Journal of Enterocolitis

Original Article

Experience with Ustekinumab and Vedolizumab in Patients with Inflammatory Bowel Disease: Single-Center Data

Halit Kandemir, Beril Demir, Enes Cömert, Derya Kirman, Kenan Moral, Gülden Bilican, Ali Karataş, Murat Kekilli, Mehmet Cindoruk, Tarkan Karakan

Department of Internal Medicine, Division of Gastroenterology Gazi University Faculty of Medicine, Ankara, Türkiye

Cite this article as: Kandemir H, Demir B, Cömert E, et al. Experience with Ustekinumab and Vedolizumab in Patients with Inflammatory Bowel Disease: Single-Center Data. *J Enterocolitis.* 2025;4(2):35-39.

Corresponding author: Halit Kandemir, e-mail: halitkandemir@gazi.edu.tr

Received: June 12, 2025 **Accepted:** June 23, 2025

DOI:10.14744/Jenterocolitis.2025.76424

Abstract

Objective: In patients with moderate-to-severe inflammatory bowel disease who do not respond adequately to anti-TNF therapies, ustekinumab and vedolizumab offer alternative biologic treatment strategies. This study investigates and compares their clinical effectiveness and therapeutic response rates in a real-world setting.

Methods: A total of 156 patients treated at a tertiary university hospital from January 2017 to October 2024 were included, with 80 patients receiving vedolizumab and 76 receiving ustekinumab. Data on gender, age, previous treatments, CRP levels, and disease activity (Mayo or Harvey–Bradshaw Index) were collected. Primary non-responders were defined as patients who did not achieve a clinical, laboratory, or endoscopic response within the first 24 weeks. Secondary non-responders were those who failed to respond within 52 weeks.

Results: Among the patient group, 49.4% were diagnosed with ulcerative colitis (UC), and 50.6% with Crohn's disease (CD). The median treatment duration was similar for both drugs. No significant differences were found in pre- and post-treatment Mayo scores for UC patients (P = 0.151; P = 0.158), whereas there were statistically significant differences between the two groups in pre- and post-treatment Harvey–Bradshaw Index for CD patients (P = 0.013; P = 0.007). At week 24, primary non-response rates were 15.78% for ustekinumab and 22.50% for vedolizumab (P = 0.316). At week 52, secondary non-response rates were 11.47% for ustekinumab and 21.25% for vedolizumab (P = 0.302).

Conclusion: Among individuals with inflammatory bowel disease who fail to respond to anti-TNF therapy, ustekinumab and vedolizumab demonstrated comparable effectiveness. No statistically significant difference was observed in rates of primary or secondary non-response. Larger, more comprehensive studies are needed to confirm these findings.

Keywords: Crohn's disease, ulcerative colitis, ustekinumab, vedolizumab

INTRODUCTION

Ulcerative colitis (UC) and Crohn's disease (CD), the two main subtypes of inflammatory bowel disease (IBD), are chronic inflammatory disorders affecting the gastrointestinal system. In recent years, both the prevalence and incidence of IBD have been rising worldwide, particularly in developed countries.[1] In addition to intestinal inflammation, IBD can present with extraintestinal complications, significantly impacting patients' quality of life.[2]

Biologic therapies—especially anti-TNF drugs—have significantly transformed the treatment landscape of IBD. Nonetheless, around 30–40% of patients fail to achieve an initial therapeutic response to these medications, while others experience a secondary loss of response over time.[3] In this context, biologic agents with different mechanisms of action have expanded treatment options, offering new hope for patients with treatment-resistant disease.

By targeting the shared p40 subunit of interleukins 12 and 23, ustekinumab functions as a monoclonal antibody with proven efficacy and safety in both initial and long-term therapy.[4] Vedolizumab, which specifically targets integrins, selectively inhibits gastrointestinal inflammation by blocking the interaction between MAdCAM-1 and α4β7 integrin.

