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Vedolizumab in Paediatric Inflammatory Bowel Disease: A Retrospective Multi-Centre Experience From the Paediatric IBD Porto Group of ESPGHAN

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Abstract

Background: Vedolizumab, an anti-integrin antibody, has proven to be effective in adults with inflammatory bowel disease [IBD], but the data in paediatrics are limited. We describe the short-term effectiveness and safety of vedolizumab in a European multi-centre paediatric IBD cohort.

Method: Retrospective review of children [aged 2–18 years] treated with vedolizumab from 19 centres affiliated with the Paediatric IBD Porto group of ESPGHAN. Primary outcome was Week 14 corticosteroid-free remission [CFR].

Results: In all, 64 children were included (32 [50%] male, mean age 14.5 ± 2.8 years, with a median follow-up 24 weeks [interquartile range 14–38; range 6–116]); 41 [64%] cases of ulcerative colitis/inflammatory bowel disease unclassified [UC/IBD-U] and 23 [36%] Crohn's disease [CD]. All were previously treated with anti-tumour necrosis factor [TNF] [28% primary failure, 53% secondary failure]. Week 14 CFR was 37% in UC, and 14% in CD [$P = 0.06$]. CFR by last follow-up was 39% in UC and 24% in CD [$p = 0.24$]. Ten [17%] children required surgery, six of whom had colectomy for UC. Concomitant immunomodulatory drugs did not affect remission rate [42% vs 35%; $p = 0.35$ at Week 22]. There were three minor drug-related adverse events. Only 3 of 16 children who underwent endoscopic evaluation had mucosal healing after treatment (19%).

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Conclusions: Vedolizumab was safe and effective in this cohort of paediatric refractory IBD. These data support previous findings of slow induction rate of vedolizumab in CD and a trend to be less effective compared with patients with UC.

Key Words: Vedolizumab; paediatric; inflammatory bowel disease

1. Background

Vedolizumab is a humanised immunoglobulin G1 monoclonal antibody acting against α4β7 integrin which modulates lymphocyte trafficking specifically to the gut. Results from the GEMINI 1[1] and GEMINI 2[2] trials demonstrated effectiveness of vedolizumab in induction and maintenance of remission in both ulcerative colitis [UC] and Crohn's disease [CD], respectively, but the clinical benefit seems slightly superior in UC. In GEMINI 1, 106/225 [47%] of patients had a clinical response by Week 6 and 107/247 [43% of responders and 18% of all comers to the trial] were in clinical remission by 1 year. In CD, 69/220 [31%] showed clinical response by 6 weeks, with 116/308 [38%] of responders in clinical remission by 1 year, representing 12% of all comers to the trial. CD patients who failed anti-tumour necrosis factor [TNF] treatments were assessed in the induction of remission trial GEMINI 3. In this study, 39% exhibited clinical response by Week 6, but the clinical remission rate did not surpass the placebo arm until 10 weeks [27% vs 12%], suggesting that the effects of vedolizumab on clinical remission may not be evident in the initial weeks of treatment, especially in CD.[3] Subsequent real-life cohort studies in adults support the effectiveness of vedolizumab in inducing and maintaining remission, both in CD and UC.[4–10]

In children, vedolizumab is available off-label and it is typically reserved for patients who have exhausted other treatment options including anti-TNF. Two case series on vedolizumab from North America have recently been published with inconsistent results, one with 52 children[11] and the second with 21 patients.[12]

The aim of this multi-centre observational study is to report on the short- and long-term outcomes of vedolizumab therapy in paediatric IBD.

2. Methods

This retrospective observational study reports the collective experience of vedolizumab in children [2–18 years] from 19 centres affiliated with the Paediatric IBD Porto and with Interest groups of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition [ESPGHAN], in Europe and Israel. All children were diagnosed with CD, UC or IBD-U by accepted criteria[13] and were commenced on vedolizumab for any reason, combined with any other medications. To avoid selection bias, we included all patients receiving at least one infusion, even if treatment had been discontinued for any reason.

