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Original Article

Efficacy and Safety of Vedolizumab and Ustekinumab Treatment in Anti-TNF-Exposed Inflammatory Bowel Disease Patients

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Abstract

Objective: Patients with inflammatory bowel disease (IBD) who fail anti–tumor necrosis factor (anti-TNF) therapy require alternative biologics with different mechanisms of action. Vedolizumab (VDZ) and ustekinumab (UST) are established effective options. However, real-world comparative data remain limited.
Methods: We conducted a retrospective, single-center study of 114 anti-TNF-experienced IBD patients (40 ulcerative colitis [UC], 74 Crohn's disease [CD]) treated with VDZ or UST between 2017 and 2024. Clinical and laboratory parameters were collected at baseline, at 3 and 12 months, and at the last follow-up. Disease activity was assessed using the partial Mayo score (UC) and the Harvey–Bradshaw Index (CD). Treatment response, persistence, adverse events, and the need for surgery were analyzed.
Results: Of the 40 UC patients, 34 (85%) were treated with VDZ and 6 (15%) with UST. Among the 74 CD patients, 34 (46%) were treated with VDZ and 40 (54%) with UST. In UC, VDZ led to significant reductions in pMayo scores at 3 and 12 months ($p<0.0001$), whereas UST showed numerical improvement without statistical significance. In CD, both VDZ and UST significantly reduced HBI scores at 3 and 12 months ($p<0.001$). Treatment persistence did not differ significantly between VDZ and UST in the overall, UC, or CD cohorts. Adverse events occurred in 9 patients (7.9%), mostly mild, with no serious complications. Surgical interventions were required in 9 patients, most of whom were treated with VDZ.
Conclusion: Both agents were effective and safe in anti-TNF-experienced IBD patients. Our real-world data indicate distinct response patterns between UC and CD, underscoring the clinical utility of both agents as therapeutic options after anti-TNF failure.
Keywords: Clinical efficacy, Crohn's disease, safety profiles, ulcerative colitis, ustekinumab, vedolizumab.

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic, relapsing condition requiring long-term management.[1] The primary therapeutic goals are to suppress inflammation, achieve mucosal healing, and maintain long-term remission.[2-5] Primary and secondary nonresponse to anti–tumor necrosis factor (anti-TNF) agents has highlighted the need for novel biologic therapies with alternative mechanisms of action, such as vedolizumab (VDZ) and ustekinumab (UST).[6,7]

VDZ is a gut-selective IgG1 monoclonal antibody that binds to the α4β7 integrin, thereby inhibiting the migration of T lymphocytes from the circulation into the gastrointestinal mucosa.[8-10] UST is a fully human IgG1 monoclonal antibody that binds to the p40 subunit shared by interleukin-12 (IL-12) and interleukin-23 (IL-23), thereby preventing these cytokines from binding to their cell surface receptors and blocking downstream inflammatory signaling pathways. By inhibiting the IL-12/23 axis, UST suppresses both Th1- and Th17-mediated immune responses.[11]

VDZ and UST have been evaluated in numerous studies. Comparative studies have not demonstrated consistent superiority of one agent over the other, with both showing favorable efficacy profiles and low rates of adverse events. In a multicenter retrospective study, UST demonstrated similar efficacy when used as second- or third-line therapy, whereas VDZ was less effective as third-line treatment than when used as a second-line option.[12] Another large multicenter study in biologic-naïve patients with CD reported similar clinical response rates between VDZ and UST. However, mucosal healing was observed more frequently in the VDZ group, whereas treatment persistence was higher in the UST group. No significant differences were observed between the two groups regarding safety or the need for surgery.[13]

Compared with CD, fewer studies have assessed the comparative effectiveness of VDZ and UST in ulcerative colitis (UC). In a cohort from Japan, no significant differences were observed between the VDZ and UST groups in terms of remission and response rates. The safety profiles of both agents were similar, and no serious adverse events were reported.[14]

Multiple clinical studies have demonstrated that the safety profiles of UST and VDZ are comparable in both biologic-naïve patients and those with anti-TNF-refractory Crohn's disease.[11-18] Rates of serious adverse events and treatment-related complications were low and similar between the two therapies.[11,12,14,15] Furthermore, both agents were well tolerated in elderly patients, with comparable adverse event rates in these subgroups.[15,16]

In this study, we aimed to evaluate the effectiveness, treatment persistence, and safety of VDZ and UST in anti-TNF-experienced IBD patients in a real-world setting.

