Comparison of Real-World Treatment Outcomes With Vedolizumab Versus Infliximab in Biologic-Naive Patients With Inflammatory Bowel Disease

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Background: Little is known about long-term real-world effectiveness of vedolizumab versus infliximab in biologic-naive patients with inflammatory bowel disease (IBD).

Methods: Biologic-naive IBD patients who received vedolizumab or infliximab in the US Explorys Universe database (May 2014–September 2018) were weighted using Entropy-balancing.

Results: Persistence rates were higher for vedolizumab (N = 542) versus infliximab (N = 1,179) cohort at 12 (84.5% vs 77.5%; P = 0.0061) and 24 (77.6% vs 64.6%; P = 0.0005) months post-maintenance therapy. Healthcare resource utilization composite end point rates were lower in vedolizumab versus infliximab cohort at 12 (36.2% vs 48.2%; P < 0.0001) and 24 (46.9% vs 59.9%; P < 0.0001) months post-treatment initiation.

Conclusions: Biologic-naive IBD patients who received vedolizumab had better long-term real-world effectiveness measures versus infliximab patients.

Key Words: Crohn disease, healthcare resource utilization, inflammatory bowel disease, persistence, ulcerative colitis

INTRODUCTION

The incidence of inflammatory bowel diseases (IBD), which include ulcerative colitis (UC) and Crohn disease (CD), peaks at about 20–29 years of age and may be rising in the US.1 The total economic burden of IBD is substantial, with national estimates ranging between $14.6 and $31.6 billion.2–6 With the growing number of biologics approved for IBD complementing conventional therapies, there is a need to optimize treatment sequencing to alleviate the disease burden.7

Current US guidelines for IBD recommend a treatment algorithm whereby antitumor necrosis factor alpha (TNFα) agents, such as infliximab,8 are used in patients who are resistant or refractory to conventional therapy with corticosteroids, thiopurines, or methotrexate.9,10 Although clinical experience with infliximab is extensive,11 about 30%–40% of infliximab-treated patients do not respond to treatment.10,12,13 Until the introduction of newer advanced therapeutics other than anti-TNFα agents, treatment options were limited for these patients.14

Vedolizumab is a gut-selective monoclonal antibody that binds to the αβ7 integrin complex.15 This drug was approved on May 20, 2014 for the treatment of adult patients with moderately to severely active UC or CD who have had an inadequate response, lost response to, or were intolerant to conventional therapy or a TNFα antagonist.16,17 The American College of Gastroenterology recommends vedolizumab for use in patients with moderately to severely active UC or CD, an updated version of UC guidelines is awaiting publication (last version published in 2010 prior to vedolizumab approval).9

There is evidence from post-hoc analyses of the GEMINI trials suggesting that vedolizumab may be more effective in biologic-naive patients than in patients who previously failed anti-TNFα therapy.18,19 With the recent clinical practice trend of introducing biologics earlier during the course of treatment,20 it is important to understand the long-term, real-world comparative effectiveness of TNFα antagonist and new therapeutic options in biologic-naive patients with IBD.

Three real-world studies have previously assessed the efficacy and safety of vedolizumab versus infliximab or anti-TNFα therapy (any agent).21–23 However, these studies were limited by a short duration of follow-up (before the initiation of the maintenance phase)23 or inadequate control for previous
anti-TNFα exposure. Furthermore, although several network meta-analyses of comparative drug effectiveness have been published,24–30 these relied on data from randomized controlled trials (RCTs), which may not adequately reflect trends in US real-world clinical practice. To date, no direct comparison of the long-term effectiveness of vedolizumab and infliximab has been performed. In light of this knowledge gap, the objective of this study was to compare real-world outcomes related to treatment effectiveness in biologic-naïve patients with IBD initiated on vedolizumab versus infliximab with a focus on long-term time points in a real-world setting in the US.

