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Biologic Therapy Sequencing in Ulcerative Colitis: A Real-World Observational Study of Second-Line Therapy After Vedolizumab

Precious A. Anyanwu,[1] Christopher Fernandes,[2] Lucinda J. Van Anglen,[1] Chiahung Chou,[3] Marie Sanchirico,[3] Harry Sarles,[4] Casey Chapman,[4] Jeanne Jiang,[3] Tao Fan,[3] Lisa Young,[3] Timothy E. Ritter[4]

[1]Healix Infusion Therapy, LLC, Sugar Land, TX, USA; [2]Anne Marion Burnett School of Medicine at Texas Christian University, Fort Worth, TX, USA; [3]Takeda Pharmaceuticals U.S.A., Inc., Lexington, MA, USA; [4]GI Alliance, Southlake, TX, USA

Background

- Biologics have revolutionized the management of ulcerative colitis (UC). Nonetheless, some patients do not experience an adequate response to first-line biologic treatment and switch to a second-line biologic
- Anti-tumor necrosis factor α (anti-TNFα) treatments were the first biologics approved for the treatment of people with UC and are commonly used as first-line biologic treatments.[1] If an adequate response to anti-TNFα treatments does not occur, patients are often switched to a second-line biologic with a different mechanism of action
- In clinical studies, the gut-selective α4β7 integrin antagonist vedolizumab has also shown favorable efficacy and safety outcomes when used as a first-line biologic treatment in people with UC[2,3]
- Findings from real-world studies, including the EVOLVE study, suggest that use of vedolizumab as a first-line biologic does not compromise the therapeutic effectiveness of subsequent anti-TNFα treatment[4–6]
- However, for patients who do not have an adequate response with vedolizumab as a first-line biologic and switch to a second-line anti-TNFα treatment, it remains unclear whether first-line use of vedolizumab impacts the effectiveness of second-line anti-TNFα treatment

Aim

- The aim of this real-world observational study was to assess rates of response to second-line anti-TNFα treatment in patients with UC who had previously received vedolizumab as a first-line biologic

Methods

- This retrospective study included biologic-naïve adult patients with moderate to severe UC who were treated at a large, multicenter, private gastroenterology practice
- Patients who received vedolizumab as a first-line biologic between January 2018 and May 2020 were identified through electronic medical records
- Eligible patients, who discontinued vedolizumab treatment and switched to a second-line anti-TNFα treatment, were observed for up to 12 months after switching or until discontinuation of anti-TNFα treatment
- The primary endpoint was the proportion of patients who received anti-TNFα treatment who had a clinical response (defined as a ≥ 2-point reduction in partial Mayo score from baseline)
- The secondary endpoint was the proportion of patients who received anti-TNFα treatment who had clinical remission (defined as a partial Mayo score of < 2)
- Clinical response and clinical remission were assessed at 3, 6, 9, and 12 months after second-line anti-TNFα treatment initiation

Table 1. Patient demographics and baseline characteristics

Baseline characteristics	N = 53
Age,[a] years, n (%)	
18–34	16 (30.2)
35–64	33 (62.3)
≥ 65	4 (7.5)
Sex, n (%)	
Male	25 (47.2)
Female	28 (52.8)
Smoking status, n (%)	
Never	34 (64.2)
Former	16 (30.2)
Current	3 (5.7)
BMI, median (IQR)	25.2 (22.2–32.2)
Charlson comorbidity score, median (IQR)	0 (0–2)
Disease characteristic, median (IQR)	
Disease duration, years	5 (2–10)
Time from diagnosis to first-line vedolizumab, years	3.8 (0.1–34.2)
Duration of first-line vedolizumab treatment, months	7.6 (5.0–14.2)
Time from diagnosis to second-line anti-TNFα treatment, years	5.3 (1.8–10.0)
Time from vedolizumab discontinuation to anti-TNFα, months	1.5 (1.0–2.1)
Duration of second-line anti-TNFα treatment, months	8.8 (3.5–12.0)
Reason for vedolizumab discontinuation, n (%)	
Loss of response	44 (83.0)
Payer/financial issues	6 (11.3)
Development of antibodies	2 (3.8)
Adverse events	1 (1.9)

anti-TNFα, anti-tumor necrosis factor α; BMI, body mass index; IQR, interquartile range.
[a]Age at the start of second-line anti-TNFα treatment.