METHODS

We enrolled patients with IBD who received VDZ or UST after treatment with an anti-TNF agent in our IBD-specific gastroenterology outpatient clinic between 2017 and 2024. The diagnoses of UC and CD were established based on clinical, endoscopic, and histological findings in accordance with the guidelines current at the time of diagnosis. Patients who had completed the induction regimen of VDZ or UST with prior exposure to anti-TNF treatment were included in the study. Exclusion criteria were age <18 years, absence of prior anti-TNF exposure, failure to complete the induction regimen, or a diagnosis of indeterminate colitis.

Demographic variables (age, sex), clinical characteristics (diagnosis, disease activity, behavior, location/extent according to the Montreal classification[17]), endoscopic activity, biochemical parameters (leukocyte count, C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], albumin), and adverse events were extracted from patient records and the hospital electronic database. Data were collected at baseline (initiation of VDZ or UST), at the 3rd month, 12th month, and the last follow-up visit.

The retrospective evaluation included adverse events, number of disease flares, new-onset complications, IBD-related surgery, and hospitalizations. Disease activity was assessed at the 3rd month, 12th month, and the last follow-up visit.

Disease activity was assessed using the Partial Mayo (pMayo) score for patients with UC and the Harvey–Bradshaw Index (HBI) for patients with CD at treatment initiation and during follow-up.

Treatment response was determined by changes in disease activity scores (pMayo and HBI) from baseline to the 3rd and 12th months. Clinical remission was defined using disease-specific indices: for UC, remission was defined as a pMayo score ≤2 with no individual subscore >1; for CD, remission was defined as an HBI ≤4, whereas clinical response was defined as a decrease of ≥3 points from baseline. In addition, treatment persistence and adverse events were retrospectively evaluated separately within each treatment group.

Statistical Analysis

Data were presented as mean±standard deviation (SD) or median (range), depending on the distribution characteristics of the variables. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Continuous variables were analyzed using either the independent-samples t test or the Mann–Whitney U test, depending on data distribution. These statistical methods were used to comprehensively evaluate relationships and differences between variable groups. Associations between variables and potential risk factors were analyzed using appropriate statistical techniques throughout the study period. A p value <0.05 was considered statistically significant.

Ethics Statement

This study was designed as a retrospective observational analysis. In accordance with national regulations and institutional policies, the requirement for written informed consent was waived by the local Institutional Review Board because of the retrospective nature of the study and the exclusive use of fully anonymized data. All patient information was obtained from electronic medical records and irreversibly anonymized before analysis; no identifiable personal data were accessed at any stage of the study. The study protocol was approved by Marmara University Faculty of Medicine, Non-Drug and Medical Device Research Ethics Committee (Approval Number: 09.2024.243, Date: 09.02.2024) and conducted in accordance with the Declaration of Helsinki.

RESULTS

Demographic and Clinical Characteristics

Overall Patient Group:

A total of 114 patients with a confirmed diagnosis of IBD were included in the study. The mean age of the patient group was 41.0±11.6 years, and the mean age at diagnosis was 29.0±9.9 years. Fifty-one (44.7%) were female and 63 (55.3%) were male (Table 1). In terms of diagnosis, 40 patients (35.1%) had UC and 74 (64.9%) had CD (Figure 1).

Ulcerative Colitis Subgroup:

Forty patients with a diagnosis of UC were included in the study. The mean age was 39.3±9.8 years, and the mean age at diagnosis was 27.9±8.8 years. Sixteen patients (40.0%) were female and 24 (60.0%) were male. Regarding disease extent, 11 patients (27.5%) had left-sided colitis, 7 (17.5%) had extensive colitis, and 22 (55.0%) had pancolitis (Table 1).