MATERIALS AND METHODS

Data Source

Electronic medical records from the IBM Explorys Universe database (January 2000–November 2018) were used. The database includes electronic health records for over 50 million unique patients, representing approximately 19% of the US population, sourcing from more than 39 large US healthcare systems including integrated delivery networks, clinically integrated networks, and accountable care organizations. This database is Health Insurance Portability and Accountability Act (HIPAA) compliant and only contains de-identified data; thus, an internal review board approval was not required.

Study Design and Study Sample

Included patients were required to meet the following criteria: adult biologic-naïve patients initiated on vedolizumab or infliximab on or after May 20, 2014 (per vedolizumab approval date),8,15 with the date of initiation defined as the index date; ≥1 diagnosis for IBD (UC or CD) on or before the index date; induction therapy (ie, received ≥3 infusions of index biologic within 98 days post-index) was completed and maintenance therapy (ie, a fourth infusion of the index biologic ≤146 days after the third infusion) was initiated, without concurrent biologic use8,15; and evidence of continuous medical activity 365 days pre-index (baseline period) and until the initiation of maintenance therapy.

Patients initiated on infliximab were excluded if they had ≥1 diagnosis for an autoimmune disease other than IBD ≤30 days before the index date (only infliximab is indicated for autoimmune diseases other than IBD).8 Eligible patients were classified into 2 mutually exclusive cohorts based on the index biologic received for IBD (ie, vedolizumab or infliximab). Study outcomes were compared for all patients with IBD and separately for patients with UC and CD.

Study Outcomes

Study outcomes included treatment persistence, intensification of dosing frequency, and a healthcare resource utilization (HRU) composite end point. Treatment persistence was measured from the start of maintenance therapy initiation and was defined as the absence of treatment discontinuation or initiation of another biologic during maintenance therapy. Based on the recommended maintenance dosing schedule of 8 weeks for both index biologics, treatment discontinuation was defined as a gap of ≥90 days between the 56th imputed day of supply and the next dose or the end of continuous medical activity.16,17,31,32

Intensification of dosing frequency was measured from the start of maintenance therapy initiation and was defined as ≥3 consecutive infusions of the index biologic during maintenance therapy with infusions received more frequently than the recommended once-every-8-weeks maintenance dosing schedule (56 days).5,15 Although dose escalation via increased dose can be used with infliximab as indicated per product label,8 dosage strength was not readily available in the data and, consequently, was not assessed.

The HRU composite end point was measured during the index biologic therapy (ie, from the initiation of induction therapy) and included the following: (1) IBD-related hospitalization, defined as a hospitalization with a diagnosis for UC or CD; (2) IBD-related surgery, defined as a medical record with a procedure for one of the major IBD-related surgical procedures (ie, incision, excision, and anastomosis of intestine; operations on rectum, recto-sigmoid, and perirectal tissue; or operations on anus); (3) and administration of intravenous corticosteroids administered in an inpatient or outpatient setting.

Statistical Analysis

Because the nature of observational studies makes results vulnerable to confounding, reweighting via entropy balancing (e-balance) was used to control for potential unbalanced confounders between cohorts. This mitigates the impact of confounders to better isolate the effect of treatment by rendering cohorts more comparable at baseline.33,34 This process can be viewed as an approach to mimic—but by no means as powerful as—randomization in RCTs.

Similar to inverse probability of treatment weighting (IPTW), e-balance is a weighting technique, which reweights patients in each cohort (who initially have a weight equal to 1), so that covariates are comparable at baseline. E-balance was chosen over other commonly used weighting methods such as IPTW because it achieves better covariate balance without relying on correct propensity score model specification. Although recently developed, e-balance is increasingly used in observational studies.35–38 The infliximab cohort was reweighted, so that the overall distribution of patient characteristics (type of IBD [UC/CD]; as of the index date: age, sex, index year, disease duration in years; during the baseline: Charlson comorbidity index, presence of fistulas, location of UC/CD as a proxy of UC/CD severity, nonbiologic therapies during the 90 days before the index date, number of IBD-related surgeries, most recent measured serum albumin and C-reactive protein level;
and number of IBD-related hospitalizations at any time before the index date) had the exact same mean and SD as the distribution of patient characteristics in the vedolizumab cohort.33,34 Standardized differences were reported to assess the balancing of patient characteristics; a small effect size was defined as a score of <0.2.39–41

