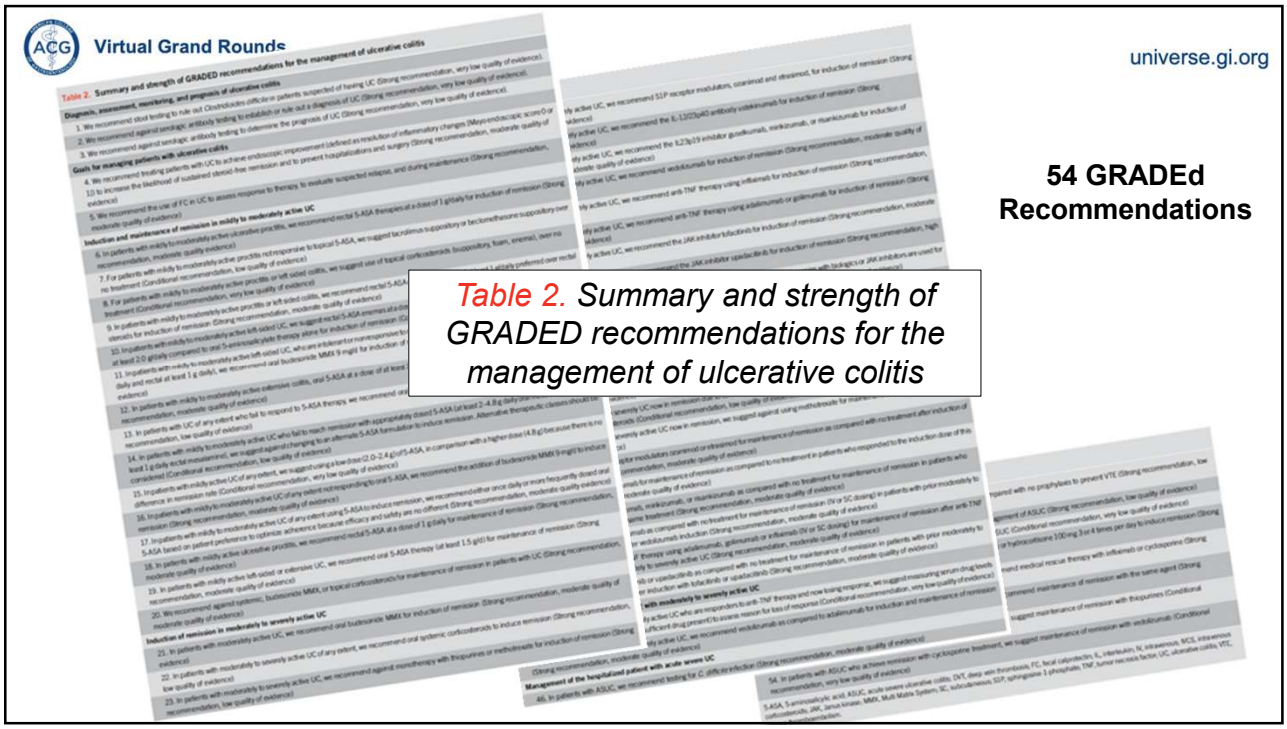
universe.gi.org

Sections of the ACG Ulcerative Colitis Practice Guidelines in Adults 2025

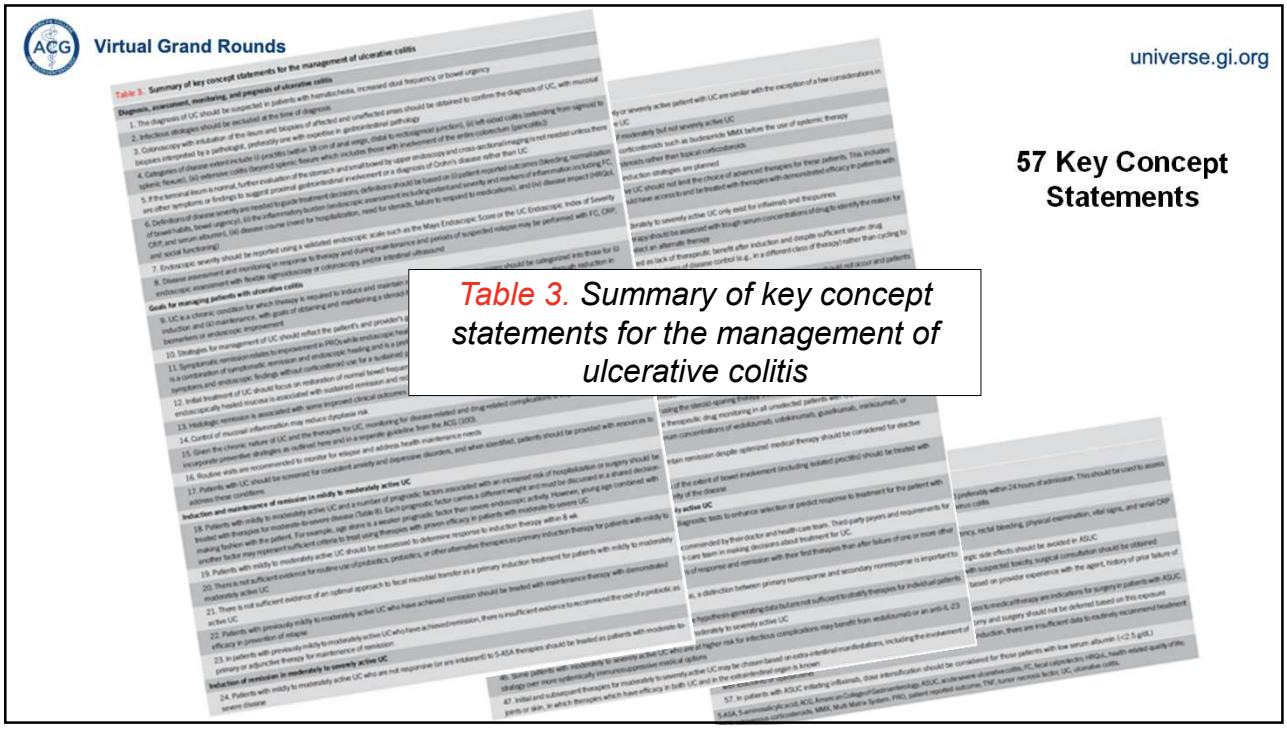
1. **Diagnosis, assessment, monitoring, and prognosis of ulcerative colitis**
2. **Goals for managing patients with ulcerative colitis**
3. **Induction and maintenance of remission in mildly to moderately active UC**
4. **Induction of remission in moderately to severely active UC**
5. **Maintenance of remission in patients with previously moderately to severely active UC**
6. **Positioning considerations for the patient with moderately to severely active UC**
7. **Management of the hospitalized patient with acute severe UC**

Rubin DT, Ananthakrishnan AN, Siegel CA, Barnes EL, Long MD. *Am J Gastroenterol*. 2025;120(6):1187-1224

18


Virtual Grand Rounds
universe.gi.org
54 GRADEd Recommendations
Table 2. Summary and strength of GRADED recommendations for the management of ulcerative colitis

19


Virtual Grand Rounds
universe.gi.org
57 Key Concept Statements
Table 3. Summary of key concept statements for the management of ulcerative colitis

20

Sections of the 2025 Ulcerative Colitis Practice Guidelines in Adults

1. Diagnosis, assessment, monitoring, and prognosis of ulcerative colitis

21

Ulcerative Colitis

- **305 (95% CI, 302–308), with a 2020 census extrapolated US prevalence of 1.253 million people living with UC[1]**
- **Initial presentation of new UC is usually characterized by symptoms of an inflamed rectum that include bleeding, urgency, and tenesmus (a sense of pressure)**
- **Consequences of UC:**
  - Comorbid psychological conditions of anxiety and depression and are more likely to have impaired social interactions or career progression
  - Defined risk of dysplasia and colorectal cancer (CRC) which is believed to be primarily related to more extensive bowel involvement and longstanding mucosal inflammatory activity
- **Management of UC must involve a prompt and accurate diagnosis, assessment of the patient's risk for poor outcomes, and early initiation of effective, safe, and tolerable medical therapies**

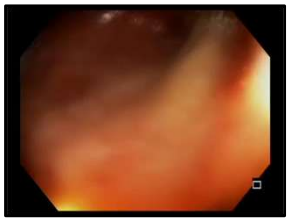
Am J Gastroenterol. 2025;120(6):1187-1224.