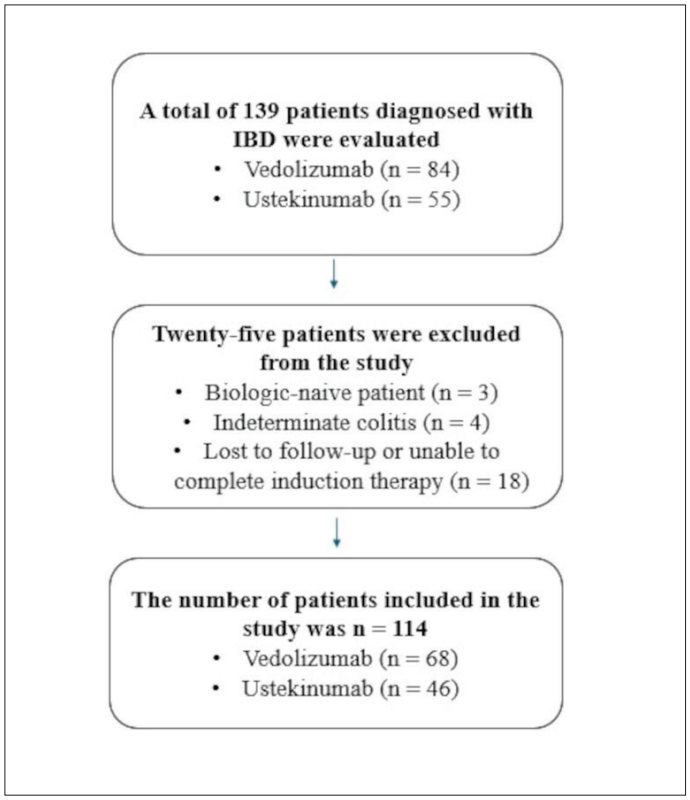


Figure 1. Flow diagram of the inclusion and exclusion of IBD patients treated with VDZ or UST.

Table 1. Patient demographics and clinical features

Characteristics	All Patients (N=114)	UC Subgroup (N=40)	CD Subgroup (N=74)
Age (years, mean ± SD)	41.0 ± 11.6	39.3 ± 9.8	42.0 ± 12.4
Age at diagnosis (years, mean ± SD)	29.0 ± 9.9	27.9 ± 8.8	29.6 ± 10.4
Female sex, n (%)	51 (44.7)	16 (40.0)	35 (47.3)
Male sex, n (%)	63 (55.3)	24 (60.0)	39 (52.7)
Left-sided colitis, n (%)	–	11(27.5)	–
Extensive colitis, n (%)	–	7(17.5)	–
Pancolitis, n (%)	–	22(55.0)	–
Age at diagnosis <16 years, n (%)	–	–	9 (12.2)
Age at diagnosis 17–40 years, n (%)	–	–	51 (68.9)
Age at diagnosis >40 years, n (%)	–	–	14 (18.9)
Ileal involvement, n (%)	–	–	10 (13.5)
Colonic involvement, n (%)	–	–	9 (12.2)
Ileocolonic involvement, n (%)	–	–	55 (74.3)
Inflammatory behavior, n (%)	–	–	5 (6.8)
Stricturing behavior, n (%)	–	–	14 (18.9)
Fistulizing behavior, n (%)	–	–	22 (29.7)
Both stricturing and fistulizing, n (%)	–	–	33 (44.6)
Presence of perianal fistula, n (%)	–	–	51 (68.9)
Presence of internal fistula, n (%)	–	–	24 (32.4)

SD :Standard deviation; UC : Ulcerative Colitis; CD : Crohn's Disease; (–) not.

Table 2. Treatment distribution and concomitant medication use in UC and CD patients

Characteristics	UC Patients (N = 40)	CD Patients (N = 74)
Vedolizumab (VDZ), n (%)	34 (85.0)	34 (45.9)
Ustekinumab (UST), n (%)	6 (15.0)	40 (54.1)
Oral mesalamine, n (%)	31 (77.5)	30 (40.5)
Azathioprine, n (%)	15 (37.5)	23 (31.1)

UC: Ulcerative Colitis; CD: Crohn's Disease; VDZ: Vedolizumab; UST: Ustekinumab. Concomitant medications refer to oral mesalamine or azathioprine used at the time of vedolizumab or ustekinumab initiation.

Crohn's Disease Subgroup:

Seventy-four patients with a diagnosis of CD were included in the study. The mean age was 42.0±12.4 years, and the mean age at diagnosis was 29.6±10.4 years. Of these, 35 (47.3%) were female and 39 (52.7%) were male. Analysis of age at diagnosis showed that 9 patients (12.2%) were diagnosed before the age of 16, 51 (68.9%) between 17 and 40 years, and 14 (18.9%) after 40 years (Table 1).

Ten patients (13.5%) had ileal involvement, 9 (12.2%) had colonic involvement, and 55 (74.3%) had ileocolonic involvement. Five patients (6.8%) had an inflammatory phenotype, 14 (18.9%) had a stricturing phenotype, 22 (29.7%) had a penetrating phenotype, and 33 (44.6%) had both stricturing and penetrating phenotypes. Stenosis was observed in 46 patients (62.2%), perianal fistula in 51 (68.9%), and internal fistulas in 24 (32.4%) (Table 1).

