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Observations and Research

Vedolizumab Experience in Children and Adolescents With Inflammatory Bowel Disease: A Multicenter Observational Study

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Background: Vedolizumab is increasingly used off-label to treat children and adolescents with inflammatory bowel disease (IBD). In the absence of rigorous clinical trial experience, multicenter observational data are important to establish expectations for efficacy and safety. We examined 1-year outcomes following vedolizumab therapy in a large multicenter pediatric IBD cohort.

Methods: We performed a retrospective study of 159 pediatric patients (4–17 years old) with IBD [78, Crohn disease (CD); 81, ulcerative colitis/IBD-unspecified (UC/IBD-U)] treated with vedolizumab for 1 year at 8 pediatric medical centers in the United States. Demographics, clinical outcomes, laboratory data, and vedolizumab dosing were recorded. The primary outcome was corticosteroid (CS)-free clinical remission at 1 year. Other measured outcomes were clinical remission at 12 and/or 24 weeks, laboratory outcomes at 1 year, and endoscopy/histology results at 1 year.

Results: Among the 159 patients (mean age, 14.5 ± 2.4 years; 86% anti-TNF experienced), 68/159 (43%) achieved CS-free clinical remission at 1 year (CD, 35/78, 45%; UC/IBD-U, 33/81, 40%). Vedolizumab therapy failed and was discontinued in 33/159 (21%) patients prior to 1 year (CD, 18/78, 23%; UC/IBD-U, 15/81, 19%). While week 12 clinical remission was not predictive of 1-year clinical remission in either CD or UC/IBD-U, week 24 clinical remission was predictive of 1-year clinical remission only in CD patients. No infusion reactions or serious side effects were noted.

Conclusions: Vedolizumab was safe and effective in this pediatric population with approximately 43% achieving CS-free clinical remission at 1 year. Similar efficacy was noted in both CD and UC.

Lay Summary

There is limited information on the safety and efficacy of vedolizumab therapy in children with inflammatory bowel disease. We report a multicenter experience with vedolizumab and find that not far from half are in remission off steroids at 1 year.

Key Words: vedolizumab, biologic therapy, pediatric IBD

Background

Vedolizumab (manufactured by Takeda), a humanized monoclonal immunoglobulin G1 antibody that binds to α4β7 integrin on lymphocytes, has been shown to be superior to placebo in clinical trials to induce and maintain clinical remission in adult patients with inflammatory bowel disease (IBD) and has been found to be safe and effective in real-world experience for adult and pediatric patients with IBD.[1–7] Vedolizumab is used off-label in pediatric patients with IBD, primarily in the setting of primary nonresponse or loss of response to anti-TNF agents.[5–7] Data on efficacy of vedolizumab in pediatric patients are limited, with published studies reporting week 14 clinical remission of 14%–42% in Crohn disease (CD) patients and 37%–76% in ulcerative

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colitis (UC) patients.[5–7] These studies are short term and have small sample sizes.

It is likely that it will take many years before there is a regulatory approval of vedolizumab in children. Therefore, we sought to describe current real-world experience in a large multicenter cohort of pediatric patients receiving vedolizumab focusing on corticosteroid (CS)-free remission at 1 year.

Materials and Methods

Study Subjects and Eligibility

A retrospective chart review was conducted from 8 large pediatric IBD centers across the United States: Connecticut Children's, Hartford, CT; Cincinnati Children's Hospital Medical Center, Cincinnati, OH; Cohen Children's Medical Center of NY, New Hyde Park, NY; Nationwide Children's Hospital, Columbus, OH; Goryeb Children's Hospital, Morristown, NJ; Children's Healthcare of Atlanta, Atlanta, GA; Hasbro Children's Hospital, Providence, RI; North Carolina Children's Hospital, Chapel Hill, NC. Patients between 4 and 17 years old diagnosed with CD, UC, or IBD-unspecified (IBD-U) based on established clinical, radiologic, endoscopic, and pathologic criteria[8] and who started vedolizumab prior to March 2018 and completed 1 year of vedolizumab therapy were included in the study. Research Electronic Data Capture (REDcap) was used to collect the information across the centers. Patients with IBD-U were grouped with those with UC for analysis purposes. Patients started on vedolizumab for postoperative prophylaxis in CD, or those without sufficient follow-up information were excluded from the study. Six patients from Connecticut Children's were included in a previous report.[6]

