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Real-World Clinical Effectiveness and Safety of Vedolizumab and Adalimumab in Biologic-Naïve Patients With Crohn's Disease: Results From the EVOLVE Study

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Background

- Approved advanced therapies for Crohn's disease (CD) include vedolizumab and adalimumab, among others[1]
  - Vedolizumab is a gut-selective humanized monoclonal anti-$\alpha_4\beta_7$ integrin antibody that reduces lymphocyte trafficking into intestinal tissue[2]
  - Adalimumab is an anti-tumor necrosis factor agent
- Data comparing the effectiveness and safety of vedolizumab versus adalimumab as first-line therapy may help to better position biologics in the therapeutic algorithm

Aim

- To evaluate the real-world clinical effectiveness and safety of vedolizumab versus adalimumab in biologic-naïve patients diagnosed with CD

Methods

- The EVOLVE retrospective cohort study examined medical records of patients diagnosed with CD receiving first-line biologic treatment with vedolizumab or adalimumab (date of initiation defined as the index date) between May 2014 and March 2018
- The study population included biologic-naïve adults diagnosed with CD who had ≥6 months of follow-up data after treatment initiation
- Pre-index baseline data collected included patient demographics, clinical and treatment history, and disease severity
- The following clinical outcomes were defined based on the following hierarchical algorithm during the postindex period[3]:
  - ***Clinical response***, defined as a positive change in CD activity index (CDAI) category from baseline (CDAI categories: score of <150, score of 151-219, score of 220-450, score of >450); or if CDAI score unknown, decrease of ≥3 points from baseline in Harvey-Bradshaw index (HBI) score; or if HBI unknown, decrease of ≥3 points from baseline in modified HBI (mHBI) score; or if mHBI unknown, treatment response recorded in medical chart as "complete response" or "partial response"
  - ***Clinical remission,*** defined as a CDAI score of <150 points; or if CDAI unknown, HBI score of ≤4 points; or if HBI unknown, mHBI score of ≤4 points; or if unknown, remission status recorded in medical chart as "in remission"
  - ***Mucosal healing,*** defined as an endoscopic assessment score of 0 or 1 (normal or inactive); or if unknown, a Simple Endoscopic Score for CD of <3, or lack of ulcerations, or other medical chart entries indicating an absence of active disease, inflammatory activity, or pathologic findings following endoscopy
  - ***Treatment persistence,*** defined as patients who did not discontinue their index treatment for any reason during the study follow-up period
- Additional outcomes evaluated were CD-related exacerbations and surgeries, serious adverse events (SAEs), and serious infections (SIs)
- Adjusted analyses were performed using inverse probability weighting (IPW). The baseline covariates included in the IPW model were age, sex, disease location, disease duration, CD-related hospitalizations, disease severity, steroid dependency status, fistula status, and a composite biochemical marker (fecal calprotectin, C-reactive protein, and albumin)

Results

- The demographic and baseline characteristics of patients treated with vedolizumab (n=218) and adalimumab (n=144) are presented in **Table 1**
- After IPW adjustment, patient demographic and baseline characteristics were similar between the treatment groups (standardized difference <0.10; data not shown)

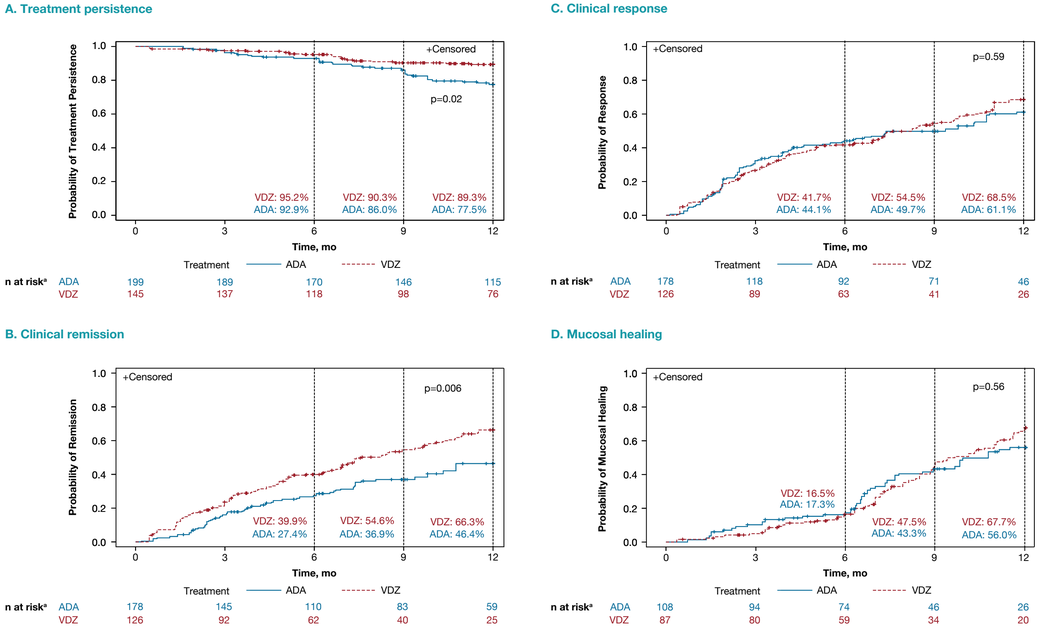
Table 1. Unadjusted baseline characteristics of biologic-naïve patients diagnosed with CD and treated with vedolizumab or adalimumab

