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Review article

Janus Kinase Inhibitors, Monoclonal Antibodies, and Fecal Microbiota Transplantation: Promising Therapies for Ulcerative Colitis

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Abstract

Ulcerative colitis (UC) is a chronic inflammatory bowel disease involving genetic, environmental, immunological, and microbial factors. Traditional treatments often fail in certain patient populations, necessitating exploration of more personalized therapies. This review aims to evaluate the efficacy, safety, and clinical potential of three emerging therapies for UC: Janus kinase (JAK) inhibitors, anti-TL1A monoclonal antibodies, and fecal microbiota transplantation (FMT). This narrative review was conducted by searching PubMed and Google Scholar for relevant peer-reviewed literature. Inclusion criteria focused on studies published in the last 10 years that investigated the mechanisms, clinical efficacy, or safety of JAK inhibitors, anti-TL1A antibodies, or FMT in UC. Both randomized controlled trials and observational studies were included. This narrative review explores emerging therapeutic strategies for ulcerative colitis, including Janus kinase inhibitors, monoclonal antibodies, and fecal microbiota transplantation. These approaches may support personalized treatment planning, particularly in patients who are refractory to conventional therapies.JAK inhibitors including tofacitinib, upadacitinib, and filgotinib demonstrated effectiveness in inducing and maintaining remission, although safety profiles varied based on selectivity. Anti-TL1A monoclonal antibodies, particularly PF-06480605 and tulisokibart, showed dual anti-inflammatory and anti-fibrotic activity, especially in patients with specific genetic biomarkers. FMT emerged as a non-pharmacological intervention capable of modulating gut microbiota and mucosal immunity, contributing to clinical and endoscopic remission in patients refractory to standard treatments. These three therapeutic modalities represent a significant shift toward individualized, pathophysiology-based treatment of UC. Future research should focus on biomarker-guided therapy selection, optimization of FMT protocols, and long-term safety data to support integration into clinical practice.

Keywords: Fecal microbiota transplantation, janus kinase inhibitors, monoclonal antibodies, ulcerative colitis

Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease that predominantly affects the colon and rectum, characterized by continuous mucosal inflammation beginning in the rectum and extending proximally. Although its clinical presentation can resemble that of Crohn's disease, UC typically spares the upper gastrointestinal tract. The differentiation between the two conditions is based on a combination of clinical, endoscopic, and histopathological findings [1].

The global prevalence of UC is influenced by environmental and genetic factors. Studies have shown a steady rise in the prevalence of inflammatory bowel disease (IBD), including UC, in regions such as Canada, the United States, and Europe [2]. In Japan, the age-standardized prevalence of ulcerative colitis (UC) increased significantly from 5 per 100,000 in 2010 to 98 per 100,000 in 2019, with a crude prevalence reaching 266 per 100,000 in the same year. This marked upward trend reflects a growing burden of UC in Japan and highlights the urgent need for continued surveillance, preventive strategies, and in-depth research into its etiology and environmental risk factors [3]. UC pathogenesis involves a complex interplay between genetic predisposition, environmental triggers, and immune dysregulation,

particularly an exaggerated T-helper 2 (Th2) immune response [4]. This dysregulated immune response promotes oxidative stress, which stimulates the production of reactive oxygen species (ROS) and activates transcription factors such as NF-κB, AP-1, p53, and STAT. These factors subsequently enhance the expression of pro-inflammatory cytokines like TNF-α, IL-6, and IL-8, aggravating mucosal inflammation and contributing to progressive tissue damage [5]. In ulcerative colitis, mucosal barrier dysfunction is characterized by defective epithelial tight junctions, increased epithelial cell death, and reduced mucus layer thickness due to goblet cell depletion. These changes promote microbial translocation and amplify mucosal immune responses. Concurrently, dysbiosis notably a decrease in butyrate-producing bacteria and an increase in facultative anaerobes disrupts epithelial metabolism and contributes to chronic inflammation [6]. These pathological processes culminate in persistent inflammation and chronic intestinal damage.

In the past decade, significant advancements have been made in therapies that target specific immune-mediated inflammatory pathways in UC [7]. Prominent among these are Janus kinase (JAK) inhibitors, monoclonal antibodies, and fecal microbiota transplantation (FMT). Oral JAK inhibitors such as tofacitinib have demonstrated efficacy in inducing and maintaining remission in moderate-to-severe UC with an acceptable safety profile [8]. Anti-TNF agents such as infliximab have proven effective in inducing and maintaining remission in ulcerative colitis, with therapeutic drug monitoring (TDM) strategies enhancing treatment outcomes by optimizing drug exposure and reducing immunogenicity [9]. Meanwhile, FMT is gaining attention as a non-pharmacological approach in UC management, restoring gut microbial diversity and promoting mucosal healing through immunologic rebalancing and engraftment of donor microbiota resembling healthy profiles [10].