Weighted Kaplan–Meier (WKM) analyses were used to describe time to first occurrence of each of the study outcomes, and log-rank tests were used to compare WKM rates at 3, 12, and 24 months. Rates of treatment persistence were measured from the initiation of maintenance therapy to first event of treatment discontinuation or initiation of another biologic. Follow-up was censored at evidence of end of continuous medical activity or end of data, whichever occurred first. Rates of dosing frequency intensification were measured from the initiation of maintenance therapy to the first dosing frequency intensification (event) among a subgroup of patients with ≥3 infusions during maintenance therapy. Follow-up was censored at the earliest event among index biologic discontinuation, initiation of another biologic, evidence of end of continuous medical activity, or end of data availability. Rates of the HRU composite end point were measured from the index date to the first HRU composite end point (event). Follow-up was censored at the earliest event among index biologic discontinuation, initiation of another biologic, evidence of end of continuous medical activity, or end of data availability.

As part of a sensitivity analysis performed among all patients with IBD included in this study, treatment persistence and the HRU composite end point were compared between cohorts after using 3 different statistical approaches other than e-balance to account for potential unbalanced confounding factors between cohorts: a matching technique (propensity score [PS] matching); another weighting technique (IPTW); and multivariable Cox proportional hazards model. All 3 additional approaches adjusted for the full list of variables to be balanced between cohorts (listed above). After PS matching and IPTW, unweighted and weighted KM, respectively, were used as described above. The multivariable Cox proportional hazards model was used to estimate hazard ratios (HR) with 95% confidence intervals (CIs) and P values. Then, adjusted survival curves were estimated based on this model.

All analyses were conducted using Statistical Analysis System (SAS) Enterprise Guide software, version 7.1 (Cary, NC).

RESULTS

In total, 1721 patients with IBD met the selection criteria, including 542 (31.5%) who received vedolizumab and 1179 (68.5%) who received infliximab. After reweighting with e-balance, patient characteristics were perfectly balanced between cohorts (all standardized differences = 0.000). Mean age was 51.4 years, 50.6% of patients were female, 55.2% used nonbiologic therapies for IBD in the 90 days before index biologic initiation, and the median time from first IBD diagnosis to index biologic initiation was 2.7 years in both cohorts (Table 1). Median follow-up duration (from the index date to the first event among end of continuous medical activity or end of data availability) was 16 months for patients in the vedolizumab cohort (30% were observed for ≥24 months following the index date) and 20 months in the infliximab cohort (41% were observed for ≥24 months following the index date).

Treatment Persistence

Among all patients with IBD, the WKM rates of treatment persistence were significantly higher for the vedolizumab cohort compared with the infliximab cohort at 12 months (84.5% vs 77.5%, P = 0.0061) and 24 months after the initiation of the maintenance phase (77.6% vs 64.6%, P = 0.0005; Fig. 1).

In both UC and CD patients, separately, WKM rates of treatment persistence were numerically higher at 3 and 12 months after the initiation of the maintenance phase for vedolizumab compared with infliximab, and the difference was statistically significant at 24 months after the initiation of the maintenance phase (UC: 78.5% vs 63.5%, P = 0.0466; CD: 77.1% vs 65.7%, P = 0.0158; Fig. 4A).

Intensification of Dosing Frequency

Overall, WKM rates of dosing frequency intensification were significantly lower for the vedolizumab cohort compared with the infliximab cohort at 12 months (7.1% vs 17.0%, P = 0.0002) and at 24 months after the initiation of the maintenance phase (14.3% vs 22.1%, P = 0.0006; Fig. 2).