Data Collection and Disease Activity Scoring

Demographics, clinical information including disease behavior and location, and medication history were recorded. vedolizumab dose, dosing frequency, and total number of doses received were recorded along with any infusion reactions or adverse events. Laboratory testing collected at the initiation and at 1 year of vedolizumab therapy included: Hemoglobin (g/dL), platelet count (Thousand/μL), erythrocyte sedimentation rate (ESR; mm/h), serum albumin (g/dL), and C-reactive protein (CRP) [CRP levels were reported as ×ULN to standardize different cutoffs from different laboratories; 1.0 corresponds to 1 time the upper limit of normal (×ULN)]. When available, colonoscopy information was collected at the initiation and at 1 year of vedolizumab therapy. Due to the retrospective nature of this study, we report colonoscopy data as visual evidence of IBD (reported in this study as macroscopic disease), only histologic evidence of IBD (reported in this study as microscopic disease only by site pathologist), or normal colonoscopy and histology (reported in this study as mucosal healing). Clinical disease activity was determined by the Paediatric Crohn's Disease Activity Index (PCDAI) for CD[9] and pediatric ulcerative colitis activity index (PUCAI) for UC,[10] and was documented at vedolizumab initiation, at 12 ± 6 weeks, at 24 ± 6 weeks, and at 1 year (±3 months) of vedolizumab therapy.

Outcome

The primary outcome was corticosteroid-free (CS-free) clinical remission at 1 year following the initiation of vedolizumab therapy. Remission was defined as a PCDAI ≤10 points for CD[9] or a PUCAI <10 points for UC.[10] Secondary outcomes included clinical remission rates at 12 and/or 24 weeks, clinical remission at 1 year, normalization of inflammatory markers, predictors of remission, and safety data. Colonoscopy outcomes when available were also observed and noted.

Statistical Analysis

Continuous variables were described and summarized as mean, median with SD, ranges, or interquartile range (IQR). Comparative analyses were performed to examine whether the distribution of observations between 2 separate groups on therapeutic efficacy are systematically different for each clinical characteristic of interest. Continuous independent variables were compared using independent sample *t*-test or Wilcoxon rank sum 2-sample test, respectively, depending on the sample distribution across groups. Categorical variables, summarized by frequency and percentage, were also compared across independent groups by the chi-square and Fisher's exact tests. Predictors of 1-year clinical remission for CD or UC patients were assessed by univariate and multivariate logistic regressions models. All analyses used SAS 9.4 (SAS Institute Inc.). All tests were 2-tailed and a *P* value of less than .05 was considered significant.

Ethical Considerations

This study was approved by the institutional ethics review board (IRB) at all involved institutions.

Results

Patient Characteristics

A total of 159 patients (CD, 78, 49%; UC, 74, 47%; IBD-U, 7, 4%) were included in the study; IBD-U patients were grouped with the UC cohort for analysis purposes. Patient demographics, baseline disease characteristics, previous anti-TNF therapy, and concomitant medication history are listed in Table 1. Age range of the IBD-U population was 4–7 years old and 5/7 (72%) were female. CD patients had longer disease duration than UC patients at vedolizumab start (7.1 ± 3.7 vs 4.9 ± 3.1 years; $P < .00$; respectively). A total of 101/159 (64%) patients were on CS at vedolizumab start and the median (range) CS dose was 30 mg (5–60). Median [IQR] baseline PCDAI was 27.5 [15–40] and PUCAI was 50 [35–65] (see Table, Supplementary Data Content 1, which demonstrates mean clinical activity scores for each timepoint).

