Journal of Enterocolitis

Review

Treatment of Ulcerative Colitis: Induction of Remission, Maintenance, and Management of the Remission Period

İsmail Hakkı Kalkan

Department of Gastroenterology, TOBB University of Economics and Technology, Ankara, Türkiye

Cite this article as: Kalkan IH. Treatment of Ulcerative Colitis: Induction of Remission, Maintenance, and Management of the Remission Period. *J Enterocolitis.* 2025;4(Suppl 1):S38-S46.

Corresponding author: İsmail Hakkı Kalkan, e-mail: drismailster@gmail.com

Received: March 10, 2025 **Accepted:** March 17, 2025

DOI: 10.14744/Jenterocolitis.2025.84898

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Abstract

Ulcerative colitis (UC) is a chronic inflammatory bowel disease that requires a tailored therapeutic approach based on disease location and severity. This review outlines treatment strategies, including conventional therapies, biologic medications, and small molecules, for inducing and maintaining remission in patients with mild to moderate and moderate to severe UC. Additionally, it addresses the management of acute severe colitis.

Keywords: Ulcerative colitis, treatment, conventional therapy, biologics

GENERAL PRINCIPLES OF TREATMENT OF ULCERATIVE COLITIS

In the treatment of ulcerative colitis, the disease location-proctitis, left-sided, or extensive-and activity level determine the type and method of treatment administration. After achieving clinical remission through induction therapy, the primary goal is to maintain remission. The initial response to induction therapy is typically observed between the second and fourth weeks, while the optimal time to assess the treatment response is between the 12th and 16th weeks. The main objectives of treatment are to achieve remission-clinical, endoscopic, and histological-and maintain it.[1]

REMISSION INDUCTION TREATMENT IN MILD TO MODERATE ULCERATIVE COLITIS

Oral Mesalazine

In the treatment of mild to moderate ulcerative colitis (UC), oral mesalazine has been shown to be more effective than a placebo in achieving both clinical remission and response. Raine T. and colleagues[2] evaluated the results of eleven randomized controlled trials through a meta-analysis and found that oral mesalazine was significantly more effective than a placebo in achieving clinical remission in 2,156 patients after 4 to 12 weeks of induction therapy [RR: 1.56; 95% CI: 1.24–1.97]. Similarly, oral mesalazine demonstrated a significantly greater effect on endoscopic response [RR: 1.73; 95% CI: 1.0–3.0]. The rate of serious adverse events during the maximum 12-week period was 6.1% in the oral mesalazine group and 9% in the placebo arms. A recent Cochrane meta-analysis found that the use of oral mesalazine in single or divided daily doses, as well as different 5-ASA formulations, did not result in differences in treatment responses.[3] Despite ongoing debate over whether differences in the colonic distribution of mesalazine preparations affect efficacy, comparative studies have not shown significant differences between formulations.

The same Cochrane meta-analysis found that higher oral doses of mesalazine in induction therapy were not superior to standard doses.[3] However, subgroup analyses of the ASCEND study indicated that a 4.8 g/day dose of mesalazine preparations with pH-dependent release may be more effective than a 2.4 g/day dose.[4] Conversely, no difference was observed between high-dose and standard-dose treatments of the pH-dependent multimatrix (MMX) preparation.[5]

Topical Mesalazine and Topical Steroids

Topical 5-ASA (suppository or enema) at a dose of ≥1 g/day for 2 to 8 weeks was found to be superior to topical steroids for remission induction in 1,395 adult patients with active distal UC [RR: 1.36; 95% CI: 1.19–1.56]. However, no significant difference was observed between the two groups regarding clinical and endoscopic response.[2] Patients are generally recommended to be treated with a single topical agent; however, only one study has suggested that a combination of rectal 5-ASA and rectal corticosteroids may be beneficial.[6] This combined approach may be appropriate for patients with UC proctitis who do not initially improve with topical 5-ASA alone.

Oral Mesalazine and Topical Mesalazine Combination Therapy

In the 2022 guideline on UC treatment, a meta-analysis evaluated a small number of studies comparing the combination of oral and topical mesalazine with oral mesalazine monotherapy for remission induction. The analysis indicated that combination therapy was more effective than

monotherapy, with a nearly significant difference [clinical remission: RR: 1.45; 95% CI: 0.98–2.13; endoscopic healing: RR: 1.21; 95% CI: 0.91–1.61]. It was concluded that combination therapy may be preferred over monotherapy, although the recommendation was based on weak evidence.[2]

MAIN POINTS

In remission induction treatment of mild to moderate UC:

- Oral mesalazine (at doses of 2.4 g and above) and colonic-released budesonide in MMX form are effective.
- Combined oral and topical mesalazine therapy is more effective than oral mesalazine monotherapy.
- Topical steroids can be added for patients with proctitis who do not respond to topical mesalazine.
- Systemic corticosteroids may be considered a second-line treatment option for patients who do not respond to mesalazine therapy.
- Thiopurines are not recommended due to their delayed onset of action.

