Long-Term Efficacy of Vedolizumab in Pediatric Inflammatory Bowel Disease

Harry E. Sarles, MD[1]; Annette E. Whitney, MD[2]; Samantha A. Kuten, PharmD[3]; Lucinda J. Van Anglen, PharmD[3]

[1]DHAT Research Institute, Richardson, TX; [2]Digestive Health Associates of Texas, Dallas, TX; [3]Healix Infusion Therapy, Sugar Land, TX

Background

Pediatric patients with inflammatory bowel disease (IBD) who have failed anti-TNF therapy have limited treatment options. Vedolizumab (VDZ), a humanized anti-integrin antibody, has proven to be safe and effective for adults with refractory IBD.[1-2] While short-term data (≤30 weeks) of VDZ in pediatric IBD patients are promising, information on long-term outcomes remain limited.[3-5]

We have previously described our long-term, real-world experience with VDZ in pediatric IBD patients.[6] This study aimed to expand upon our initial population and continue to validate results.

Methods

A retrospective observational study of pediatric patients (≤18 years) who received VDZ for the treatment of ulcerative colitis (UC) or Crohn's disease (CD) at a large gastroenterology private practice.

- Data collection included demographics, disease activity, prior and concurrent therapy, VDZ discontinuation, adverse events, and IBD-related ED visits and/or hospitalizations.
- Disease activity was assessed using the short pediatric Crohn's disease activity index (shPCDAI) and pediatric ulcerative colitis activity index (PUCAI) at baseline, 14 weeks, 6, 12 and 24 months in those patients who were on continued therapy.
- Clinical remission was defined by shPCDAI score <15 or PUCAI score <10.
- 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. Change in disease activity scores from baseline were compared using Wilcoxon signed-rank test.

Study Cohort

Pediatric IBD patients treated with VDZ since drug approval in 2014
n=29

↓

1-year efficacy data
n=24
VDZ discontinued by 1 year (n=5)

↓

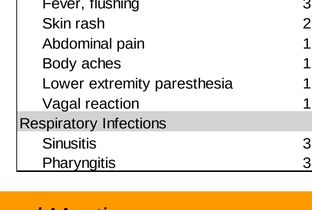
2-year efficacy data
n=14
VDZ discontinued by 2 years (n=5)
Less than 2-year data available (n=5)

Results

Table 1. Baseline Demographics

	CD n=16	UC n=13	All IBD n=29
Age (yrs), mean ± SD	14.1±3.2	13.6±3.3	13.9±3.2
Age, n (%)			
≤10	3 (19%)	1 (8%)	4 (14%)
11-15	6 (38%)	9 (69%)	15 (52%)
16-18	7 (44%)	3 (23%)	10 (34%)
Male gender, n (%)	10 (63%)	7 (54%)	17 (59%)
Disease duration (yrs), median (IQR)	4.4 (2.3-6.6)	2.3 (1.1-3.4)	3.0 (2.0-5.2)
VDZ duration (mos), median (IQR)	33.9 (16.3-39.1)	16.8 (11.7-29.7)	21.3 (13.8-39.1)

Figure 1. Prior Biologic Therapies



- All 29 patients were previously treated with a biologic, which were anti-TNF agents in all cases.
- Prior failed biologics included:
  - 17 (59%) failed infliximab only
  - 10 (34%) failed infliximab and adalimumab
  - 2 (7%) failed infliximab, adalimumab, and certolizumab

Table 2. Vedolizumab Dosing & Concomitant Therapy

	CD n=16	UC n=13	All IBD n=29
VDZ dose (mg/kg), mean ± SD	6.7±3.5	6.2±2.1	6.5±2.9
Dose escalation, n(%)	3 (19%)	8 (62%)	11 (38%)
Every 6 weeks	1	8	9
Every 4 weeks	2	--	2
Time to dose escalation (months), mean ± SD	11.0±2.4	13.8±8.0	13.0±6.9

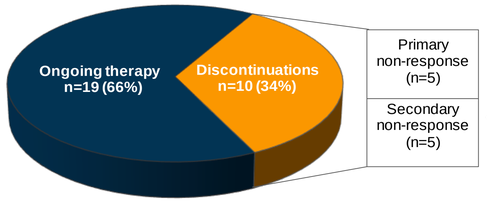
- 28 patients were initiated on a standard dose of 300 mg intravenously at weeks 0, 2, 6, and then every 8 weeks. The remaining patient (5 y/o, 21 kg) was initiated on a dose of 200 mg.
- 27 patients were on concomitant therapy, including 22 on systemic corticosteroids, 10 on 5-ASA, and 7 on immunomodulators.
- 14 of 22 patients were weaned off systemic corticosteroids at a median of 12.4 weeks (IQR 9.8-19.5), with 9 discontinuing steroids by week 14.

