Second-Line Biologic Therapy After Vedolizumab

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Abstract

Introduction: Vedolizumab (VDZ), an anti-integrin monoclonal antibody approved for the treatment of Crohn's disease (CD) and ulcerative colitis (UC), is increasingly being utilized as first-line biologic therapy in bio-naïve inflammatory bowel disease (IBD) patients (pts) with moderate-to-severe disease. While prior studies have described the efficacy of VDZ after anti-TNF failure, there is little guidance on the use of alternative biologics following initial VDZ therapy. This study describes the clinical response of IBD pts treated with a second (2nd) biologic following VDZ discontinuation.

Methods: We performed a retrospective review of all bio-naïve IBD pts started on VDZ as first-line therapy at a large multicenter gastroenterology private practice since drug approval in 2014. Pts were identified who failed initial VDZ treatment and were switched to a 2nd biologic agent. Data collection included demographics, diagnosis, therapy, and disease activity scores using the partial Mayo score (pMayo) for UC pts and the Harvey-Bradshaw Index (HBI) for CD pts. Clinical remission was assessed for those pts with ≥6 months of data and defined as pMayo less than 2 or HBI less than 5.

Results: A total of 135 IBD pts receiving VDZ as first-line biologic therapy were identified, of which VDZ was discontinued in 30 (22%). Our study cohort included 25 pts who received a 2nd line biologic following VDZ failure (11 primary non-response, 14 secondary non-response). Second-line biologic agents included 19 infliximab, 3 adalimumab, 2 ustekinumab, and 1 tofacitinib. Baseline demographics of the 25 pts were as follows: mean age 47±18 years, male gender 13 (52%), UC 19 (76%), CD 6 (24%), time to 2nd biologic 8.2±4.5 weeks. Disease severity scores prior to and following initiation of the 2nd line biologic are depicted. Clinical remission assessment was available for 18 of 25 patients. Remission was achieved in 11 of 18 pts (61%), driven by UC pts treated with infliximab. Overall, pts treated with anti-TNF agents following VDZ had higher rates of remission compared to those treated with other biologics.

Discussion: Biologic-naïve IBD pts treated initially with VDZ have high treatment persistence. In addition, rates of remission with 2nd-line biologic therapy are greater than expected when first-line failure is VDZ. Further studies are warranted to determine the optimal order in which advanced therapies should be initiated.

Background

Use of vedolizumab (VDZ) as initial biologic therapy for the management of patients with moderate-to-severe inflammatory bowel disease (IBD) is increasing, largely due to its favorable safety profile.[1-4] While the efficacy of VDZ in treating patients who fail initial anti-TNF biologic therapy has been reported, there are little data to address the efficacy of alternative biologics in IBD patients who fail initial VDZ therapy.[4-5] We have previously described our real-world experience of IBD patients treated with a second-line biologic following VDZ discontinuation, in which prior VDZ therapy did not appear to diminish the response to second-line therapy. This study aimed to expand upon our initial population, and continue to validate previous results.

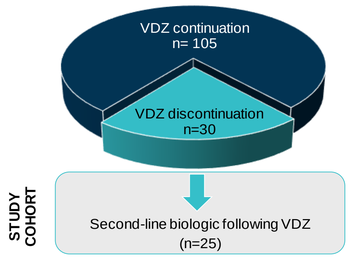
Methods

We conducted a retrospective review of all bio-naïve IBD patients started on VDZ as first-line therapy at a large multicenter gastroenterology private practice. Patients who failed initial VDZ therapy and were subsequently switched to a second-line biologic were identified.