In the maintenance of remission in mild to moderate UC:

- For patients with proctitis in remission, topical 5-ASA is recommended at dosages ranging from 1 g every three days to 1 g daily for 12 to 24 months.
- Thiopurines are recommended as maintenance therapy for patients who are mesalazine-intolerant or steroid-dependent.
- Continuing treatment with the same mesalazine formulation is recommended to reduce the risk of relapse.

In remission induction treatment of moderate to severe UC:

- Oral prednisolone, anti-TNF agents (infliximab, adalimumab, and golimumab), vedolizumab, ustekinumab, and Janus kinase inhibitors can be used as first-line treatments.
- Adding immunomodulators to anti-TNF therapy to reduce immunogenicity increases treatment success.
- In biologic treatment-experienced patients, infliximab, ustekinumab, Janus kinase inhibitors, vedolizumab*, and adalimumab* are preferred.
- Janus kinase inhibitor therapy should be administered to an appropriate patient population, considering the risk group (individuals >65 years of age with at least one cardiovascular disease risk factor).
- Etrasimod and ozanimod are approved for the induction treatment of moderate to severe UC.

  * In moderately active UC.

In maintenance of remission in moderate to severe UC

- Maintenance of remission should be continued with the induction drug (except systemic steroids).
- Anti-TNF drugs, vedolizumab, ustekinumab, and Janus kinase inhibitors are effective in maintaining remission.
- Etrasimod and ozanimod are approved for the maintenance treatment of moderate to severe UC.

In the treatment of acute severe UC:

- The initial treatment involves either a single 100 mg intravenous dose of hydrocortisone, given four times, or a 60 mg intravenous dose of methylprednisolone, administered through multiple injections or as a continuous infusion over 24 hours.
- In patients who do not respond to systemic corticosteroids, infliximab (standard dose) or IV cyclosporine (7-day induction of 2–4 mg/kg followed by oral administration in responding patients) may be administered.
- Thiopurine should be added to treatment when cyclosporine is switched to the oral form.

Budesonide MMX

The efficacy of once-daily budesonide MMX 9 mg for remission induction in adult patients with active mild to moderate UC was assessed by reviewing the results of three studies. At the end of week 8, among a total of 542 patients, budesonide MMX was found to be superior to placebo in inducing clinical remission [RR: 2.86; 95% CI: 1.62–5.04] and clinical response [RR: 1.46; 95% CI: 1.11–1.93], as well as in achieving an endoscopic response [RR: 1.43; 95% CI: 1.10–1.84]. Across all three studies, the rates of serious adverse events and any adverse events did not differ between the budesonide MMX and placebo groups [RR: 0.88; 95% CI: 0.33–2.41 and RR: 1.04; 95% CI: 0.79–1.37, respectively].[2,7-9]

Systemic Steroids

In mild to moderate UC, systemic corticosteroids are used as second-line therapy for remission induction when mesalazine therapy fails. Evidence supporting this approach is based on a comparison between systemic corticosteroids and sulfasalazine, which demonstrated remission induction rates of 76% versus 58% in favor of corticosteroids.[10]

Thiopurines

Two randomized controlled trials (RCTs) have evaluated azathioprine monotherapy for remission induction. In these studies assessing the efficacy of azathioprine in inducing UC remission, no significant difference was found between azathioprine and placebo for clinical remission induction. There are no studies on mercaptopurine or thioguanine.[2 11 12] Due to the relatively slow onset of action of azathioprine, it should generally be added to treatment in patients with active disease only when used in combination with an effective induction agent for remission maintenance. Figure 1 illustrates the treatment algorithm for mild to moderate UC.

MAINTENANCE OF REMISSION IN MILD TO MODERATE ULCERATIVE COLITIS

Oral Mesalazine

Two separate randomized controlled trials involving 306 participants evaluated the use of oral mesalazine for the maintenance treatment of UC. These studies found that oral mesalazine at doses of ≥2 g/day was superior to placebo in achieving clinical remission after 48 to 52 weeks of follow-up [RR: 1.54; 95% CI: 1.11–2.14]. Additionally, oral mesalazine demonstrated a near-significant superiority over placebo in achieving endoscopic remission [RR: 1.20; 95% CI: 1.00–1.44].[2,13,14]

