# Upadacitinib, Infliximab Lead for Rapid Ulcerative Colitis Relief

Written by The Life Science Feed Editorial Team · Published 6 July 2026 · Edited by Mara Voss

> Ulcerative colitis, a chronic inflammatory condition of the colon, continues to present a significant therapeutic challenge for European GPs and specialists. Patients often endure debilitating symptoms, including bloody diarrhoea, abdominal pain, and urgency, which severely impact quality of life and necessitate swift, effective intervention.1 Identifying therapies that offer not only sustained remission but also rapid symptom relief remains a critical unmet need in clinical practice.

**KEY TAKEAWAYS**

- The Pivot: Upadacitinib and infliximab demonstrate superior speed to clinical response in ulcerative colitis compared to other established biologics.
- The Data: Upadacitinib achieved clinical remission in a significantly higher proportion of patients by week 8 (26% vs 5% for placebo, PThe Action: Clinicians should consider upadacitinib or infliximab when rapid symptom control is a priority for patients with moderate to severe ulcerative colitis.

Patients with moderate to severe ulcerative colitis frequently cycle through therapies, seeking not just long-term disease control but also prompt alleviation of acute flares. The urgency of symptom resolution often dictates treatment choice, particularly for those experiencing severe disease activity. Current treatment algorithms include aminosalicylates, corticosteroids, immunomodulators, and a growing array of biologics and small molecules, each with varying onset of action and efficacy profiles. The goal is always to induce remission quickly and maintain it, thereby reducing hospitalisations and improving patient outcomes.

Upadacitinib, an oral selective JAK1 inhibitor, and infliximab, an intravenous anti-TNF monoclonal antibody, have both established efficacy in inducing and maintaining remission in ulcerative colitis. Upadacitinib works by inhibiting the Janus kinase pathway, thereby disrupting the signalling of several cytokines implicated in inflammation, including IL-6, IL-12, IL-23, and IFN-³ Infliximab, on the other hand, neutralises tumour necrosis factor-alpha (TNF-⇶ a key pro-inflammatory cytokine. The mechanisms of action differ, but both aim to quell the immune response driving colitis. Clinicians have long sought to understand which of these agents, or others in the class, offers the fastest path to meaningful symptom improvement.

## The numbers on speed to relief

Clinical trials evaluating upadacitinib in ulcerative colitis, such as the U-ACCOMPLISH and U-ACHIEVE induction studies, enrolled patients with moderately to severely active disease who had failed or were intolerant to conventional or biologic therapies. These trials typically defined clinical remission as a total Mayo score of 2 or less, with no subscore

greater than 1, and a rectal bleeding subscore of 0. Endoscopic improvement was also a key secondary endpoint, often defined as a Mayo endoscopic subscore of 1 or less. The patient populations in these studies were representative of those seen in specialist clinics, often with a history of extensive colitis and prior exposure to multiple lines of treatment. The U-ACCOMPLISH trial, for example, included patients who had failed at least one prior biologic therapy, reflecting a real-world refractory population.1

Upadacitinib demonstrated a rapid onset of action. In the U-ACHIEVE induction study, a significantly higher proportion of patients receiving upadacitinib 45 mg once daily achieved clinical remission by week 8 compared to placebo (26% vs 5%, P1 Clinical response, defined as a decrease from baseline in total Mayo score of at least 3 points and at least 30%, plus a decrease in rectal bleeding subscore of at least 1 point or an absolute rectal bleeding subscore of 0 or 1, was also achieved more rapidly. By week 2, 50% of upadacitinib-treated patients achieved clinical response, compared to 23% of those on placebo (P1 This early separation from placebo is a critical indicator of rapid symptomatic improvement, suggesting that patients experience relief within weeks rather than months.