Vedolizumab Administration and Dosing

Vedolizumab administration details are shown in Table 2. The most common indication for vedolizumab initiation was failure to respond to an anti-TNF (87%). When examining the subset of patients who had inactive disease at baseline ($n = 22$), vedolizumab therapy was started because of anti-TNF complications (CD, 3; UC, 6) or inability to wean off steroids while on an immunomodulator (CD, 9; UC, 4); Table 2. vedolizumab dose of 300 mg was received by 143/159 (90%) patients during the study period. A total of 39/159 (25%) patients weighed <40 kg and 16/39 (weight range 16–39 kg) had a starting dose <300 mg (range, 100–200 mg; median, 5.97 mg/kg; range, 4.9–10.2 mg/kg). Seven of these 16 had dose escalation during the last 3 months of vedolizumab therapy (median, 200 mg; range,

Table 1. Demographic, baseline disease characteristics, and medication exposure history

	Total *n* = 159	CD *n* = 78 (49%)	UC/IBD-U *n* = 81 (51%)	*P*
Age at vedolizumab start (yr)	14.5 ± 2.4	15.1 ± 1.0	14.0 ± 1.7	<.001
Female	88 (55)	42 (54)	46 (57)	.7
Weight at vedolizumab start (kg)	52.0 ± 17.2	52.5 ± 17.1	51.5 ± 17.4	.9
Weight at vedolizumab end (kg)	56.7 ± 17.5	57.1 ± 17.8	56.4 ± 17.0	.8
Disease duration prior to vedolizumab start (yr)	5.9 ± 3.6	7.1 ± 3.7	4.9 ± 3.1	<.001
CD				
Ileocolonic [L3]	—	62 (80)	—	—
Inflammatory [B1]	—	44 (56)	—	—
Stricturing [B2]	—	17 (22)	—	—
Penetrating [B3]	—	6 (8)	—	—
Stricturing and penetrating disease [B2/B3]	—	11(14)	—	—
UC/IBD-U Extensive/Pancolitis [E3/E4]	—	—	67 (83)	—
Previous anti-TNF exposure	136 (86)	70 (90)	66 (81)	.6
Concomitant thiopurines	9 (3)	4 (5)	5 (6)	.6
Concomitant methotrexate	46 (29)	25 (32)	21 (26)	.5
CS therapy at start of vedolizumab[a]	101 (64)	50 (64)	51 (63)	—
Baseline PCDAI/PUCAI	—	27.5 [15–40]	50 [35–65]	—
Hospitalized at vedolizumab start (Yes)	27 (17)	12 (15)	15 (19)	.6

Data shown in mean ± SD, *n* (%), or median [IQR]. Abbreviations: CD, Crohn disease; CS, corticosteroid; IBD-U, inflammatory bowel disease-unspecified; IQR, interquartile range; PCDAI, Paediatric Crohn's Disease Activity Index; PUCAI, pediatric ulcerative colitis activity index; UC, ulcerative colitis.
[a]Inactive/mild disease activity (*n* = 27), moderated to severe disease activity (*n* = 74).

Table 2. Vedolizumab indication and dosage details

	All patients *n* = 159	CD *n* = 78 (49%)	UC/IBD-U *n* = 81 (51%)	*P*
Vedolizumab indication (s)[a]				
Initial biologic	18 (11)	5 (6)	13 (16)	.07
Anti-TNF failed therapy[b]	139 (87)	76 (97)	63 (78)	.1
Prednisone dependent	36 (23)	17 (47)	19 (23)	.85
Allergic reaction to anti-TNF[c]	10 (6)	5 (6)	5 (6)	1
Psoriasis from anti-TNF[c]	7 (4)	3 (4)	4 (5)	.8
Dose per weight (mg/kg)				
At vedolizumab start	6.0 ± 1.8	5.9 ± 1.7	6.0 ± 1.9	.9
At vedolizumab end	5.2 ± 1.9	5.2 ± 2.0	5.2 ± 1.7	.9
Absolute dose (mg)				
At vedolizumab start	286 ± 45	287 ± 41	285 ± 48	.9
At vedolizumab end	275 ± 70	272 ± 76	278 ± 64	.6
Duration of induction (d)	47 ± 29.0	49 ± 25.7	46 ± 31.5	.003
Total number of doses	10 ± 3.0	9.8 ± 3.0	10.0 ± 2.9	.5
Dose interval at study end (wks)	5.7 ± 1.9	5.7 ± 1.9	5.6 ± 1.9	.9
Duration on vedolizumab prior to discontinuation (wks)[d]	23 ± 13	23 ± 11	22 ± 16	.15

Data shown in *n* (%) or mean ± SD. Abbreviations: CD, Crohn disease; IBD-U, IBD-U, inflammatory bowel disease-unspecified; UC, ulcerative colitis.
[a]Some had multiple.
[b]Eighty patients failed anti-TNF therapy at or prior to 6 weeks of therapy.
[c]Nine patients started vedolizumab with inactive disease: 7 developed psoriasis and 2 had an immune mediate allergic reaction to anti-TNF.
[d]For patients who failed vedolizumab prior to 1 year.