There is limited data on the impact of switching mesalazine formulations on disease activity in patients with UC in remission. A study by Robinson et al. examining 1,200 cases found that patients in remission who switched mesalazine formulations had a 3.5-fold higher likelihood of relapse compared to those who continued their original formulation.[15]

Topical Mesalazine

An analysis of four placebo-controlled studies investigating the efficacy of topical 5-ASA in the maintenance treatment of patients with distal colitis or proctitis showed that 5-ASA, in suppository or enema form at doses ranging from 1 g three times a week to 1 g daily, was superior to placebo in achieving clinical remission after 12 to 24 months of use [RR: 2.22; 95% CI: 1.26–3.90].[2,16-20] Additionally, for the maintenance of endoscopic remission, 1 g of 5-ASA enemas was shown to be superior to placebo at the end of the first year.[21]

Thiopurines

Four placebo-controlled trials found that azathioprine was more effective than placebo in maintaining clinical remission in UC patients who were steroid-dependent or 5-ASA-intolerant at the end of the first year

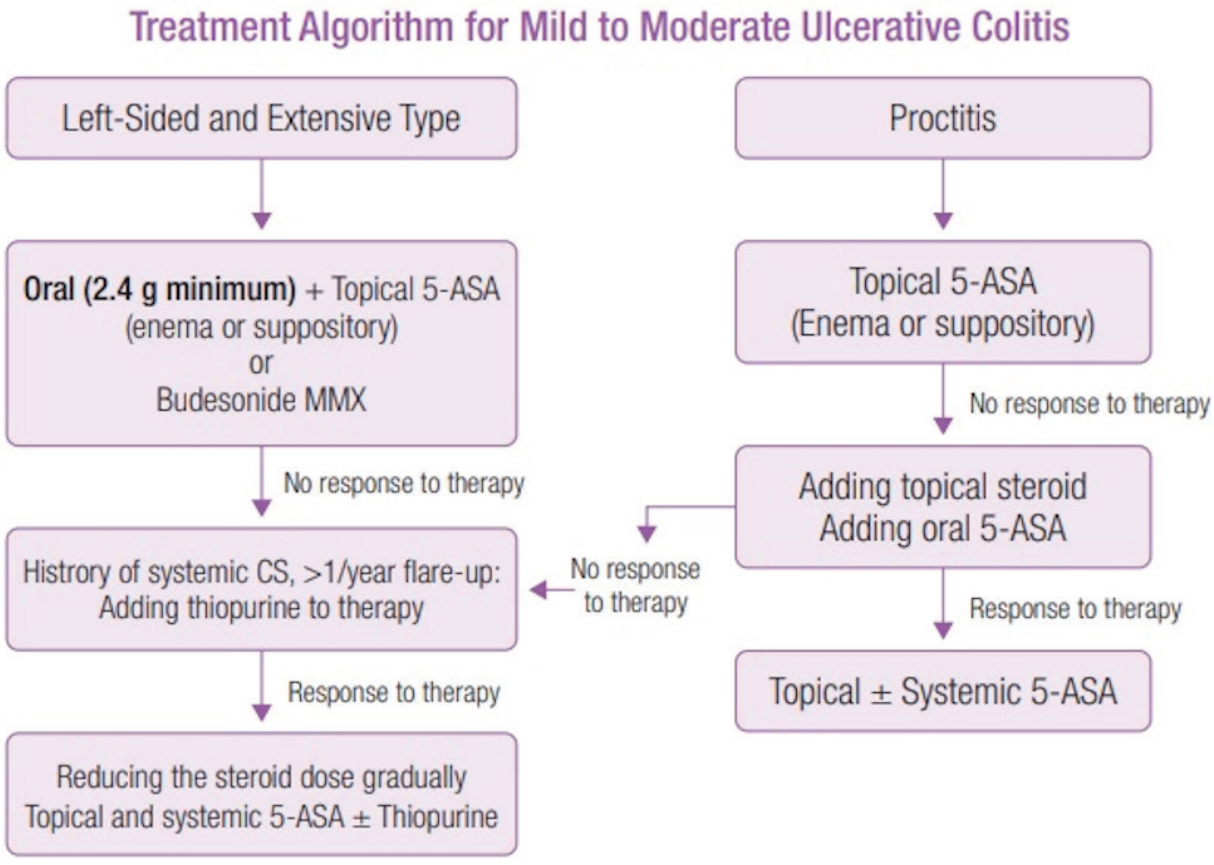

Figure 1. Treatment Algorithm for Mild to Moderate Ulcerative Colitis.