22

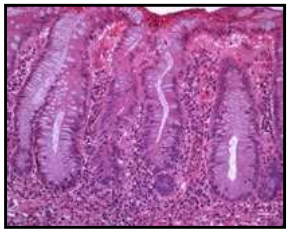
Virtual Grand Rounds

Diagnosis of UC

- Clinical suspicion
- Exclusion of infection
- Endoscopic assessment
- Histologic assessment showing chronicity
  - Histology of endoscopically normal mucosa
- Examination of terminal ileum
- Assessment of IC valve
- Upper GI not needed in adults unless other symptoms or unexplained findings



Endoscopically moderate colitis



Chronic inflammation with increase in plasma cells in the lamina propria and crypt architectural distortion

Images compliments David T. Rubin, MD

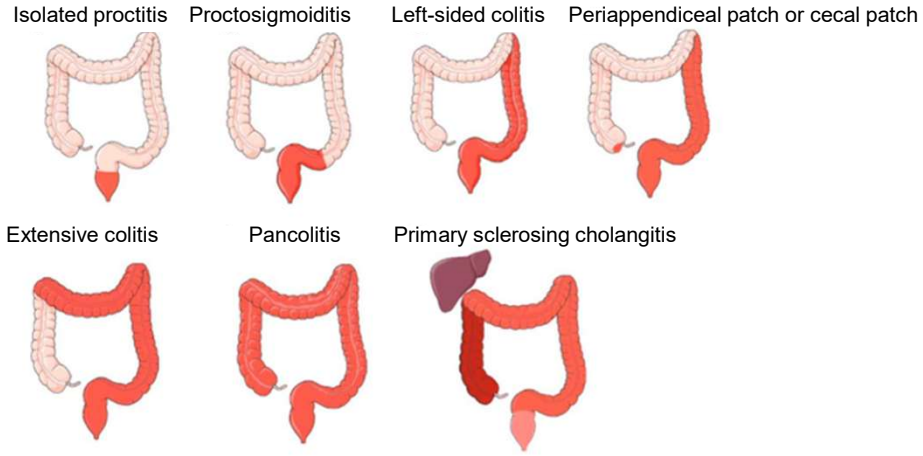
Am J Gastroenterol. 2025;120(6):1187-1224.

23

Virtual Grand Rounds

universe.gi.org

Different UC Clinical Phenotypes



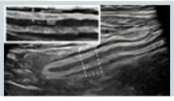
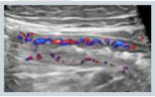
Am J Gastroenterol. 2025;120(6):1187-1224.

24

Virtual Grand Rounds

universe.gi.org

Updated ACG Ulcerative Colitis Activity Index

	Remission	Mild-Moderate	Moderate-Severe	Fulminant
Stools (#/day)	Formed stools	<4	>6	>10
Blood in stools	None	Intermittent	Frequent	Continuous
Urgency	None	Mild, occasional	Often	Continuous
Hemoglobin	Normal	Normal	<75% of normal	Transfusion required
Fecal calprotectin (µg/g)	<150-200	>150-200	>150-200	>150-200
Mayo Endoscopic Score	0	1-2	2-3	3
Intestinal ultrasound	Colonic BWT≤3 mm Rectal BWT<4 mm mLimberg=0		Colonic BWT>3 mm Rectal BWT≥4 mm mLimberg>0	

ACG GRADEd Recommendation

5. We recommend the use of fecal calprotectin in ulcerative colitis to assess response to therapy, to evaluate suspected relapse, and during maintenance (Strong recommendation, moderate quality of evidence)

Modified from Truelove SC & Witts LJ. *Br Med J*. 1955 Oct 29;2(4947):1041-8.
Maaser C, et al. *Gut*. 2020;69(9):1629-1636.
Am J Gastroenterol. 2025;120(6):1187-1224.

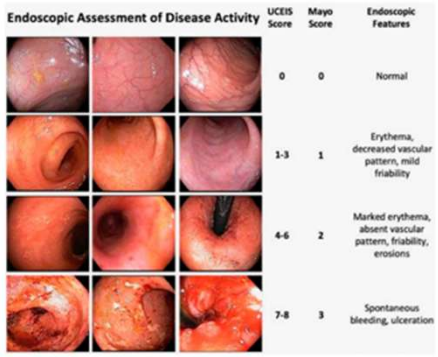
25

Virtual Grand Rounds

universe.gi.org

Remission in UC

- **Patient Reported Outcomes (Symptoms)**
  - No blood
  - Normal stool frequency
  - No urgency
- **Endoscopic Improvement**
  - Mayo Endoscopic Score of 0 or 1
  - Surrogates (benchmarked) calprotectin, CRP



Am J Gastroenterol. 2025;120(6):1187-1224.

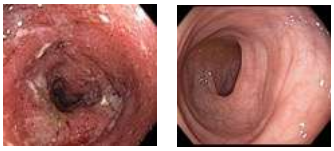
26

Virtual Grand Rounds

universe.gi.org

Remission Concepts and Targets

- **Mucosal healing:** Mayo Endoscopic Score 0,1[1,2]
  - Fecal calprotectin as surrogate for endoscopy when endoscopy not feasible to assess for mucosal healing and disease activity[1,2]



- **Disease Modification:** *changing the natural history of the UC toward positive long-term outcomes*
- **Incorporation of patient preferences:** shared decision making

Histological healing is distinct from endoscopic mucosal healing[3] and **is not yet a target**
"Histological remission" = absence of neutrophils

[1]*Am J Gastroenterol*. 2025;120(6):1187-1224.
[2]Wei CS, et al. *Intest Res.* 2017;15(3):266-284.
[3]Turner D, et al. *Gastroenterology*. 2021;160:1570-1583.

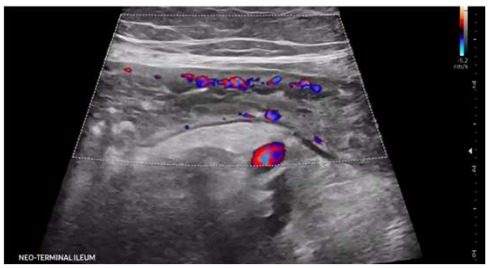
27

Virtual Grand Rounds

universe.gi.org

What is Intestinal Ultrasound?