120–300 mg; median, 7.6 mg/kg; range 5.2–9.5 mg/kg). The median (range) number of doses given over the study period for the entire cohort was 10 (3–15) doses and the mean ± SD infusion frequency given during the last 3 months of the study period was 5.7 ± 1.9 weeks. The last 3 months of the study period, 102/159 (64%) patients had dose interval less than every 8 weeks and 63/159 (39%) patient received vedolizumab every 4 weeks.

Medication Exposure

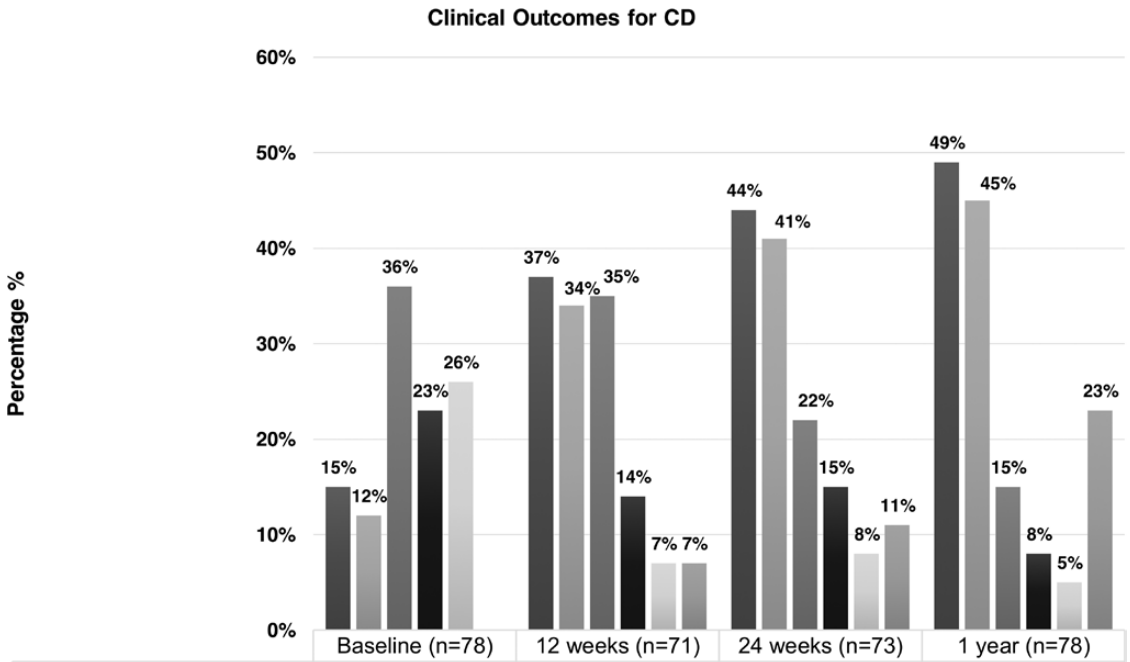
When examining number of patients exposed to biologics prior to vedolizumab initiation, 18/159 (11%) patients had no previous biologic exposure (CD, 5; UC, 13), 136/159 (86%) patients were exposed to anti-TNF therapy, and 5/159 (3%) had received ustekinumab. Furthermore, 62/159 (39%) received ≥2 anti-TNF agents prior to vedolizumab initiation. The median (range) time from last anti-TNF exposure to vedolizumab start was 4 weeks (2–8) (see Table, Supplementary Data Content 2, which demonstrates the number of patients exposed to each individual biologic, duration of exposure, and time from discontinuation to start of vedolizumab therapy for each biologic agent). There was no significant difference between UC and CD in exposure to immunomodulators, however, UC patients were more likely to be exposed to rectal mesalamine ($P < .003$) and oral aminosalicylates ($P < .02$) (see Table, Supplementary Data Content 3, which demonstrates details for medication exposure).

