#P2222

Real-World Experience of Vedolizumab in Pediatric Inflammatory Bowel Disease

Annette E. Whitney, MD[1], Harry E. Sarles, Jr., MD, FACG[2], Claudia P. Schroeder, PharmD, PhD[3], Tracy C. Okoro, PharmD[3], Lucinda J. Van Anglen, PharmD[3]

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

Abstract

Introduction: Vedolizumab (VDZ) is a humanized monoclonal antibody approved for use in adults with inflammatory bowel disease (IBD). There are limited data on VDZ in pediatric patients (pts), but it may be a viable treatment option in children unresponsive to other biologic therapy. We describe our real-world experience of VDZ in pediatric IBD pts treated at a large private practice.

Methods: A retrospective study was conducted of IBD pts ≤18 years (yrs) who received VDZ for at least 12 months (mo) since drug approval in 2014. Data included demographics, disease characteristics, therapy and adverse events. Disease activity scores were assessed at 0, 6 and 12 mo using the short pediatric Crohn's disease (CD) activity index (sPCDAI) and pediatric ulcerative colitis (UC) activity index (PUCAI). Activity was assessed again at 24 mo for those on continued therapy. Clinical remission was defined by sPDCAI score less than 15 or PUCAI score less than 10.

Results: We identified 20 pts (age: 14±4 years, mean disease duration: 4.5±3 years, 65% male) including 14 CD and 6 UC. Mean dose at initiation of VDZ was 6.5±3 mg/kg infused at 0, 2, 6 and every 8 wks. All pts had previously failed anti-TNF agents, 35% (n=7) failed 2 anti-TNFs and 10% (n=2) failed 3 anti-TNFs. Twenty percent were on VDZ monotherapy with 80% on combination corticosteroids. An additional 4 pts also received immunomodulators. The effects of VDZ on disease activity scores and remission during the first year are shown in Figure 1 and 2. Significant reduction of sPCDAI scores in CD pts occurred at 6 mo (72%) and 12 mo (76%). Although not significant, reductions were also seen in PUCAI scores for UC pts at 6 mo (82%) and 12 mo (75%). Sustained clinical remission at 12 mo was achieved in 65% of pts (10/14 CD, 3/6 UC). Eight of 11 pts (73%) still receiving VDZ at 24 mo had ongoing clinical remission (7/8 CD, 1/3 UC). Discontinuation of VDZ occurred in 5 pts (2 under 6 mo, 3 between 12-24 mo). Sixteen adverse events were reported in 9 pts with 2 serious who were treated without sequelae. No drug discontinuations occurred due to adverse events.

Discussion: Although limited in sample size, our experience supports the use of VDZ in pediatric IBD pts who failed prior anti-TNF therapy. The majority of pts experienced sustained clinical remission with VDZ at 12 mo with no safety concerns. Additional larger studies are needed to establish the role of VDZ in treatment of pediatric IBD.

Background

Vedolizumab, a gut-selective anti-α4β7 integrin monoclonal antibody, was approved by the FDA in May 2014 for moderate to severe CD and UC[1]. Current research has established its safety and efficacy in adult pts.[2-3] Although VDZ may be warranted in refractory or severe pediatric IBD, there are limited data on its long-term use in this population.

Objectives

The objective was to describe our long-term real-world experience with VDZ in pediatric IBD pts treated at a large gastroenterology private practice.

Methods

A retrospective observational study was conducted of pediatric IBD pts ≤18 years (yrs) old who received VDZ for at least 12 mo since drug approval in 2014 at multiple centers within a larger practice.

- Data collection included demographics, disease characteristics, prior and concurrent therapy, disease activity score, and adverse events.
- Disease activity was assessed by the Short Pediatric Crohn's Disease (CD) Activity Index (sPCDAI) in CD pts and the Pediatric Ulcerative Colitis (UC) Activity Index (PUCAI) in UC pts at 0, 6 and 12 mo and at 24 mo in those pts who were on continued therapy.
- Clinical remission was defined by sPCDAI score <15 or PUCAI <10.
- Remission rates were based upon the population available at each follow-up period. Associated risk factors for remission were assessed at 12 mo.
- VDZ discontinuations and adverse events were assessed throughout the study period.
- Data analysis included descriptive statistics, Wilcoxon signed-rank test for changes in disease activity score from baseline, discontinuation-free survival using Kaplan-Meier method with log rank test to measure the difference in the curves by IBD diagnosis, and Altman method including odds ratio (OR) and 95% confidence interval (CI) with a p value <0.05 to be statistically significant for factors associated with clinical remission.