- Ultrasound examination done by scanning the abdominal wall to visualize the bowel
- Assesses for inflammation in the small and large intestine
- Used in both UC and CD
- A point-of-care test to be done during a clinic visit
- Billing codes exist (Limited Abdominal Ultrasound)



Dolinger MT, Krugliak Cleveland N, Rubin DT, Dubinsky MC. Guide to Intestinal Ultrasound Credentialing, Documentation, and Billing for Gastroenterologists in the United States. *Am J Gastroenterol*. 2023;118(9):1528-1531.

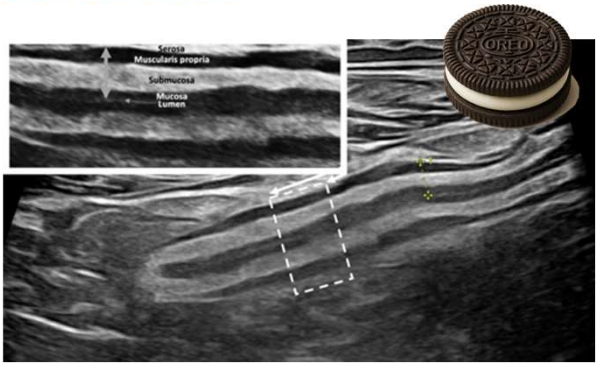
28

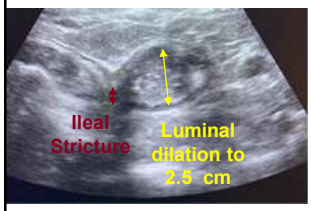
Virtual Grand Rounds

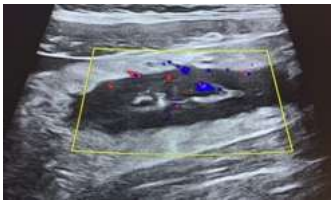
Standard Ultrasound Parameters

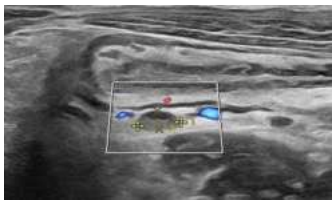
universe.gi.org

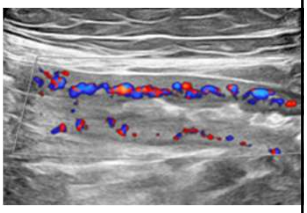
- Bowel wall thickness (normal ≤3 mm in TI and colon, ≤4 mm in rectum)
- Bowel wall hyperemia by color Doppler imaging
- Bowel wall layer stratification
- Presence of inflammatory/mesenteric fat
- Lymphadenopathy
- Complications (stricture, abscess, fistula)











29

Virtual Grand Rounds

universe.gi.org

IUS IN UC CORRELATES TO ENDOSCOPY

UC-IUS index

- EMS: r = 0.830; p <0.001
- UCEIS: r = 0.759; p <0.001
- Strong interobserver correlation of IUS scores ρ = 0.877

Parameters	Points [0–7]
Bowel wall thickness	
> 2 mm	1
> 3 mm	2
> 4 mm	3
Doppler signal	
Spots	1
Stretches	2
Abnormal haustrations	1
Fat wrapping	1

Milan Ultrasound Criteria

- EMS: ρ = 0.653; p <0.001
- Ultrasound remission: MUC >6.2 predicts endoscopic inflammation (Mayo endoscopic subscore >1)

MUC = 1.4 × BWT + 2 × BWF	
BWT	Bowel wall thickness in mm
BWF	Bowel wall flow (0 = absence; 1 = presence)

Bots S, et al. *J Crohns Colitis*. 2021;15(8):1264-1271.
Allocca M, et al. *United European Gastroenterol J*. 2022;10(2):190-197.

30

Virtual Grand Rounds

universe.gi.org

Assessment of Disease Risk "Severity" in UC

Ulcerative Colitis

Low Risk for Colectomy

- Limited anatomic extent
- Mild endoscopic disease

High Risk for Colectomy

- Extensive colitis
- Deep ulcers
- Age <40
- High CRP and ESR
- Steroid-requiring disease
- History of hospitalization
- *C. difficile* infection
- CMV infection

Rubin DT, et al. *Am J Gastroenterol*. 2025;120(6):1187-1224.
Dassopoulos T, et al. *Gastroenterology*. 2015;149(1):238-45.

Other Considerations

Moderate/High Risk for Complications

- Extra-intestinal manifestations (joints, skin, PSC)
- Steroid-dependence
- Delayed growth
- Mental health disorders
- Under/Un-insured

Jose FA, et al. *J Pediatr Gastroenterol Nutr*. 2008;46(2):124-33.
Waljee AK, et al. *PLoS One*. 2016;11(6):e0158017.
Amaro F, et al. *Biomedicines*. 2020;8(11):458.
Szigethy E, et al. *Clin Gastroenterol Hepatol*. 2017;15(7):986-997.
Nguyen GC, et al. *Inflamm Bowel Dis*. 2009;15(5):726-33.

31

Virtual Grand Rounds

universe.gi.org

Prognosis Should Guide Therapy as Much as Activity

This updated guideline emphasizes that patients with moderately to severely active UC or those who have UC with high risk of hospitalization or colectomy should be treated with therapies that have evidence for their efficacy in this degree of active disease or with this specific prognosis, based on evidence in clinical trials and real-world observational studies.

We recommend that prognosis should guide choice of therapy as much as activity of inflammation at the time of acute illness.

Am J Gastroenterol. 2025;120(6):1187-1224.

32

Sections of the 2025 Ulcerative Colitis Practice Guidelines in Adults

2. Goals for managing patients with ulcerative colitis

33

Optimal Goals of Management of UC

- Sustained and durable steroid-free remission
- Appropriate psychosocial support
- Normal health-related quality of life and social functioning
- Prevention of morbidity including hospitalization and surgery
- Prevention of cancer

Am J Gastroenterol. 2025;120(6):1187-1224.

34

Virtual Grand Rounds

universe.gi.org

Updated Goals of Management of UC

- **Diagnosis including extent of disease and biopsy**
- **Movement to separate activity and severity**
- **Induction of clinical response/remission and mucosal healing**
- **Maintenance therapy identified based on induction therapy and prognosis**
- **Screen and treat for anxiety/depressive disorders**
- **Prevention of complications (cancer, hospitalization, infections, other drug-related)**

Am J Gastroenterol. 2025;120(6):1187-1224.