Primary Outcome

The primary outcome of CS-free clinical remission was achieved in 35/78 (45%) of all CD patients and in 33/81 (41%) of all UC patients; Figures 1 and 2, respectively. Of the subgroup of patients who continued on vedolizumab therapy for 1 year, 33/60 (55%) of CD patients and 33/66 (50%) of UC patient achieved CS-free clinical remission. Baseline disease activity for patients who achieve CS-free clinical remission is listed in Table 3. Failure to control disease was the reason for discontinuing vedolizumab in the cohort that discontinued vedolizumab prior to 1 year.

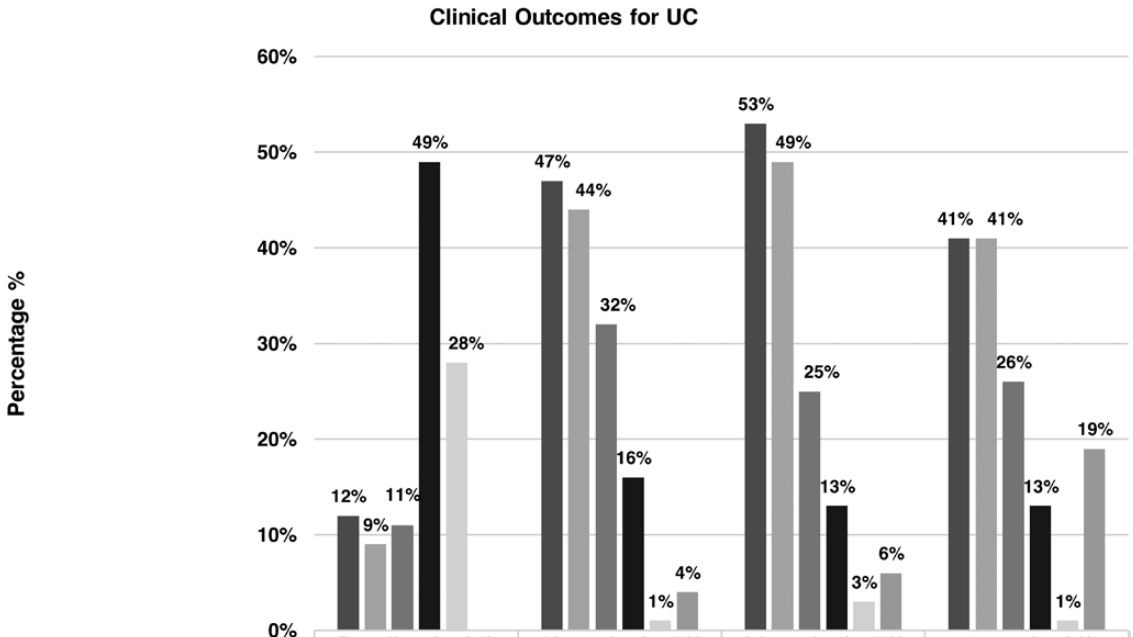
Secondary Outcomes

Clinical disease activity at baseline, 12 weeks, 24 weeks, and 1 year for CD and UC patients is shown in Figures 1 and 2, respectively. Vedolizumab therapy failed and was discontinued prior to 1 year in 18/78 (23%) of CD patients and 15/81 (19%) of UC patients. All CD patients who were biologic naive ($n = 5$) and 6/13 UC patients who were biologic naive achieved CS-free clinical remission at 1 year. Baseline disease characteristics for patients who discontinued vedolizumab prior to 1 year shown in Table 3. When examining sustained clinical remission rates, 36/159 (23%) patients achieved clinical remission at 12 weeks and had sustained clinical remission at 24 weeks *and* 1 year. Additionally, 24/159 (15%) patients did *not* achieve clinical remission at 12 weeks but achieved clinical remission at 1 year. For patients who had baseline inactive disease, 10/12 of CD and 6/10 UC patients continued to have inactive disease at 1 year (1 CD and 1 UC patients failed therapy and discontinued vedolizumab prior to 1 year). Sustained remission rates and surgeries while on vedolizumab therapy are shown in Table 3. Univariate and multivariate analysis showed that clinical remission at 24 weeks and not hospitalized at vedolizumab start were the only predictors of CS-free clinical remission at 1 year for CD patients. No predictors of 1-year CS-free clinical remission were found for UC patients. Week 12 clinical remission, concomitant immunomodulators, or biologics exposure were *not*