Recent real-world evidence supports the rapid effectiveness and safety of mechanism-driven therapies such as upadacitinib for ulcerative colitis (UC). In a prospective cohort of treatment-resistant UC patients, upadacitinib achieved clinical remission in 81.5% and clinical response in 85.2% by week 8, with improvements observed as early as week 2. These findings highlight upadacitinib's potential as a rapid and effective option even in patients with prior exposure to multiple advanced therapies, including tofacitinib [11]Meanwhile, bispecific monoclonal antibodies that target TL1A and integrin α4β7 have shown synergistic anti-inflammatory and anti-fibrotic effects in preclinical models of colitis, paving the way for dual-targeted strategies [12]. Furthermore, long-term data from randomized studies support the efficacy of maintenance FMT in sustaining clinical remission and microbial balance in UC patients unresponsive to standard pharmacologic therapies [13]. These findings underscore the growing shift toward targeted, personalized, and microbiome-centered approaches in the management of UC

Therapeutic strategies for UC have undergone a significant transformation over the past decade, driven by a deeper understanding of the disease's pathophysiology, particularly the roles of immune dysregulation and gut microbiota alterations [14]. Although conventional treatments such as corticosteroids, aminosalicylates, and immunomodulators remain foundational in UC management, many patients exhibit suboptimal responses or develop secondary loss of efficacy, necessitating the development of more targeted and personalized therapeutic approaches [15]. In this context, three novel modalities have emerged at the forefront of UC treatment innovation: Janus kinase (JAK) inhibitors, monoclonal antibodies targeting specific immune pathways, and fecal microbiota transplantation (FMT). These strategies not only differ mechanistically from traditional therapies, but also represent advances in molecular therapeutics and microbiome-based interventions aimed at the root causes of UC.

The following sections explore how these three approaches are reshaping the therapeutic landscape and establishing themselves as new pillars in the management of ulcerative colitis. Emerging clinical evidence supports the efficacy and safety of these three therapeutic modalities, particularly in patients with inadequate response to conventional treatments. Therefore, a narative review of these approaches through the lens of evidence-based medicine is essential to guide their implementation in clinical practice.

Methods

This narrative review aims to examine relevant scientific literature that has evaluated the efficacy, safety, and potential clinical application of three emerging therapies for ulcerative colitis (UC): Janus kinase (JAK) inhibitors, anti-TL1A monoclonal antibodies, and fecal microbiota transplantation (FMT). Literature was searched through two major databases—PubMed and Google Scholar—with a publication range from January 2015 to March 2025. The keywords used in the search included: "ulcerative colitis" AND "Janus kinase inhibitors", "ulcerative colitis" AND "monoclonal antibodies", and "ulcerative colitis" AND "fecal microbiota transplantation", which yielded a substantial number of initial results.

Inclusion criteria comprised English-language, full-text, peer-reviewed articles focusing on the efficacy, safety, mechanism of action, or clinical application of the three aforementioned therapies in UC management. Articles were excluded if they discussed only other diseases (e.g., Crohn's disease), were review papers without primary data, commentaries or conference abstracts lacking methodological rigor, or were not published in English. Titles and abstracts were screened to assess relevance, followed by full-text review for final inclusion.

Quality assessment of the selected articles was conducted narratively, based on methodological robustness and thematic relevance. Evaluated aspects included research focus, study design (e.g., clinical trials, observational studies, systematic reviews), data collection methods, key findings, and study limitations. Data extraction was performed independently by two reviewers using a structured charting template. Extracted information included study title, therapeutic category (JAK inhibitors, monoclonal antibodies, or FMT), methodological approach, primary objective, and principal findings and interpretations.

This review was developed to address two primary questions. What is the clinical efficacy and safety profile of JAK inhibitors, anti-TL1A antibodies, and FMT in the treatment of ulcerative colitis? How do these therapies contribute to a more personalized and mechanism-based therapeutic approach in UC? Although conventional therapies remain the standard of care, an evolving understanding of UC pathogenesis has led to the rise of targeted treatment modalities. However, significant evidence gaps remain particularly regarding long-term safety, predictive biomarkers, and integration into practical treatment algorithms. This review thus aims to enhance current understanding of the positioning and clinical potential of these three therapies within the evolving landscape of ulcerative colitis management.

Results and Discussion

An initial search of the literature was conducted using specified keyword combinations, after which duplicate records were eliminated. Titles and abstracts were reviewed to assess their relevance. Only studies that specifically investigated ulcerative colitis and included at least one of the three therapeutic strategies Janus kinase (JAK) inhibitors, monoclonal antibodies targeting TL1A, or fecal microbiota transplantation (FMT) were selected for inclusion. Papers were excluded if they focused exclusively on other conditions such as Crohn's disease, were not published in English, or lacked adequate methodological clarity or clinical pertinence. All eligible studies were then grouped according to the type of therapeutic intervention evaluated. The subsequent sections provide an integrated analysis of the findings, beginning with JAK inhibitors, followed by monoclonal antibodies, and concluding with FMT. Each part highlights key insights into therapeutic efficacy, safety outcomes, underlying mechanisms, and the broader clinical significance based on the most up-to-date scientific evidence.