35

Virtual Grand Rounds

universe.gi.org

Sections of the New Ulcerative Colitis Practice Guidelines in Adults 2025

Goals for managing patients with ulcerative colitis
9. UC is a chronic condition for which therapy is required to induce and maintain remission; therapeutic decisions should be categorized into those for (i) induction and (ii) maintenance, with goals of obtaining and maintaining a steroid-free remission and obtaining biological response through reduction in biomarkers or endoscopic improvement
10. Strategies for management of UC should reflect the patient's and provider's goals and recognize the chronic nature of the disease
11. Symptomatic remission relates to improvement in PROs while endoscopic healing is defined as restoration of intact mucosa without friability. Deep remission is a combination of symptomatic remission and endoscopic healing and is a preferred goal of management. Corticosteroid-free remission is defined based on symptoms and endoscopic findings without corticosteroid use for a sustained period of time (usually more than 12 wk)
12. Initial treatment of UC should focus on restoration of normal bowel frequency and control of the primary symptoms of bleeding and bowel urgency. An endoscopically healed mucosa is associated with sustained remission and reduced risk of colectomy
13. Histologic remission is associated with some improved clinical outcomes but has not yet been validated prospectively as a preferred target for treatment
14. Control of mucosal inflammation may reduce dysplasia risk
15. Given the chronic nature of UC and the therapies for UC, monitoring for disease-related and drug-related complications is important. This should incorporate preventive strategies as outlined here and in a separate guideline from the ACG (100).
16. Routine visits are recommended to monitor for relapse and address health maintenance needs
17. Patients with UC should be screened for coexistent anxiety and depressive disorders, and when identified, patients should be provided with resources to address these conditions

36

Virtual Grand Rounds

universe.gi.org

Treatment Options for Ulcerative Colitis, 2025

Class of Therapy Treatment	Treatment	Comment	
5-ASA	Mesalamine Sulfasalazine	Oral and rectal	Conventional Therapies (Traditional)
Corticosteroids	Budesonide Prednisone/Methylpred	Oral and rectal	
Thiopurines	6-mercaptopurine Azathioprine	Pharmacogenomics TPMT, NUDT15	Conventional Synthetic Therapies (Immunomodulators)
Calcineurin inhibitors	Cyclosporine Tacrolimus	IV and oral	
Anti-integrin	Vedolizumab	IV and SC maintenance	Biological Therapies
Anti-IL-23 (p40: IL-12/23 p19: IL-23)	Guselkumab (p19/CD64) Mirikizumab (p19) Risankizumab (p19) Ustekinumab (p40)	IV and SC maintenance Biosimilars to ustekinumab	
Anti-TNF	Adalimumab Golimumab Infliximab	Infliximab IV and SC maintenance Biosimilars to IFX and ADA	
Janus kinase inhibitors	Filgotinib (JAK1) Tofacitinib (JAK1,2,3) Upadacitinib (JAK1)	Oral Filgotinib EU only	Targeted Synthetic Small Molecules
S1P receptor modulators	Etrasimod ($S1P_{1,4,5}$) Ozanimod ($S1P_{1,5}$)	Oral	

Am J Gastroenterol. 2025;120(6):1187-1224

37

Virtual Grand Rounds

universe.gi.org

Treatment Options for Ulcerative Colitis, 2025

New since 2019 ACG Guideline

Class of Therapy Treatment	Treatment	Comment	
5-ASA	Mesalamine Sulfasalazine	Oral and rectal	Conventional Therapies (Traditional)
Corticosteroids	Budesonide Prednisone/Methylpred	Oral and rectal	
Thiopurines	6-mercaptopurine Azathioprine	Pharmacogenomics TPMT, NUDT15	Conventional Synthetic Therapies (Immunomodulators)
Calcineurin inhibitors	Cyclosporine Tacrolimus	IV and oral	
Anti-integrin	Vedolizumab	IV and SC maintenance	Biological Therapies
Anti-IL-23 (p40: IL-12/23 p19: IL-23)	Guselkumab (p19/CD64) Mirikizumab (p19) Risankizumab (p19) Ustekinumab (p40)	IV and SC maintenance Biosimilars to ustekinumab	
Anti-TNF	Adalimumab Golimumab Infliximab	Infliximab IV and SC maintenance Biosimilars to IFX and ADA	
Janus kinase inhibitors	Filgotinib (JAK1) Tofacitinib (JAK1,2,3) Upadacitinib (JAK1)	Oral Filgotinib EU only	Targeted Synthetic Small Molecules
S1P receptor modulators	Etrasimod ($S1P_{1,4,5}$) Ozanimod ($S1P_{1,5}$)	Oral	

Am J Gastroenterol. 2025;120(6):1187-1224

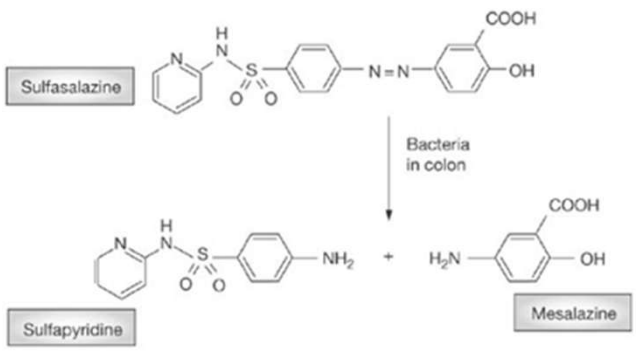
38

Sections of the 2025 Ulcerative Colitis Practice Guidelines in Adults

3. Induction and maintenance of remission in mild to moderate UC

39

5-ASA Formulations



- **Mesalamine**
  - **Delayed release (pH)**
  - **MMX**
  - **Moisture release**
  - **Enema**
  - **Suppository**
- **Pro-drugs**
  - **Sulfasalazine**
  - **Balsalazide**
  - **Olsalazine**

40

Virtual Grand Rounds

universe.gi.org

Management of Mildly-to-Moderately Active UC

Induction:

- Mild proctitis→ **rectal 5-ASA** recommended (1 g/day)[1,2,3,4,5]
- Mild proctitis not responsive to topical 5-ASA →suggest **tacrolimus suppository or beclomethasone suppository** over no treatment[6]
- Left-sided mild UC→ **rectal 5-ASA** (≥1 g/day) in combination with **oral 5-ASA** (≥ 2.0 g/day)[1,2,3,4,5,6]
- Mild extensive UC→ **oral 5-ASA** (≥ 2.0 g daily)[1,5]
- Mild UC (any extent)→ use a low dose (2.0-2.4 g) of **5-ASA**[2], in comparison with a higher dose (4.8 g)[1]
- Mild-moderate UC not responding to **oral 5-ASA**→ +**budesonide MMX** 9 mg/day[1,2,3,5]

Maintenance:

- Mildly active proctitis→ **rectal 5-ASA** (1 g daily)[1,2,7]
- Mildly active left-sided or extensive UC→ **oral 5-ASA** therapy (≥ 2 g/day)[1,2,3,4]
- **Recommend against** **systemic steroids**[1,3,6]

[1]Rubin DT, et al. *Am J Gastroenterol.* 2025;120(6):1187-1224.
[2]Hardbord M, et al. *J Crohns Colitis.* 2017;11(7):769-784.
[3]Bressler B, et al. *Gastroenterology.* 2015;148(5):1035-1058.
[4]Coi CH, et al. *Intest Res.* 2017;15(1):7-37.
[5]Ko CW, et al. *Gastroenterology.* 2019; 156(3):748-764.
[6]Lie M, et al. *Clin Gastroenterol Hepatol.* 2020;18(8):1777–84.
[7]Wei CS, et al. *Intest Res.* 2017;15(3):266-284.