- Data collection included demographics, disease characteristics, VDZ discontinuation, second-line biologic therapy, and disease activity
- Patients with ≥6 months data were included in efficacy analyses
- Disease activity was assessed using the partial Mayo (pMayo) for UC patients and the Harvey-Bradshaw Index (HBI) for CD patients at the following time points: VDZ discontinuation; second-line biologic initiation; 3 months; and 6 months
- Clinical remission was defined by pMayo score <2 or HBI score <5
- Descriptive data were reported as frequencies and proportions for categorical variables, and as mean ± standard deviation (SD) or median (interquartile range, IQR) for continuous variables

Results

Patient Selection



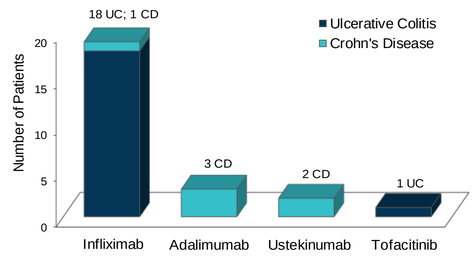
- 135 bio-naïve IBD patients were initiated on VDZ as first-line therapy, median VDZ treatment duration was 9.8 (IQR 4.1-21.7) months.
- Following VDZ discontinuation, 25 of 30 patients (19 UC, 6 CD) were initiated on a second-line biologic therapy.

Baseline Demographics

	UC n=19	CD n=6	All IBD n=25
Age (yrs), means ± SD	48.8±16.2	43.3±25.4	47.5±18.3
Male gender, n(%)	10 (53%)	3 (50%)	13 (52%)
Disease duration (yrs), median (IQR)	9.0 (2.6-13.3)	3.8 (1.4-8.0)	6.0 (1.8-13.1)
VDZ duration (mos), median (IQR)	6.7 (3.3-17.0)	6.0 (4.3-7.2)	6.7 (3.3-13.6)
Reason for VDZ discontinuation, n(%)			
Primary non-reponse*	7 (37%)	4 (67%)	11 (44%)
Secondary non-response†	12 (63%)	2 (33%)	14 (56%)

* Lack of response to induction therapy; † Loss of response during treatment

Second-Line Biologic Therapy Following VDZ

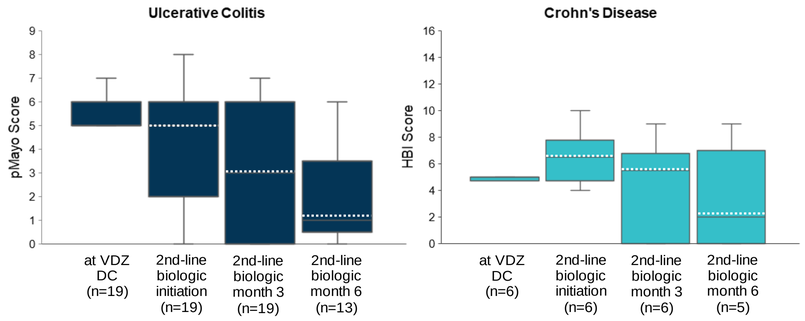


- Anti-TNF agents were the most common second-line biologic following VDZ.
- Mean time to second-line biologic following VDZ was 8.2±4.5 weeks.

Second-Line Biologic Therapy Dosing & Concomitant Medications

	UC n=19	CD n=6	All IBD n=25
Second-Line Biologic Dosing			
Infliximab (mg/kg), mean ± SD	5.3±0.25	4.9 (-)	5.2±0.26
Adalimumab (mg), mean ± SD	-	40 (-)	40 (-)
Ustekinumab (mg/kg), mean ± SD	-	90 (-)	90 (-)
Tofacitinib daily dose (mg), mean ± SD	20 (-)	-	20 (-)
Concomitant Medications, n(%)	16 (84%)	5 (83%)	21 (84%)
Steroids	13	5	18
5-Aminosalicylates	6	3	9
Immunomodulators	4	2	6