Janus kinase 2 inhibitors

Janus kinase (JAK) inhibitors are small-molecule drugs that block the activity of JAK enzymes—key components in the JAK-STAT signaling pathway—by competitively binding to the ATP-binding pocket of the kinase domain [16]. Due to structural variations in the ATP-binding sites of different JAK isoforms, these inhibitors can be selectively designed to target specific JAKs. Some JAK inhibitors demonstrate higher selectivity for JAK1 over JAK2 or JAK3, enabling more tailored immunomodulatory effects [17]. To provide a comprehensive overview of the development and clinical positioning of JAK inhibitors in the treatment of ulcerative colitis, this review synthesizes findings from molecular studies, clinical trials, and real-world evidence. Table 1 summarizes five key scientific articles that collectively illustrate the efficacy, safety profiles, and mechanisms of action of JAK inhibitors in UC management.

Tofacitinib, the first-generation JAK inhibitor approved for ulcerative colitis (UC), primarily targets JAK1 and JAK3. Its efficacy in both induction and maintenance of clinical remission has been well established in the OCTAVE 1, 2, and SUSTAIN trials, which demonstrated significant improvements in mucosal healing and remission compared to placebo over a 52-week period [18][19].A systematic review further confirmed its superiority over placebo in achieving endoscopic remission and clinical response; however, concerns remain regarding serious adverse events such as herpes zoster and thromboembolism [20]. Nonetheless, therapeutic response to tofacitinib is not universal. A study by Melón-Ardanaz et al., utilizing single-cell RNA sequencing (scRNA-seq), revealed distinct molecular differences between responders and non-responders. Non-responders exhibited heightened NF-κB activation and IL-10-dominant macrophage infiltration in colonic mucosa, whereas responders showed elevated baseline JAK-STAT activity prior to treatment. These findings highlight the importance of molecular biomarkers in predicting therapeutic outcomes and pave the way for personalized treatment approaches [21].

Second-generation agents, such as upadacitinib and filgotinib, were developed with enhanced selectivity for JAK1, aiming to deliver higher efficacy with improved safety profiles. Upadacitinib has demonstrated robust clinical remission and mucosal healing, even in patients with prior biologic therapy failure, as shown in the U-ACHIEVE and SELECTION studies. In contrast, filgotinib has shown the greatest effectiveness in biologic-naïve patients and is associated with a lower risk of systemic adverse effects [18]. From a safety perspective, a dose-dependent relationship has been observed with tofacitinib, particularly regarding thromboembolic events and major adverse cardiovascular events (MACE), especially in elderly patients with comorbidities. In comparison, upadacitinib and filgotinib appear to pose lower risks, likely due to their higher JAK1 selectivity. Accordingly, it is recommended that the lowest effective dose be used for maintenance therapy, alongside rigorous patient risk stratification prior to treatment initiation [22].

Table 1. Key studies on janus kinase inhibitors in ulcerative colitis

Article Title (Author, Year)	Drug(s) Discussed	Study Type	Main Focus	Key Findings
Understanding the mechanisms underlying the lack of response to Janus kinase inhibition in ulcerative colitis (Melón-Ardanaz et al., 2024)	Tofacitinib	Observational + scRNA-seq on UC biopsy samples	Explains why some UC patients do not respond to tofacitinib	Non-responders show high NF-κB activation and IL-10-dominant macrophages; responders exhibit higher baseline JAK-STAT activity
Efficacy and Safety of Janus Kinase Inhibitors in Ulcerative Colitis (Neri et al., 2024)	Tofacitinib, Upadacitinib, Filgotinib	Narrative review + clinical trial and real-world data	Comparison of efficacy and safety of approved JAK inhibitors for UC	All agents effective for induction and maintenance; upadacitinib is most promising; patient selection important due to varied AE profiles
JAK Inhibitors: A New Dawn for Oral Therapies in Inflammatory Bowel Diseases (Herrera-deGuise et al., 2023)	All JAK inhibitors (e.g., Tofacitinib, Upadacitinib)	Narrative review + molecular mechanism discussion	General overview of JAK-STAT role and JAKi mechanism in IBD	Fast-acting, non-immunogenic, multi-target drugs; newer candidates (e.g., deucravacitinib) still in development
Oral Janus Kinase Inhibitors for Maintenance of Remission in UC (Cochrane Review) (Davies et al., 2020)	Tofacitinib	Systematic review and meta-analysis of RCTs	Evaluation of tofacitinib's efficacy and safety as a maintenance therapy	Effective for maintaining clinical and mucosal remission for 52 weeks; AE profile similar to placebo; SAE data requires cautious interpretation
Safety of Janus Kinase Inhibitors in Inflammatory Bowel Diseases (Núñez et al., 2023)	Tofacitinib, Upadacitinib, Filgotinib	Narrative review focusing on safety	Assessment of long-term AE risks and appropriate patient selection	Main risks: infections, hypercholesterolemia, thromboembolism, MACE; safest in younger patients without cardiovascular risk