[RR: 1.59; 95% CI: 1.19–2.11].[2 11 12 22 23] However, there are no controlled trials comparing thiopurines with a placebo for the maintenance of endoscopic remission. Despite this, extensive cohort studies and a recent real-world investigation have demonstrated that azathioprine is effective in maintaining clinical remission and reducing the need for colectomy.[24,25]

REMISSION INDUCTION THERAPY IN MODERATE TO SEVERE ULCERATIVE COLITIS

Systemic Steroids

Systemic steroids have been widely used worldwide for the induction treatment of moderate to severe UC. The benefits of short-term use in induction therapy are expected to outweigh potential risks. Systemic steroid therapy has been shown to be superior to budesonide and budesonide MMX, although it may increase steroid-related side effects.[26,27]

Anti-TNFs (Infliximab, Adalimumab, Golimumab)

In ECCO's recent UC treatment guideline, a meta-analysis evaluating the efficacy of anti-TNF agents in remission induction analyzed nine RCTs and found that anti-TNF agents were superior to placebo in achieving clinical remission [RR: 2.23; 95% CI: 1.81–2.76], clinical response [RR: 1.56; 95% CI: 1.38–1.76], and mucosal healing [RR: 1.49; 95% CI: 1.32–1.68].[2,28-36] Additionally, in the same meta-analysis and several large population cohort studies, anti-TNFs demonstrated similar safety outcomes to placebo.[2,37,38]

Although no studies have directly compared anti-TNF agents, two recent network meta-analyses have indicated that infliximab is superior to adalimumab and golimumab in achieving clinical remission.[39,40] In a subgroup analysis of a phase 3 study, the efficacy of adalimumab in inducing remission in infliximab-treated patients was found to be low.[35]

Furthermore, a meta-analysis including six studies on ulcerative colitis examined the efficacy of adalimumab following infliximab treatment, revealing remission rates ranging from 0% to 50%.[41] However, there is insufficient data regarding the use of anti-TNF agents after other biological therapies. Studies investigating the efficacy of combining immunomodulators with anti-TNF therapy for remission induction have demonstrated that the combination of infliximab and azathioprine is more effective than infliximab alone.[42] Although no randomized controlled trials have been conducted for adalimumab, data from observational studies suggest a comparable advantage when used in combination with immunomodulators.[43] Research by Roblin et al. found that for patients who develop antibodies to anti-TNF drugs, combination therapy with immunomodulators yields better results than switching to a different anti-TNF agent.[44]

Anti-Integrin (Vedolizumab)

In two separate RCTs, in which 620 patients were examined regarding the efficacy and safety of vedolizumab in induction treatment in patients with moderate to severe UC, a 6- to 10-week follow-up was performed.[45,46] A meta-analysis of these studies found that vedolizumab was superior to placebo for the induction of remission [RR: 2.14; 95% CI: 1.03–4.43]. The rate of serious adverse events in patients treated with vedolizumab did not differ from that in patients receiving placebo [RR: 0.71; 95% CI: 0.39–1.30]. In the GEMINI I phase 3 induction

study, the endoscopic remission rate at week 6 was 40.9% in patients receiving vedolizumab compared to 24.8% in patients receiving placebo (P = 0.001).[45] A more recent meta-analysis analyzed three separate trials[45-48] and found vedolizumab superior to placebo in the induction of remission in UC [OR: 2.21; 95% CI: 1.49–3.27]. In addition, this meta-analysis showed that vedolizumab was more effective in inducing remission in patients without anti-TNF therapy experience than in experienced patients.

IL-12/23 Inhibitor (Ustekinumab)

In an RCT investigating the efficacy of ustekinumab in patients with moderate to severe active UC who were refractory to conventional (steroid-thiopurine) therapy and biologics (anti-TNF and/or vedolizumab) or who were steroid-dependent, ustekinumab (6 mg/kg) was superior to placebo in terms of the induction of clinical remission (15.5% vs. 5.3%) [RR: 2.91; 95% CI: 1.72–4.94], clinical response (61.8% vs. 31.3%) [RR: 1.97; 95% CI: 1.64–2.37], and endoscopic healing (27.0% vs. 13.8%) [RR: 1.96; 95% CI: 1.41–2.72]. The frequency of serious adverse events did not differ between the ustekinumab and placebo groups (5.2% vs. 7.9%) [RR: 0.67; 95% CI: 0.39–1.17].[49] A 2020 indirect network meta-analysis found no statistical difference between the efficacy of ustekinumab and anti-TNF agents or tofacitinib in biologically naïve patients with moderate to severe UC but demonstrated the superiority of ustekinumab over adalimumab or vedolizumab in anti-TNF-experienced patients.[40]

Janus Kinase Inhibitors (Tofacitinib, Upadacitinib)