Results

Table 1. Demographics

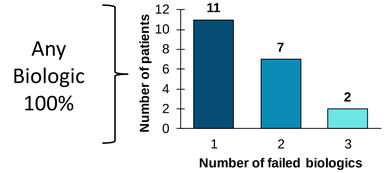
Characteristics	CD (n=14)	UC (n=6)	Total (n=20)
Gender, n (%)			
Male	9	4	13 (65)
Age, n (%)			
<10	3	1	4 (20)
11-15	4	4	8 (40)
16-18	7	1	8 (40)
Duration of therapy, mean (SD)			
Months of VDZ	26	23.8	25 (12)
Disease duration, mean (SD)	5.3	2.5	4.5 (3)

Table 2. Clinical Characteristics

Characteristics	CD (n=14)	UC (n=6)	Total (n=20)
IBD characteristics, n (%)			
Prior complications	3	-	3 (15)
Prior surgeries	3	-	3 (15)
Perianal involvement	6	2	8 (40)
Concurrent medications, n (%)			
5-Aminosalicylates (5-ASA)	1	-	1 (5)
Corticosteroids	7	2	9 (45)
Immunomodulators	2	-	2 (10)
Corticosteroids+5-ASA	-	3	3 (15)
Corticosteroids+Immunomodulators	3	1	4 (20)

Prior complications include bowel obstruction, fistulas, stricture, polyps, diverticulosis.

Figure 1. Prior Failed Biologics



- Prior failed biologics included:
  - 1 failed: 10 infliximab, 1 adalimumab
  - 2 failed: infliximab and adalimumab;
  - 3 failed: infliximab, adalimumab, certolizumab

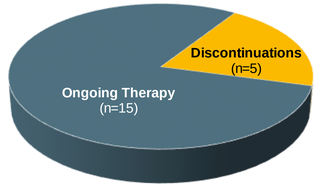
Table 3. VDZ Regimen

Dosage	CD (n=14)	UC (n=6)	Total (n=20)
Mean dose, mg/kg (range)			
Induction	6.7 (3-15)	5.9 (4-10)	6.5 (3-15)
Maintenance	7.1 (3-19)	5.9 (4-10)	6.7 (3-19)

Therapy optimization	Time to change	CD (n=4)	UC (n=1)	Total (n=5)
Dose escalation	mean mo (range)	n	n	n
Shortened interval	14 (8-15)	3	1	4
Increased dosage	15	1	0	1

- All pts received initial doses at 0, 2, 6 then every 8 weeks.

Figure 2. VDZ Discontinuations



20 pediatric pts were initiated on VDZ therapy

- **18 completed 12 mo of therapy (2 discontinuations; 1 CD, 1 UC)**
- **11 completed 24 mo of therapy (3 discontinuations; all CD)**
  - **4 were still on continued therapy at study completion**

Table 4. Time and Reasons for Discontinuation

Dx	No. of pts	Time to D/C (mean mo)	Reason	Subsequent therapy
CD	1	1.3	pt choice	non-biologics; VDZ restarted at 11 mo
CD	3	19	loss of response	UST (n=2) IFX (n=1)
UC	1	5.5	loss of response	colectomy

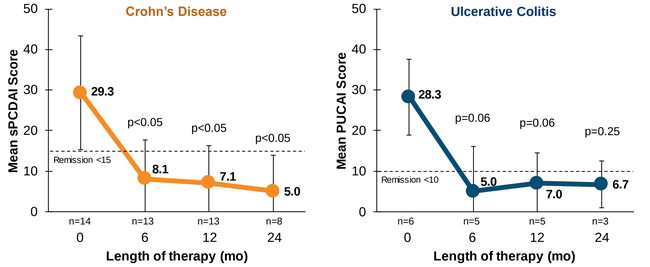
D/C: discontinuation; IFX: infliximab; UST: ustekinumab

Table 5. Safety and Adverse Events

Adverse event (AE)	Frequency	Time to event (mean mo)
Bone and Joint	**19%**	
Arthralgia	3	17.5
Gastrointestinal	**12.5%**	
Nausea	1	0.5
Reflux	1	12.4
Infections	**31%**	
Influenza	2	16.6
Pharyngitis	1	0.5
Sinusitis	2	19.2
Systemic	**25%**	
Headache	1	14.5
Flushing	1	initial dose
Fatigue	2	17.8
Others	**12.5%**	
Oral spasm	1	0.5
Vagal reaction	1	initial dose

- None of the AEs led to VDZ discontinuation.
- 16 AEs were observed in 9/20 pts (45%).
- Pts who experienced headache and vagal reaction required emergent care without sequelae.