Explicit clinical and demographic data, baseline disease characteristics, previous medications and surgeries, and anthropometric data were recorded 6 months preceding initiation of vedolizumab, at vedolizumab onset and at 6, 14, 22, and 54 weeks thereafter, when available, as well as at last follow-up. The following data were recorded at each time point: disease activity (captured by the weighted Paediatric Crohn's Disease Activity Index [wPCDAI] in CD and the Paediatric Ulcerative Colitis Activity Index [PUCAI] in UC as well as by physician global assessment [PGA]), medications, blood tests, and explicit data on adverse events. When available, data on surgery, endoscopic evaluations (captured by the Simple Endoscopic Score in CD [SES-CD] and the UC Endoscopic Index of Severity [UCEIS] in UC/IBD-U) and stool calprotectin were recorded. De-identified patient data were recorded on standardised REDcap web-based case-report forms, managed by the data coordinating centre [DCC] at Shaare Zedek Medical Center in Jerusalem. All contributing centres obtained individual ethical approval from their local ethics board.

The primary outcome was treatment success at Week 14, defined as steroid- and exclusive enteral nutrition [EEN]-free remission [ie wPCDAI < 12.5 or PUCAI < 10] without the need for new medications or surgical intervention.

Secondary outcomes included remission rate at last follow-up, mucosal healing [defined as SES-CD < 3 in CD[14] or UCEIS = 0 in UC/IBD-U[15]], deep remission [defined as clinical remission with fecal calprotectin < 100 mcg/g[16]], need for surgical interventions, growth, weight gain, and adverse events. Linear growth was assessed by its most sensitive measure, height velocity, during the 6-months preceding starting vedolizumab therapy vs the paired measure after starting therapy. Anthropometric measurements are expressed as standard deviation z-scores [SDS] using age- and gender-matched reference standards.[17,18] Height velocity data were standardised using the Stata JMP-derived polynomial calculations based on percentile data.[17,19]

2.1. Statistical analyses

Data are presented as mean ± standard deviation, or medians (interquartile range [IQR]), as appropriate for the distribution normality. Intention-to-treat [ITT] analysis was calculated using the modified non-response imputation [NRI], whereby patients in whom vedolizumab was ceased before the visit were considered treatment failures in all outcomes. If data were missing due to lack of sufficient follow-up [but the drug was not discontinued] and the 6-week vedolizumab induction period was completed, then the last observation carried forward [LOCF] was used. Patients in whom follow-up did not extend beyond vedolizumab induction were included only in the safety analysis and the NRI [if the drug was discontinued] to reflect a conservative yet fair reflection of the drug effect. Data were compared using chi square or Fisher's exact test for categorical variables and Student's t test or Wilcoxon rank sum test for continuous variables. Paired data with a non-normal distribution were compared with the Sign test, including pre vs post treatment measures of anthropometric data. Statistical analyses were performed using SPSS [IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY] with $p < 0.05$ taken as the significance threshold.

3. Results

3.1. Patient characteristics

A total of 64 children were included with a median follow-up of 24 weeks [IQR 14–38] [Table 1]; 52 [81%] patients were followed for at least 14 weeks, 38 [59%] followed for at least 22 weeks and 10 [16%] followed

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Table 1. Baseline patient characteristics: frequency [%], mean ± SD, or median [IQR] are presented as appropriate.

	Total [*n* = 64]	CD [*n* = 23]	UC [*n* = 33] / IBD-U [*n* = 8]
Male	32 [50%]	13 [57%]	19 [46%]
Age at diagnosis [years]	10.7 ± 3.6	9.5 ± 3.5	11.4 ± 3.5
Disease duration [months]	37 [22–60]	61 [34–92]	33 [20–43]
Follow-up [weeks]	24 [14–38; range 6–116]	22 [14–38; range 6–56]	24 [14–36; range 6–116]
Location/extent		L2 4 [17%]	E1 1 [2%]
		L3 11 [48%]	E2 4 [10%]
		L3/L4a 6 [26%]	E3 6 [15%]
		L3/L4b 2 [9%]	E4 30 [73%]
		Perianal 4 [17%]	
Behaviour		Inflammatory 17 [74%]	Severe 37 [90%]
		Stricturing 5 [22%]	
		Penetrating 1 [4%]	
		Growth delay 15 [65%]	
Extra-intestinal manifestations	16 [25%]	8 [35%]	8 [20%]
Clinical assessment			
Baseline PGA			
Severe	22 [37%]	7 [33%]	15 [39%]
Moderate	24 [41%]	7 [33%]	17 [45%]
Mild	11 [19]	6 [29%]	5 [13%]
Remission	2 [3%]	1 [5%]	1 [3%]
Baseline wPCDAI/PUCAI		37.5 [24–61]	45 [30–65]
Baseline endoscopy [SES-CD/UCEIS]		19.5 [10.5–23.3]	20 [15–25]
Anti-TNF	64 [100%]	23 [100%]	41 [100%]
Primary failure	18 [28%]	6 [26%]	12 [29%]
Secondary failure	34 [53%]	10 [44%]	24 [59%]
Adverse event	9 [14%]	5 [22%]	4 [10%]
Second anti-TNF	36 [56%]	18 [78%]	18 [44%]
Third-line therapy			
Tacrolimus	4 [6%]		4 [10%]
Thalidomide	1 [2%]	1 [4%]	
Previous surgery	5 [8%]	4 [17%]	1 [2%]