41

Virtual Grand Rounds

universe.gi.org

Sections of the 2025 Ulcerative Colitis Practice Guidelines in Adults

4. Induction of remission in moderately to severely active UC

42

Virtual Grand Rounds

universe.gi.org

Induction of Remission: Moderately-to-Severely Active UC

- UC failing to respond to **5-ASA** therapy→ **oral systemic corticosteroids**[1,2,3,4]
- Moderate UC→ **oral budesonide MMX**[1]
- Moderate-severe UC of any extent→ **oral systemic corticosteroids**[1,3,4]
- S1P receptor modulator inhibitor **ozanimod**[1,5] or **etrasimod**[1,6]
- IL-12/23p40 antibody **ustekinumab**[1,7] or IL23p19 inhibitor **guselkumab**[1,8], **mirikizumab**[1,9], or **risankizumab**[1,10]
- **Vedolizumab**[1,2,3]
- **Anti-TNF** therapy using **adalimumab**, **golimumab** or **infliximab**[1,3]
  - **Infliximab** in combination with a **thiopurine**[1,2,3,4]
- **Tofacitinib**[1,11] or **upadacitinib**[1,12]
- **Recommend against** monotherapy with **thiopurines** *or* **methotrexate**[1,3]

[1]Rubin DT, et al. *Am J Gastroenterol*. 2025;120(6):1187-1224.
[2]Hardbord M, et al. *J Crohns Colitis*. 2017;11(7):769-784.
[3]Bressler B, et al. *Gastroenterology*. 2015;148(5):1035-1058.
[4]Coi CH, et al. *Intest Res*. 2017;15(1):7-37.
[5]Sands BE, et al. *Clin Gastroenterol Hepatol*. 2024;22(10):2084-95.
[6]Sandborn WJ, et al. *Lancet*. 2023;401(10383):1159-71.
[7]Sands BE, et al. *N Engl J Med*. 2019;381:1215-26.
[8]Rubin DT, et al. *Lancet*. 2025;405(10472):33-49.
[9]D'Haens G, et al. *N Engl J Med*. 2023; 388(26):2444-55.
[10]*Gastroenterol Hepatol* (NY). 2023;19(12 Suppl 9):9-10.
[11]Sandborn WJ, et al. *N Engl J Med*. 2017;376(18):1723-36.
[12]Vermeire S, et al. *Lancet Gastroenterol Hepatol*. 2023;8(11):976-989.

43

Virtual Grand Rounds

universe.gi.org

Sections of the 2025 Ulcerative Colitis Practice Guidelines in Adults

5. Maintenance of remission in patients with previously moderately to severely active UC

44

Virtual Grand Rounds

universe.gi.org

Maintenance of Remission: Moderate-Severe UC

- **Recommend against** systemic steroids[1,2,3]
- Thiopurines[1,2,3,4,5]
- **Against** using methotrexate[1,2,3]
- S1P receptor modulator inhibitor ozanimod[1,6] or etrasimod[1,7]
- IL-12/23 ustekinumab[1,8] or IL23 guselkumab[1,9], mirikizumab[1,10], or risankizumab[1,10]
- Vedolizumab (IV or SC)[1,5,15]
- **Anti-TNF therapy** using **adalimumab**, **golimumab** or **infliximab (IV or SC)**[1,2,3,4,5,14]
- Tofacitinib[1,12] 5mg or 10 mg PO BID or upadacitinib[1,13] 15mg or 30mg PO QD

[1]Rubin DT, et al. *Am J Gastroenterol.* 2025;120(6):1187-1224.
[2]Bressler B, et al. *Gastroenterology.* 2015;148(5):1035-1058.
[3]Wei CS, et al. *Intest Res.* 2017;15(3):266-284.
[4]Hardbord M, et al. *J Crohns Colitis.* 2017;11(7):769-784.
[5]Coi CH, et al. *Intest Res.* 2017;15(1):7-37.
[6]Sands BE, et al. *Clin Gastroenterol Hepatol.* 2024;22(10):2084-95.
[7]Sandborn WJ, et al. *Lancet.* 2023;401(10383):1159-71.
[8]Sands BE, et al. *N Engl J Med.* 2019;381(13):1201-14.
[9]Rubin DT, et al. *Lancet.* 2025;405(10472):33-49.
[10]D'Haens G, et al. *N Engl J Med.* 2023; 388(26):2444-55.
[11]*Gastroenterol Hepatol* (NY). 2023;19(12 Suppl 9):9-10.
[12]Sandborn WJ, et al. *N Engl J Med.* 2017;376(18):1723-36.
[13]Vermeire S, et al. *Lancet Gastroenterol Hepatol.* 2023;8(11):976-989.
[14]Hanauer SB, et al. Gastroenterology. 2024;167(5):919-933.
[15]Sandborn WJ, et al. *Gastroenterology.* 2020;158(3):562-572.

45

Virtual Grand Rounds

universe.gi.org

Variable Dosing from Induction to Maintenance in Moderate-to-Severe UC

Treatment	Induction	SC Maintenance
Vedolizumab (anti-integrin)	IV: 300mg at wks 0 and 2	Wk 6: 108mg q2wks
Infliximab (anti-TNF)	IV: 5mg/kg at wks 0, 2, 6	Wk 10: 120mg q2wks
Guselkumab (p19/CD64: IL-23)	IV: 200mg wks 0, 4, 8	Wk 12: 200mg q4wks Wk 16: 100mg q8wks
Mirikizumab (p19: IL-23)	IV: 300mg wks 0, 4, 8	Wk 12: 200mg q4wks
Risankizumab (p19: IL-23)	IV: 1200mg wks 0, 4, 8	Wk 12: 180mg/1.2 mL or 360mg/2.4 mL q8wks
Ustekinumab (p40: IL-12/23)	IV: ≤55 kg: 260mg at wk 0 ≤85 kg: 390mg at wk 0 ≥85 kg: 520mg at wk 0	Wk 8: 90mg q8wks
Tofacitinib (JAKi)	10mg PO BID for 8 weeks	5mg PO BID or 10mg PO BID
Upadacitinib (JAKi)	45mg PO QD for 8 weeks	15mg PO qd or 30mg PO qd

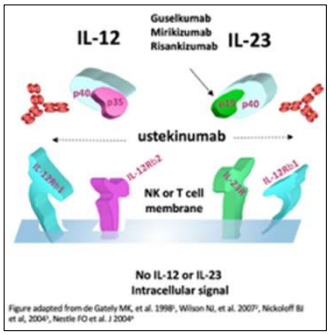
46

Virtual Grand Rounds

universe.gi.org

General Considerations of IL-23 Inhibitors in UC

- **Effective, very safe**
- **Excellent for concomitant skin**
- **Safety:**
  - **Will worsen chronic Hep B, monitor carefully**
  - **NO risk of TB**
- **Unclear if p19 antibody is better than p40 antibody in UC**
- **Likely can cycle (based on psoriasis and Crohn's experience[3])**



[1]Sandborn WJ, et al. *N Engl J Med*. 2017;376(18):1723-1736.
[2]Danese S, et al. *Lancet*. 2022;399(10341):2113-2128.
[3]Zinger A, et al. *Clin Gastroenterol Hepatol*. 2024;S1542-3565(24)00968-6.