	Baseline (n=78)	12 weeks (n=71)	24 weeks (n=73)	1 year (n=78)
Clinical remission	15%	37%	44%	49%
CS-free clinical remission	12%	34%	41%	45%
Mild disease activity	36%	35%	22%	15%
Moderate disease activity	23%	14%	15%	8%
Severe disease activity	26%	7%	8%	5%
Failed vedolizumab therapy		7%	11%	23%

Figure 1. Clinical outcomes for CD patients on vedolizumab therapy for all time periods. Abbreviations: CD, Crohn disease; CS, corticosteroid.



	Baseline (n=81)	12 weeks (n=79)	24 weeks (n=79)	1 year (n=81)
Clinical remission	12%	47%	53%	41%
CS-free clinical remission	9%	44%	49%	41%
Mild disease activity	11%	32%	25%	26%
Moderate disease activity	49%	16%	13%	13%
Severe disease activity	28%	1%	3%	1%
Failed vedolizumab therapy		4%	6%	19%

Figure 2. Clinical outcomes for UC patients on vedolizumab therapy for all time periods. Abbreviations: CS, corticosteroid; UC, ulcerative colitis.

Table 3. Baseline disease activity for the CS-free clinical remission cohort and vedolizumab failed cohort, and secondary and surgery outcomes

	All *n* = 159	CD *n* = 78	UC/IBD-U *n* = 81
One-year CS-free clinical remission, *n*	68	35	33
Baseline disease activity			
Inactive/mild disease	34	24	10
Moderate/severe disease	34	11[a]	23
Vedolizumab therapy failed, *n*	33	18	15
Baseline disease activity			
Inactive/mild disease	9	6	3
Moderate/severe disease	24	12	12
Hospitalized at vedolizumab start for patients that vedolizumab therapy failed[b]	8	5	3
On CS therapy at vedolizumab start for patients that vedolizumab therapy failed	24	13	11
Clinical remission at 12 weeks *and* sustained remission at 24 weeks *and* 1 year	36	16	20
Not clinical remission at 12 weeks but CR at 1 year	24	14	10
Surgery while on vedolizumab for all patients	26	18[c]	8 [Colectomy]

Abbreviations: CD, Crohn disease; CR, clinical remission; CS, corticosteroid; IBD-U, IBD-U, inflammatory bowel disease-unspecified; UC, ulcerative colitis.
[a]Hospitalized (*n* = 2).
[b]On CS (CD, 3; UC, 2).
[c]Colectomy (*n* = 3), ileocecectomy (*n* = 6), diverting ileostomy (*n* = 6), ileostomy closure (*n* = 2), small bowel resection (*n* = 1).

predictors of 1-year CS-free clinical remission for CD or UC patients.

Laboratory and Endoscopic Outcomes

There was an overall significant reduction in mean CRP, ESR, and platelet counts and a significant increase in mean hemoglobin and albumin levels from baseline versus the end of 1-year therapy ($P < .001$) (see Table, Supplementary Data Content 4, which demonstrates details on laboratory outcomes). When examining patients who had CRP values at both vedolizumab start and end ($n = 115$), 68/115 (59%) patients had abnormal CRP at vedolizumab start and 59/115

(51%) had elevated CRP and clinical disease activity. At the end of vedolizumab therapy, 18 patients achieved clinical remission *and* normalization of CRP and 21 patients continued to have elevated CRP levels despite clinical remission at 1 year. When further examining ESR values, 90/159 (57%) patients had elevated ESR at vedolizumab start and 55/90 (61%) had elevated ESR and clinically active disease. At the end of therapy, 19 achieved clinical remission *and* normalization of ESR and 15 continued to have elevated ESR values despite clinical remission. When examining available endoscopic outcomes, 40/159 (25%) patients had a colonoscopy at the start and end of vedolizumab therapy. All had evidence of endoscopic activity at vedolizumab start and only 4 achieved mucosal healing at vedolizumab end. Out of the 32/68 patients who achieved CS-free clinical remission and had a colonoscopy at 1 year, only 4/32 had mucosal healing.

