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Ustekinumab Therapy in Inflammatory Bowel Disease: Outcomes from Routine Clinical Practice

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Abstract

Background:
Ustekinumab has emerged as an effective therapeutic option for patients with Crohn's disease, including those with prior exposure to other biologic agents. However, data from routine clinical practice remain essential to better characterize its effectiveness and safety in heterogeneous patient populations.

Methods:
We conducted a retrospective observational study including patients with Crohn's disease treated with ustekinumab. Patients previously exposed to another biologic agent within three months before ustekinumab initiation were excluded to limit potential confounding. Clinical, biological, and treatment-related data were collected at baseline and during follow-up. Clinical response, remission rates, and safety outcomes were assessed according to predefined criteria.

Results:
Thirty-five patients with inflammatory bowel disease were included, including **26 with Crohn's disease (74.3%)** and **9 with ulcerative colitis (25.7%)**; mean age at inclusion was **44.2 years**, with a male predominance (**62.9%**). Ustekinumab was mainly initiated after **anti-TNF failure or intolerance (94.3%)**. After **6–24 months of follow-up**, **71.4%** of patients achieved a marked clinical response, while **20.0%** required dose interval shortening to every 6 weeks, and **8.6%** discontinued treatment due to lack of efficacy. A significant biological response was observed, with a **>50% reduction in CRP** and fecal calprotectin in the majority of patients by week 13. Endoscopic improvement was documented in most patients, and **no treatment-related adverse events** were reported.

Conclusion:
In this cohort, ustekinumab demonstrated sustained effectiveness and a favorable safety profile in patients with Crohn's disease, including those with prior biologic exposure. These findings support its use as a valuable therapeutic option in routine clinical practice and are consistent with previously published observational and clinical trial data.

Keywords: Ustekinumab; Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Anti-TNF failure; Treatment outcomes

1. Introduction

Inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis, is a chronic immune-mediated condition characterized by relapsing intestinal inflammation and significant morbidity. Despite major therapeutic advances, a substantial proportion of patients experience primary non-response, secondary loss of response, or intolerance to conventional treatments and tumor necrosis factor (TNF) antagonists, underscoring the need for effective and durable alternative therapies (1,2).

Ustekinumab is a fully human monoclonal antibody targeting the p40 subunit shared by interleukins 12 and 23, cytokines that play a central role in Th1 and Th17-mediated inflammation. This distinct mechanism of action differentiates ustekinumab from anti-TNF agents and integrin inhibitors and supports its use in patients with moderate-to-severe IBD, particularly those with previous biologic exposure (14).

The efficacy of ustekinumab in Crohn's disease has been established in pivotal randomized controlled trials, demonstrating significant improvements in clinical response and remission during induction, as well as sustained efficacy during maintenance and long-term follow-up (1–3). In ulcerative colitis, the UNIFI clinical trial program similarly confirmed the superiority of ustekinumab over placebo for both induction and maintenance of remission, with consistent benefits across clinical, endoscopic, and mucosal outcomes in patients with moderate-to-severe disease (4–6).

However, the generalizability of randomized trial data may be limited by strict inclusion criteria, as patients encountered in routine clinical practice often present with more complex disease profiles, prior biologic failures, and comorbidities. Observational clinical studies conducted in routine care settings therefore provide complementary information regarding treatment effectiveness and safety in broader patient populations (7–9).

The aim of the present study was to assess the clinical, biological, and endoscopic outcomes of ustekinumab in patients with inflammatory bowel disease treated in routine clinical practice, as well as to evaluate its safety profile in a prospective observational setting.

Materials and Methods

This prospective observational study was conducted to evaluate the effectiveness and safety of ustekinumab in the management of IBD. A total of 35 patients with confirmed IBD were consecutively included and followed at the Department of Gastroenterology I of the Military Teaching Hospital of Rabat between January 2022 and January 2025.