We sought to analyze real-world data from a single center regarding the use of ustekinumab and vedolizumab in the treatment of IBD patients. Our study aims to assess the clinical efficacy of these agents, determine primary and secondary non-response rates, and investigate potential differences between the two treatment groups.

METHODS

This study was based on a retrospective review of patient data from a single tertiary care hospital, involving IBD patients who received usteki-

MAIN POINTS

- Ustekinumab and vedolizumab demonstrated comparable clinical effectiveness as second-line treatments in patients with moderate-to-severe Crohn's disease and ulcerative colitis who were refractory to anti-TNF therapy.
- Primary and secondary non-response rates at weeks 24 and 52 did not differ significantly between the ustekinumab and vedolizumab groups, indicating similar long-term treatment efficacy.
- Ustekinumab showed significantly greater improvement in Harvey–Bradshaw Index and post-treatment CRP levels in Crohn's disease patients compared to vedolizumab.
- No life-threatening adverse effects or opportunistic infections were observed in either treatment group, supporting the safety and tolerability of both biologics in real-world clinical practice.
- The study provides valuable real-world evidence from a 7-year single-center experience, highlighting the practical utility of ustekinumab and vedolizumab in anti-TNF-experienced IBD patients.

numab or vedolizumab at Gazi University's Gastroenterology Clinic between January 2017 and October 2024.

Patient Selection

The inclusion criteria were as follows:
1. Patients aged ≥18 years
2. Diagnosis of CD or UC based on a combination of endoscopic evidence, clinical presentation, and imaging
3. Initiation of ustekinumab or vedolizumab treatment with at least 52 weeks of follow-up

The exclusion criteria for the study were as follows:

1. Missing clinical or laboratory data
2. Concurrent immunosuppressive therapy
3. Ineligibility for treatment due to malignancy or severe comorbidities

Treatment Protocol

Ustekinumab was administered as an initial intravenous loading dose (260, 390, or 520 mg/kg), followed by maintenance treatment with 90 mg subcutaneous injections every eight weeks. Vedolizumab was administered as an initial intravenous loading dose of 300 mg at weeks 0, 2, and 6, followed by maintenance infusions of 300 mg every eight weeks.

Response Assessment

The response to treatment was evaluated using two primary criteria:
1. Primary non-response: Treatment modification within the first 24 weeks
2. Secondary non-response: Treatment modification between weeks 24 and 52

Before starting treatment, patients' age, gender, previous medications, disease activity scores (HBI or Mayo), and levels of CRP and fecal calprotectin were recorded. Clinical response was assessed using the HBI or Mayo score, while biochemical response was evaluated based on CRP and fecal calprotectin levels. Endoscopic response was determined using endoscopic scoring systems based on the patients' clinical status. Ethics committee approval was obtained from Gazi University Non-Interventional Clinical Research Ethics Committee (Approval Number: 12, Date: 14.02.2025). All study participants provided informed consent prior to inclusion. This research was conducted in accordance with the guidelines of the Declaration of Helsinki.

Collection and Examination of Data

Demographic characteristics, disease subtype (CD or UC), pre- and post-treatment clinical parameters, laboratory values, and imaging findings were retrospectively retrieved from electronic medical records.

Statistical Analysis

Statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Continuous data are presented as mean ± standard deviation, whereas categorical data are expressed as percentages. The chi-square test was used to evaluate differences in primary and secondary non-response rates. For comparisons between pre- and post-treatment values, paired t-tests or Wilcoxon signed-rank tests were applied, as appropriate. A p-value less than 0.05 was considered statistically significant.

RESULTS

Between May 2019 and October 2024, a total of 89 patients were initiated on ustekinumab treatment. During the follow-up period, 11 patients discontinued follow-up for various reasons, 1 patient discontinued treatment due to side effects, and 1 patient passed away. These patients were excluded from the study, leaving 76 patients in the ustekinumab group. Between January 2017 and October 2024, a total of 106 patients were initiated on vedolizumab treatment. Among them, 21 patients discontinued follow-up, 2 patients stopped treatment due to side effects, and 3 patients passed away. After excluding these patients, 80 patients remained in the vedolizumab group. The study cohort consisted of 156 patients in total.