SD, standard deviation; IQR, interquartile range; CD, Crohn's disease; UC, ulcerative colitis; IBD-U, inflammatory bowel disese unclassified; PGA, physician global assessment; wPCDAI, weighted Paediatric Crohn's Disease Activity Index; PUCAI, Paediatric Ulcerative Colitis Activity Index; SES-CD, Simple Endoscopic Score in CD; UCEIS, Ulcerative Colitis

Endoscopic Index of Severity; TNF, tumour necrosis factor.

to at least 1 year. Of the 12 patients with less than 14 weeks' follow-up, 10 ceased vedolizumab and only two lacked sufficient follow-up data.

All children were previously exposed to anti-TNF, 57 [89%] of whom failed intensified dosing regimen and almost half failing a second anti-TNF or third-line therapy [Table 1]. At vedolizumab initiation, disease activity was moderate or severe in 40 [63%] of patients, despite 49 [77%] patients taking concomitant corticosteroids or nutritional therapy [Table 1].

3.2. Drug administration

A total of 52 [81%] children received the adult dose of 300 mg and the others [weighing 19.5-48 kg] received 150-250 mg or 3.6–10.3 mg/kg (median 7.3 mg/kg [IQR 5.6–9.8]). The smallest child to receive 300 mg weighed 28.5 kg, and the largest child to receive a reduced dose weighed 48 kg [received 200 mg] [Supplementary Figure 1, available as Supplementary data at *IJE* online]. Of those who commenced lower doses, four subsequently had the dose increased throughout the treatment course. One of these children [UC] achieved better response on the higher dose but did not achieve remission, two [both UC] were already in remission before the dose escalation, and the fourth [CD] did not respond to the higher dose.

Vedolizumab was ceased in 14 [22%] of patients throughout follow-up within a median of 14 weeks [IQR 12–22], all but one due to poor response; 10/14 [71%] discontinued within 14 weeks and 13/14 [93%] within 6 months. One patient ceased due to chronic itch as a suspected adverse event of vedolizumab, which resolved following drug cessation.

3.3. Remission rate

ITT steroid- and EEN-free remission rates at Week 14 were observed in 15/41 [37%] of the UC/IBD-U children and 3/21 [14%] of CD [$p = 0.06$; Figure 1]. The ITT remission rates at 22 weeks were 14/41 [34%] in UC/IBD-U and 4/21 [19%] for CD [$p = 0.22$; Figure 1]. Three UC patients who were in remission at Week 14 were not in remission at Week 22, with two new patients entering remission over that period. In CD, two patients in remission at Week 14 lost remission at Week 22, but three new patients entered remission over that period.

At last follow-up, ITT remission rates were 16/41 [39%] for UC/IBD-U and 5/21 [24%] in CD [$p = 0.24$; Figure 1]. Clinical activity scores and C-reactive protein [CRP] improved during the treatment course [Table 2].

Corticosteroid and nutritional therapy were used as directed by the treating physician, with variable dosing courses as per clinical need. A total of 41 patients [67%] were on corticosteroid therapy at commencement, 12 of whom received high dose induction therapy [above 0.8 mg/kg]. There was no impact of initial high dose steroid use on Week 14 remission rates in either CD or UC/IBD-U [$p = 1.0$ and $p = 0.89$, respectively]. Throughout follow-up there were fewer patients on corticosteroid therapy, with a drop in median dose of steroids over time [Table 2].