WKM rates of dosing frequency intensification were significantly lower in patients with UC who received vedolizumab at 12 months (6.4% vs 21.8%, P = 0.0008) and 24 months after the initiation of the maintenance phase (12.8% vs 25.1%, P = 0.0022) relative to patients who received infliximab. Similar results were found in patients with CD at 12 months (7.6% vs 15.2%, P = 0.0372) and at 24 months after the initiation of the maintenance phase (15.5% vs 20.0%, P = 0.0671; Fig. 4B).

HRU Composite End point

Overall, WKM rates of the HRU composite end point were significantly lower among patients in the vedolizumab cohort compared with those in the infliximab cohort at 12 months (36.2% vs 48.2%, P < 0.0001) and 24 months post-index (46.9% vs 59.9%, P < 0.0001; Fig. 3; see Supplementary Table 1 for the rates of the individual end points). WKM rates of the HRU composite end point were significantly lower in patients with UC who received vedolizumab at 12 months (36.5% vs 48.0%, P = 0.0259) and 24 months post-index (47.1% vs 58.8%, P = 0.0151) relative to those who received infliximab. Similar results were found in patients with CD at 12 months (35.8% vs 48.5%, P = 0.0003) and 24 months post-index (46.9% vs 63.2%, P = 0.0001; Fig. 4C).
|                      | IBD Patients (Overall) | UC Patients | CD Patients |
|----------------------|------------------------|-------------|-------------|
|                      | Vedolizumab | Infliximab | Vedolizumab | Infliximab | Vedolizumab | Infliximab |
| **N = 542**          | N = 1179    |             | N = 247    | N = 469    | N = 295    | N = 710    |
| **Age at index date (y), mean ± SD [median]** | 51.4 ± 16.6 [52] | 51.4 ± 16.6 [53] | 51.3 ± 16.8 [52] | 51.3 ± 16.8 [53] | 51.4 ± 16.4 [52] | 51.4 ± 16.4 [52] |
| Female               | 274 (50.6) | 596 (50.6) | 109 (44.1) | 207 (44.1) | 165 (55.9) | 397 (55.9) |
| IBD type             |             |             |             |             |             |             |
| UC                   | 267 (49.3) | 598 (50.7) |             |             |             |             |
| Disease duration (time from first diagnosis for IBD to index date, mo), mean ± SD [median] | 51.7 ± 53.0 [32] | 51.7 ± 53.0 [33] | 50.6 ± 54.9 [30] | 50.6 ± 54.9 [26] | 52.7 ± 51.4 [37] | 52.7 ± 51.4 [37] |
| Index year           |             |             |             |             |             |             |
| 2014                 | 19 (3.5)   | 41 (3.5)   | 4 (1.6)    | 8 (1.6)    | 15 (5.1)   | 36 (5.1)   |
| 2015                 | 121 (22.3) | 263 (22.3) | 44 (17.8)  | 84 (17.8)  | 77 (26.1)  | 185 (26.1) |
| 2016                 | 161 (29.7) | 350 (29.7) | 67 (27.1)  | 127 (27.1) | 94 (31.9)  | 226 (31.9) |
| 2017                 | 149 (27.5) | 324 (27.5) | 83 (33.6)  | 158 (33.6) | 66 (22.4)  | 159 (22.4) |
| 2018                 | 92 (17.0)  | 200 (17.0) | 49 (19.8)  | 93 (19.8)  | 43 (14.6)  | 103 (14.6) |
| CCIb                 | 0.7 ± 1.2 [0] | 0.7 ± 1.2 [0] | 0.7 ± 1.2 [0] | 0.7 ± 1.2 [0] | 0.7 ± 1.2 [0] | 0.7 ± 1.2 [0] |
| Laboratory results, N (%)c |             |             |             |             |             |             |
| Serum albumin (g/dL) |             |             |             |             |             |             |
| NA, N (%)            | 169 (31.2) | 368 (31.2) | 90 (36.4)  | 171 (36.4) | 79 (26.8)  | 190 (26.8) |
| Normal value, N (%)d | 260 (48.0) | 566 (48.0) | 115 (46.6) | 218 (46.6) | 145 (49.2) | 349 (49.2) |
| C-reactive protein (mg/L) |             |             |             |             |             |             |
| NA, N (%)            | 389 (71.8) | 846 (71.8) | 191 (77.3) | 363 (77.3) | 198 (67.1) | 477 (67.1) |
| Normal value, N (%)e | 76 (14.0)  | 165 (14.0) | 28 (11.3)  | 53 (11.3)  | 48 (16.3)  | 116 (16.3) |
| Fistulising, N (%)b  | 48 (8.9)   | 104 (8.9)  |             |             | 41 (13.9)  | 99 (13.9)  |
| Nonbiologic therapies for IBD, N (%)f | 299 (55.2) | 650 (55.2) | 140 (56.7) | 266 (56.7) | 159 (53.9) | 383 (53.9) |
| IBD-related surgery, N (%)b | 67 (12.4) | 146 (12.4) | 27 (10.9)  | 51 (10.9)  | 40 (13.6)  | 96 (13.6)  |
| Hospitalization, N (%)g | 224 (41.3) | 487 (41.3) | 92 (37.2)  | 175 (37.2) | 132 (44.7) | 318 (44.7) |
| Disease location of UCb |             |             |             |             |             |             |
| Ulcerative ileocolitis |             |             | 107 (43.3) | 203 (43.3) |             |             |
| Ulcerative proctitis |             |             | 7 (2.8)    | 13 (2.8)   |             |             |
| Ulcerative proctosigmoiditis |             |             | 32 (13.0) | 61 (13.0)  |             |             |
| Pseudopolyposis of colon |             |             | 31 (12.6) | 59 (12.6)  |             |             |
| Left-sided ulcerative colitis |             |             | 36 (14.6) | 68 (14.6)  |             |             |
| Universal ulcerative colitis |             |             | 36 (14.6) | 68 (14.6)  |             |             |
| Other ulcerative colitis |             |             | 7 (2.8)   | 13 (2.8)   |             |             |
| Disease location of CDb |             |             |             |             |             |             |
| Regional enteritis |             |             |             |             | 285 (96.6) | 686 (96.6) |
| Regional enteritis of small intestine |             |             |             |             | 120 (40.7) | 289 (40.7) |
| Regional enteritis of large intestine |             |             |             |             | 104 (35.3) | 250 (35.3) |
| Regional enteritis of small intestine with large intestine involvement |             |             |             |             | 111 (37.6) | 267 (37.6) |