Among the UC patients, 34 (85%) were treated with VDZ and 6 (15%) with UST. Of these, 31 (77.5%) were using oral mesalamine concurrently, while 15 (37.5%) received concomitant azathioprine therapy (Table 2).

In the CD cohort, 34 (45.9%) were treated with VDZ and 40 (54.1%) with UST. Among them, 30 patients (40.5%) were using oral mesalamine and 23 (31.1%) were receiving concomitant azathioprine therapy (Table 2).

Vedolizumab dose intensification was administered in 3 UC patients (7.5%) and in 5 CD patients (6.8%). Three patients with Crohn's disease who were anti-TNF-naïve were excluded from the study.

Among the included patients, 78 (68.4%) had been exposed to a single anti-TNF agent, 33 (28.9%) to two anti-TNF agents, and 3 (2.6%) to three different anti-TNF agents (Table 3). When comparing the number of patients with prior exposure to a single versus multiple anti-TNF agents between the UST and VDZ groups, exposure to more than one anti-TNF agent was significantly higher in the UST group (p=0.013).

Among patients with UC, 5 (12.5%) had been exposed to more than one anti-TNF agent, compared with 31 (41.9%) of those with CD. This difference was also statistically significant (p=0.001).

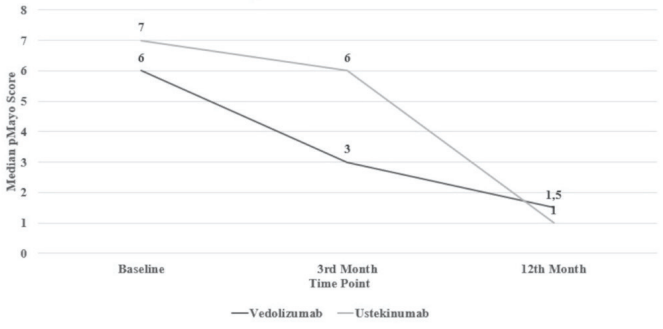
Assessment of Treatment Response

In UC patients treated with VDZ, the median pMayo score at treatment initiation was 6 (range: 0–9), which decreased to 3 (range: 0–8) at the 3rd month and further to 1.5 (range: 0–8) at the 12th month (Figure 2). A statistically significant reduction in pMayo scores was observed

Table 3. Number of biologic therapy exposures in study population

Single anti-TNF agent, n (%)	78 (68.4)
Two anti-TNF agents, n (%)	33 (28.9)
Three anti-TNF agents, n (%)	3 (2.6)

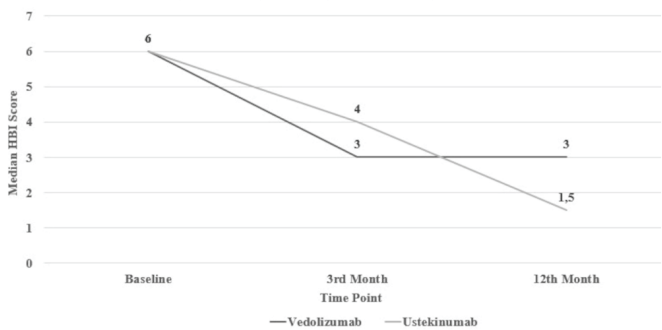
TNF: Tumor necrosis factor.



Time Point	VDZ Remission	UST Remission
3rd Month	14/34 (41.2%)	0/6 (0%)
12th Month	20/34 (58.8%)	3/6 (50.0%)

(Remission definitions: pMayo ≤2 for UC).

Figure 2. Median pMayo scores over time in UC patients treated with VDZ and UST.



Time Point	VDZ Remission	UST Remission
3rd Month	22/34 (64.7%)	24/40 (60.0%)
12th Month	22/34 (64.7%)	38/40 (95.0%)

(Remission definitions: HBI ≤4 for CD)

Figure 3. Median HBI scores over time in patients treated with VDZ and UST.

when baseline scores were compared with those at the 3rd and 12th months, respectively (p<0.0001 and p<0.0001).

In UC patients treated with UST, the median pMayo score was 7 (range: 5–9) at baseline, 6 (range: 6–6) at the 3rd month, and 1 (range: 1–6) at the 12th month. Although pMayo scores decreased from baseline to the 3rd and 12th months, these reductions were not statistically significant (p=0.15 and p=0.06, respectively) (Figure 2).

Among UC patients, no statistically significant difference was observed in baseline pMayo scores between the VDZ and UST groups (p=0.17). In both treatment groups, pMayo scores decreased significantly from pretreatment to the 3rd month and from pretreatment to the 12th month (p<0.0001 and p<0.0001) (Figure 2).