Vedolizumab Safety

Minor side effects to vedolizumab were reported in 32/159 (24%); some had multiple side effects. Reported side effects include nausea and vomiting (5/32), headache (6/32), dizziness and fatigue (4/32), mild—nonurticarial—rash (7/32), respiratory symptoms including sinusitis, flu like symptoms, and/or cough (6/32), and joint pain (4/32). One patient with a history of primary sclerosing cholangitis had ascending cholangitis while on vedolizumab therapy. No reported infusion-related reactions, malignancy, progressive multifocal leukoencephalopathy or deaths were noted.

Discussion

In this large real-world multicenter study of vedolizumab treatment in pediatric IBD, we show that vedolizumab is safe and effective in achieving 1-year CS-free clinical remission in pediatric IBD with rates of 45% and 41% in CD and UC/IBD-U, respectively. Our 1-year CS-free remission rates are comparable to those from a previous real-world series in adults on vedolizumab.[11] Notably, the CS-free remission rate was similar for both CD and UC. Not surprisingly, 88% of our vedolizumab-treated patients were biologic experienced, with 86% having had anti-TNF therapy and 39% with 2 or more biologic drugs that failed to control their disease. Just over 50% of the cohort were on CS therapy prior to starting vedolizumab, and a significant percentage had moderate to severe clinical disease activity (CD, 50%; UC, 77%) at the start of vedolizumab therapy. These data suggest that pediatric patients previously exposed to anti-TNF agents and receiving CS can still achieve favorable outcomes.

Because of a lack of controlled clinical trials there is little evidence on which to base pediatric dosing. The majority of our patients receiving the adult dose of 300 mg. A need to decrease the interval between maintenance dosing of every 8 weeks was noted in 64% of our patients, with a mean interval of 5.7 weeks at the end of observation, and 39% receiving infusions every 4 weeks. This vedolizumab dose is similar to that reported in previous pediatric studies.[5,6] No systematic therapeutic drug level monitoring was performed.

Our 1-year remission rates are lower than that reported in the GEMINI LTS study at 52 weeks (CD, 71%; UC,74%).[12,13] Comparing our results to the GEMINI LTS clinical trial is potentially confounded by different patient populations, study design, and lack of standardized dosing in our study. This difference is also possibly due to the real-world nature of our study; in the GEMINI LTS study patients were escalated to vedolizumab every 4 weeks, which might have impacted clinical outcomes. Although the majority of our patients received an adult dose of 300 mg/dose and mean ± SD vedolizumab frequency given at the end was 5.7 ± 1.9 weeks, in our study the dose and frequency of vedolizumab were at the discretion of the treating physician and doses were nonstandardized.

Our 12-week clinical remission rate for CD (34%) is comparable to the week 14 remission rates in pediatric patients reported previously by Singh et al (42%),[6] but significantly higher than that reported by Conrad et al and Ledder et al (week 14 remission, 15%, and 14%, respectively).[5,7] Moreover, our 12-week clinical remission rate for UC (44%) was comparable to that reported by Ledder et al at 14 weeks (37%),[5] but significantly lower than that reported by Singh et al (week 14 clinical remission, 76%); this variation in clinical remission outcomes is also noted in adult studies[14–16] and possibly due to the real-world nature of these studies.

Our data showed that 21% of CD and 25% of UC patients who achieved clinical remission at 12 weeks had sustained clinical remission up to 1 year. Although clinical remission at 12 weeks was not predictive of 1-year clinical remission, this suggests that early clinical remission can be sustained up to 1 year on vedolizumab therapy in pediatric patients with IBD. Importantly, 15% of patients not in clinical remission at week 12 did reach clinical remission by 1 year. Clinical remission at 24 weeks was predictive of clinical remission at 1 year for CD but not for UC patients, this is consistent with the findings by Conrad et al and in GEMINI 3 that showed a slower response to vedolizumab in CD patients; especially CD patients exposed to biologics (94% of our cohort).[3,7]

In our cohort, remission at 24 weeks and outpatient status at the start of therapy were predictors of remission in CD patients but not UC patients; this was not reported in previous pediatric studies. No other predictors of remission were identified in CD patients and no predictors of remission in UC patients including disease severity and location were identified in our cohort. This is similar to that reported by Ledder et al. Our study did not corroborate the findings presented by the Singh et al study that patients with colonic-only disease were more likely to have clinical remission at 6 and 24 weeks.