Eighty-seven patients (55.8%) were female, and 69 (44.2%) were male. Of all patients, 77 (49.4%) had UC, and 79 (50.6%) had CD. At the time of diagnosis, the mean patient age was 35.01 years. The mean age at diagnosis was 33.88 years in the ustekinumab group and 36.08 years in the vedolizumab group, with no statistically significant difference between the two groups (P = 0.170). Of the patients, 102 (65.4%) had previously used infliximab and 60 (38.5%) had used adalimumab as anti-TNF agents, while 115 (73.7%) had prior experience with azathioprine. A total of 27 patients who started ustekinumab and 35 patients who started vedolizumab required concomitant steroids at treatment initiation (62 patients [39.7%] in total) (Table 1).

The pre-treatment Mayo score of 31 UC patients who started ustekinumab was 8.29, while the post-treatment score was 3.00. In 46 UC patients treated with vedolizumab, the pre-treatment Mayo score was 7.72 and the post-treatment score was 3.83. No statistically significant differences were observed between the two groups regarding the Mayo score both before (P = 0.151) and after (P = 0.158) treatment.

The pre-treatment Harvey–Bradshaw Index (HBI) of 45 patients with CD who started ustekinumab was 7.24, while the post-treatment HBI was 2.13. In 34 patients with CD who started vedolizumab, the pre-treatment HBI was 8.62, and the post-treatment HBI was 3.76. There was a statistically significant difference between the two groups in terms of both pre-treatment (P = 0.013) and post-treatment HBI values (P = 0.007).

In 31 UC patients who started ustekinumab treatment, CRP levels were 32.7 mg/L before treatment and 16.61 mg/L after treatment. In 46 UC patients receiving vedolizumab, CRP levels were 40.93 mg/L before treatment and 19.74 mg/L after treatment. There was no statistically significant difference between the two drug groups in terms of

Table 1. Demographic and Clinical Characteristics of Patients Using Ustekinumab and Vedolizumab

	Patients Using Ustekinumab (76)		Patients Using Vedolizumab (80)	
	UC	CD	UC	CD
Number of Patients, n (%)	31 (40.8)	45 (59.2)	46 (57.5)	34 (42.5)
Gender n (%)				
Female	16 (51.6)	30 (66.6)	20 (43.5)	21 (61.8)
Male	15 (48.4)	15 (33.4)	26 (56.5)	13 (38.2)
Mean Age at Diagnosis (years)	32.26	35.69	35.96	36.24
Anti-TNF Experience Before Treatment, n (%)				
INF	24 (77)	25 (55)	30 (65)	23 (67)
ADA	10 (32)	23 (51)	13 (28)	14 (41)
INF+ADA	4 (13)	6 (13)	4 (8)	7 (20)
AZA Use Before Treatment, n (%)	16 (51.6)	44 (97,7)	25 (54.3)	30 (88.2)
Steroid Requirement, n (%)	13(41.9)	14(31.1)	20(43.5)	15 (44.1)
Primary Non-Responder at 24 Weeks, n (%)	6 (19.3)	6 (13.3)	10 (21.7)	8 (23.5)
Secondary Non-Responder at 52 Weeks, n (%)	6 (19.3)	5 (11.1)	9 (19.5)	8 (23.5)
Number of Patients Continuing Treatment (n) and Duration (months-median)	19, 18.3 (2-34) months	32, 22.1 (1-65) months	24, 22.8 (2-87) months	14, 25.5 (1-82) months
Number of Patients with Treatment Change (n) and Duration (months-median)	12, 7.5 (3-28) months	13, 10.4 (4-32) months	22, 11.6 (2-69) months	20, 13.5 (2-52) months
CRP Before Treatment (mean)	32.71	46.07	40.93	40.06
CRP After Treatment (mean)	16.61	11.93	19.74	23.91
HBI Score Before Treatment (mean)	-	7.24	-	8.62
HBI Score After Treatment (mean)	-	2.13	-	3.76
Mayo Score Before Treatment (mean)	8.29	-	7.72	-
Mayo Score After Treatment (mean)	3.00	-	3.83	-

UC: Ulcerative Colitis, CD: Crohn's Disease, INF: Infliximab, ADA: Adalimumab, AZA: Azathioprine, CRP: C-Reactive Protein, HBI: Harvey-Bradshaw Index.

pre-treatment (P = 0.176) and post-treatment (P = 0.333) CRP values among UC patients.