A systematic comparison of the three agents, tofacitinib, upadacitinib, and filgotinib, concluded that all are effective in both induction and maintenance phases, with rapid onset of action. However, each agent has distinct advantages and limitations. Tofacitinib stands out for its fast clinical response but carries higher vascular and metabolic risk. Upadacitinib and filgotinib, while safer in high-risk populations, currently lack validated predictive biomarkers for individualized therapy. Neri et al. also noted the potential benefit of combining JAK inhibitors with immunomodulators, although supporting data remain limited [23].

Looking ahead, newer-generation JAK inhibitors such as deucravacitinib and izencitinib are under development with greater molecular selectivity and gut-specific targeting. These innovations aim to preserve therapeutic efficacy while minimizing systemic exposure and reducing the risk of serious adverse events [18]. In summary, JAK inhibitors have introduced a new paradigm in the treatment of UC. The three approved agents, tofacitinib, upadacitinib, and filgotinib, have demonstrated efficacy in both clinical trials and real-world practice. Optimal agent selection should be guided by individual risk profiles, pharmacodynamic characteristics, and, potentially, biomarker data. Moving forward, personalized treatment strategies and the advancement of next-generation, selective JAK inhibitors remain central to optimizing UC management.

Antibody monoklonal TNF-like ligand 1A (TL1A)

TNF-like ligand 1A (TL1A) is a circulating cytokine that functions downstream of tumor necrosis factor (TNF) signaling. A bispecific antibody (bsAb) targeting both TL1A and the integrin α4β7 has recently been developed for the treatment of inflammatory bowel disease (IBD), showing promising outcomes in preclinical studies [12][24].

To provide a comprehensive perspective on the therapeutic potential of anti-TL1A monoclonal antibodies in ulcerative colitis, several recent studies have explored this pathway across molecular mechanisms, preclinical models, and early-phase clinical trials. Table 2 summarizes four key scientific publications that reflect strategic advances in targeting the TL1A–DR3 axis. These studies address clinical efficacy, safety profiles, and precision medicine approaches based on genetic biomarkers.

Table 2. Key studies on anti-TL1A monoclonal antibodies in ulcerative colitis

Article Title (Author, Year)	Drug(s) Discussed	Study Type	Main Focus in UC	Key Findings
Anti-TL1A Antibody PF-06480605 Safety and Efficacy for Ulcerative Colitis: A Phase 2a Single-Arm Study (Danese et al., 2021) [77]	PF-06480605	Phase 2a clinical trial (TUSCANY)	Evaluation of safety and efficacy of PF-06480605 in moderate-to-severe UC	38.2% of patients showed endoscopic improvement at week 14; mild adverse events; TL1A target engagement preserved; histological improvement observed
Phase 2 Trial of Anti-TL1A Monoclonal Antibody Tulisokibart for Ulcerative Colitis (Sands et al., 2024) [78]	Tulisokibart (PRA023)	Phase 2 clinical trial (ARTEMIS-UC)	Clinical efficacy and genetic biomarker-based diagnostic approach in UC	Significant clinical remission (26% vs 1% placebo); higher response rates in TL1A-positive patients (32% vs 11%)
TL1A Inhibition for Inflammatory Bowel Disease Treatment: From Inflammation to Fibrosis (Solitano et al., 2024) [76]	PF-06480605, PRA023, TEV-48574	Narrative review + translational and clinical data	TL1A–DR3 as a therapeutic target in UC: anti-inflammatory, anti-fibrotic, and immunomodulatory effects	Anti-TL1A reduces Th1/Th17 activity, downregulates IFN-γ and IL-6 expression; potential therapeutic role in UC through fibrosis and cytokine regulation
An Anti-TL1A Antibody for the Treatment of Asthma and Inflammatory Bowel Disease (Clarke et al., 2018) [75]	C03V (anti-TL1A)	Preclinical (in vitro & in vivo murine UC model)	Evaluation of C03V antibody in mouse model of colitis	C03V highly selective for TL1A; suppresses Th1/Th17; reduces fibrosis without triggering ADCC; supports clinical development potential

Recent advancements in UC therapy have shifted toward more selective immunotherapy strategies, particularly those targeting novel cytokines such as tumor necrosis factor-like ligand 1A (TL1A). TL1A is a member of the TNF superfamily involved in effector T cell activation (Th1 and Th17), pro-inflammatory cytokine production, and tissue fibrosis. The TL1A–death receptor 3 (DR3) signaling pathway has been shown to be overexpressed in intestinal tissues of patients with active IBD, including UC, positioning it as a promising target for next-generation biologics [25].