In the ECCO guideline of 2022, a meta-analysis of two RCTs showed that tofacitinib was superior to placebo in achieving clinical remission [RR: 3.26; 95% CI: 1.95–5.43] and clinical response [RR: 1.79; 95% CI: 1.49–2.14] in 1,220 patients who were treatment-intolerant or refractory to biological/conventional (mesalazine and steroids and/or thiopurine) therapy.[2,50,51] However, adverse events and endoscopic response results have not been evaluated due to the lack and uncertainty of these data.[2]

In a meta-analysis investigating the efficacy of tofacitinib in UC, a subgroup analysis showed similar efficacy of tofacitinib in anti-TNF-naïve and anti-TNF-experienced patients with UC.[52] In addition, network meta-analyses demonstrated that tofacitinib, anti-TNFs, and ustekinumab were superior to vedolizumab and adalimumab in patients with prior biologic treatment experience.[2,39,40]

In two separate parallel-arm RCTs examining the efficacy of upadacitinib in the treatment of moderate to severe UC, more than two-thirds of the subjects had a history of at least one biologic treatment. Upadacitinib 45 mg induction therapy was shown to be superior to placebo in achieving clinical remission and endoscopic improvement.[53]

In a network meta-analysis of indirect comparisons, upadacitinib was superior to all other biological agents and small molecules, including infliximab [OR: 2.70; 95% CI: 1.18–6.20], in achieving clinical remission in UC (SUCRA: 0.996).[54] Another network meta-analysis found that upadacitinib demonstrated rapid efficacy in the treatment of moderate to severe UC. According to this meta-analysis, upadacitinib was superior to all biologics and small molecules, including infliximab, in achieving clinical remission at 2, 4, and 6 weeks.[55]

Sphingosine-1 Phosphate Receptor Modulators (Etrasimod, Ozanimod)

Etrasimod and ozanimod are oral S1P receptor modulators that have been approved for the treatment of moderate to severe UC. There are five subtypes of S1P receptors (S1P1–S1P5), each exhibiting varying levels of expression in lymphoid and hematopoietic tissues, as well as in specific organs, including the brain, heart, and gastrointestinal tract.

These S1P receptor modulators are hypothesized to function by binding to S1P receptors on the surface of immune cells. This binding mechanism sequesters activated immune cells in the lymph nodes, reducing the number of immune cells entering the bloodstream. Consequently, fewer immune cells are available to migrate to areas of active inflammation, such as the colon, in patients with UC.[56]

Etrasimod was approved for the treatment of moderate to severe UC in 2023. It demonstrated efficacy as an induction therapy in a phase III RCT (ELEVATE UC 12 trial) involving 354 participants, with 238 assigned to the etrasimod group and 116 to the placebo group. The primary outcome analysis showed that etrasimod was significantly more effective in inducing clinical remission by the end of the 12-week induction phase (25% for etrasimod vs. 15% for placebo; P = 0.026). The ELEVATE UC 12 trial met all key secondary objectives. Notably, a higher percentage of patients treated with etrasimod showed endoscopic improvement (31% vs. 19%; P = 0.0092), achieved symptomatic remission (47% vs. 29%; P = 0.0013), and exhibited both endoscopic improvement and histological remission (16% vs. 9%; P = 0.036) at 12 weeks.[57]

Ozanimod was approved for the induction treatment of moderate to severe UC in 2021 based on a phase 3, 10-week trial conducted as part of the TRUE NORTH program. The study demonstrated ozanimod's superiority over placebo in achieving the primary endpoint of clinical remission at Week 10 (18% vs. 6%) and key secondary endpoints, including clinical response (48% vs. 26%), endoscopic improvement (27% vs. 12%), and mucosal healing (13% vs. 4%). The rates of achieving clinical and endoscopic endpoints were higher in biologic-naïve patients compared with biologic-exposed patients, with treatment differences at Week 10 of 16%, 9%, and 3% versus placebo for biologic-naïve, single biologic-exposed, and multiple biologic-exposed patients, respectively.[58,59]

Given the recency of its approval, there are no published real-world data on etrasimod and limited published real-world experience with ozanimod in UC. Therefore, this article will not address the positioning of both drugs in the treatment algorithm. Figure 2 shows the treatment algorithm for moderate to severe UC.