In 45 CD patients receiving ustekinumab, CRP values were 46.07 mg/L before treatment and 11.93 mg/L after treatment. In 34 CD patients in the vedolizumab group, CRP values were 40.06 mg/L before treatment and 23.91 mg/L after treatment. Among patients with CD, there was no significant difference between the two drug groups in pre-treatment CRP values (P = 0.317), while a statistically significant difference was observed in post-treatment CRP values (P = 0.038).

Among patients who continued to use vedolizumab during follow-up, the median duration of drug use was 22.8 months (range: 2–87) in 24 UC patients and 25.5 months (range: 1–82) in 14 CD patients. For patients who continued to use ustekinumab, the median duration of drug use was 18.3 months (range: 2–34) in 19 UC patients and 22.1 months (range: 1–65) in 32 CD patients. There was no statistically significant difference between the two groups in terms of duration of drug use in both UC and CD patients (P = 0.284 and P = 0.179, respectively).

At the end of the 24th week, based on the evaluation of primary non-response: 6 of the 12 patients who switched from ustekinumab were UC, and 6 were CD. The mean duration of drug use was 4.5 months in both groups. Among the 18 patients who switched from vedolizumab, 10 had UC and 8 had CD. The average duration of drug therapy was 3.6 months in UC patients and 4.375 months in CD patients. There was no statistically significant difference in the duration of drug use during the period of primary non-response in both UC and CD patients (P = 0.481 and P = 0.771). Additionally, there was no statistically significant difference in the primary non-response rates between the two drug groups (P = 0.316).

At the end of the 52nd week, 6 of the 11 patients who switched from ustekinumab were UC and 5 were CD. The mean time to drug switching was 10.5 months for UC patients and 9.8 months for CD patients. Among the vedolizumab group, 9 patients who switched were UC and 8 were CD. The mean duration of drug switching was 9.6 months for both UC and CD patients. There was no statistically significant difference in the duration of drug use during the period of secondary non-response between UC and CD patients (P = 0.533 and P = 1.000). Likewise, there was no statistically significant difference in the rates of secondary non-response between the two drug groups (P = 0.302).

During follow-up, only one patient in the ustekinumab group and two patients in the vedolizumab group experienced a non-life-threatening allergic drug reaction during the first infusion. These patients were treated with drug discontinuation and symptomatic therapy. No life-threatening complications or opportunistic infections were observed in any patient during the follow-up period.

DISCUSSION

In this real-world, single-center retrospective analysis, the goal was to evaluate and compare the efficacy of ustekinumab versus vedolizumab as second-line therapies in patients with moderate-to-severe CD and

UC who had prior anti-TNF treatment experience. We aimed to analyze patients' demographic characteristics, prior treatments, steroid requirements, pre-treatment HBI and Mayo scores, clinical remission rates, and primary/secondary non-response rates.