The diagnosis of IBD was established on the basis of clinical, endoscopic, radiological, and histopathological criteria, in accordance with current international standards. All patients initiated treatment with ustekinumab as part of routine clinical care.

Ustekinumab was administered according to the approved dosing regimen, with weight-based intravenous induction (260 mg for <55 kg, 390 mg for 55–85 kg, and 520 mg for >85 kg), followed by subcutaneous maintenance therapy of 90 mg every 8 weeks.

Patients were excluded if they had received another biologic within 3 months prior to ustekinumab initiation. Additional exclusion criteria included inability to ensure regular follow-up, contraindications to ustekinumab, incomplete medical records, or a history of hematological disorders or malignancy.

Clinical, biological, endoscopic, and radiological data were prospectively collected using a standardized case report form. Patients were evaluated at predefined time points: at week 8, week 16, month 6, and month 12 after treatment initiation. Clinical assessment was performed at each visit. Biological monitoring included measurement of C-reactive protein (CRP) and, when available, fecal calprotectin. Endoscopic evaluation was performed according to clinical indication during follow-up.

Clinical response was defined as the resolution of digestive symptoms, including abdominal pain, diarrhea, and rectal bleeding. Biological response was defined as a reduction greater than 50% in CRP levels and/or fecal calprotectin compared with baseline values.

Endoscopic disease activity was assessed using validated scoring systems. In patients with Crohn's disease, the Crohn's Disease Endoscopic Index of Severity (CDEIS) was used, whereas in patients with ulcerative colitis, endoscopic activity was evaluated using the Mayo endoscopic subscore. Endoscopic response was defined as a reduction of at least 50% in the endoscopic score, while endoscopic remission was defined as an endoscopic score <3.

All data were analyzed descriptively to assess treatment effectiveness and tolerance in a real-world clinical setting. Patient confidentiality was strictly respected throughout the study.

Results

Baseline characteristics of the study population

A total of 35 patients with inflammatory bowel disease were included in the study. Among them, 26 patients (74.3%) were diagnosed with Crohn's disease, while 9 patients (25.7%) had ulcerative colitis. The mean age at inclusion was 44.2 years, with a range from 22 to 75 years. The largest proportion of patients was aged between 31 and 45 years. The study population showed a male predominance, with 22 male patients (62.9%) and 13 female patients (37.1%). A family history of inflammatory bowel disease was reported in three patients, all of whom had Crohn's disease.

Disease characteristics

Disease location

In patients with Crohn's disease, disease distribution was predominantly ileocolonic, observed in 16 patients (61.5%). Isolated colonic involvement was reported in 3 patients (11.5%), isolated ileal disease in 6 patients (23.1%), and ileocecal involvement in 1 patient (3.8%).

Among patients with ulcerative colitis, disease extent was mainly pancolitis, observed in 4 patients (44.4%), followed by left-sided colitis in 3 patients (33.3%), and rectosigmoid involvement in 2 patients (22.2%).

Crohn's disease phenotype

Among the 26 patients with Crohn's disease, the inflammatory phenotype was the most frequent, observed in 15 patients, followed by the fistulizing phenotype in 6 patients, and the stricturing phenotype in 5 patients. Perianal disease was present in 7 patients (26.9%) with Crohn's disease.

Clinical manifestations at baseline

At baseline, abdominal pain was reported in 65.5% of patients and was frequently associated with Koenig's syndrome in 24.1%. Diarrhea, including mucous or bloody diarrhea (rectal bleeding), was the most common symptom, reported by 82.2% of patients.

Extraintestinal manifestations were observed in 7 patients, mainly involving osteoarticular and cutaneous manifestations. Arthralgia was the most frequent extraintestinal manifestation, followed by lumbosciatica, gonalgia, and erythema nodosum.

Among patients with Crohn's disease, perianal manifestations were identified in approximately 17.2%, including anal fissures, external fistulous openings (single or multiple), anal stenosis, and isolated proctalgia.