MAINTENANCE OF REMISSION IN MODERATE TO SEVERE ULCERATIVE COLITIS

Anti-TNFs (Infliximab, Adalimumab, Golimumab)

A meta-analysis of data from 10 RCTs[28-36,60] showed that anti-TNF agents were effective in maintaining remission in moderate to severe UC.[2] Anti-TNF agents were superior in maintaining clinical remission [RR: 1.98; 95% CI: 1.60–2.45], steroid-free clinical remission [RR: 2.86; 95% CI: 1.67–4.90], improvement in quality of life [RR: 1.71; 95% CI: 1.27–2.32], and sustained maintenance of clinical remission [RR: 2.76; 95% CI: 1.78–4.28]. There was no difference in serious adverse events between anti-TNF agents and placebo [RR: 0.84; 95% CI: 0.64–1.09].[2]

Anti-Integrin (Vedolizumab)

In the 2022 ECCO guideline**,** which analyzed the data of three separate RCTs, the maintenance of clinical remission [RR: 2.37; 95% CI: 1.74–3.23] and sustained maintenance of clinical remission [20.7% vs. 9.4%; RR: 2.16; 95% CI: 1.34–3.50] were superior to placebo after 52–60 **weeks** of follow-up in patients with remission induction with vedoli-

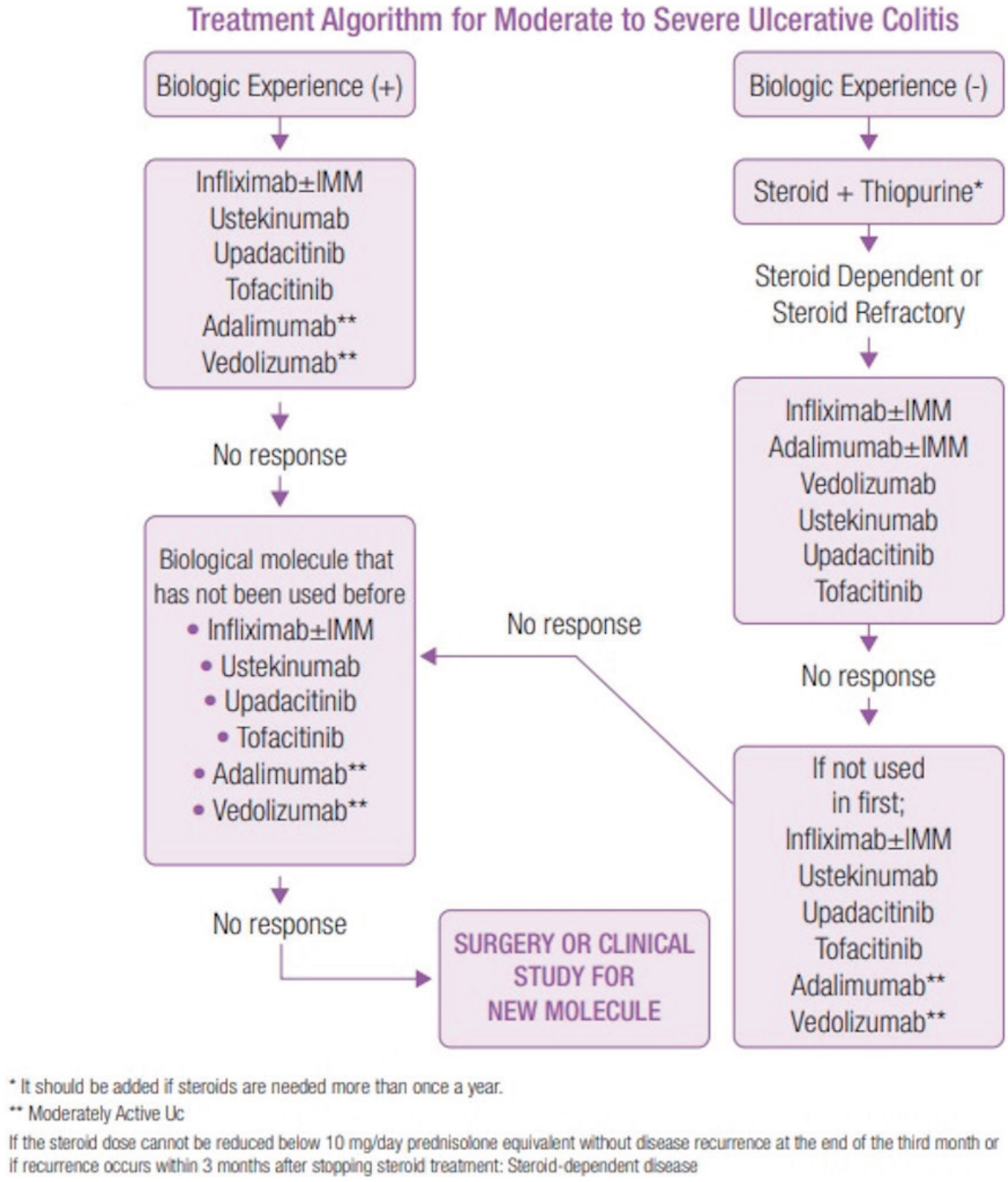

Figure 2. Treatment Algorithm for Moderate to Severe Ulcerative Colitis.

