AGA LIVING GUIDELINES: PHARMACOLOGICAL MANAGEMENT OF MODERATE-TO-SEVERE ULCERATIVE COLITIS

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REVIEWING FOR POTENTIAL UPDATE
Meeting: July 8, 2025

DECISION: After reviewing updated evidence, the guideline panel decided not to issue any new recommendations or amend any existing recommendations in AGA's 2024 guideline on ulcerative colitis (Singh, 2024)**.**

Next anticipated evidence review: December 2025

STEPS

1. We reviewed focused questions that were previously identified by the panel as being in the “living mode” (**Table 1**). No new agent has received regulatory approval since the last version of the guideline (December 2024).

S#	Focused Question	PICO Question			
		Patients	**Intervention**	**Comparator**	**Critical Outcomes**
1. (Living)	In adult outpatients with moderate-to-severe UC, what is the efficacy of TNF antagonists (infliximab, adalimumab, golimumab), vedolizumab, ustekinumab, JAK-inhibitors (tofacitinib, filgotinib, upadacitinib), S1P receptor modulators (ozanimod, etrasimod) and IL-23 antagonists (mirikizumab, risankizumab, guselkumab), for induction and maintenance of remission in patients with moderate-severe UC?	Adult outpatients with moderate-to-severe UC	• TNF antagonists (infliximab, adalimumab, golimumab) • Vedolizumab • Ustekinumab • JAK-inhibitors (tofacitinib, filgotinib, upadacitinib) • S1P receptor modulators (ozanimod, etrasimod) • IL-23 antagonists (mirikizumab, risankizumab, guselkumab)	Placebo	• Induction of clinical remission • Maintenance of clinical remission
2. (Living)	In adult outpatients with moderate-to-severe UC who are **naïve to advanced therapies**, what is the comparative efficacy of infliximab, adalimumab, golimumab, vedolizumab, ustekinumab, tofacitinib, filgotinib, upadacitinib, ozanimod, etrasimod, mirikizumab, risankizumab and guselkumab for induction and maintenance of remission?	Adult outpatients with moderate-to-severe UC who are naïve to advanced therapies	• Infliximab • Adalimumab • Golimumab • Vedolizumab • Ustekinumab • Tofacitinib • Filgotinib • Upadacitinib • Ozanimod • Etrasimod • Mirikizumab • Risankizumab • Guselkumab	Placebo or another active comparator	• Induction of clinical remission • Maintenance of clinical remission
3 (Living)	In adult outpatients with moderate-to-severe UC who **have been exposed to advanced therapies**,	Adult outpatients with moderate-to-severe UC	• Infliximab • Adalimumab • Golimumab	Placebo or another active comparator	• Induction of clinical remission

	what is the comparative efficacy of infliximab, adalimumab, golimumab, vedolizumab, ustekinumab, tofacitinib, filgotinib, upadacitinib, ozanimod, etrasimod, mirikizumab, risankizumab and guselkumab for induction and maintenance of remission?	who have been exposed to advanced therapies	• Vedolizumab • Ustekinumab • Tofacitinib • Filgotinib • Upadacitinib • Ozanimod • Etrasimod • Mirikizumab • Risankizumab • Guselkumab		• Maintenance of clinical remission
4. (Living)	In adult outpatients with moderate-to-severe UC, is combination therapy of TNF antagonists with an immunomodulator (thiopurines or methotrexate) superior to TNF monotherapy or immunomodulator monotherapy for induction and maintenance of remission?	Adult outpatients with moderate-to-severe UC	Combination therapy with a TNF antagonist and an immunomodulator (thiopurines or methotrexate)	• TNF antagonist monotherapy • Immunomodulator monotherapy (thiopurines or methotrexate)	• Induction of clinical remission • Maintenance of clinical remission
5. (Living)	In adult outpatients with moderate-to-severe UC, is combination therapy of a non-TNF biologic with an immunomodulator (thiopurines or methotrexate) superior to TNF monotherapy or immunomodulator monotherapy for induction and maintenance of remission?	Adult outpatients with moderate-to-severe UC	Combination therapy with a non-TNF antagonist biologic and an immunomodulator (thiopurines or methotrexate)	• Non-TNF antagonist biologic monotherapy • Immunomodulator monotherapy (thiopurines or methotrexate)	• Induction of clinical remission • Maintenance of clinical remission
6. (Living)	In adult outpatients with moderate-to-severe UC in steroid-free remission on combination therapy of biologic + immunomodulator, is discontinuation of (a) an immunomodulator or (b) discontinuation of a biologic, superior to continuation of combination therapy?	Adult outpatients with moderate-to-severe UC in steroid-free remission on combination therapy	• Discontinuation of an immunomodulator • Discontinuation of a biologic	Continuation of combination therapy	• Prevention of relapse