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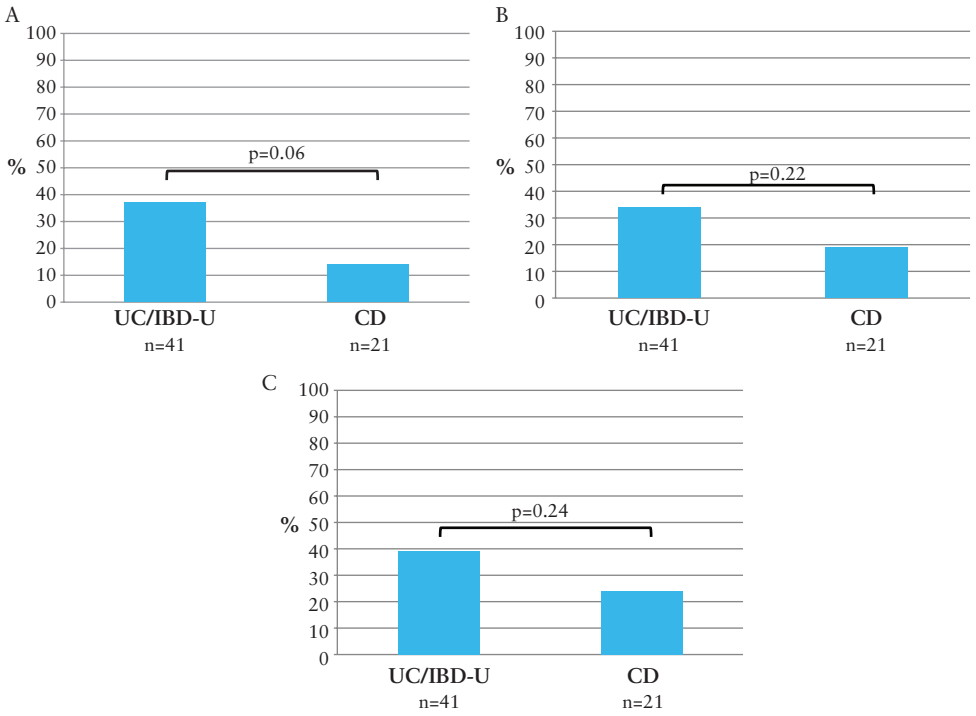

Figure 1. Steroids- and exclusive enteral nutrition [EEN]-free intention-to-treat remission rate in Week 14 [a], Week 22 [b], and last follow-up [c]; intention-to-treat analysis.

Table 2. Indicators of disease activity over time (frequency [%] or medians [IQR] are reported as appropriate).

	Week 0	Week 6	Week 14	Week 22	Week 52
CD	*n* = 22	*n* = 22	*n* = 16	*n* = 14	*n* = 4
wPCDAI	38 [24–61]	31 [14–46]	19 [9–29]	18 [8–26]	18 [9–39]
Clinical remission	2 [9%]	5 [23%]	4 [25%]	5 [36%]	1 [25%]
CRP [mg/dL]	1.6 [0.37–4.9]	0.72 [0.2–3.36]	0.8 [0.46–2.94]	0.85 [0.34–2.19]	1.9 [0.58–5.48]
Number normal	6 [27%]	8 [36%]	6 [38%]	5 [36%]	1 [25%]
Steroid use	14 [64%]	9 [41%]	2 [13%]	1 [7%]	0
Dose [mg]	25 [15–40]	20 [7.5–33]	17.5 [10–17.5]	5	
Enteral nutrition	7 [32%]	7 [32%]	3 [19%]	2 [14%]	1 [25%]
UC/IBD-U	n = 39	n = 38	n = 34	n = 26	n = 10
PUCAI	45 [30–65]	25 [9–40]	10 [0–28]	10 [0–15]	2.5 [0–22.5]
Clinical remission	2 [5%]	9 [24%]	16 [47%]	12 [46%]	6 [60%]
CRP [mg/dL]	0.41 [0.1–1.4]	0.23 [0.07–0.67]	0.14 [0.05–0.71]	0.15 [0.04–0.51]	0.09 [0.04–0.28]
Number normal	24 [62%]	28 [74%]	19 [56%]	19 [73%]	9 [90%]
Steroid use	27 [69%]	19 [50%]	9 [26%]	4 [15%]	0
Dose [mg]	25 [20–40]	20 [10–40]	12.5 [10–20]	15 [6–24]	