Summary and Conclusions

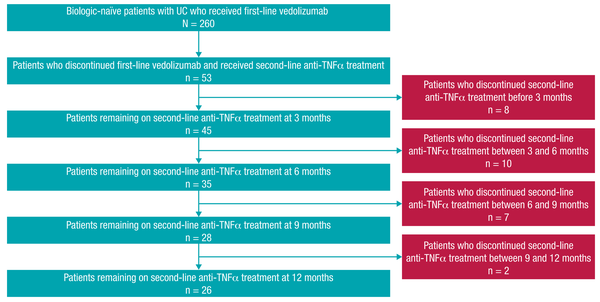
- **Rates of clinical response and clinical remission for second-line anti-TNFα treatments following vedolizumab as a first-line biologic treatment suggest that vedolizumab can be used as a first-line biologic treatment in patients with UC without concerns about the effectiveness of using second-line anti-TNFα treatments**
- **Among those who remained on anti-TNFα treatment, approximately 60% of patients had a clinical response at 3 months and about half had a clinical response at 12 months**
- **Approximately 20–25% of all patients who received second-line anti-TNFα treatment had clinical remission over the 12-month follow-up period. Approximately 40% of those who remained on anti-TNFα treatment at 12 months had clinical remission**
- **There was no difference in clinical response and remission rates between adalimumab and infliximab, suggesting both can be used as second-line treatments following vedolizumab**

- Primary and secondary outcomes are reported for two groups
  - All patients who initiated second-line anti-TNFα treatment. This group included patients who discontinued or were lost to follow-up at each of the 3, 6, 9, and 12-month assessments
  - Only patients who remained on second-line anti-TNFα treatment at each time point. This group excludes patients who discontinued treatment or were lost to follow-up at each of the 3, 6, 9, and 12-month assessments
- Descriptive data are reported as frequencies and proportions for categorical variables, and median (interquartile range [IQR]) for continuous variables
- The Kaplan–Meier method was used to describe time to remission stratified by anti-TNFα treatment and analyzed by the log-rank χ^2 test

Results

- Patient demographics and baseline characteristics are shown in **Table 1**
  - In total, 260 adult patients with moderate to severe UC received vedolizumab as a first-line biologic (**Figure 1**)
  - Vedolizumab was discontinued after a median (IQR) duration of 7.6 months (5–14) in 53 patients (20.4%) who subsequently received second-line anti-TNFα treatment with infliximab (n = 39, 73.6%) or adalimumab (n = 14, 26.4%)
  - Median (IQR) anti-TNFα treatment duration was 8.8 months (3.5–12.0); 49.1% (n = 26/53) completed 12 months of anti-TNFα treatment
- Details of second-line anti-TNFα treatment and concurrent medications are shown in **Table 2**
  - Most patients (64.2%) were receiving a corticosteroid at initiation of anti-TNFα treatment and approximately half were concurrently receiving 5-aminosalicylates (5-ASA)
- During the study period, 4 patients switched to a second anti-TNFα treatment; 3 switched from infliximab to adalimumab and 1 switched from adalimumab to infliximab-dyyb
  - Patients received the first anti-TNFα treatment for a median (IQR) of 5 months (4–6) before switching
  - The reasons for switching to a second anti-TNFα treatment were development of antibodies (infliximab, n = 1; adalimumab, n = 1), payer/financial issues (infliximab, n = 1), and adverse events (infliximab, n = 1)
  - Both patients who switched owing to the development of antibodies achieved clinical remission with the alternative anti-TNFα treatment by the 12-month assessment

Figure 1. Patient population



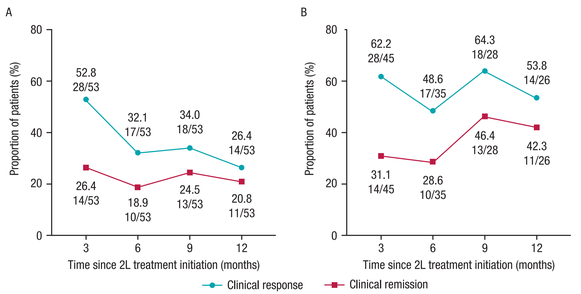
anti-TNFα, anti-tumor necrosis factor α; UC, ulcerative colitis.