Radiological and endoscopic findings at baseline

All patients underwent baseline imaging evaluation, including CT enterography and/or MR enterography, and pelvic MRI when perianal disease was suspected. Imaging findings revealed a predominance of ileocolonic involvement, with associated complications such as ileal strictures, enteroenteric or ileocolonic fistulas, and inflammatory bowel wall thickening in several cases. Pelvic MRI identified various types of perianal fistulas, including complex fistulas and intersphincteric and transsphincteric tracts.

Baseline colonoscopy was performed in all patients prior to initiation of ustekinumab therapy. In Crohn's disease, endoscopic severity ranged from minimal to severe lesions. In ulcerative colitis, colonoscopy confirmed active disease, with moderate Mayo endoscopic scores in six patients and severe scores in three patients. Histopathological examination of biopsy specimens confirmed active disease in all cases, without evidence of dysplasia or malignancy.

Baseline biological inflammation

At baseline, inflammatory markers showed a wide range of activity. CRP levels were elevated in approximately 70.6% of patients, reflecting active inflammation, while 29.4% had normal or near-normal values. The mean CRP level was 38.8 mg/L, indicating a high inflammatory burden at treatment initiation.

Treatment indications and dosing

All patients included in the study received ustekinumab according to standard therapeutic recommendations for inflammatory bowel disease. The main indication for ustekinumab initiation was secondary loss of response to anti–TNF therapy, observed in 24 patients (68.6%). In 3 patients (8.5%), ustekinumab was introduced due to lack of response to immunosuppressive therapy and contraindication to anti–TNF agents. Five patients (14.3%) received ustekinumab because of significant adverse events related to anti–TNF therapy, including severe infusion reactions, with two cases of anaphylactic shock, leading to permanent discontinuation of infliximab. Additionally, two patients (5.7%) had a

contraindication to continued anti–TNF therapy, related to dilated cardiomyopathy with reduced ejection fraction in one case and unexplained neurological disorders in another.

Ustekinumab was used as first-line biologic therapy in one patient (2.9%).

The induction dose of ustekinumab was weight-based. Patients weighing between 55 and 85 kg received 390 mg (51.7%), those weighing more than 85 kg received 520 mg (10.3%), and patients weighing less than 55 kg received 260 mg (34.5%).

Following induction, all patients received a maintenance dose of 90 mg every 8 weeks, with dose interval shortening to every 6 weeks in selected cases of partial response.

Clinical response

After a minimum follow-up of 6 months and a maximum of 24 months, clinical outcomes were assessed. A marked clinical improvement was observed in 25 patients, characterized by a significant reduction in abdominal pain and stool frequency.

Seven patients showed a moderate clinical response, requiring shortening of the maintenance interval to 6 weeks instead of the initial 8-week regimen to achieve sustained symptom control. Three patients did not respond to ustekinumab therapy, leading to treatment discontinuation after 6 months.

Biological response

Biological response was evaluated using CRP and FC levels. At baseline, CRP levels varied widely, ranging from <1 mg/L to 255 mg/L, reflecting heterogeneous systemic inflammatory activity. A reduction greater than 50% in CRP levels was observed in several patients by week 13, with post-treatment values ranging from 1 mg/L to a maximum of 75 mg/L.

Baseline fecal calprotectin levels were markedly elevated in most patients, frequently exceeding 1000 µg/g, indicating severe intestinal inflammation. By week 13, 23 patients experienced a significant reduction (>50%) in fecal calprotectin levels, with post-treatment values ranging from 149 µg/g to 588 µg/g.

Endoscopic response

Endoscopic assessment demonstrated a favorable response to ustekinumab therapy.

A good endoscopic response with clear improvement in disease activity scores was observed in 20 patients, while 15 patients showed a partial endoscopic response.

Three patients did not achieve a favorable endoscopic response during follow-up.

Safety and tolerability

Throughout the follow-up period, no clinical or biological adverse events related to ustekinumab were reported among the 35 patients.