IQR, interquartile range; CD, Crohn's disease; UC, ulcerative colitis; IBD-U, inflammatory bowel disese unclassified; wPCDAI, weighted Paediatric Crohn's Disease Activity Index; PUCAI, Paediatric Ulcerative Colitis Activity Index; CRP, C-reactive protein.

At vedolizumab commencement, 21/64 [67%] patients were on concomitant thiopurines or methotrexate therapy. This dropped to 20/40 [50%] at 22 weeks and 7/14 [50%] at 1 year. Remission rates did not differ in those with combination therapy at 14 weeks vs those on monotherapy (11/30 [37%] vs 7/21 [33%]; $p = 0.52$) and not at 22 weeks (8/19 [42%] vs 7/20 [35%]; $p = 0.35$).

3.4. Secondary outcomes

Univariate analysis showed no association between remission rates and gender, age at diagnosis, disease duration, CRP, presence of perianal disease, or reason for previous anti-TNF failure either in UC/IBD-U or in CD [all $p > 0.28$; data not shown]. There was no association between remission rates and disease location in CD or disease extent in UC. All CD patients who achieved remission by last follow-up had ileocolonic disease; however, the remission rate of ileocolonic distribution was not significantly different in the smaller cohort with isolated colonic disease (5/19 [26%] vs 0/4 [0%], respectively; $p = 0.26$).

There was no demonstrated catch-up growth in the CD patients. The reduced height velocity seen overall before vedolizumab therapy did not improve over the 6 months thereafter (median z-score –1.55 [IQR -4.9–2.8] vs -1.88 [-2.9- 1.2]; $p = 0.96$). To more accurately

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evaluate height velocity changes requires bone age or Tanner score to assess pubertal stage, data which were largely missing. Sub-analysis of height velocity was performed in those patients with Tanner stage recorded between 1–3, in whom linear growth is assumed to be ongoing. Among this cohort there remained no significant improvement in height velocity (median z-score -4.98 [-6.4–-3.3] vs -3.55 [-6.12–-1.88]; p = 0.36). Catch-up growth was noted among the five CD patients who achieved remission by end of follow-up, (post-treatment height velocity z-score 5.96 [IQR -1.9-5.96]]), higher than pre-treatment height velocity z-score (-0.67 [IQR -1.9–0.67]); however, with the limited number of patients who met these criteria, this did pnot reach statistical significance [P = 0.18]. None of these patients had Tanner stage recorded as 1–3.

Weight gain was not seen over the 6 months following treatment commencement, either among UC/IBD-U patients (median weight z-score at baseline -0.57 [-1.1-0.38] vs -0.46 [-1.0-0.78) after 6 months; p = 0.07) or among CD patients (-1.22 [-1.8-0.1] vs -0.89 [-2.2-0.04]; p = 0.92].

In all, 56 children [88%] had a standard induction course with 8-weekly maintenance infusions; eight [12%] commenced 4-weekly infusions from the outset. Of the former, seven [13%] increased dosing to 4- or 6-weekly infusions, due to poor response. Of these, four patients had CD, one of whom subsequently achieved remission, and three had UC, of whom one subsequently achieved remission, another partially responded and the third had no response. There was no difference in success rate between those who commenced on 8-week dosing intervals and those who commenced on 4-week dosing intervals from the outset (20/45 [44%] vs 1/7 [14%] respectively; p = 0.14).

Nineteen children had both baseline and follow-up colonoscopic assessment. Among these children, both UCEIS in UC and SES-CD in CD dropped significantly [Figure 2]. Two of 13 UC/IBD-U patients [15%, 5% of all UC/IBD-U patients] and 1/6 CD patients [17%, 4% overall CD] achieved mucosal healing.