The majority of the biologic naive patients were in clinical remission at 1 year (11/18, 61%; CD, 5/5, 100%; UC, 6/13, 46%), consistent with previous pediatric reports.[6] However, it is challenging to draw a conclusion from our study due to the small sample size of biologic naive patients in our cohort. Additional clinical trials are necessary to study the efficacy of vedolizumab in biologic naive versus biologic exposed pediatric IBD patients.

As this was a retrospective study there was no systematic methodology to perform and record endoscopic outcomes, and no mechanism for central review. We sought to understand whether serial CRP measures might indicate mitigation of inflammation. Despite the limitations in our data when examining CRP values in patients who achieved clinical remission at 1 year, our study showed that a small number of these patients had normalizations of CRP at 1 year. This raises an important point regarding the importance of colonoscopy and fecal markers in assessing the efficacy of vedolizumab, with them being superior to CRP levels in assessing mucosal healing and remission as note in the literature.[17] Of the

32 patients who had a colonoscopy and were in clinical remission at 1 year, only 4 patients achieved both visual and biopsy normalization. We recognize that this observation is limited by its uncontrolled nature and the small number of patients. Prospective clinical trials in pediatric patients assessing mucosal healing after 1 year of vedolizumab therapy are warranted.

There were no major side effects such as infusion reaction, major infections (such as tuberculosis, histoplasmosis, septicemia), progressive multifocal leukoencephalopathy, or deaths. Minor side effects were reported in 24% of our cohort and were similar to those reported in other pediatric studies[5,7] and adult studies[1,2,16] including constitutional symptoms, upper respiratory tract symptoms, joint pains, and minor—nonurticarial—rash. One patient with primary sclerosing cholangitis developed ascending cholangitis thought to be unrelated to vedolizumab therapy.

Limitations to our study include the retrospective design and thus the lack of standardized dosing and the lack of standardized blood work, vedolizumab levels, fecal markers (such as calprotectin), and endoscopic evaluation. However, our study is representative of real-world data of 1-year vedolizumab clinical remissions rates in pediatric patients with complex IBD who failed anti-TNF therapy. Our findings are similar to those reported in the real-world data in adults with IBD.[11]

In conclusion, our study showed that vedolizumab is safe and associated with a 1-year CS-free remission rate of around 45% in both UC and CD in a largely anti-TNF experienced population of children and adolescents. It does raise the important question of whether better rates could be achieved in anti-TNF naive patients, as has been described previously.[3,7] We show that there is a delayed response to vedolizumab in CD patients exposed to biologics and that clinical remission at 12 weeks can be sustained up to 1 year of therapy (23% of all CD and 25% of all UC). Despite the retrospective nature of this study, these data support the efficacy and safety of vedolizumab therapy in children and adolescents with IBD and can be used by practitioners when discussing vedolizumab therapy with third-party payers who may request supporting data. Further studies and clinical trials of vedolizumab are required to better evaluate the dose, long-term efficacy, and rate of mucosal healing in pediatric IBD.

Supplementary Data

Supplementary data is available at *Crohn's and Colitis 360* online.

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No funding was received for this study.

Author Contributions

All authors have made substantial contributions to all of the following: (1) the conception and design of the study, acquisition of data, analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and (3) final approval of the version to be submitted.

Conflicts of Interest

James Markowitz serves as a consultant to Janssen Pharmaceuticals; Francisco Sylvester is a member of the scientific advisory board for Landos Biopharma; Jeffrey S. Hyams serves on an Advisory Board for Janssen, AbbVie, and consultant to Takeda, Pfizer, Boehringer-Ingelheim, Lilly, Bristol Myers Squibb. All other authors have no disclosures or conflict of interests.

Data Availability

Data are available upon request. No new data were created or analyzed.

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