2. The evidence synthesis team conducted an updated literature search from November 2023 till June 10, 2025, addressing these six focused questions. We searched MEDLINE, Embase, and Cochrane CENTRAL via Ovid. The search combined controlled vocabulary and text words related to UC, with validated RCT filters applied to MEDLINE and Embase. We excluded pediatric studies and non-English language studies. The search identified 4,320 potential studies (3,744 full-text papers and 576 conference abstracts). The search strategy is listed in the appendix.
3. The identified title/abstracts were then reviewed by the AGA's validated large language model pipeline (Chung *et al*. *Gastroenterology* 2025; doi: 10.1053/j.gastro.2025.03.034) for evidence synthesis for clinical guidelines. With this pipeline and after excluding duplicates, 527 articles were selected for further review. Two guideline panel members (Siddharth Singh and Yuhong Yuan) reviewed these studies independently.
4. After review, eight new RCTs (five published as conference abstracts) that met our inclusion criteria were identified. These included six RCTs that informed PICO #1: four new RCTs comparing ozanimod (n=2 RCTs, one induction + one maintenance trial; 198 patients) or etrasimod (n=2 RCTs; 212 patients) vs. placebo for treatment of moderate-to-severe UC, one new RCT comparing Efmarodocokin alfa, a novel IL-22 agonist vs. placebo (n=22) and including vedolizumab as an active comparator (n=43), one new RCT comparing subcutaneous guselkumab vs. placebo (n=557). We identified two head-to-head RCTs informing PICOs #2 and #3: one RCT compared the efficacy of infliximab vs. vedolizumab vs. ustekinumab as first-line therapy for biologic-naïve patients with moderate-to-severe UC (n=97), and one RCT compared the efficacy of infliximab vs. vedolizumab in patients with moderate-to-severe UC with previous failure of adalimumab or golimumab (n=151). No new RCTs informing PICOs 4, 5 and 6 were identified.

Study	**Title**	**Abstract**	**DOI**
Matsuoka 2024 (Conference abstract)	Ozanimod as a once-daily oral therapy for Japanese patients with ulcerative colitis: results from the induction period of a Phase 2/3 study (J-True North)	Background Ozanimod is an oral, small molecule sphingosine 1-phosphate (S1P) receptor modulator that selectively targets the S1P1 and S1P5 receptor subtypes. Ozanimod is approved in multiple countries outside Japan for the treatment of moderately to severely active ulcerative colitis (UC) and/or relapsing forms of multiple sclerosis. We herein report the efficacy and safety results during the induction period of J-True North, a multi-centre, randomised, double-blind, placebo-controlled clinical Phase 2/3 study consisting of a 12-week induction period, followed by a 40-week maintenance period and an open-label extension period in Japanese patients with moderately to severely active UC. Methods Japanese male and female UC patients aged 18 to 75 years with moderately to severely active UC (defined as Mayo score of 6 to 12, with endoscopic subscore ≥2, rectal bleeding score (RBS) ≥1, and stool frequency score ≥1) were randomised in a 1:1:1 ratio to receive either 0.46 mg or 0.92 mg ozanimod, or placebo capsules orally once daily. All patients had received prior treatment with aminosalicylates or corticosteroids. The primary endpoint was clinical response at Week 12 (defined as a reduction from baseline in the complete Mayo score of ≥ 3 points and ≥ 30%, and a reduction from baseline in the RBS of ≥ 1 point or an absolute	https://doi.org/10.1093/ecco-jcc/jjad212.0817