In CD patients treated with VDZ, the median HBI score at baseline was 6 (range: 1–17), decreasing to 3 (range: 0–15) at the 3rd month and remaining 3 (range: 0–12) at the 12th month. Comparisons of baseline HBI scores with those at the 3rd and 12th months showed statistically significant reductions (p<0.0001 and p=0.001, respectively) (Figure 3). In CD patients treated with UST, the median HBI score was 6 (range: 0–19) at baseline, 4 (range: 0–18) at the 3rd month, and 1.5 (range: 0–10) at the 12th month. Significant reductions in HBI scores were observed from baseline to the 3rd month and from baseline to the 12th month (p<0.0001 for both comparisons) (Figure 3). No statistically significant difference in baseline HBI scores was observed between the VDZ and UST groups (p=0.95), indicating comparable baseline disease activity.

A significant decline in ESR was observed at weeks 26 and 52, and CRP levels showed a significant reduction at week 52 in both the vedolizumab and ustekinumab groups (Supplementary Table 1).

Treatment Persistence

No significant difference in treatment response was observed between patients who received VDZ and those who received UST in the overall cohort or in the UC and CD subgroups (p=0.51, p=0.69, and p=0.36, respectively) (Figure 4).

Treatment Discontinuation

Treatment with VDZ or UST was discontinued in 40 patients. Of these, 15 patients (37.5%) had UC and 25 patients (62.5%) had CD. Among those who discontinued treatment, 9 patients (22.5%) had been receiving UST and 31 patients (77.5%) had been receiving VDZ.

Reasons for Treatment Discontinuation

In our study, 4 patients chose not to continue treatment, and therapy was discontinued. One patient was lost to follow-up during the COVID-19

Supplementary Table 1. Changes in laboratory parameters according to treatment group

Parameter	Treatment	Baseline (Median)	Week 6 (Median)	p	Week 14 (Median)	p	Week 26 (Median)	p	Week 52 (Median)	p
WBC (×10³/μL)	VDZ	9450	7700	0.80	7440	0.36	7350	0.16	7575	0.21
	UST	9610	8640	0.75	8140	0.40	8150	0.31	8580	0.22
CRP (mg/L)	VDZ	25.7	18.3	0.19	17.4	0.40	16.5	0.10	17.6	0.02
	UST	29.0	14.5	0.12	12.8	0.07	14.1	0.09	17.4	0.04
ESR (mm/h)	VDZ	25.2	22.7	0.62	20.5	0.02	21.5	0.053	20.7	0.003
	UST	44.9	29.6	0.50	27.8	0.04	28.3	0.03	15.4	0.01

WBC: White blood cell; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; VDZ: Vedolizumab; UST: Ustekinumab. Values are expressed as medians due to non-normal data distribution. p-values indicate within-group comparisons versus baseline (Wilcoxon signed-rank test). Statistical significance was defined as p < 0.05.