zumab. There was no significant difference between vedolizumab and placebo in terms of safety data [RR: 0.71; 95% CI: 0.39–1.30].[2,45,46,61,62]

In a meta-analysis of 48 observational studies, the maintenance of the remission rate with vedolizumab therapy was 45% [95% CI: 40%–50%] and the endoscopic healing rate was 45% [95% CI: 36%–54%]. The rate of maintenance of clinical remission was higher in biologic-naïve subjects than in biologic-experienced subjects [OR: 1.47; 95% CI: 1.17–1.85].[63]

IL-12/23 Inhibitor (Ustekinumab)

The role of ustekinumab in the maintenance of UC was evaluated in two RCTs. In the first maintenance study, subcutaneous ustekinumab 90 mg every 8 weeks was superior to placebo in achieving clinical re-

mission [RR: 1.82; 95% CI: 1.33–2.49] and steroid-free remission [RR: 1.79; 95% CI: 1.30–2.47] at the end of week 44 in patients who responded to the induction therapy. There was no significant difference in serious adverse events between the treatment and placebo arms [5.2% vs. 7.9%; RR: 0.67; 95% CI: 0.39–1.17]. Comparable results were observed when ustekinumab 90 mg was administered subcutaneously at 12-week intervals.[2,49]

In the UNIFI long-term extension study, which examined the efficacy and safety of ustekinumab treatment for up to three years, steroid-free remission rates at the end of week 152 were 51.2% (q12w) and 55.1% (q8w). Remission rates were higher in biologic-naïve patients. No deaths, major cardiovascular adverse events, or tuberculosis were observed between weeks 96 and 156.[64]

Janus Kinase Inhibitors (Tofacitinib, Upadacitinib)

In an RCT examining the long-term efficacy of tofacitinib in UC, tofacitinib 5 mg or 10 mg twice daily was shown to be superior to placebo in achieving clinical remission [RR: 3.37; 95% CI: 2.23–5.10], maintenance of clinical remission [RR: 4.71; 95% CI: 2.51–8.84], and steroid-free clinical remission [RR: 2.54; 95% CI: 1.39–4.65] in patients responding to induction therapy. In terms of safety, an increased risk of infection was observed with tofacitinib [OR: 1.56; 95% CI: 1.18–2.06].[51]

In the U-ACHIEVE upadacitinib maintenance study, subjects who responded to 8 weeks of 45 mg induction therapy were randomized to receive 30 mg, 15 mg, or placebo daily. At the end of 52 weeks, clinical remission, maintenance of clinical remission, steroid-free clinical remission, endoscopic improvement, and histological–endoscopic mucosal improvement were superior to those of placebo in the upadacitinib 30 mg and 15 mg groups. No statistically significant increase in the risk of serious adverse events was observed when compared with placebo at either dose.[53]

In a meta-analysis of safety data over approximately 4.5 years, no mortality or other serious adverse events (opportunistic infections, malignancies, non-melanoma skin cancer, gastrointestinal perforations, or major cardiovascular events) were observed for tofacitinib use, except for serious infections [RR: 2.0; 95% CI: 1.4–2.8] and herpes zoster infection [RR: 4.1; 95% CI: 3.1–5.2]. This risk was shown to be dose-dependent and higher with tofacitinib 10 mg twice daily than with tofacitinib 5 mg twice daily.[65]

A safety study of tofacitinib in patients with rheumatoid arthritis reported an increased risk of venous thromboembolism compared to anti-TNFs with tofacitinib 10 mg twice daily in patients aged ≥50 years with at least one known cardiovascular risk factor. A similar increase in risk was not observed with a twice-daily dose of 5 mg of tofacitinib.[66] Based on these data, the European Medicines Agency (EMA) has recommended that tofacitinib be used at the lowest effective dose for maintenance and that twice-daily doses of 10 mg should be avoided.[2]

The potential benefits of the oral route of administration, the absence of immunogenicity risk, efficacy in biologic treatment-experienced patients, and the rapid effect-especially more pronounced with upadacitinib-stand out as important advantages of Janus kinase inhibitors in the treatment of UC. Therefore, the treatment decision should be evaluated on a patient-specific basis, considering the risk-benefit ratio.

Sphingosine-1 Phosphate Receptor Modulators (Etrasimod, Ozanimod)

A recent meta-analysis[67] of four studies[58,68-70] evaluated the effectiveness of S1P receptor modulators, ozanimod and etrasimod, as maintenance therapy (32–52 weeks). The analysis found S1P receptor modulator therapy more effective in maintaining clinical remission than placebo, with an RR of 2.92 (95% CI: 1.63–5.21, P = 0.07). This effectiveness was consistent for both drugs. However, only ozanimod showed superiority over placebo in maintaining clinical response, with an RR of 1.65 (95% CI: 1.15–2.36, P = 0.16) compared to etrasimod's RR of 1.71 (95% CI: 0.98–2.99, P = 0.14).