Specifically, no cases of headache, recurrent infections (including upper respiratory tract infections), or injection-site allergic reactions were observed.

The absence of adverse events highlights the favorable safety profile of ustekinumab in this cohort and supports its good tolerability in the management of inflammatory bowel disease.

Discussion

In this prospective observational study conducted in routine clinical practice, ustekinumab demonstrated favorable clinical, biological, and endoscopic outcomes in patients with inflammatory bowel disease (IBD), along with an excellent safety profile. These findings are consistent with previously published evidence from randomized controlled trials and observational clinical studies.

The efficacy of ustekinumab in moderate-to-severe Crohn's disease has been well established by pivotal randomized trials. In the UNITI-1 and UNITI-2 induction studies, ustekinumab significantly improved clinical response and remission rates compared with placebo in patients with prior failure of conventional therapy or anti-TNF agents (1,2). These benefits were sustained during the maintenance phase in the IM-UNITI trial, with durable clinical remission observed up to three years of follow-up (3). Our findings are in line with these results, supporting the sustained effectiveness of ustekinumab beyond the controlled setting of clinical trials.

Similarly, in ulcerative colitis, the UNIFI trial program demonstrated the superiority of ustekinumab over placebo for induction and maintenance of clinical remission, endoscopic improvement, and mucosal healing in patients with moderate-to-severe disease (4,5). Long-term extension studies further confirmed the durability of response and the favorable safety profile of ustekinumab over prolonged treatment periods (6). The biological and endoscopic improvements observed in our study are consistent with these data.

Observational clinical studies conducted in routine care settings provide complementary evidence, particularly in heterogeneous and refractory patient populations. Several cohort studies and meta-analyses have shown that ustekinumab maintains meaningful effectiveness in patients with previous biologic exposure, including anti-TNF failure, with response and remission rates comparable to those reported in clinical trials (7–9). These findings support the robustness of ustekinumab across different clinical contexts.

Patients with prior anti-TNF failure represent a challenging therapeutic subgroup. Evidence suggests that ustekinumab remains effective in this population and may offer advantages over other biologic options. Comparative observational studies have reported higher rates of endoscopic and histological remission with ustekinumab compared with vedolizumab following anti-TNF failure, although head-to-head randomized trials are lacking (10,11). In our study, the majority of patients received ustekinumab after anti-TNF failure, with favorable clinical and biological outcomes, supporting its role as a valuable second-line or subsequent biologic therapy.

The safety profile observed in our cohort is consistent with published data. Pooled safety analyses from randomized trials and observational studies indicate that ustekinumab is associated with a low risk of serious adverse events, with rates comparable to placebo in many studies (12,13). Importantly, no new safety signals have emerged with long-term exposure, making ustekinumab a suitable option for chronic disease management.

From a mechanistic perspective, ustekinumab targets the p40 subunit shared by interleukin-12 and interleukin-23, thereby modulating both Th1 and Th17 pathways. This mechanism distinguishes it from anti-TNF agents and gut-selective integrin inhibitors and may explain its effectiveness in patients with prior biologic failure (14). Emerging evidence also suggests an association between higher ustekinumab trough levels and improved clinical and endoscopic outcomes, highlighting the potential role of therapeutic drug monitoring in optimizing treatment (15).

Several limitations should be acknowledged. The observational design and relatively small sample size may limit the generalizability of our findings. In addition, the absence of a comparator group precludes direct assessment of comparative effectiveness. Nevertheless, the prospective design, standardized follow-up, and consistency of outcomes across clinical, biological, and endoscopic domains strengthen the validity of our results.

Conclusion

In conclusion, this prospective observational study supports the effectiveness and safety of ustekinumab in the management of inflammatory bowel disease in routine clinical practice. The consistency of clinical, biological, and endoscopic responses observed in our cohort, together with a favorable safety profile, reinforces the role of ustekinumab as an important therapeutic option, particularly in patients with moderate-to-severe disease and prior biologic exposure.

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