		RBS of ≤ 1 point), and key secondary endpoints were clinical remission, clinical response, endoscopic improvement, mucosal healing and safety at Week 12 and 52. Results Patients were randomised to the ozanimod 0.46 mg group (n=68), 0.92 mg group (n=65), and the placebo group (n=65). At baseline, 36.4% of patients were female, mean age was 42.6 y and mean complete Mayo score was 8.4. The clinical response rate at Week 12 was 52.9%, 61.5%, and 32.3% in the ozanimod 0.46 mg, 0.92 mg, and placebo groups, respectively, demonstrating a statistically significant improvement of ozanimod vs placebo (Figure 1). Similarly, higher improvement rates were observed in all key secondary clinical and endoscopic endpoints in the ozanimod groups compared with the placebo group at Week 12. Frequent adverse events (AEs) observed in the induction period were nasopharyngitis, headache, et.al. (Table 1). AEs observed in the study were similar to those in the global phase 3 True North study with 0.92 mg ozanimod, and there were no new safety signals with ozanimod in the J-True North study. Conclusion Ozanimod as a once-daily oral therapy was effective as induction therapy for Japanese patients with moderately to severely active UC, and the safety profile was consistent with the results of previous studies.	
Nakase 2024 (conference abstract)	Ozanimod as induction and maintenance therapy for ulcerative colitis: a randomized, double-blind, placebo-controlled study in japan (j-true north)	Background: Ozanimod (OZA) is an oral, small molecule sphingosine 1-phosphate (S1P) receptor modulator that selectively targets the S1P1 and S1P5 receptor subtypes. OZA is approved in multiple countries outside Japan for the treatment of moderately to severely active ulcerative colitis (UC). We herein report the efficacy and safety results in induction and maintenance period from the J-True North study in Japanese patients with moderately to severely active UC (NCT03915769). Method: Japanese male and female UC patients aged 18 to 75 years with moderately to severely active UC (defined as Mayo score of 6 to 12 inclusive, with endoscopic subscore ≥2, a rectal bleeding score (RBS) ≥1, and a stool frequency score ≥1) were randomized in a 1:1:1 ratio to receive either 0.46 mg or 0.92 mg OZA, or placebo (PBO) capsules orally once daily. All patients had received prior treatment with aminosalicylates or corticosteroids. Following the 12-wk induction period (IP), patients who responded to treatment continued their respective 0.46 mg, 0.92 mg OZA or PBO treatment during the 40-wk maintenance period (MP), whereas non-responders transferred to the open-label extension and received 0.92 mg OZA. The primary endpoint was clinical response at Week 12 (defined as a reduction from baseline in the complete Mayo score of ≥3 points and ≥30%, and a reduction from baseline in the RBS of ≥1 point or RBS ≤1). Key secondary endpoints were clinical remission, clinical response, endoscopic improvement, mucosal healing and safety at Weeks 12 and 52. Results: Patients were randomized to the OZA 0.46 mg group (n=68), 0.92 mg group (n=65), and the PBO group (n=65). At baseline, 36.4% of patients were female, mean age was 42.6 y and mean complete Mayo score was 8.4. The patients who achieved clinical response at Week 12 were 52.9%, 61.5%, and 32.3% in the OZA	https://doi.org/10.1016/S0016-5085(24)02359-X