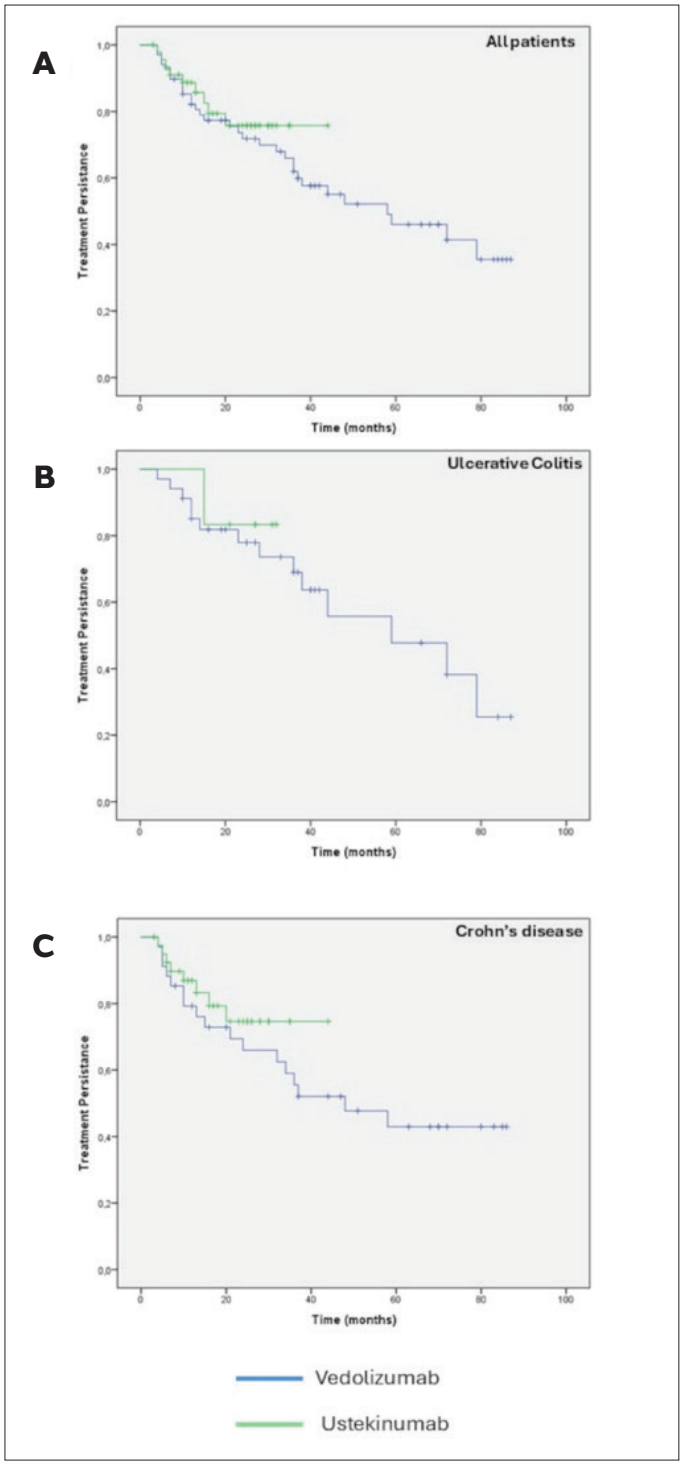


Figure 4. Comparison of treatment persistence between VDZ and UST.

pandemic and discontinued treatment. In 7 patients, treatment was discontinued due to adverse events, including arthritis (n=3), dyspnea (n=1), hypoglycemia (n=1), weight loss (n=1), and scalp rash (n=1).

Evaluation of Treatment Nonresponse

Primary nonresponse (lack of clinical improvement during the induction phase) was observed in 9 patients, whereas secondary loss of response (loss of clinical efficacy during the maintenance phase after initial improvement) occurred in 19 patients (Figure 5).

Adverse Reactions and Surgery

A total of 9 patients experienced treatment-related adverse events. In the UST group, 1 patient developed vertigo following the loading dose and another developed arthritis. In the VDZ group, adverse events were reported in 7 patients, including exertional dyspnea, hypoglycemic episodes, weight loss, scalp rash, arthritis, and cutaneous rashes.

Nine patients required surgical intervention. Among them, 3 underwent right hemicolectomy; all had CD and were receiving vedolizumab therapy. In one case, surgery was performed due to primary nonresponse, in another due to secondary loss of response, and in the third case treatment was continued postoperatively after remission was achieved.
One CD patient receiving VDZ underwent subtotal colectomy due to secondary loss of response, resulting in treatment discontinuation. Another patient with UC receiving VDZ underwent total proctocolectomy due to primary nonresponse, and treatment was discontinued accordingly. Additionally, abscess drainage procedures were performed in 4 patients due to perianal or intra-abdominal abscesses (Table 4).

DISCUSSION

In this study, real-world data on VDZ and UST treatments were compared in 114 patients with IBD who were unresponsive to at least one anti-TNF agent. The therapeutic efficacy and safety of both biologic agents were assessed by recording clinical response, treatment discontinuation rates, adverse event profiles, and safety outcomes during induction and maintenance therapy.

In UC patients, VDZ achieved statistically significant clinical remission in both the induction and maintenance phases, as measured by the pMayo score. In contrast, UST was associated with a numerical reduction in the pMayo score that did not reach statistical significance. Among CD patients, both the UST and VDZ treatment groups achieved statistically significant clinical remission during the induction and maintenance phases, as measured by the HBI. Numerical improvement in HBI scores was observed in both groups during induction, whereas a more pronounced numerical reduction was noted in UST-treated patients compared with those receiving VDZ during maintenance therapy. No statistically significant difference in treatment persistence was observed between the two agents, either in the overall IBD cohort or within the UC and CD subgroups. Both treatments were safe, with similar adverse event and safety profiles.