One of the earliest anti-TL1A candidates studied was PF-06480605, a humanized IgG1 monoclonal antibody with high specificity for TL1A. In the phase 2a TUSCANY trial, this therapy induced endoscopic improvement in 38.2% of patients with active UC after 14 weeks. Although 82% of participants developed anti-drug antibodies, most adverse events were mild and did not interfere with treatment continuation. Histological assessments revealed mucosal healing, and elevated free TL1A levels indicated sustained target engagement [26].

Further evidence of clinical potential comes from the ARTEMIS-UC phase 2 trial of tulisokibart (PRA023), a next-generation anti-TL1A monoclonal antibody developed using a genetic biomarker-guided approach. Tulisokibart achieved a 26% remission rate compared to only 1% in the placebo group. In patients who tested positive for predictive TL1A genetic biomarkers, remission rates increased to 32%. These findings support the feasibility of molecular biomarker-based patient stratification, aligning with the broader trend toward personalized medicine in clinical immunology [27].

At the molecular level, a comprehensive review of key anti-TL1A candidates, PF-06480605, PRA023, and TEV-48574, has highlighted their therapeutic mechanisms. TL1A activation stimulates the Th1/Th17 axis and induces pro-inflammatory cytokines including IFN-γ, IL-6, and IL-17. It also promotes extracellular matrix remodeling, contributing to chronic fibrosis. Inhibiting TL1A thus offers dual benefits: reducing inflammation while simultaneously attenuating fibrotic progression—a therapeutic advantage not commonly observed with conventional biologics [27].

Preclinical findings further strengthen the case for anti-TL1A therapy. In murine models of colitis, the antibody C03V exhibited high affinity and specificity for TL1A, effectively suppressing Th1/Th17 signaling and reducing fibrotic damage without inducing antibody-dependent cellular cytotoxicity (ADCC). This safety profile underscores its potential for clinical development, particularly in contrast to cytotoxic biologics [25].

Taken together, clinical, molecular, and preclinical data suggest that anti-TL1A monoclonal antibodies such as PF-06480605 and tulisokibart represent promising biologic therapies for UC, especially for patients unresponsive to conventional or anti-TNF treatments. Their dual-action profile simultaneously targeting inflammation and fibrosis positions them as ideal candidates for precision medicine approaches guided by genetic biomarkers. Large scale

confirmatory trials will be essential to establish their clinical validity and support their future integration into UC treatment guidelines.

Fecal microbiota transplantation (FMT)

Fecal microbiota transplantation (FMT) is a therapeutic intervention aimed at restoring gut microbial balance by transferring stool from a healthy donor to a recipient [28]. Initially developed for the treatment of recurrent *Clostridioides difficile* infections, FMT has since gained attention as a potential adjunct therapy for UC particularly in patients who are refractory to conventional pharmacologic treatments [10]. Randomized controlled trials have indicated that fecal microbiota transplantation (FMT) may lead to clinical remission in about one-third of patients with active ulcerative colitis, particularly when using stool from multiple donors and administering treatment at higher frequencies. These findings highlight the promise of microbiome-based therapies in treating inflammatory bowel disease [19]. To provide a comprehensive understanding of FMT's therapeutic role in UC, multiple studies have assessed its efficacy from various perspectives ranging from immunological mechanisms to systematic reviews and meta-analyses of randomized controlled trials. Table 3 summarizes five key studies that contribute to the evidence base regarding the clinical utility, safety, and mechanistic rationale of FMT in UC management.