		0.46 mg, 0.92 mg, and PBO groups, respectively, demonstrating a statistically significant improvement of OZA vs PBO. Continued OZA treatment maintained significant improvements in clinical response and clinical remission through Week 52 in patients who entered the MP (Figure 1). Similarly, higher proportions of patients achieved other key secondary endpoints in the OZA groups compared with the PBO group both at Week 12 and Week 52. Frequent adverse events observed in the IP and MP were presented in Table 1. Safety results of the J-True North study were consistent with findings of a previously conducted global phase 3 study in moderately to severely active UC with 0.92 mg OZA, and no new safety signals were identified. Conclusion: OZA as a once-daily oral therapy was effective and well tolerated as induction and maintenance therapy in Japanese patients with moderately to severely active UC. This large-scale Japanese clinical trial results verified the efficacy and safety of OZA in an Asian population for the first time. [figure presented] [table presented]	
Takeuchi 2025	Efficacy and safety of etrasimod in Japanese patients with ulcerative colitis: results from a phase 2 dose-ranging study.	Background/Aims: Etrasimod is an oral, once-daily, selective sphingosine 1-phosphate1,4,5 receptor modulator for the treatment of moderately to severely active ulcerative colitis (UC). However, its efficacy, safety, and the appropriate dosage have not been extensively investigated in the Japanese population., Methods: This phase 2, multicenter, randomized, double-blind, placebo-controlled dose-ranging, 12-week trial was carried out among Japanese patients with moderately to severely active UC. Patients were randomized 1:1:1 to receive etrasimod 1 mg once daily (QD), etrasimod 2 mg QD, or placebo. The primary efficacy endpoint was the proportion of patients achieving clinical remission at week 12. Secondary efficacy endpoints and treatment emergent adverse events (TEAEs) were also investigated. Efficacy endpoints were presented as proportions of patients achieving each outcome., Results: Overall, 17, 19, and 18 patients received etrasimod 1 mg QD, etrasimod 2 mg QD, and placebo, respectively. One patient receiving etrasimod 1 mg (6.7%), 5 patients receiving etrasimod 2 mg (26.3%), and no patients receiving placebo (0%) achieved clinical remission. More patients receiving etrasimod versus placebo achieved secondary endpoints, except endoscopic normalization, at week 12. TEAEs were experienced by 9 patients receiving etrasimod 1 mg (52.9%), 13 patients receiving etrasimod 2 mg (68.4%), and 10 patients receiving placebo (55.6%). None of the TEAEs were serious and none experienced by patients receiving etrasimod led to treatment discontinuation., Conclusions: Overall, etrasimod 2 mg QD for up to 12 weeks appeared efficacious and safe in these Japanese patients with moderately to severely active UC. All TEAEs were mild to moderate in severity. (ClinicalTrials.gov: NCT05061446).	https://dx.doi.org/10.5217/ir.2024.00213
Naganuma 2025	First-line biologics as a treatment for	Background:	https://dx.doi.org/10

	ulcerative colitis: a multicenter randomized control study	Despite the availability of several biologics for ulcerative colitis (UC), there remains a critical need to identify first-line treatment biologics. The superiority of infliximab (IFX) over vedolizumab (VED) and ustekinumab (UST) was evaluated as initial UC treatments in patients with biologic-naive UC. Method(s): This multicenter, randomized control trial was conducted across 20 Japanese medical institutions. An independent center randomly allocated patients with UC (Mayo score >= 6) who had not previously used biologics to three treatment groups (IFX, VED, UST). The primary endpoint was the clinical remission (CR) rate at week 12, with other endpoints including the treatment continuation rate at week 26 and adverse events (AEs). Result(s): From May 2021 to June 2023, 107 cases were registered, including 104 for safety and 97 for efficacy evaluation. CR rate at week 12 was 36.4% (95%CI:20.4-54.9), 32.4% (95%CI:17.4-50.5) and 43.3% (95%CI:25.5-62.6) in IFX, VED, and UST group, respectively. Continuation rates at week 26 were 50.0%(IFX), 58.3% (VED), and 82.4% (UST). AEs related to study medication were 14.7% (IFX), 16.7% (VED), and 5.9% (UST). Predictors for CR at week 12 were thiopurine use in IFX (p = 0.04), lower baseline Mayo score (p = 0.007), and lower Patient report outcome 2 (p = 0.003) at week 2 in VED. Conclusion(s): Due to small sample size, it is challenging to make conclusions for main endpoints from this study while our study suggested that use of thiopurines in IFX group and lower activity at enrollment in VED group may enhance treatment efficacy. (jRCT1031200329; available at https://jrct.niph.go.jp/).Copyright Â¬Â© Japanese Society of Gastroenterology 2025.	.1007/s00535-025-02216-0
Danese 2025	A Randomized Phase II Study of Efmarodocokin Alfa, an interleukin-22 Agonist, Versus Vedolizumab in Patients With Ulcerative Colitis	Background & Aims: Efmarodocokin alfa is an interleukin (IL)-22 agonist, with favorable pharmacokinetic properties and an acceptable safety profile. This study further explored the therapeutic potential of efmarodocokin alfa compared with vedolizumab in patients with ulcerative colitis (UC). Method(s): This randomized phase II trial evaluated the efficacy, safety, pharmacokinetics, and pharmacodynamics of 3 doses of efmarodocokin alfa administered intravenously every 4 weeks (30 mug/kg [n = 43], 60 mug/kg [n = 44], and 90 mug/kg [n = 43]) compared with placebo (n = 22) and with vedolizumab (n = 43) in the treatment of moderate to severe UC. Key clinical outcomes were assessed through the modified Mayo Clinic Score, and endoscopic evaluations by a central reader. Result(s): Efmarodocokin alfa was adequately tolerated with an acceptable safety profile. Although efmarodocokin alfa did not show statistically significant improvement in clinical remission, clinical response, endoscopic healing, or endoscopic remission at week 8 compared with placebo, vedolizumab demonstrated some efficacy. Clinical remission was achieved by 12%, 9%, and 12% of patients in the 30, 60, and 90 mug/kg dose arms,	https://dx.doi.org/10.1016/j.cgh.2024.11.013