aAfter e-balance, all covariates were adequately balanced according to a threshold of standardized difference < 0.2.
bDuring the 365 days before the index date.
cMost recent measure during the 365 days before the index date.
dReference range of serum albumin is 3.5–5.1 g/dL.
eReference range of C-reactive protein is <0.8 mg/L.
fDuring the 90 days before the index date.
gAny time before the index date.
CCI, Charlson comorbidity index; NA, not available.
Sensitivity Analysis

Regardless of the statistical approach, vedolizumab was associated with higher rates of persistence and lower rates of the HRU composite end point versus infliximab in patients with IBD. E-balance and IPTW preserved sample sizes, whereas PS matching reduced sample sizes (vedolizumab, N = 499; infliximab, N = 804). All 3 matching/weighting methods yielded adequate balancing, although e-balance performed better, with patient characteristics being perfectly balanced after reweighting (ie, all standardized differences = 0.000; Supplementary Fig. 1).

Among all patients with IBD, rates of treatment persistence were significantly higher in the vedolizumab cohort relative to the infliximab cohort using e-balance (WKM rates at 24 months: vedolizumab = 77.6%, infliximab = 64.6%; P = 0.0005), IPTW (WKM rates at 24 months: vedolizumab = 76.8%, infliximab = 68.5%; P = 0.0253), and PS matching (WKM rates at 24 months: vedolizumab = 77.3%, infliximab = 67.2%; P = 0.0016). Results from the Cox proportional hazards model showed that patients who received vedolizumab were less likely to have a treatment discontinuation or to initiate another biologic versus those who received infliximab (HR [95% CI] = 0.70 [0.55–0.88]; P = 0.0030).