Table 3. Key Studies on fecal microbiota transplantation in ulcerative colitis

Article Title (Author, Year)	Study Design / Population	Main Focus	Key Findings
Efficacy of Fecal Microbiota Transplantation in the Treatment of Active Ulcerative Colitis: A Systematic Review and Meta-Analysis of Double-Blind Randomized Controlled Trials (El Hage Chehade et al., 2023)	Systematic review and meta-analysis of 6 RCTs	Efficacy of FMT for induction of clinical and endoscopic remission in active UC	FMT was superior to placebo for combined remission (OR 4.11); no significant difference based on route, frequency, or donor type (single/pooled); adverse events were similar to placebo
Modulation of Gut Microbiota and Th17/Treg Cell Balance in Response to Fecal Microbiota Transplantation in Ulcerative Colitis (Huang et al., 2022)	8-week clinical trial, 15 patients with mild-to-moderate UC	Microbiota changes and immune response post-FMT	Increased *Faecalibacterium* in responders, decreased Th17 and increased Treg; reduced inflammation; improved barrier function
Fecal Microbiota Transplantation for Patients with Ulcerative Colitis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials (Gefen et al., 2025)	Meta-analysis of 14 RCTs (n=600)	Evaluation of efficacy and combination therapy strategies	FMT improved clinical and endoscopic remission (OR 2.25); pooled donors more effective; methotrexate or steroid pre-FMT improved outcomes
Efficacy and Safety of Fecal Microbiota Transplantation in the Treatment of Ulcerative Colitis: A Meta-Analysis (Feng et al., 2023)	Meta-analysis of 13 RCTs	Evaluation of FMT efficacy and safety in active UC	Higher rates of clinical (RR 1.73) and endoscopic (RR 1.74) remission with FMT vs control; no significant increase in adverse events
Fecal Microbiota Transplantation for Ulcerative Colitis: An Evolving Therapy (Sood et al., 2020)	Narrative review focused on practical and immunologic aspects	Donor/patient selection, delivery route, duration, and mechanisms	Multisession FMT improved remission and microbiota diversity; Treg/Th17 balance improved; specific microbial role remains inconsistent

Intestinal dysbiosis—marked by reduced microbial diversity and an imbalance between pro-inflammatory and anti-inflammatory bacterial populations—plays a central role in the pathogenesis of ulcerative colitis (UC). Studies have shown that FMT not only increases the abundance of beneficial microorganisms such as *Faecalibacterium prausnitzii*, but also reduces Th17 cell populations while enhancing regulatory T cell (Treg) activity. These immunomodulatory effects are thought to restore mucosal immune homeostasis, leading to inflammation control and epithelial barrier reinforcement [29].

Clinically, FMT has demonstrated efficacy in inducing remission. A meta-analysis of 13 randomized controlled trials (RCTs) reported that FMT significantly outperformed control interventions in achieving both clinical remission (RR 1.73) and endoscopic remission (RR 1.74). Importantly, adverse events did not significantly differ between treatment and control groups, supporting the relative safety of FMT in clinical settings [30]. Similar findings were

observed in a separate meta-analysis of six RCTs, which concluded that FMT was consistently more effective than placebo in achieving combined remission. The analysis found no meaningful differences in effectiveness based on delivery route (e.g., colonoscopy, oral capsules, or enema) or donor type (single vs pooled), suggesting considerable logistical flexibility in clinical application [31].

Further systematic reviews support the efficacy of FMT, with emerging evidence that adjunctive strategies—such as pre-treatment with corticosteroids or methotrexate—may enhance therapeutic outcomes. These findings highlight a new direction in personalized, microbiota-based therapy, where FMT could serve as a component of multimodal treatment regimens [32]. However, several challenges remain. No consensus has been reached regarding the optimal frequency of administration, donor selection criteria, or treatment duration. Additionally, the specific microbial taxa most responsible for therapeutic success remain unidentified, as microbial biomarkers among responders vary widely across studies. The immunological mechanisms underlying FMT, including T cell modulation, IL-10 production, and restoration of intestinal memory T cell populations—require further investigation through focused and well-controlled trials [10]. Overall, FMT represents a promising supportive and potentially primary therapy for select subgroups of UC patients, particularly those who fail to respond to first- or second-line pharmacologic treatments. Its strength lies in its multimodal mechanism of action: restoring the gut microbial ecosystem, reinforcing mucosal integrity, and rebalancing immune responses. Nevertheless, long-term efficacy, safety, and integration of FMT into UC treatment algorithms will depend on future research focused on response predictors, protocol standardization, and durable outcomes.

Conclusion

This review explored the current clinical landscape of three innovative therapeutic strategies for ulcerative colitis: Janus kinase (JAK) inhibitors, monoclonal antibodies targeting TL1A, and fecal microbiota transplantation (FMT). Janus kinase inhibitors, anti-TL1A monoclonal antibodies, and fecal microbiota transplantation each represent promising advancements in the treatment landscape of ulcerative colitis, especially for patients with inadequate response to standard therapies. While current evidence supports their efficacy and safety in clinical trials, further long-term, real-world studies are essential to establish optimal patient selection, timing, and cost-effectiveness. Among these, FMT offers unique potential as a non-pharmacological, microbiota-targeted strategy, although standardization remains a major challenge. Future research should focus on integrating precision medicine approaches, identifying predictive biomarkers, and refining treatment algorithms to ensure effective and individualized care in ulcerative colitis management.

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References

[1] B. S. Pabla and D. A. Schwartz, "Assessing Severity of Disease in Patients with Ulcerative Colitis," *Gastroenterol. Clin. North Am.*, vol. 49, no. 4, pp. 671–688, 2020, doi: 10.1016/j.gtc.2020.08.003.