		respectively, compared with 9% and 26% of patients in the placebo and vedolizumab arms at week 8. Similarly, endoscopic healing at week 8 was achieved by 14%, 14%, and 12% of patients in the 30, 60, and 90 mug/kg dose arms, respectively, compared with 14% and 33% of patients in the placebo and vedolizumab arms. A dose-dependent increase in pharmacodynamic biomarkers was observed (regenerating islet-derived protein 3-alpha and C-reactive protein levels). Conclusion(s): Efmarodocokin alfa did not demonstrate efficacy compared with placebo, and this phase II study was ended early for futility; however, there was evidence of target engagement (skin adverse events, regenerating islet-derived protein 3-alpha levels). ClinicalTrials.gov, Number: NCT03558152.	
Bouguen 2025 (conference abstract)	Comparative efficacy of infliximab and vedolizumab after failure of a first anti-TNF in patients with ulcerative colitis: a double-blind randomized controlled trial (EFFICACI)	Background: No clinical trial has previously assessed the best therapeutic strategy between switching to another anti-TNF or swapping to another class of biologic class after the failure of a first anti-TNF in ulcerative colitis (UC). The aim of the EFFICACI trial was to compare the efficacy of vedolizumab with infliximab in patients who had failed a first sub-cutaneous anti-TNF (golimumab and/or adalimumab). Methods: EFFICACI was a French double-blind multicenter randomized controlled trial (1:1) comparing intravenous vedolizumab 300 mg at weeks 0-2-6 to intravenous infliximab 5 mg/kg at weeks 0-2-6. Eligible patients had moderate-to-severe UC, defined by a total Mayo score ≥ 6, despite at least 12 weeks (W) of treatment with adalimumab or golimumab as first line of advanced therapy. The primary endpoint was steroid free clinical remission at W14. The number of patients (N=150) was estimated for a 20% difference in favor of vedolizumab with a type 1 risk of 5% and a power of 80%. Patients were subsequently followed in an open-label fashion until week 54. The analysis was performed on an intention-to-treat basis. Only results at W14 will be presented. (CPP: 2018-002673-21; Clinical Trial: 35RC17_8841_EFFICACI) Results: From January 2018 to December 2023, 151 patients were randomized among 19 centers: 78 in the vedolizumab arm and 73 in the infliximab arm. Characteristics and demographics at inclusion were similar between groups, with 102/151 (67.5%) patients failing adalimumab and 49/151 (32.5%) failing golimumab. Concomitant immunosuppressive treatment with thiopurine or methotrexate was associated with infliximab and vedolizumab for 37/72 (51.4%) patients and 43/78 (55.1%) patients, respectively. At W14, proportions of patients in clinical remission (primary endpoint) were 34.6% (27/78) with vedolizumab and 19.2% (14/73) with infliximab (p=0.033). The clinical response rates were 46/78 (59.0%) with vedolizumab and 36/72 (50.0%) with infliximab (p=0.27). Proportions of patients in clinical response at W2, W6 and W14 are shown in Figure 1. At W14, endoscopic improvement (Mayo endoscopic subscore 0 or 1) was observed in 36/77 (46.8%) patients in the vedolizumab arm and 21/72 (29.2%) in the infliximab arm (p=0.027). No factor at inclusion was predictive of remission at week 14, including pharmacokinetic data for the first-line anti-TNF. Adverse event rates were similar in both groups - 46 (63.9%) infliximab arm, 55/78 (70.51%) vedolizumab arm. Eight	https://doi.org/10.1093/ecco-jcc/jjae190.0038