Table 2. Second-line anti-TNFα treatment details and concurrent medications

Second-line anti-TNFα treatment	Infliximab n = 39 (73.6%)	Adalimumab n = 14 (26.4%)
Maintenance dose, mg/kg, median (IQR)	5.2 (5.0–5.7)	40 mg
Maintenance dose frequency	Q8W	Q2W
Dose escalation, n (%)	14 (35.9)	4 (28.6)
Increased dose	11 (78.6)	0 (0)
Increased frequency	3 (21.4)	4 (100)
Concurrent medication, n (%)		
Corticosteroids	22 (56.4)	12 (85.7)
5-ASA	19 (48.7)	8 (57.1)
Immunomodulator	3[b] (7.7)	1[b] (7.1)
Corticosteroids + 5-ASA	12 (30.8)	8 (57.1)
Corticosteroids + thiopurine	2 (5.1)	1 (7.1)
5-ASA + thiopurine	2 (5.1)	1 (7.1)
Corticosteroids + 5-ASA + thiopurine	1 (2.6)	1 (7.1)

5-ASA, 5-aminosalicylates; anti-TNFα, anti-tumor necrosis factor α; IQR, interquartile range; Q2W, every 2 weeks; Q8W, every 8 weeks.
[a]One patient was on 6-mercaptopurine and the other two patients were on azathioprine.
[b]The patient was on azathioprine.

Figure 2. The proportion of patients with clinical response or clinical remission after switching to 2L anti-TNFα treatment in A) the total population and in B) the patients who remained on treatment at each time point



2L, second-line; anti-TNFα, anti-tumor necrosis factor α.

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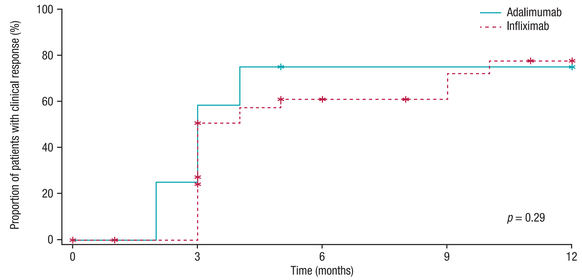
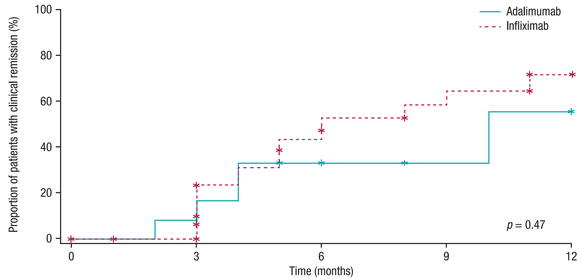
- **Figure 2** shows the proportions of patients who had clinical remission and clinical response at 3, 6, 9, and 12 months for all patients who received second-line anti-TNFα treatment and those who remained on the treatment
- At 3 months, 62.2% of patients who remained on anti-TNFα treatment had a clinical response. Following a slight decline at 6 months, response rates were stable at 9 and 12 months (**Figure 2**)
- There were no significant differences ($p = 0.29$) in clinical response rates between patients who received infliximab and those who received adalimumab (**Figure 3**)
- Throughout the follow-up period, approximately 20–25% of all patients had clinical remission after receiving second-line anti-TNFα treatment. At 12 months, 42.3% of those still receiving an anti-TNFα treatment had clinical remission (**Figure 2**)
- There were no significant differences ($p = 0.47$) in clinical remission rates between patients who received infliximab and those who received adalimumab (**Figure 4**)

Figure 3. Cumulative time to first clinical response[a] following initiation of second-line anti-TNFα treatment in patients with UC who had previously received vedolizumab as a first-line biologic[b]



anti-TNFα, anti-tumor necrosis factor α; UC, ulcerative colitis.
[a]Defined as a ≥ 2-point reduction in partial Mayo score from baseline.
[b]At the end of 12 months, the Kaplan–Meier curve shows the proportion of patients who had a clinical response at least once during the follow-up period.

Figure 4. Cumulative time to first clinical remission[a] following initiation of second-line anti-TNFα treatment in patients with UC who had previously received vedolizumab as a first-line biologic[b]



anti-TNFα, anti-tumor necrosis factor α; UC, ulcerative colitis.
[a]Defined as a partial Mayo score of < 2.
[b]At the end of 12 months, the Kaplan–Meier curve shows the proportion of patients who had a clinical remission at least once during the follow-up period.

Disclosures

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