[2] G. G. Kaplan and J. W. Windsor, "The four epidemiological stages in the global evolution of inflammatory bowel disease," *Nat. Rev. Gastroenterol. Hepatol.*, vol. 18, no. 1, pp. 56–66, 2021, doi: 10.1038/s41575-020-00360-x.

[3] M. Yamazaki, H. Chung, Y. Xu, and H. Qiu, "Trends in the prevalence and incidence of ulcerative colitis in Japan

and the US," *Int. J. Colorectal Dis.*, vol. 38, no. 1, pp. 1–13, 2023, doi: 10.1007/s00384-023-04417-6.

[4] Y. Long *et al.*, "The Imbalance of Circulating Follicular Helper T Cells and Follicular Regulatory T Cells Is Associated With Disease Activity in Patients With Ulcerative Colitis," *Front. Immunol.*, vol. 11, no. February, pp. 1–14, 2020, doi: 10.3389/fimmu.2020.00104.

[5] L. Chen *et al.*, "Oncotarget 7204 www.impactjournals.com/oncotarget Inflammatory responses and inflammation-associated diseases in organs," *Oncotarget*, vol. 9, no. 6, pp. 7204–7218, 2018, [Online]. Available: www.impactjournals.com/oncotarget/

[6] T. Kobayashi *et al.*, "Ulcerative colitis," *Nat. Rev. Dis. Prim.*, vol. 6, no. 1, 2020, doi: 10.1038/s41572-020-0205-x.

[7] R. Pietschner, T. Rath, M. F. Neurath, and R. Atreya, "Current and Emerging Targeted Therapies for Ulcerative Colitis," *Visc. Med.*, vol. 39, no. 2, pp. 46–53, 2023, doi: 10.1159/000530983.

[8] W. J. Sandborn *et al.*, "Tofacitinib as Induction and Maintenance Therapy for Ulcerative Colitis," *N. Engl. J. Med.*, vol. 376, no. 18, pp. 1723–1736, 2017, doi: 10.1056/nejmoa1606910.

[9] S. Singh, M. H. Murad, M. Fumery, P. S. Dulai, and W. J. Sandborn, "First- and Second-Line Pharmacotherapies for Patients With Moderate to Severely Active Ulcerative Colitis: An Updated Network Meta-Analysis," *Clin. Gastroenterol. Hepatol.*, vol. 18, no. 10, pp. 2179-2191.e6, 2020, doi: 10.1016/j.cgh.2020.01.008.

[10] A. Sood *et al.*, "Fecal microbiota transplantation for ulcerative colitis: An evolving therapy," *Crohn's Colitis 360*, vol. 2, no. 4, pp. 1–7, 2020, doi: 10.1093/crocol/otaa067.

[11] S. Friedberg *et al.*, "Upadacitinib Is Effective and Safe in Both Ulcerative Colitis and Crohn's Disease: Prospective Real-World Experience," *Clin. Gastroenterol. Hepatol.*, vol. 21, no. 7, pp. 1913-1923.e2, 2023, doi: 10.1016/j.cgh.2023.03.001.

[12] H. Ran *et al.*, "Clinical : Therapy and Observation Abstract citation ID : jjae190 . 1022 Engineering and Development of a Novel Bispecific Antibody Targeting both TL1A and α 4 β 7 for the Treatment of IBD," p. 2025, 2025.

[13] H. Fang *et al.*, "Long-term efficacy and safety of monotherapy with a single fresh fecal microbiota transplant for recurrent active ulcerative colitis: a prospective randomized pilot study," *Microb. Cell Fact.*, vol. 20, no. 1, pp. 1–14, 2021, doi: 10.1186/s12934-021-01513-6.

[14] S. L. Zhang, S. N. Wang, and C. Y. Miao, "Influence of microbiota on intestinal immune system in Ulcerative colitis and its intervention," *Front. Immunol.*, vol. 8, no. NOV, pp. 1–11, 2017, doi: 10.3389/fimmu.2017.01674.

[15] Z. Cai, S. Wang, and J. Li, "Treatment of Inflammatory Bowel Disease: A Comprehensive Review," *Front. Med.*, vol. 8, no. December, pp. 1–24, 2021, doi: 10.3389/fmed.2021.765474.

[16] S. Kwon, "Molecular dissection of Janus kinases as drug targets for inflammatory diseases," *Front. Immunol.*, vol. 13, no. December, pp. 1–9, 2022, doi: 10.3389/fimmu.2022.1075192.

[17] C. M. Lin, F. A. Cooles, and J. D. Isaacs, "Basic Mechanisms of JAK Inhibition," *Mediterr. J. Rheumatol.*, vol. 31, no. Supp 1, pp. 100–1404, 2020, doi: 10.31138/MJR.31.1.100.