Disease Activity Scores with Second-Line Biologic Therapy



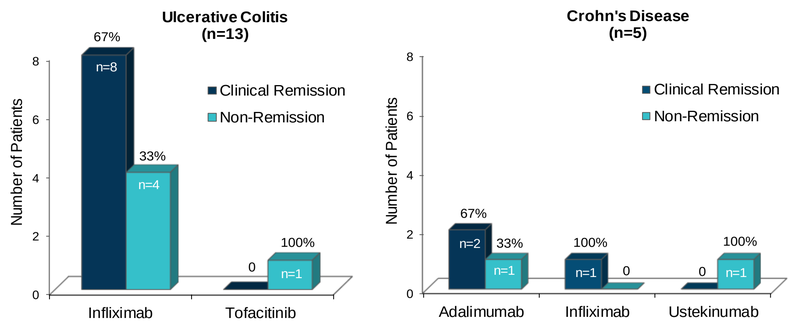
- Of 25 patients who were started on second-line biologic therapy following VDZ, 6-month efficacy data were available for 18 of 25 patients
  - 3 patients discontinued second-line infliximab <6 months, 2 for lack of response and 1 for intolerance
  - 4 patients had <6 month data available

Disease Activity Sub-Scores with Second-Line Biologic Therapy

Disease activity scores	2nd-line biologic initiation	2nd-line biologic month 3	2nd-line biologic month 6	% Score Reduction at month 6
Ulcerative colitis patients	n=19	n=19	n=13	
pMayo, median	5.0	3.0	1.0	80
Stool frequency	1.0	1.0	0.0	100
Rectal bleeding	1.0	0.0	0.0	100
Physician global assessment	2.0	1.0	1.0	50
Crohn's disease patients	n=6	n=6	n=5	
HBI, median	6.5	5.5	2.0	69
General well-being	1.0	1.0	0.0	100
Abdominal pain	1.0	0.5	0.0	100
Liquid stool frequency	3.5	2.5	1.0	71
Additional manifestations	0.0	0.0	0.0	n/a

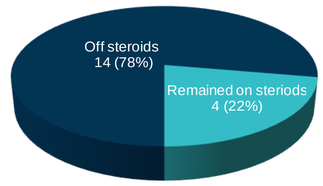
- Median disease activity score reduced by 80% (pMayo 5.0 to 1.0) and 69% (HBI 6.5 to 2.0) at month 6 for UC and CD patients, respectively.

Clinical Remission at 6 Months with Second-Line Biologic Therapy



- Overall clinical remission at month 6 of second-line biologic therapy was achieved in 11 of 18 (61%) patients.
- Month 6 remission rates were 62% and 60% in UC and CD patients, respectively.
- These data were driven primarily by UC patients treated with infliximab.

Steroids at 6 Month of Second-Line Biologic Therapy



- Of 25 patients, 18 were on concomitant steroids at time of second-line biologic therapy initiation.
- 14 (78%) were successfully weaned by month 6.

Discussion

- 135 biologic-naïve IBD patients were initiated on VDZ, with 115 remaining on therapy. Our study evaluates 25 patients (19 UC, 6 CD) initiated on a second-line biologic following VDZ discontinuation.
- Ulcerative Colitis
  - 18 of 19 UC patients were started on infliximab; the remaining patient was started on tofacitinib.
  - Disease activity scores at month 6 compared to time of second-line biologic therapy initiation reduced by 80%.
  - Clinical remission at month 6 of second-line biologic therapy was achieved in 62% of patients.
- Crohn's Disease
  - CD patients were started on infliximab (n=1), adalimumab (n=3), or ustekinumab (n=2).
  - Disease activity scores at month 6 compared to time of second-line biologic therapy initiation reduced by 69%.
  - Clinical remission at month 6 of second-line biologic therapy was achieved in 60% of patients.
- We observed clinical remission at 6 months exclusively in patients transitioned from VDZ to an anti-TNF agent as second-line biologic therapy.
- Most patients on steroids were successfully weaned by month 6.
- This study is limited by small sample size and retrospective design.

Conclusion

- Biologic-naïve IBD patients treated with vedolizumab as first-line therapy have high treatment persistence.
- Clinical remission rates achieved with second-line biologic therapy are considerably greater than we expected following vedolizumab treatment failure.
- Further studies are warranted to determine the optimal order in which advanced biologic therapies should be initiated.

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