		patients were hospitalized for a severe flare (5 in the infliximab arm and 3 in the vedolizumab arm). Conclusion: After failure of a first subcutaneous anti-TNF, induction therapy with vedolizumab was superior to infliximab in achieving steroid free clinical remission at week 14 in patients with UC.	
Peyrin-Biroulet 2025 (Conference abstract)	Efficacy and safety of subcutaneous guselkumab induction therapy in patients with Ulcerative Colitis: results through week 12 from the phase 3 ASTRO study	Background: Guselkumab (GUS) is a selective dual-acting IL-23p19 subunit inhibitor that potently blocks IL-23 and binds to CD64, a receptor on cells that produce IL-23. GUS demonstrated efficacy in patients (pts) with ulcerative colitis (UC) who received GUS intravenous (IV) induction and subcutaneous (SC) maintenance (QUASAR). We evaluated the efficacy and safety of GUS SC induction in ASTRO, a phase 3, randomised, double-blind, placebo (PBO)-controlled, parallel-group, multicenter trial in pts with moderately to severely active UC. Methods: Eligible pts had a history of inadequate response or intolerance to corticosteroids, immunosuppressants, biologics, Janus kinase inhibitors, and/or sphingosine 1-phosphate inhibitors (BIO/JAKi/S1Pi-IR) or were BIO/JAKi/S1Pi naïve. Randomisation was stratified by baseline (BL) BIO/JAKi/S1Pi status and Mayo endoscopic subscore (MES) with 418 pts allocated 1:1:1 to GUS 400 mg SC q4w (x3)→GUS 200 mg SC q4w (N=140), GUS 400 mg SC q4w (x3)→GUS 100 mg SC q8w (N=139), or PBO (N=139). The primary endpoint was clinical remission (Mayo stool frequency subscore 0/1 not increased from BL, rectal bleeding subscore 0, MES 0/1 with no friability) at week (W) 12. Multiplicity-controlled W12 secondary endpoints are clinical response, symptomatic remission, endoscopic improvement, and histo-endoscopic mucosal improvement (HEMI). The prespecified analysis plan compared the combined GUS 400 mg SC treatment group to PBO at W12, and safety was assessed throughout. Results: BL characteristics were similar across treatment groups (overall mean age, 41.7 years; mean UC duration, 7.6 years; mean modified Mayo score, 6.7; MES=3, 56.0%; BIO/JAKi/S1Pi-IR, 40.2%). The primary endpoint and all secondary endpoints were met. At W12, significantly greater proportions of pts treated with GUS 400 mg SC induction than PBO achieved clinical remission (27.6% vs 6.5%, respectively; adj Δ: 21.1%; P<0.001), clinical response (65.6% vs 34.5%; adj Δ: 31.0%; P<0.001), symptomatic remission (51.3% vs 20.9%; adj Δ: 30.4%; P<0.001), endoscopic improvement (37.3% vs 12.9%; adj Δ: 24.3%; P<0.001), and HEMI (30.5% vs 10.8%; adj Δ: 19.6%; P<0.001). In prespecified analyses of subpopulations defined by prior BIO/JAKi/S1Pi history, greater proportions of GUS-treated versus PBO-treated pts achieved the endpoints (Figure). The proportions of GUS-treated pts with ≥1 adverse event (AE), serious AE, or AE leading to treatment discontinuation were not greater than PBO (Table). Conclusion: ASTRO established the efficacy of GUS SC induction in UC, with no new safety concerns identified. These results build on the QUASAR IV induction data, demonstrating that both GUS IV and SC induction are highly efficacious in pts with moderately to severely active UC.	https://doi.org/10.1093/ecco-jcc/jjae190.0010