Baseline Characteristics	Vedolizumab (n=218)	Adalimumab (n=144)	p Value
Mean (SD) age, y	51.7 (16.8)	40.0 (14.9)	<0.001
Male, n (%)	114 (52.3)	75 (52.1)	0.969
Disease duration, n with available data	176	111	0.016
<2 years, n (%)	50 (28.4)	50 (45.0)	
2 to <5 years, n (%)	32 (18.2)	16 (14.4)	
≥5 years, n (%)	94 (53.4)	45 (40.5)	
Missing, n (%)	42 (19.3)	33 (22.9)	
Median (min-max) observation period, months[a]	15.7 (4.2-45.9)	19.3 (6.1-49.3)	<0.001
CD location at index, n with available data	196	121	0.047
Colonic with/without upper GI disease, n (%)	42 (21.4)	35 (28.9)	
Illeal with/without upper GI disease, n (%)	85 (43.4)	36 (29.8)	
Illeocolonic with/without upper GI disease, n (%)	69 (35.2)	50 (41.3)	
Unknown, n (%)	22 (10.1)	23 (16.0)	
Disease severity at index, n with available data	180	116	0.161
Moderate, n (%)	84 (46.7)	58 (50.0)	
Severe, n (%)	17 (9.4)	17 (14.7)	
Pre-index CD-related hospitalizations, n (%)			
Yes	22 (10.1)	14 (9.7)	0.909
No	196 (89.9)	130 (90.3)	
Composite biochemical marker,[b] n (%)			0.382
Within normal range	41 (18.8)	21 (14.6)	
Outside of normal range	50 (22.9)	50 (34.7)	
Unknown	32 (14.7)	16 (11.1)	
Steroid dependency status, n (%)			0.004
Dependent	32 (14.7)	22 (15.3)	
Intolerant	6 (2.8)	0	
Not dependent or intolerant	86 (39.4)	37 (25.7)	
Not dependent, intolerant, or refractory	47 (21.6)	54 (37.5)	
Refractory	5 (2.3)	2 (1.4)	
Unknown	42 (19.3)	29 (20.1)	
Active fistulae prior to index event, n (%)			0.052
Yes	8 (3.7)	14 (9.7)	
No	181 (83.0)	109 (75.7)	
Unknown	29 (13.3)	21 (14.6)	
Disease behavior, n (%)			0.371
Nonstricturing, nonpenetrating, with or without perianal disease	92 (42.2)	53 (36.8)	
Penetrating, with or without perianal disease	17 (7.8)	9 (6.3)	
Stricturing, with or without perianal disease	45 (20.6)	27 (18.8)	
Unknown	64 (29.4)	55 (38.2)	

CD, Crohn's disease; GI, gastrointestinal; max, maximum; min, minimum.
[a]Although all patients were required to have 6 months of follow-up from time of treatment initiation to data abstraction, some patients were lost to follow-up; therefore, the minimum duration during the observation periods was <6 months.
[b]The composite biochemical marker used a hierarchical algorithm for the 3 baseline biochemical disease indicators, based on data availability, with fecal calprotectin at the top of the hierarchy (fecal calprotectin [≥250 mg/kg] → C-reactive protein [≥5 mg/L] → albumin [<35 g/L]).

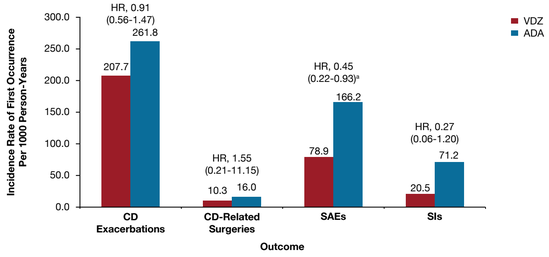
- Cumulative treatment persistence, clinical remission, clinical response, and mucosal healing in biologic-naïve patients diagnosed with CD and treated with vedolizumab or adalimumab are shown in **Figure 1**
- Vedolizumab-treated patients were significantly less likely to experience SAEs over 12 months versus adalimumab-treated patients (**Figure 2**)
- There were no statistical differences in CD-related exacerbations, CD-related surgeries, or SIs between the treatment cohorts (**Figure 2**)

Figure 1. Cumulative A) treatment persistence, B) clinical remission, C) clinical response, and D) mucosal healing in biologic-naïve patients diagnosed with CD and treated with vedolizumab or adalimumab



p values are log-rank from time-to-event analyses. Inverse probability weighting included the following covariates in the model: age, sex, disease location, disease duration (≤2 years, 2-5 years, 5-10 years, >10 years, and unknown), disease-related hospitalizations, disease severity, steroid dependency status, fistula status, and a composite biochemical marker (fecal calprotectin, C-reactive protein, and albumin).
ADA, adalimumab; CD, Crohn's disease; VDZ, vedolizumab.
[a]The sum of the patient weights for each group of patients still receiving treatment and who have clinical outcomes that can still be assessed.

Figure 2. CD-related exacerbations, surgeries, SAEs, and SIs in biologic-naïve patients with CD treated with VDZ or ADA over 12 months



Data are unadjusted incidence rates and adjusted HRs (95% CI). p values are from time-to-event analyses.
ADA, adalimumab; CD, Crohn's disease; HR, hazard ratio; SAE, serious adverse event; SI, serious infection; VDZ, vedolizumab.
[a]Denotes statistically significant differences between cohorts.

Conclusions

- In a real-world setting, biologic-naïve patients with CD treated with vedolizumab had equivalent rates of response and mucosal healing but demonstrated a greater likelihood of continuing with treatment and achieving clinical remission versus patients treated with adalimumab
- Patients were less likely to experience SAEs with vedolizumab than with adalimumab

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