VDZ induced clinical remission in 42% of UC patients at the 3rd month and 60% at the 12th month, closely resembling the results of the GEMINI I trial.[8] In the UST-treated UC group, no clinical remission was observed at the 3rd month, whereas 60% of patients achieved clinical remission at the 12th month. The results in this cohort were not statistically significant; however, they were consistent with published data. In the UNIFI trial, clinical remission rates were relatively low during the induction phase (15.6% at week 8) but more than doubled during the maintenance phase, reaching 43.8% at week 44.[18] Similar to the UNIFI trial, our study demonstrated a marked increase in remission rates during the maintenance phase among patients treated with UST, with 60% achieving remission at the 12th month. The slightly higher remission rate observed in our cohort compared with UNIFI may be attributable to differences in patient characteristics and study design. While UNIFI was a phase 3 randomized controlled trial evaluating the efficacy of UST in a heterogeneous UC population under strict protocol-defined remission criteria, our study represents real-world data, potentially involving a more selected patient population and a less rigid definition of remission.[18]

Table 4. Surgical outcomes and indications in patients under biologic treatment

Surgical Procedure	Number of Patients	Diagnosis	Biologic Agent	Reason for Surgery / Outcome
Right Hemicolectomy	3	CD	VDZ	1 primary NR*, 1 secondary NR*, 1 continued post-op due to remission
Subtotal Colectomy	1	CD	VDZ	Secondary NR*, treatment discontinued
Total Proctocolectomy	1	UC	VDZ	Primary NR*, treatment discontinued
Intraabdominal Abscess Drainage	4	CD and UC	VDZ	Perianal or intra-abdominal abscess

NR: Non-response; CD: Crohn's disease; UC: Ulcerative colitis; VDZ: Vedolizumab; UST: Ustekinumab.

Another important consideration is that the number of UC patients receiving UST in our study was relatively low (n=6). This disproportionality in patient numbers represents a limitation in comparing response among UC patients. The apparent delay in short-term clinical improvement should therefore be interpreted cautiously. Furthermore, the rate of multiple anti-TNF resistance was higher in this group; only 5% (n=2) of patients in the VDZ group had failed more than one anti-TNF agent, compared with 50% (n=3) in the UST group.

Several studies have included anti-TNF-naïve patients in comparative analyses. In one study involving 106 UC patients (64 treated with VDZ and 42 with UST) who were either anti-TNF-naïve or experienced, no significant differences were observed between the two treatments in terms of remission and response rates at weeks 6, 22, and 54. The Clinical Activity Index (CAI) was used to assess disease activity in that study.[14] Another study using the same remission index as our study (pMayo ≤2) reported no significant differences in clinical remission at weeks 14 and 52.[19]

In our CD cohort, VDZ induced remission in 65% at the 3rd month and 66% at the 12th month, whereas the corresponding rates for UST were 60% and 95%, respectively. These findings are consistent with previous studies.[20-25] Multiple studies in anti-TNF-experienced CD populations have shown that UST may be more effective than VDZ during the maintenance phase. However, studies in anti-TNF-naïve populations yielded mixed results, with some showing similar outcomes and others demonstrating differences.[13,26,27] Another study including anti-TNF-experienced CD patients demonstrated that the superiority of UST over VDZ was particularly evident in patients with ileal involvement and penetrating disease behavior.[28] A prospective study reported that, in anti-TNF-experienced CD patients, both clinical remission (HBI ≤4) and biochemical remission (CRP ≤5 mg/L and fecal calprotectin ≤250 µg/g) rates at week 52 were significantly higher in the UST group.[24] Long disease duration and the presence of perianal disease have generally been associated with poorer outcomes for VDZ. In contrast, ileocolonic disease has been linked to higher remission rates in response to UST.[22,29]

In most comparable studies conducted in UC patients, treatment persistence rates were similar to those observed in our study, with no significant differences between the two agents.[19,30] Some studies in CD patients reported comparable outcomes at week 52, whereas others demonstrated higher long-term treatment persistence with UST.[13,21-23,29,31,32]

No serious adverse events were observed with either biologic agent in our study. Most studies conducted in patients with IBD have demonstrated comparable safety profiles for both agents, and our findings support this evidence.[13,24,27,29,33]