Wu 2025 (conference abstract)	Efficacy and Safety of Vedolizumab Combined with Upadacitinib in Moderate-to-Severe Ulcerative Colitis: a Multicenter, Prospective, Randomized Controlled Trial	Background: The optimal treatment strategy for moderate-to-severe ulcerative colitis (UC) remains challenging. This study aimed to evaluate the efficacy and safety of combination therapy with vedolizumab (VDZ) plus upadacitinib (UPA) compared to VDZ monotherapy. Methods: In this multicenter, prospective, randomized controlled trial, patients with moderate-to-severe UC were randomized to receive either VDZ (300mg at weeks 0, 2, 6, then every 8 weeks through week 54) plus UPA (45mg daily for 8 weeks) or VDZ monotherapy. Primary endpoints included clinical response, sustained clinical response, clinical remission, sustained clinical remission, and CRP normalization at weeks 8 and 54. Secondary endpoints included endoscopic response, sustained endoscopic response, endoscopic remission, sustained endoscopic remission and quality of life changes. Results: 61 patients were enrolled (combination therapy: n=26; monotherapy: n=35). At week 8, the combination therapy group showed significantly higher clinical response rates compared to the monotherapy group (63.4% vs 34.3%, P=0.037). Clinical remission rates were 30.8% vs 11.4% (P=0.152). Endoscopic response rates were significantly higher in the combination group (61.5% vs 40.0%, P=0.042). Endoscopic remission (46.2% vs 25.7%, P=0.209), and histological remission (34.6% vs 14.3%, P=0.157) showed numerical improvements. Laboratory inflammatory markers and nutritional parameters improved in both groups without significant between-group differences. Conclusion: VDZ plus UPA combination therapy showed better early clinical and endoscopic outcomes compared to VDZ mono-therapy in moderate-to-severe UC. Both treatments improved inflammatory and nutritional markers. This dual-targeted approach may represent a promising treatment strategy for UC patients, though larger studies with longer follow-up are needed to confirm these findings.	https://doi.org/10.1093/ecco-jcc/jjae190.0097
Wu 2025 (Conference abstract)	Etrasimod as induction and maintenance therapy in Asian patients with moderately to severely active Ulcerative Colitis: results from the maintenance period of a randomised, double-blind, placebo-controlled,	Background: Etrasimod (ETR) is an oral, once daily (qd), selective sphingosine 1-phosphate (S1P)1,4,5 receptor modulator for the treatment of moderately to severely active ulcerative colitis (UC). ES101002 was a registrational Phase (Ph) 3 study evaluating the efficacy and safety of ETR in Asian patients (pts) with moderately to severely active UC (NCT04176588). ETR has shown significant benefit vs placebo (PBO) as induction and maintenance therapy in pts with UC, including in the 12-week (wk) induction period (IP) of ES101002.1-4 Here, we report results from the 40-wk maintenance period (MP) of ES101002. Methods: The study comprised a 12-wk IP, 40-wk MP, and open-label (OL) period (up to 40 wks). Eligible pts were enrolled from the Chinese mainland, Taiwan, and South Korea, had confirmed moderately to severely active UC, and had failed ≥1 UC treatment (conventional and/or biologics/JAK inhibitors). Pts randomised 2:1 into the IP received ETR 2 mg qd or PBO for 12 wks. Clinical responders at wk 12 were re-randomised 1:1 into the MP and received ETR or PBO for 40 wks. In the MP, stratification factors were treatment in the IP,	https://doi.org/10.1093/ecco-jcc/jjae190.0091

	multi-centre Phase 3 study (ES101002)	previous exposure to biologics/JAK inhibitors, and concomitant use of corticosteroids at IP baseline. IP non-responders or pts who experienced UC worsening in IP/MP were offered entrance into the OL period. The objectives for the MP of the study were to evaluate the efficacy and safety of ETR vs PBO. Results: A total of 158 pts were randomised into the MP and received treatment (77 ETR; 81 PBO). Baseline pt demographics and disease characteristics, including mean age (43.8 years [yrs] ETR; 40.7 yrs PBO), proportion of female pts (45.5% ETR; 40.0% PBO), and mean baseline modified Mayo Score (6.0 ETR; 5.8 PBO), were balanced between groups. A higher proportion of pts receiving ETR (89.6%) vs PBO (51.9%) completed the 40-wk MP. All efficacy objectives in the 40-wk MP were achieved (Figure 1). A significantly greater proportion of pts receiving ETR vs PBO achieved clinical remission, clinical response, endoscopic improvement, endoscopic normalisation, mucosal healing, and symptomatic remission (P<.0001 each). Most treatment-emergent adverse events (TEAEs) were mild to moderate in severity (Table 1). ETR vs PBO resulted in fewer Grade 3 TEAEs (ETR 10.4%, PBO 13.6%) and serious adverse events (ETR 7.8%, PBO 8.6%). In each group, there was a single treatment discontinuation due to a TEAE (UC worsening) with no Grade 4 TEAEs or deaths. Conclusion: Consistent with previous studies, ETR resulted in clinically meaningful and statistically significant improvement of UC in Asian pts across clinical, endoscopic, and histologic endpoints, and was safe and well-tolerated.	