Figure 3. Reduction in Disease Activity



- **CD pts had a significant reduction in sPCDAI scores from baseline at 6 mo (72%),12 mo (76%), and 24 mo (83%).**
- **PUCAI scores trended downward from baseline in UC pts at 6 mo (82%), with unappreciable changes following.**

Figure 4. Clinical Remission Rates

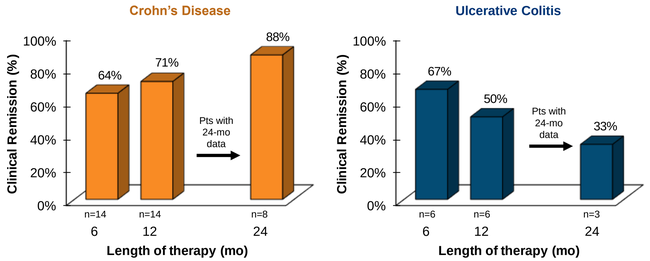


Figure 5. Steroid-Free Remission Rates

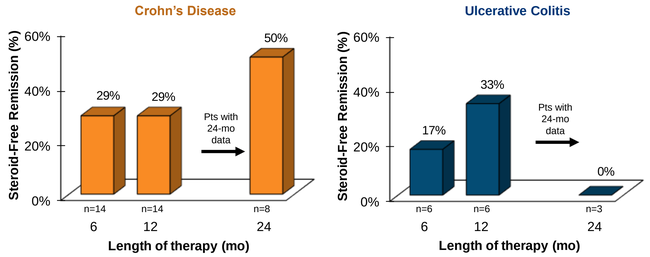


Table 6. Factors Associated with Remission

Factors	n	OR	Confidence interval	P Value
Male gender	13	13.33	1.05-169.67	0.047
Disease duration <7 years	16	0.83	0.06-10.60	1.000
Mild disease activity*	12	1.07	0.13-8.79	1.000
Active perianal disease in CD	3	0.50	0.03-8.71	1.000
Clinical remission <14 weeks	13	0.56	0.05-6.77	1.000
Concurrent steroids	16	1.20	0.09-15.26	1.000

*Mild diease activity is defined as a sPCDAI of 15-29 or PUCAI of 10-34.

- In our cohort, male pts were significantly more likely to achieve clinical remission at 12 mos.
- Other factors evaluated were not associated with clinical remission at 12 mos.

Discussion

- This is the longest available real-world evaluation of VDZ in pediatric IBD pts to date.
- Comparable to previous data, we noted the following:
  - At 6 mo, CD pts had a 72% reduction in sPCDAI score and UC pts had a 82% reduction in PUDAI score on average.
  - The majority (67%) of UC pts achieved clinical remission by 6 mo. However, the pts did not continue in remission over the 24 mo.
  - At 6 mo, 25% of pts achieved steroid-free remission with a modest increase in UC pts at 1 year (29% CD; 33% UC).
  - Higher clinical remission rates were observed in male pts at 12 mo.
  - There were no safety concerns that led to VDZ discontinuation.
- Contrary to previous data, we noted the following:
  - At 6 mo, the majority (64%) of our CD pts experienced clinical remission versus 35% and 31%.[4-5] Most pts had sustained remission over 24 mo.
  - The greatest improvement in disease activity occurred by 6 mo.
  - Younger age, disease duration, disease severity, perianal disease in CD pts, concurrent steroid use at baseline, and clinical remission at 14 weeks did not impact clinical remission at 12 mo.
- Study limitations include the small sample size and the retrospective, observational design. The low statistical power due to the small sample size may account for missed effect of VDZ on UC disease activity. The sPCDAI was used as opposed to the complete PCDAI, and biochemical and endoscopic remission were not assessed due to limited availability of necessary data.

Conclusion

- Our study suggests that VDZ is safe and effective in pediatric pts.
- This study is limited in size, therefore additional large prospective studies are warranted.

References

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