47

Virtual Grand Rounds

universe.gi.org

Efficacy of IL-23 Inhibitors in UC Clinical Remission Rates

Ustekinumab[1]						Risankizumab[2]					Mirikizumab[3]				Guselkumab[4]					
IV Induction W8 % (P-value)			SC Maintenance W44 % (P-value)			IV Induction W12 % (P-value)		SC Maintenance W52 % (P-value)			IV Induction W12 % (P-value)		SC Maintenance W40 % (P-value)		IV Induction W12 % (P-value)		SC Maintenance W44 % (P-value)		
130 mg at wk 0	6 mg/kg at wk 0	PBO	90 mg q12wks	90 mg q8wks	PBO	1200 mg at wks 0, 4, 8	PBO	360 mg q8wks	180 mg q8wks	PBO	300 mg q4wks	PBO	200 mg q4wks	PBO	200 mg at wks 0, 4, 8	PBO	200 mg q4wks	100 mg q8 wks	PBO
UNIFI								COMMAND			LUCENT 1		LUCENT 2		QUASAR Phase 3				
15.6 (<0.001)	15.5 (<0.001)	5.3	38.4 (0.002)	43.8 (<0.001)	24.0	20.3 (<0.001)	6.2	37.6 (0.002)	40.2 (<0.001)	25.1	24.2 (<0.001)	13.3	49.9 (<0.001)	25.1	22.6 (<0.001)	7.9	50 (<0.001)	45.2 (<0.001)	18.9
Delta CR Remission Over Placebo																			
130 mg: 10.3 6 mg/kg: 10.2			90 mg q12: 14.4 90 mg q8: 19.8			14.1		360 mg q8: 12.5 180 mg q8: 15.1			10.9		24.8		14.7		200 mg q4: 31.1 100 mg q8: 26.3		

Randomized responder designs: all patients in PLACEBO maintenance arms received drug and responded in induction

[1]Sands BE, et al. *N Engl J Med*. 2019;381(13):1201-1214.
[2]Louis E, et al. JAMA. 2024;332(11):881-897.
[3]D'Haens G, et al. *N Engl J Med*. 2023;389(8):772.
[4]Rubin DT, et al. *Lancet*. 2025;405(10472):33-49.

48

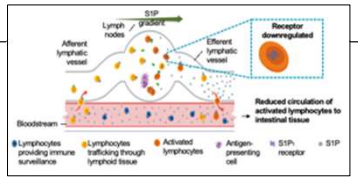
Virtual Grand Rounds

universe.gi.org

General Considerations for Small Molecules in UC

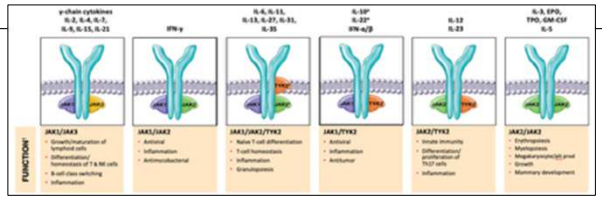
- **Favorable PK avoids pharmacodynamic challenges of protein losing colopathy**
- **Convenience of oral delivery**

- **S1P Receptor Agonists (ozanimod, etrasimod):**
  - Mechanism: prevents egress of active lymphocytes from lymph nodes
  - Likely better in moderate vs severe disease
  - Effects:
    - Expected reduction in circulating lymphocytes in periphery
    - Transient asymptomatic bradycardia
    - Rare risk of macular edema (transient)



Harris S, et al. *Neurol Neuroimunol Neuroinflamm*. 2020;7(5):e839.

- **JAK Inhibitors (tofacitinib, upadacitinib):**
  - Mechanism: inhibition of enzymes related to signal transduction
  - U.S. label positioned after anti-TNF
  - Effects:
    - Increased lipids (affects transport)
    - Risk of Herpes zoster (vaccine recommended)
    - Considerations related to VTE, MACE (but not observed in IBD)



Clark JD, et al. *J Med Chem*. 2014;57(12):5023-5038.

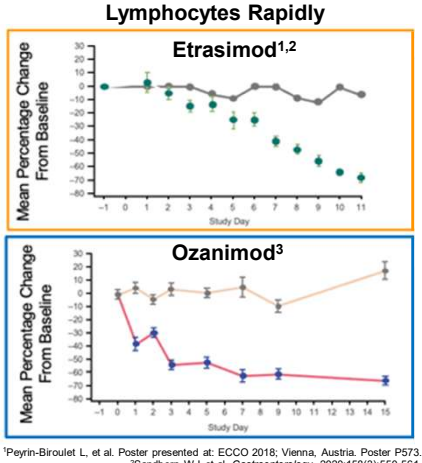
49

Virtual Grand Rounds

universe.gi.org

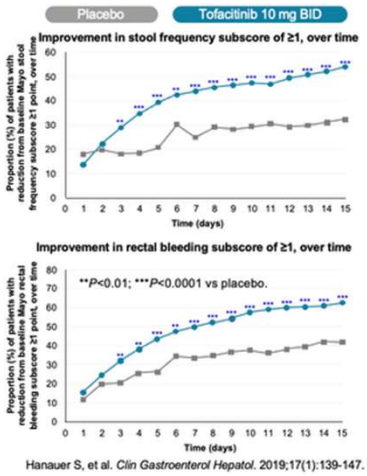
Novel Small Molecules are Fast! Consider Avoiding Steroids Entirely

S1P Receptor Modulators Affect Lymphocytes Rapidly



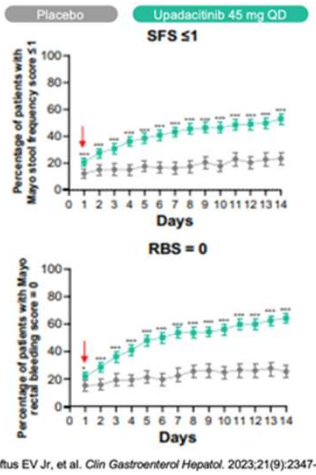
[1]Peyrin-Biroulet L, et al. Poster presented at: ECCO 2018; Vienna, Austria. Poster P573.
[2]Sandborn WJ, et al. *Gastroenterology*. 2020;158(3):550-561.
[3]Tran JQ, et al. *J Clin Pharmacol*. 2017;57(8):988-996.

Tofacitinib



Hanauer S, et al. *Clin Gastroenterol Hepatol*. 2019;17(1):139-147.

Upadacitinib



Loftus EV Jr, et al. *Clin Gastroenterol Hepatol*. 2023;21(9):2347-2358.e6.

50

Sections of the 2025 Ulcerative Colitis Practice Guidelines in Adults

6. Positioning considerations for the patient with moderately to severely active UC

51

Treatment Positioning in the New UC Guidelines GRADEd Recommendations

1. 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 antidrug antibodies** (if there is not sufficient drug present) to assess reason for loss of response. (Conditional recommendation, very low quality of evidence.)

2. In patients with moderately to severely active UC, we **recommend vedolizumab as compared to adalimumab for induction and maintenance of remission**. (Strong recommendation, moderate quality of evidence.)

Am J Gastroenterol. 2025;120(6):1187-1224.
Sands BE, et al. *N Engl J Med* 2019;381:1215-1226.

52

Virtual Grand Rounds

universe.gi.org

Treatment Positioning in the New UC Guidelines Key Concept Statements

1. There are **no validated therapeutic biomarkers or companion diagnostic tests** to enhance selection or predict response to treatment for the patient with active UC.
2. Patients with UC should have available all medical options as recommended by their doctor and healthcare team. **Third party payers and requirements for step therapy should not come between the patient and their healthcare team** in making decisions about treatment for UC.
3. Patients with moderately to severely active UC have higher rates of response and remission with their first therapies than after failure of one or more other advanced therapies.
4. Given the expanding number of therapies per mechanistic class, a **distinction between primary non-response and secondary non-response is important** in order to select the next therapeutic option.
5. Post hoc subgroup analyses and network meta-analyses provide **hypothesis-generating data but are not sufficient** to stratify therapies for individual patients.
6. **Infliximab is the preferred anti-TNF therapy** for patients with moderately to severely active UC.
7. Some patients with moderately to severely active UC who are at higher risk for infectious complications may benefit from vedolizumab or an anti-IL-23 strategy over more systemically immunosuppressive medical options.
8. Initial and subsequent therapies for moderately to severely active UC may be **chosen based on extra-intestinal manifestations**, including the involvement of joints or skin, in which therapies which have efficacy in both UC and in the extra-intestinal organ is known.