5. The guideline panel met on July 8, 2025. Dr. Yuhong Yuan was added as a new junior methodologist to the guideline. The members in attendance were Drs Singh, Ananthakrishnan, Scott, Loftus, Agrawal, Haydek, and Yuan.
6. On reviewing the new evidence in the context of existing evidence and recommendations, the panel determined that new evidence was unlikely to meaningfully change the certainty of evidence that informed prior recommendations. The panel determined that new evidence did NOT warrant a change in existing recommendations or need for new recommendation statements.
7. Additionally, the panel identified one RCT comparing the combination of upadacitinib + vedolizumab vs. vedolizumab monotherapy (n=61). The panel discussed whether new PICO(s) on advanced combination therapy should be added to the existing guideline. Upon review of the data and discussion, the panel determined that at this stage, the evidence was too preliminary to develop a new PICO that would address combination of advanced therapies. The panel will revisit new data at the next planned update.

Appendix:

Search Strategy:

1. Colitis, Ulcerative/ use medall,cctr
2. ulcerative colitis/ use oemezd
3. ulcerative colitis.ti,ab,kw,kf.
4. or/1-3 [UC]
5. 4 use cctr [UC in CENTRAL]
6. ((Randomized Controlled Trial or Controlled Clinical Trial).pt. or (Randomi?ed or Placebo or Randomly or Trial or Groups).ab. or Drug Therapy.fs.) not (exp Animals/ not Humans.sh.) [MEDLINE Cochrane RCT filter]
7. 4 and 6 use medall [UC in MEDLINE]
8. Randomized controlled trial/ or Controlled clinical study/ or randomization/ or intermethod comparison/ or double blind procedure/ or human experiment/ or (random$ or placebo or (open adj label) or ((double or single or doubly or singly) adj (blind or blinded or blindly)) or parallel group$1 or crossover or cross over or ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)) or assigned or allocated or (controlled adj7 (study or design or trial)) or volunteer or volunteers).ti,ab. or (compare or compared or comparison or trial).ti. or ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab.
9. Cross-sectional study/ not (exp randomized controlled trial/ or controlled clinical study/ or controlled study/ or randomi?ed controlled.ti,ab. or control group$1.ti,ab.)
10. (random$ adj sampl$ adj7 ("cross section$" or questionnaire$1 or survey$ or database$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.)
11. (((case adj control$) and random$) not randomi?ed controlled).ti,ab.
12. Systematic review.ti,ab. not (trial or study).ti.
13. (nonrandom$ not random$).ti,ab.
14. "random field$".ti,ab.
15. (random cluster adj3 sampl$).ti,ab.
16. "we searched".ab. and (review.ti. or review.pt.)
17. ("update review" or (databases adj4 searched)).ab.
18. (rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1).ti. and animal experiment/
19. Animal experiment/ not (human experiment/ or human/)
20. or/9-19
21. 8 not 20 use oemezd [Embase Cochrane RCT filter]
22. 4 and 21 use oemezd [UC in Embase]
23. 5 or 7 or 22 [UC RCTs in all databases]
24. limit 7 to dt=20231101-20250610 use medall [Limit not valid in CCTR,Embase; records were retained]
25. limit 22 to dc=20231101-20250610 use oemezd [Limit not valid in CCTR; records were retained]
26. (2024* or 2025*).ep.
27. 23 and 26
28. limit 23 to yr="2023 -Current" use cctr

29. 24 or 25 or 27 or 28 [UC RCTs from Nov 2023 to June10 2025]
30. limit 29 to english language
31. (exp animals/ or exp animal/ or exp nonhuman/ or exp animal experiment/ or animal model/ or animal tissue/ or non human/ or (rat or rats or mice or mouse or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or canine or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1 or basic research or cell lines or in vitro or animal model).ti,ab.) not (humans/ or human/ or (men or women or patients or participants or subjects).ti,ab.)
32. 30 not 31
33. (child/ or Pediatrics/ or Adolescent/ or Infant/ or adolescence/ or newborn/ or (baby or babies or child or children or pediatric* or paediatric* or peadiatric* or infant* or infancy or neonat* or newborn* or new born* or adolescen* or preschool or pre-school or toddler*).ti,ab.) not (adult/ or aged/ or (aged or adult* or elder* or senior* or men or women).ti,ab.)
34. 32 not 33

References

Singh, S. (2024, December). AGA Living Clinical Practice Guideline on Pharmacological Management of Moderate-to-Severe Ulcerative Colitis. *Gastroenterology, 167*(7), 1307-1343. doi:10.1053/j.gastro.2024.10.001