In addition, among patients with IBD, rates of the HRU composite end point were significantly lower for vedolizumab relative to infliximab patients when using e-balance (WKM rates at 24 months: vedolizumab = 46.9%,
infliximab = 59.9%, \(P < 0.0001\), IPTW (WKM rates at 24 months: vedolizumab = 48.9%, infliximab = 57.1%; \(P < 0.0001\)), PS matching (WKM rates at 24 months: vedolizumab = 46.6%, infliximab = 57.4%; \(P < 0.0001\)), and Cox proportional hazards model (HR [95% CI] = 0.72 [0.61–0.84]; \(P < 0.0001\)).

Similar observations were made when analyzing patients with UC and CD separately (data not shown).

**DISCUSSION**

In this retrospective observational study that included biologic-naive patients with IBD, treatment persistence—an important measure of the effectiveness of a therapy in patients with chronic diseases—was higher in the vedolizumab cohort compared with the infliximab cohort. Dosing frequency intensification was required less often among patients in the vedolizumab cohort relative to those in the infliximab cohort. With regard to the HRU composite end point, rates were found to be lower in the vedolizumab cohort relative to the infliximab cohort. These conclusions held true for all time points analyzed. The trend was maintained and even more pronounced at long-term time points such as 24 months, highlighting the potential benefits of vedolizumab over longer follow-up periods. Similar results were found when separately analyzing patients with UC and CD.

Approximately 30%–40% of anti-TNFα-naive patients have a primary nonresponse to anti-TNFα therapy; among those who initially respond to anti-TNFα therapy, approximately one third subsequently lose their response to therapy or become intolerant to therapy (ie, secondary nonresponders). There is growing evidence, both from clinical trials and real-world studies, showing that vedolizumab may have higher efficacy when used in anti-TNFα-naive patients versus in primary or secondary anti-TNFα nonresponders. The VICTORY consortium—which studied the largest cohort of patients with IBD treated with vedolizumab in a real-world clinical setting—reported a reduction in vedolizumab effectiveness when used after a TNFα antagonist. A German real-world study found that vedolizumab was significantly more effective at inducing clinical remission in anti-TNFα-naive patients than in patients with UC who previously received anti-TNFα therapy. Taken together with the findings of the present study, this growing body of evidence supports the view that the choice of the first-line biologic is crucial from a clinical perspective.

The present study reported on dosing frequency intensification instead of increased dosage. Nearly one-fifth of patients with IBD had dosing frequency intensification over 24 months, suggesting physicians do value this treatment strategy in certain circumstances. The US prescribing information of vedolizumab does not recommend increasing the frequency of dosing in patients who do not respond adequately to the standard once-every-8-weeks regimen, and that of infliximab recommends a dose escalation from 5 to 10 mg/kg in nonresponders with CD. However, there is evidence that a once-every-4-weeks regimen of vedolizumab may increase response rates in patients who have failed the once-every-8-weeks regimen. In the present study, patients with IBD who received vedolizumab had lower rates of dosing frequency intensification compared with those who received infliximab, suggesting treatment intensification is more commonly required among infliximab-treated patients. Although the proportion of patients who had their dosage strength increased (as opposed to dosing frequency) could not be assessed in the current study, prior evidence suggests that the rates of dose escalation are also lower among vedolizumab-treated patients as compared to infliximab-treated patients. Thus, the present study’s estimate of dosing frequency escalation is likely to represent an underestimation of the true rate.
of dose escalation in infliximab-treated patients. This higher rate of dosing frequency intensification not only suggests a lower clinical effectiveness for infliximab in biologic-naive patients compared to vedolizumab, but may also have significant economic implications as dosing frequency intensification entails additional HRU related to drug administration.

The rates of the HRU composite end point, which included intravenous corticosteroids, IBD-related hospitalization,
and IBD-related surgery, were significantly higher among infliximab-initiated patients compared with vedolizumab-initiated patients. These HRU end points were selected because they are likely to reflect exacerbations of disease severity, which may indicate a loss of or poorer response to IBD treatment.\(^5,10\) Therefore, the significant difference observed in the rates of the HRU composite end point suggests that the effectiveness of vedolizumab may be better than that of infliximab.