Overall, both VDZ and UST appear to be well tolerated across a wide

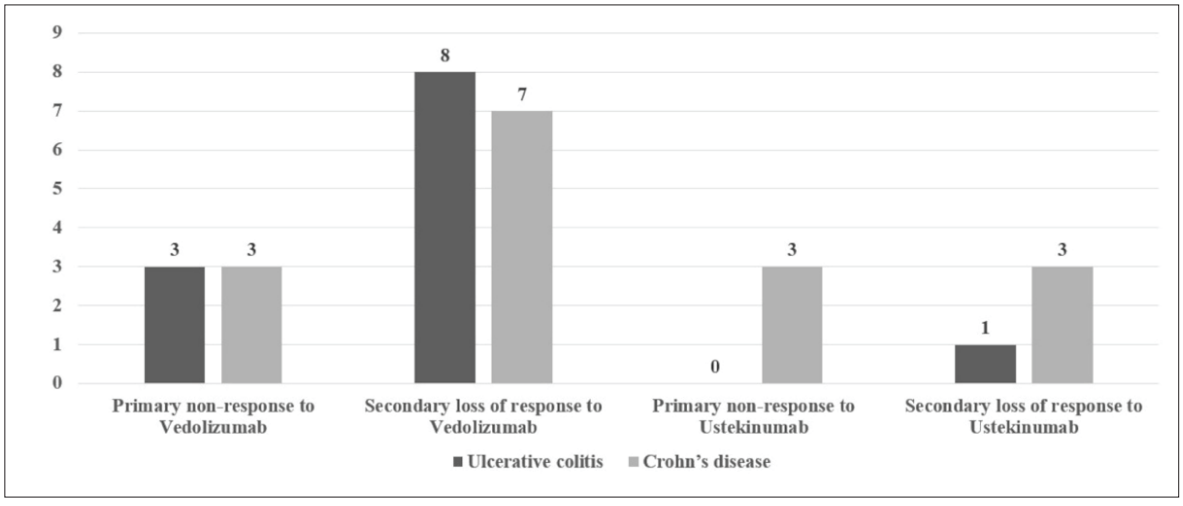


Figure 5. Patients with primary or secondary nonresponse to vedolizumab or ustekinumab.

range of patients, including older adults. In our study, 10 patients aged ≥60 years (1 with UC, 9 with CD) received biologic therapy (4 with UST and 6 with VDZ), with no serious complications or infections reported in this subgroup. These findings support the safety of both agents in elderly patients and are consistent with published evidence.[15,16,34]

A major strength of this study is its focus on real-world data evaluating the effectiveness of VDZ and UST as second- or third-line therapies in anti-TNF-experienced patients. The tertiary-center setting and access to a broad, diverse patient population further enhance the study's clinical relevance.

This study has several limitations. The retrospective, single-center design inherently limits the generalizability of the findings. In addition, the imbalance in sample sizes between the treatment groups and the overall small cohort size precluded a robust head-to-head comparative analysis. Another important limitation was the lack of adequate endoscopic and biochemical follow-up data at both 3 and 12 months, which prevented evaluation of mucosal healing and the use of a modified Mayo endoscopic subscore. The absence of fecal calprotectin evaluation during follow-up is another limitation.

Given these limitations, the primary focus of this study was not a direct comparison between VDZ and UST but rather an evaluation of their individual effectiveness, treatment persistence, and safety profiles in a real-world cohort. Future prospective, multicenter studies with standardized endoscopic and biochemical monitoring and larger sample sizes are needed to validate these findings. This study demonstrates that both UST and VDZ are effective in achieving clinical remission in anti-TNF-refractory IBD patients. High clinical success rates can be achieved with appropriate patient selection. Therefore, VDZ and UST represent effective and safe therapeutic options for achieving sustained, long-term disease control in patients with UC or CD who have failed anti-TNF therapy.

Ethics Committee Approval: The study's protocol received approval from the Ethical Committee for Clinical Investigations of the Marmara University Faculty of Medicine, Non-Drug and Medical Device Research Hospital (Approval Number: 09.2024.243, Date: 09.02.2024).

Informed Consent: Informed consent was waived by the local Clinical Research Ethics Committee due to the retrospective nature of the study and the use of anonymized patient data.

Conflict of Interest: Haluk Tarik Kani has been speaker or advisor for Abbvie, Janssen, Sanofi, Takeda and Ferring. The remaining authors declare no conflicts of interest.

Peer-review: Externally peer-reviewed.

Author Contribution: Concept – N.N., H.T.K.; Design – N.N., H.T.K.; Supervision – Y.Ö.A., Ö.A.; Data Collection and/or Processing - N.N., H.T.K.; Analysis and/or Interpretation - N.N., H.T.K.; Literature Review – N.N., T.T., H.T.K.; Writing – N.N., T.T.; Critical Review – Y.Ö.A., Ö.A., H.T.K.

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