Infliximab, a long-standing cornerstone of ulcerative colitis therapy, also exhibits a relatively rapid onset of action, particularly with intravenous administration. Data from the ACT 1 and ACT 2 trials showed that clinical response rates were significantly higher with infliximab compared to placebo as early as week 8. For instance, in ACT 1, 69% of patients on infliximab achieved clinical response at week 8, versus 37% on placebo (P2 While direct head-to-head trials comparing upadacitinib and infliximab for speed of onset are scarce, network meta-analyses have attempted to indirectly compare these agents. These analyses often place both upadacitinib and infliximab among the top contenders for rapid induction of clinical remission and response, frequently outperforming other biologics like vedolizumab or ustekinumab in terms of speed.3

The rapid symptomatic improvement observed with upadacitinib is often attributed to its oral administration and systemic distribution, allowing for quick attainment of therapeutic concentrations. Infliximab, given intravenously, also achieves high systemic concentrations quickly, which contributes to its rapid effect. Both drugs have demonstrated significant improvements in endoscopic outcomes and histological remission, but the immediate impact on patient-reported symptoms is what often drives early treatment satisfaction and adherence. For example, in the U-ACHIEVE study, patients on upadacitinib reported significant improvements in stool frequency and rectal bleeding as early as day 3.1 This level of rapid symptomatic control is highly valued by patients experiencing severe flares.

The safety profiles of these agents are well-characterised. Upadacitinib carries a boxed warning regarding serious infections, major adverse cardiovascular events (MACE), thrombosis, and malignancy, consistent with other JAK inhibitors. Infliximab is associated with risks of infusion reactions, serious infections, and reactivation of latent tuberculosis. The choice between these agents often involves a careful risk-benefit discussion, balancing the need for rapid efficacy with potential adverse events, especially in patients with comorbidities. The open-label nature of some extension studies for both drugs is an obvious caveat when interpreting long-term safety and efficacy, as patient and physician awareness of treatment can influence reported outcomes. Still, the induction phase data, typically double-blind and placebo-controlled, provides a robust assessment of early efficacy.

The trials for upadacitinib and infliximab were not powered to detect differences in specific patient subgroups, such as those with concomitant primary sclerosing cholangitis or specific genetic markers, and that gap matters for truly personalised medicine. Whether the rapid benefits extend uniformly across all phenotypes of ulcerative colitis, including

those with severe proctitis or extensive pancolitis, remains an area for further investigation. Future research should focus on head-to-head comparisons of these rapid-acting agents, particularly in real-world settings, to provide more definitive guidance on optimal sequencing and patient selection. The economic implications of faster remission, including reduced hospitalisations and improved productivity, also warrant closer examination.

### CLINICAL IMPLICATIONS

The emergence of upadacitinib and the sustained performance of infliximab as rapid-onset therapies for ulcerative colitis offer clinicians more precise tools for managing acute flares. When a patient presents with severe, active disease, the ability to achieve clinical response within weeks, rather than months, can significantly alter the disease trajectory and improve immediate quality of life. This speed is not merely a convenience; it can prevent hospitalisations and reduce the need for prolonged corticosteroid courses, thereby mitigating their associated side effects.

For patients, the prospect of rapid symptom relief is paramount. Bloody diarrhoea and urgency are debilitating symptoms that severely impact daily functioning. A therapy that can quell these symptoms quickly allows patients to regain a semblance of normalcy sooner, fostering greater adherence and satisfaction with their treatment regimen. This immediate impact can also build confidence in the chosen therapy, which is crucial for long-term management of a chronic condition.

But the choice between these agents is not solely about speed. Clinicians must weigh the oral convenience of upadacitinib against its JAK inhibitor class risks, including MACE and thrombosis, particularly in older patients or those with cardiovascular risk factors. Infliximab, while effective, requires intravenous infusion, which can be a logistical burden for some patients, though its long-established safety profile offers reassurance. The decision requires a detailed discussion of individual patient comorbidities, preferences, and prior treatment failures.

The pharmaceutical industry will undoubtedly continue to push for faster-acting agents, but the real challenge lies in identifying which patients will respond best to which rapid-onset therapy. Biomarkers that predict early response to specific mechanisms of action are still largely elusive. Until then, clinicians will continue to rely on a combination of clinical judgment, patient characteristics, and the robust, albeit indirect, evidence of comparative efficacy and speed.



### REFERENCES

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