Two recent real-world studies have assessed the effectiveness of vedolizumab and other anti-TNFα agents. Adar et al reviewed the medical record of older patients (≥60 years) with IBD treated with vedolizumab versus other anti-TNFα and concluded that both agents were similarly effective in terms of clinical remission.\(^23\) However, this study included patients who received these agents in any line of therapy, and the authors did not adjust for the large difference in the proportion of anti-TNFα-naïve patients between both cohorts (vedolizumab = 40%, anti-TNFα = 86%).\(^25\) Therefore, this study likely underestimated the real benefits of vedolizumab due to this important confounder. Furthermore, the low sample size of this study (N vedolizumab = 131, N anti-TNFα = 103) compared with the present study (N vedolizumab = 542, N anti-TNFα = 1179) may have precluded the detection of statistically significant differences.\(^22\) Another recent study by Davis et al reported numerical trends suggesting that a higher proportion of vedolizumab-treated patients may respond to treatment and have clinical remission than anti-TNFα-treated patients, but the difference was not statistically significant likely due to the small sample size of the study (N vedolizumab = 42, N anti-TNFα = 97).\(^25\) Thus, the apparent discrepancy of the conclusions of the current study versus other real-world studies may largely be explained by differences in study design and sample size. However, data from the first head-to-head trial directly comparing vedolizumab with an anti-TNFα (adalimumab) in patients with moderately to severely active UC do corroborate the findings of the present study.\(^50\) In this trial, vedolizumab was found superior to adalimumab in achieving clinical remission and endoscopic mucosal healing at week 52, whereas corticosteroid-free remission was not significantly different between trial arms.\(^50\) Both agents were generally safe and well tolerated.\(^50\) In further support of the conclusions of the present study, a network meta-analysis of 5 studies provided evidence for the benefits of vedolizumab maintenance therapy over other biologics among anti-TNFα-naïve patients with UC.\(^30\) More comparative studies focusing on vedolizumab versus infliximab are warranted to confirm the findings from the present study.

**Limitations**

This study is subject to some limitations. First, EMR databases may contain omissions and inaccuracies in diagnosis and procedure codes. However, this limitation should equally impact both study cohorts, which makes it unlikely to significantly affect the conclusions of the present study. Second, for infliximab, treatment intensification may include dose escalation via increased dosage strength in addition to dose escalation via dosing frequency intensification as indicated per label,\(^8\) which may have underestimated the proportion of patients in this cohort who had treatment intensification. However, information on dosage strength could not be reliably captured in the available data.\(^31,32\) Fourth, the present study was observational in nature and, despite the use of several approaches to control for observed potential confounders, the contribution of unobserved confounders cannot be excluded. Finally, although the outcomes assessed in the present study may be considered proxies for drug effectiveness, objective markers of disease severity, such as mucosal healing, were not available in the database. Interventional studies with such markers are warranted to validate the findings presented here and complement our understanding of the comparative effectiveness of vedolizumab and infliximab with data from a more controlled environment. Additionally, this study did not evaluate safety.

**CONCLUSION**

In this real-world study, vedolizumab was associated with significantly higher rates of treatment persistence, lower rates of dosing frequency intensification, and lower rates of the HRU composite end point compared with infliximab in biologic-naïve patients with IBD. Similar trends were observed for UC and CD separately. Notably, these differences appeared particularly pronounced over longer follow-up (eg, 24 months), suggesting the potential benefits of vedolizumab over infliximab are observed with continuous and prolonged exposure to the drug. Despite the use of statistical approaches to control for potential confounders in the present study, RCTs are warranted to provide a more comprehensive understanding of the putative differences in effectiveness between vedolizumab and infliximab.

**SUPPLEMENTARY DATA**

Supplementary data are available at Crohn’s & Colitis 360 online.

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