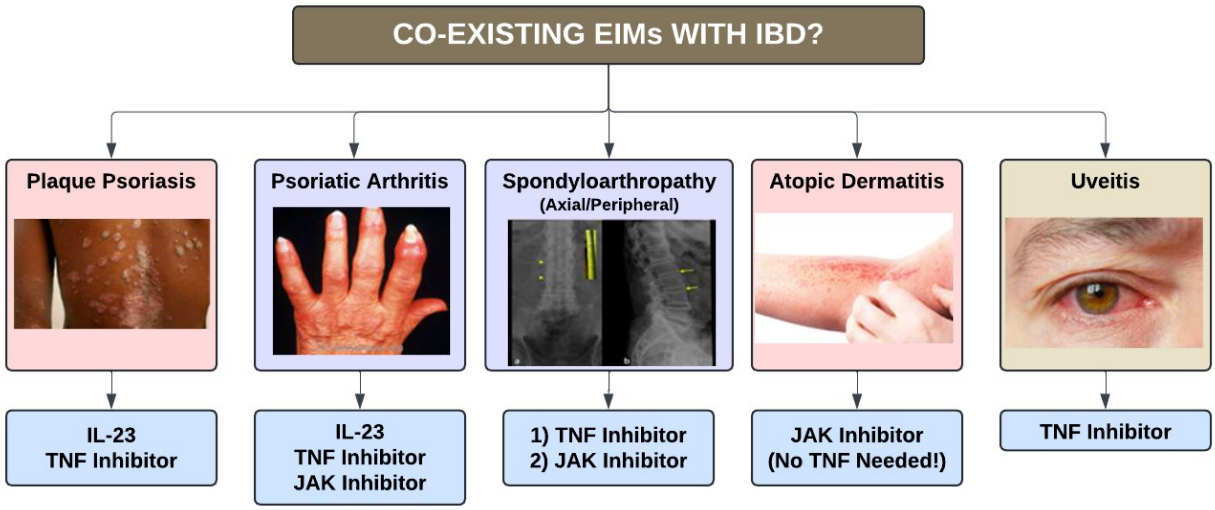
Am J Gastroenterol. 2025;120(6):1187-1224.

53

Virtual Grand Rounds

universe.gi.org

Choosing Advanced Therapies for UC Based on Concomitant Immune Conditions and Extra-Intestinal Manifestations



David T. Rubin, MD, 2024.

54

Virtual Grand Rounds

universe.gi.org

Sections of the 2025 Ulcerative Colitis Practice Guidelines in Adults

7. Management of the hospitalized patient with acute severe UC

55

Virtual Grand Rounds

universe.gi.org

Management of the Hospitalized Patient with Acue Severe Ulcerative Colitis

- DVT prophylaxis[1,4]
- Test for *C. diff*[1,4,7]; treat with vancomycin[1,8,9]
- Avoid opiods[1,4]
- Methylprednisolone 60 mg/day or hydrocortisone 100 mg 3-4x/day[1,2,3,7]
- If inadequate response to IVCS in 3-5 days→ infliximab or cyclosporine[1,2,3,4,6]
- Surgery if fail to respond to medical therapy[4,5,6,7]
- If remission with cyclosporine, maintain remission with thiopurines[1] *or* vedolizumab[1]

[1]Rubin DT, et al. *Am J Gastroenterol.* 2025;120(6):1187-1224.
[2]Hardbord M, et al. *J Crohns Colitis.* 2017;11(7):769-784.
[3]Coi CH, et al. *Intest Res.* 2017;15(1):7-37.
[4]Bitton A, et al. *Am J Gastroenterol.* 2012;107(2):179-94.
[5]Ross H, et al. *Dis Colon Rectum.* 2014;57(1):5-22.
[6]Brown SR, et al. *Colorectal Dis.* 2018;20(Suppl 8):3-117.
[7]Wei CS, et al. *Intest Res.* 2017;15(3):266-284.
[8]Johnson S, et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 focused update guidelines on management of Clostridioides difficile infection in adults. *Clin Infect Dis.* 2021;73(5):e1029–e1044.
[9]Kelly CR, et al. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of *Clostridioides difficile* Infections. *Am J Gastroenterol.* 2021;116(6):1124-1147.

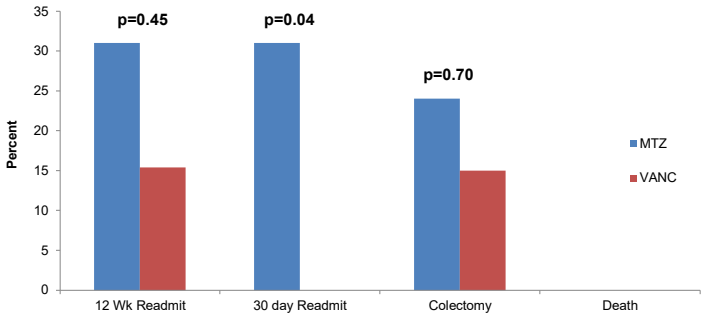
56

Virtual Grand Rounds

universe.gi.org

UC Patients with *C. difficile* Should be Treated with Vancomycin

Antibiotic choice for non-severe CDI DOES influence outcomes in UC[1]



Hospitalized UC patients with *C. difficile* should receive vancomycin regardless of severity score

[1]Horton HA, et al. *Antimicrob Agents Chemother*. 2014;58(9):5054-9.
Johnson S, et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 focused update guidelines on management of Clostridioides difficile infection in adults. *Clin Infect Dis*. 2021;73(5):e1029–e1044.
Kelly CR, et al. ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of *Clostridioides difficile* Infections. *Am J Gastroenterol*. 2021;116(6):1124-1147.

57

Virtual Grand Rounds

universe.gi.org

Considerations for JAK inhibitors and ASUC

- **Data on tofacitinib/upadacitinib for ASUC promising, may have benefit in selective patients**
- **Available studies are uncontrolled, in populations without prior anti-TNF exposure (US label), or use off-label dosing of the medications**
- Clinicians cautioned against using higher doses of the JAK inhibitors in combination with corticosteroids or as rescue therapy immediately after infliximab because of concerns about over immune suppression and risks of opportunistic infections

Therefore: We limit the recommendation of JAK inhibitor therapy as a standard option for all patients with ASUC at this time