S1P receptor modulators effectively maintained endoscopic response, with an RR of 2.44 (95% CI: 1.45–4.10; P = 0.03), though significant heterogeneity was observed. For mucosal healing maintenance, S1P receptor modulator therapy was superior to placebo, with an RR of 2.46 (95% CI: 1.61–3.76; P = 0.21). Pooled data from two trials showed ozanimod superior to placebo in maintaining histological remission, with an RR of 2.31 (95% CI: 1.48–3.62; P = 0.25).

Table-1 illustrates the administration methods and dosages for biological agents and small-molecule drugs used in UC treatment, including both the induction and maintenance phases.

Treatment of Acute Severe Ulcerative Colitis

Systemic corticosteroids are the first-choice treatment for acute severe UC. The corticosteroid choice should be hydrocortisone 100 mg IV, 4 × 1 dose, or methylprednisolone 60 mg IV dose, multiple injections, or 24-hour infusion. Various indices (Table-2) have been used to assess the response to corticosteroid therapy. IV cyclosporine treatment (2–4 mg/kg, followed by oral administration combined with thiopurine if a response is obtained after 7 days of intravenous treatment) or infliximab treatment is used in cases considered unresponsive to corticosteroid treatment according to the evaluations of these indices.[71]

It should be noted that cyclosporine may increase immunosuppression in patients receiving optimal thiopurine maintenance therapy or in those with a recent history of infliximab infusion. Therefore, its use should be avoided in patients with renal dysfunction or active infections. It should also be noted that there is a risk of anaphylaxis.[72]

Infliximab treatment is administered at a standard dose: 5 mg/kg at weeks 0, 2, and 6, and 5 mg/kg every 8 weeks after induction. A higher dose of 10 mg/kg or more frequent administration of the induction dose (accelerated induction) is not superior to the standard dose. Patients should be referred to reference centers for medical treatment after cyclosporine or infliximab failure. Successful outcomes have been achieved with the use of tofacitinib in severe active UC cases that have prior biologic treatment experience (those who failed anti-TNF treatments before hospitalization or did not respond to infliximab during admission) and required hospitalization. A small number of observational studies have shown that remission induction with cyclosporine followed by maintenance therapy with vedolizumab may be successful in patients with steroid-resistant and severely active UC, especially in those previously unresponsive to anti-TNFs or thiopurines. In a few studies, the combination of cyclosporine and ustekinumab has shown promise in patients with steroid-resistant, steroid-refractory, anti-TNF, or vedolizumab-refractory severe active UC.[71]

CONCLUSION

In conclusion, the management of UC, particularly across its various stages-from remission induction to maintenance and acute treatment-requires an individualized approach tailored to disease severity and the patient's response to therapies. For mild to moderate UC, oral mesalazine at higher doses and colonic-released budesonide have demonstrated efficacy, with combination therapies yielding superior outcomes compared to monotherapies. In cases where patients exhibit an inadequate response, the addition of topical steroids and the consideration of systemic corticosteroids provide potential alternatives, while thiopurines should be avoided due to their delayed onset of action. When addressing maintenance strategies, maintaining consistency in mesalazine formulations is essential to reduce relapse risks, with thiopurines being an option for patients intolerant of mesalazine.

In moderate to severe UC, the introduction of biologic therapies such as anti-TNF agents, vedolizumab, ustekinumab, and oral small molecules such as Janus kinase inhibitors has resulted in disease control for patients who are steroid refractory or dependent. For acute severe UC, prompt initiation of corticosteroids and multidisciplinary management, particularly in collaboration with IBD surgeons, remains crucial, with salvage options such as infliximab and cyclosporine available for patients who do not respond.

Overall, effective treatment requires close monitoring and an individualized approach to achieve optimal clinical and endoscopic responses and improve the quality of life for patients with UC.

Peer-review: Internally peer-reviewed.

Author Contributions: Concept – İ.H.K.; Design – İ.H.K.; Supervision – İ.H.K.; Resource – İ.H.K.; Materials – İ.H.K.; Data Collection and/or Processing - İ.H.K.; Analysis and/or Interpretation - İ.H.K.; Literature Review – İ.H.K.; Writing – İ.H.K.; Critical Review – İ.H.K.

Use of AI for Writing Assistance: A Large Language Model (LLM) has been used to produce submitted work.

Conflict of Interest: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study received no financial support.

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