[18] C. Herrera-deGuise, X. Serra-Ruiz, E. Lastiri, and N. Borruel, "JAK inhibitors: A new dawn for oral therapies in inflammatory bowel diseases," *Front. Med.*, vol. 10, no. March, pp. 1–13, 2023, doi: 10.3389/fmed.2023.1089099.

[19] R. P. Hirten and B. E. Sands, "New Therapeutics for Ulcerative Colitis," *Annu. Rev. Med.*, vol. 72, pp. 199–213, 2021, doi: 10.1146/annurev-med-052919-120048.

[20] S. C. Davies, I. M. Hussein, T. M. Nguyen, C. E. Parker, R. Khanna, and V. Jairath, "Oral Janus kinase inhibitors for maintenance of remission in ulcerative colitis," *Cochrane Database Syst. Rev.*, vol. 2020, no. 1, 2020, doi: 10.1002/14651858.CD012381.pub2.

[21] E. Melón-Ardanaz, M. Veny, A. M. Corraliza, A. Garrido-Trigo, V. Gudiño, Á. Sanzo-Machuca, M. Buendia, M. Esteller, M. Rodrigo, M. C. Masamunt, Á. Giner, I. Ordás, A. Fernández-Clotet, B. Caballol, Á. Corbí, B. Verstockt, S. Vermeire, J. Panés, E. Ricart, and A. Salas, "Understanding the mechanisms underlying the lack of response to Janus kinase inhibition in ulcerative colitis," https://doi.org/10.1101/2024.10.17.876478.

[22] P. Núñez, R. Quera, and A. J. Yarur, "Safety of Janus Kinase Inhibitors in Inflammatory Bowel Diseases," *Drugs*, vol. 83, no. 4, pp. 299–314, 2023, doi: 10.1007/s40265-023-01840-5.

[23] B. Neri, R. Mancone, M. Fiorillo, S. C. Schiavone, S. Migliozzi, and L. Biancone, "Efficacy and Safety of Janus Kinase-Inhibitors in Ulcerative Colitis," 2024.

[24] Y. J. Song *et al.*, "Circulating TNF-like protein 1A (TL1A) is elevated early in rheumatoid arthritis and depends on TNF," *Arthritis Res. Ther.*, vol. 22, no. 1, pp. 1–14, 2020, doi: 10.1186/s13075-020-02198-9.

[25] A. W. Clarke *et al.*, "An anti-TL1A antibody for the treatment of asthma and inflammatory bowel disease," *MAbs*, vol. 10, no. 4, pp. 664–677, 2018, doi: 10.1080/19420862.2018.1440164.

[26] S. Danese *et al.*, "Anti-TL1A Antibody PF-06480605 Safety and Efficacy for Ulcerative Colitis: A Phase 2a Single-Arm Study," *Clin. Gastroenterol. Hepatol.*, vol. 19, no. 11, pp. 2324-2332.e6, 2021, doi:

10.1016/j.cgh.2021.06.011.
[27] V. Solitano, V. Jairath, F. Ungaro, L. Peyrin-Biroulet, and S. Danese, "TL1A inhibition for inflammatory bowel disease treatment: From inflammation to fibrosis," *Med*, vol. 5, no. 5, pp. 386–400, 2024, doi: 10.1016/j.medj.2024.03.010.
[28] K. O. Kim and M. Gluck, "Fecal microbiota transplantation: An update on clinical practice," *Clin. Endosc.*, vol. 52, no. 2, pp. 137–143, 2019, doi: 10.5946/CE.2019.009.
[29] C. Huang *et al.*, "Ulcerative Colitis in Response to Fecal Microbiota Transplantation via Modulation of Gut Microbiota and Th17/Treg Cell Balance," *Cells*, vol. 11, no. 11, 2022, doi: 10.3390/cells11111851.
[30] J. Feng *et al.*, "Efficacy and safety of fecal microbiota transplantation in the treatment of ulcerative colitis: a systematic review and meta-analysis," *Sci. Rep.*, vol. 13, no. 1, pp. 1–13, 2023, doi: 10.1038/s41598-023-41182-6.
[31] N. El Hage Chehade *et al.*, "Efficacy of Fecal Microbiota Transplantation in the Treatment of Active Ulcerative Colitis: A Systematic Review and Meta-Analysis of Double-Blind Randomized Controlled Trials," *Inflamm. Bowel Dis.*, vol. 29, no. 5, pp. 808–817, 2023, doi: 10.1093/ibd/izac135.
[32] R. Gefen *et al.*, "Fecal microbiota transplantation for patients with ulcerative colitis: a systematic review and meta-analysis of randomized control trials," *Tech. Coloproctol.*, vol. 29, no. 1, 2025, doi: 10.1007/s10151-025-03113-7.