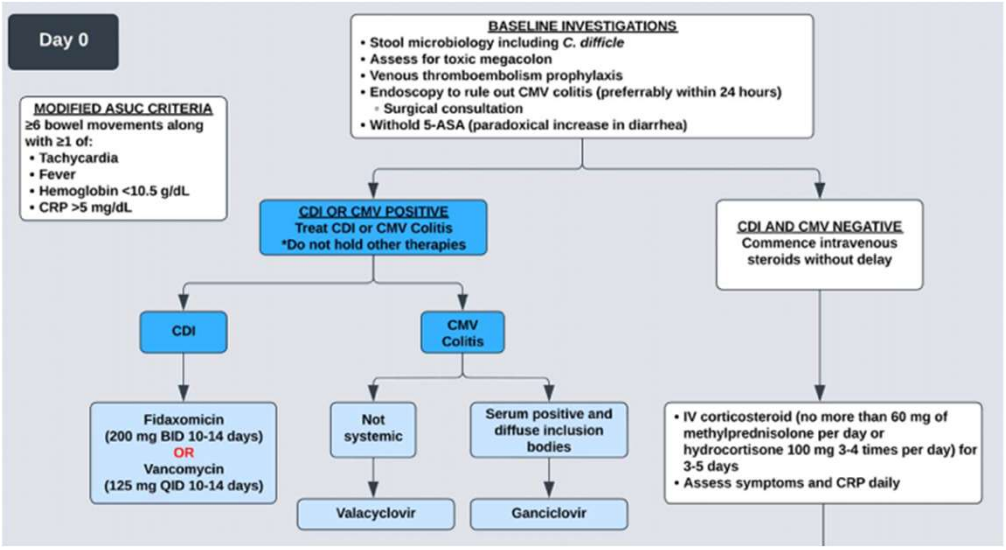
Am J Gastroenterol. 2025;120(6):1187-1224.

58

Virtual Grand Rounds

ACG Algorithm for the Management of Hospitalized Patients With Acute Severe UC

universe.gi.org

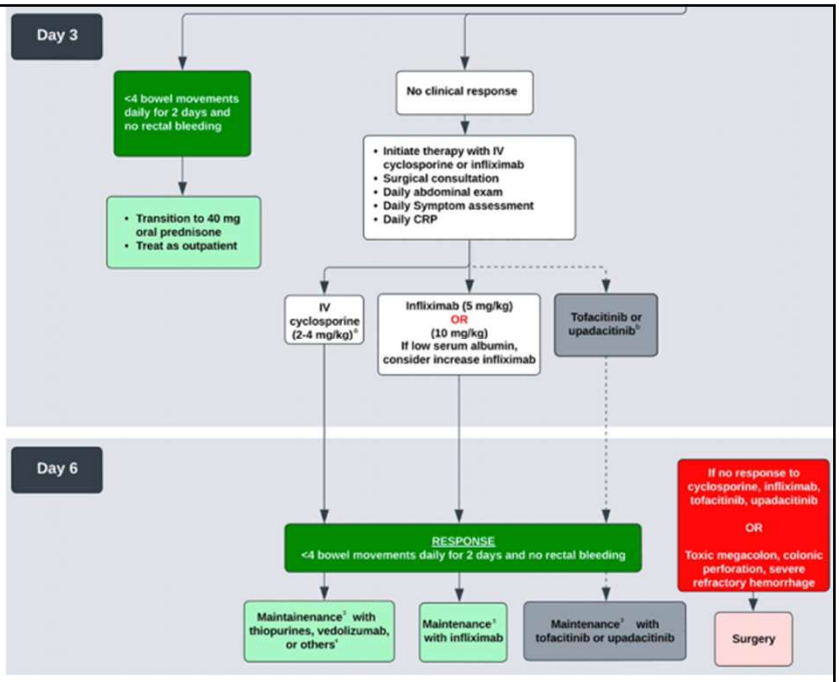


Am J Gastroenterol. 2025;120(6):1187-1224.

59

Virtual Grand Rounds

ACG Algorithm for the Management of Hospitalized Patients With Acute Severe UC



Am J Gastroenterol. 2025;120(6):1187-1224

60

Virtual Grand Rounds

universe.gi.org

Knowledge Gaps and Unresolved Issues

Pre-Diagnosis

Diagnosis

Induction and Maintenance of Remission

Disease Modification

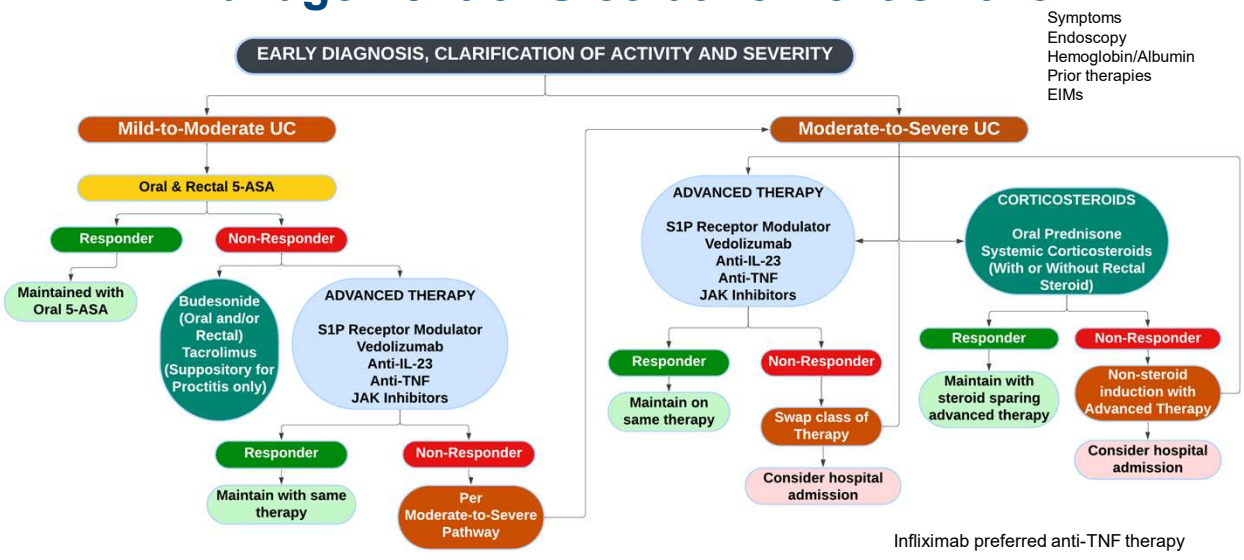
- Prevention strategies for individuals at risk for developing UC
- Predictive biomarkers to personalize therapy selection (efficacy *and* safety)
- Application of intestinal ultrasound in assessment of UC
  - Role of transmural assessment in treatment response and outcomes
- Head-to-head randomized controlled trials to clarify sequencing and positioning of therapies
- Efficacy of different therapies in the setting of failure or intolerance to non-TNF-antagonist advanced therapy.
- Better understanding of combination therapy
- Novel mechanisms of action to treat UC
- Effect of earlier advanced treatment to improve outcomes

61

Virtual Grand Rounds

universe.gi.org

Management of Ulcerative Colitis 2025



Rubin DT, Ananthakrishnan AN, Siegel CA, Barnes EL, Long MD. *Am J Gastroenterol.* 2025;120(6):1187-1224.

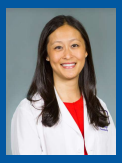
62

Virtual Grand Rounds

universe.gi.org

Questions

David T. Rubin, MD, FACG



Shannon Chang, MD, FACG

63

GI Innovation Through Collaboration

Let's talk... ACG invites you to join the conversation in the GI Circles.

ACG's Online Professional Networking Communities

Login or sign-up now at: **acg-gi-circle.within3.com**

ACG GI Circle

Connect and collaborate within GI

IBD Circle

A Partnership of the American College of Gastroenterology and the Crohn's & Colitis Foundation

64