Within the ustekinumab group, 15.8% of the 76 patients (6 with UC and 6 with CD) were classified as primary non-responders by week 24, while 14.4% (6 UC, 5 CD) were identified as secondary non-responders at week 52. In a study by Forss et al.5 in 2021, clinical remission rates were found to be 40% at the end of week 16. In a follow-up study in 2023,6 the response rates of the same patient group at the end of week 52 were found to be 44%. Primary and secondary response rates were significantly higher in our study. In a meta-analysis including 14 studies, loss of response and the requirement for dose escalation at the end of one year were determined to be 21% in CD.[7] In the UNITI 1 and 2 studies, response rates at the end of week 6 and week 52 were 34% and 52%, respectively, in patients with moderate-to-severe CD.3 In a 2021 study of 312 patients (224 ustekinumab, 88 vedolizumab), steroid-free remission rates were better in favor of ustekinumab at both week 14 and week 54 (25.9% vs. 3.8% and 49.3% vs. 41.2%, respectively).[8]

In our study, a total of 80 patients were treated with vedolizumab. Among these patients, 18 (22.5%) experienced primary non-response at week 24, while 17 (21.2%) showed secondary non-response at week 52. A meta-analysis conducted in 2019 reported remission rates of 32% in UC patients and 30% in CD patients at week 14 of vedolizumab treatment. In that study, remission rates at week 52 were 42% for UC and 30% for CD.9 A meta-analysis of 10 cohorts conducted in 2010 found secondary loss of response to treatment to be 47.9% in CD and 39.8% in UC.[10] In our study, both primary and secondary response rates to vedolizumab were higher.

In a separate study comparing infliximab and vedolizumab in UC patients, the response rate at week 52 in the vedolizumab group was found to be 75%.[11] In the GEMINI 1 and 2 studies, clinical response and remission rates at week 6 in UC patients were 47.1% and 16.9%, respectively, while in CD patients, the rates were 31.4% and 14.5%. At week 52, these rates increased to 56.6% and 41.8% in UC, and 39.0% and 43.5% in CD.[12,13] A study conducted in 2018 reported high remission rates reaching 90% and good adherence to treatment at week 52, similar to our findings.[14] Another study conducted in Italy in 2020 showed that, in biologic-naive patients, 68.2% of CD patients and 67.9% of UC patients showed a clinical response 14 weeks after starting vedolizumab. At week 52, 77.4% of CD patients and 73.8% of UC patients treated with vedolizumab showed a clinical response.[15] A recent meta-analysis comprising 14 studies and a total of 5,651 patients evaluated the efficacy of ustekinumab versus vedolizumab in CD patients who did not respond to anti-TNF treatment. The analysis revealed that remission and drug continuation rates were higher in the ustekinumab group (29–86%) compared to the vedolizumab group (38–62%).[16]

In a single-center study conducted in Norway with vedolizumab, among the 71 patients treated, a significant decrease in CRP levels was observed in CD patients, while no CRP response was achieved in UC patients.[17]

The strengths of our study lie in the analysis of real-world data from patients followed for more than 52 weeks over a period exceeding 7 years, providing important clinical insights. Limitations include the retrospective nature of the study and the relatively small sample size. Another limitation is the definition of primary and secondary non-response as a transition to another agent, such as vedolizumab or ustekinumab, without full evaluation of clinical, laboratory, and endoscopic responses in all patients. Despite these limitations, our study followed a total of 134 patients for at least 52 weeks, providing valuable real-world experience.

In summary, for individuals suffering from moderate-to-severe Crohn's disease or ulcerative colitis who are refractory to anti-TNF agents, ustekinumab and vedolizumab represent effective and well-tolerated treatment alternatives.

Ethics Committee Approval: Ethics committee approval was obtained from Gazi University Non-Interventional Clinical Research Ethics Committeel (Approval Number: 12, Date: 14.02.2025).

Informed Consent: Written informed consent was obtained from the patients participating in this study.

Peer-review: Externally peer-reviewed.

Author Contribution: Concept – H.K.; Design – H.K.; Supervision – A.K.; Resource – H.K.; Materials – H.K.; Data Collection and/or Processing - H.K., B.D., E.C., D.K., K.M., G.B.; Analysis and/or Interpretation - H.K.; Literature Review – H.K., B.D., E.C., D.K., K.M., G.B.; Writing – H.K., A.K.; Critical Review – A.K., M.K., M.C., T.K.

Declaration of Interests: The authors declare that they have no competing interest.

Funding: Authors declare that this study have not received any financial support.

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