Table 3. Adverse Events and Infections

	Frequency
Adverse Event	
Arthralgia	7
Headache	6
Fatigue	5
Nausea	3
Fever, flushing	3
Skin rash	2
Abdominal pain	1
Body aches	1
Lower extremity paresthesia	1
Vagal reaction	1
Respiratory Infections	
Sinusitis	3
Pharyngitis	3

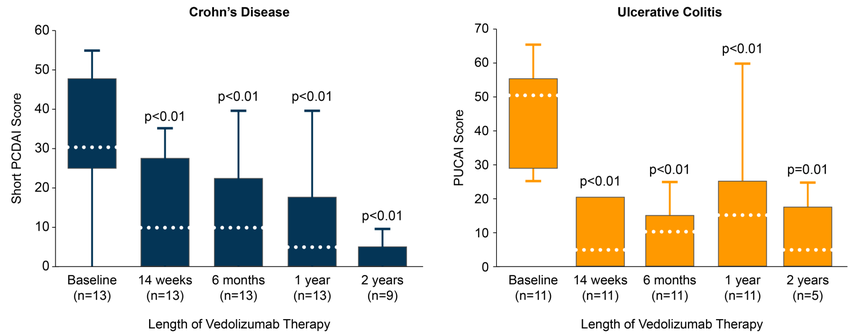
- The most commonly patient-reported AEs were arthralgia, headache, and fatigue.
- Of note, three patients developed C difficile infections while on VDZ. None of these required hospitalization.
- No drug discontinuations occurred due to AEs.

Figure 2. Vedolizumab Discontinuations



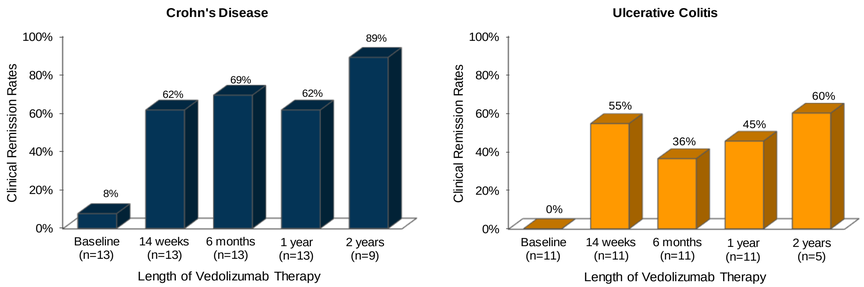
- Median time to VDZ discontinuation for primary non-response (<6 months) was 1.4 months (IQR 1.2-3.3).
- Median time to VDZ discontinuation for secondary non-response (6-24 months) was 16.2 months (IQR 14.4-16.4).
- Following VDZ discontinuation, 6 patients required surgical intervention and 4 were placed on additional biologic therapy.

Figure 3. Disease Activity Scores with Vedolizumab



- Significant reductions in disease activity scores compared to baseline were achieved in both CD and UC patients at ***all*** time points.

Figure 4. Vedolizumab Clinical Remission Rates



*One CD patient in remission at baseline was initiated on VDZ due to marked elevation of fecal calprotectin while compliant with immunomodulator therapy.

- At 1-year, clinical remission was achieved in 8 of 13 (62%) CD and 5 of 11 (45%) UC patients.
- Remission was sustained at 2 years in 11 of 14 patients (8/9 CD and 3/5 UC).

Discussion

- This is the longest available real-world evaluation of VDZ for the treatment of pediatric IBD.
- Our population consisted entirely of anti-TNF-exposed patients.
- We observed a rapid and sustained response to VDZ therapy, with significant reductions in disease severity scores compared to baseline from 14 weeks through 2 years in both CD and UC pediatric patients.
- A significant number of patients were successfully weaned off systemic corticosteroids early on with VDZ therapy.
- Drug discontinuations were attributable to primary or secondary non-response. There were no patient-reported adverse events or infections leading to drug discontinuation.
- Previous literature suggests that VDZ is more effective in pediatric UC compared to CD (week 14 remission rates 76% vs 42%, p<0.05).[3] However, we observed high remission rates in both CD and UC patients.
- Study limitations include the small sample size and retrospective design. The shPCDAI was used as opposed to the complete or weighted PCDAI, and biochemical and endoscopic remission were not assessed due to limited availability of these endpoints.

Conclusions

- Our data suggest that vedolizumab is effective in achieving clinical remission in pediatric IBD patients with prior anti-TNF agent failure.
- We observed early and sustained remission rates in both UC and CD patients.
- There were minimal safety concerns.
- These data need to be validated in larger cohorts.

References

1. Feagan BG, et al. *N Engl J Med* 2013; 369: 699-710.
2. Sandborn WJ, et al. *N Engl J Med* 2013; 369: 711-721.
3. Singh N, et al. *Inflamm Bowel Dis* 2016; 22: 2121-2126.
4. Conrad MA, et al. *Inflamm Bowel Dis* 2016; 22: 2425-2431.
5. Ledder O, et al. *J Crohns Colitis* 2017; 11: 1230-1237.
6. Whitney A, et al. *Am J Gastroenterol* 2018; 113: S396.