Stool calprotectin was measured at baseline, with follow-up measures, in 25 patients [five CD, 20 UC/IBD-U]. There was a significant drop in the calprotectin levels following treatment, with a median decrease of 518 mcg/g [IQR 202–2327] in UC/IBD-U and 499 mcg/g [39–1620] in CD, with no difference in magnitude of the drop between UC/IBD-U and CD [p = 0.62] [Figure 3]. Deep remission, defined as fecal calprotectin < 100 mcg/g, was achieved by six children [24% of those in whom calprotectin was measured, 9% overall]. All of these children had UC/IBD-U (6/41 [15%] of UC/IBD-U vs 0/23 [0%] of CD patients; p = 0.03]). Eleven children [44% of those with serial calprotectin, and 17% overall] had calprotectin < 300 mcg/g (2/23 [9%] of CD patients and 9/41 [22%] with UC; p = 0.09).

Ten [17%] patients underwent surgical resection at a median of 4 months [IQR 3.3–5.8], four of whom had CD [17% of the entire CD cohort] and six had UC/IBD-U [15% of entire UC/IBD-U cohort].

3.5. Safety

No serious drug-related adverse events were reported. Three mild potential drug-related adverse events were recorded: one [13-year-old female] developed otitis externa and periorbital oedema after the first and second infusions, which subsequently resolved and she remained on treatment; the second [17-year-old female] developed an intractable itch after the first infusion and vedolizumab was subsequently ceased; and the third [17-year-old female] developed mild shortness of breath during the fourth infusion, which improved with antihistamine medication and a slower infusion rate. Vedolizumab was continued in this patient, only ceasing later due to poor drug effectiveness.

4. Discussion

In this largest real-life cohort of vedolizumab use in paediatric IBD to date, we show that vedolizumab is safe and effective in paediatric IBD, with EEN- and steroid-free remission rates at last follow-up of 39% and 24% in UC/IBD-U and CD, respectively. In this previously refractory cohort, among those who underwent evaluation, 15% and 17% had demonstrated mucosal healing and 30% and 0% achieved calprotectin < 100 mcg/g, respectively. Consistent with the finding in GEMINI 3,[3] there was a slower response rate in CD than in UC. The slower rate of response in CD as demonstrated in our study is a finding of potential clinical significance when selecting appropriate patients for vedolizumab therapy. Considering the refractory nature of our cohort, these data show promise for this newer class of biological therapy in paediatric UC, and to a lesser extent also in CD.

Our remission rate in CD is comparable to the paediatric cohort of Conrad *et al*. who report a Week 14 remission rate of 15%,[12] but significantly lower in both UC and CD remission rates than reported by Singh *et al*. [Week 14 remission of 76% and 42%, respectively].[11]

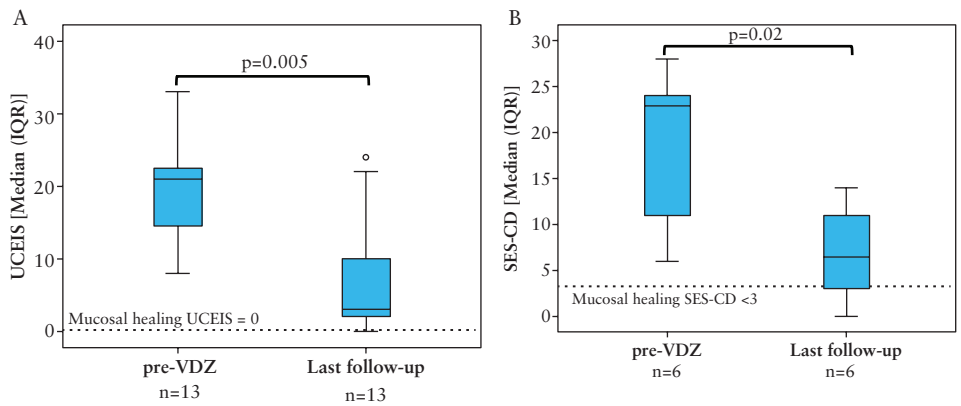

Figure 2. Change in endoscopic scores; Ulcerative Colitis Endoscopic Index of Severity [UCEIS] in ulcerative colitis [UC] [a], and Simple Endoscopic Score in Crohn's Disease [SES-CD] [b]. Repeat colonoscopy at median 14 weeks (interquartile range [IQR] 14–22).

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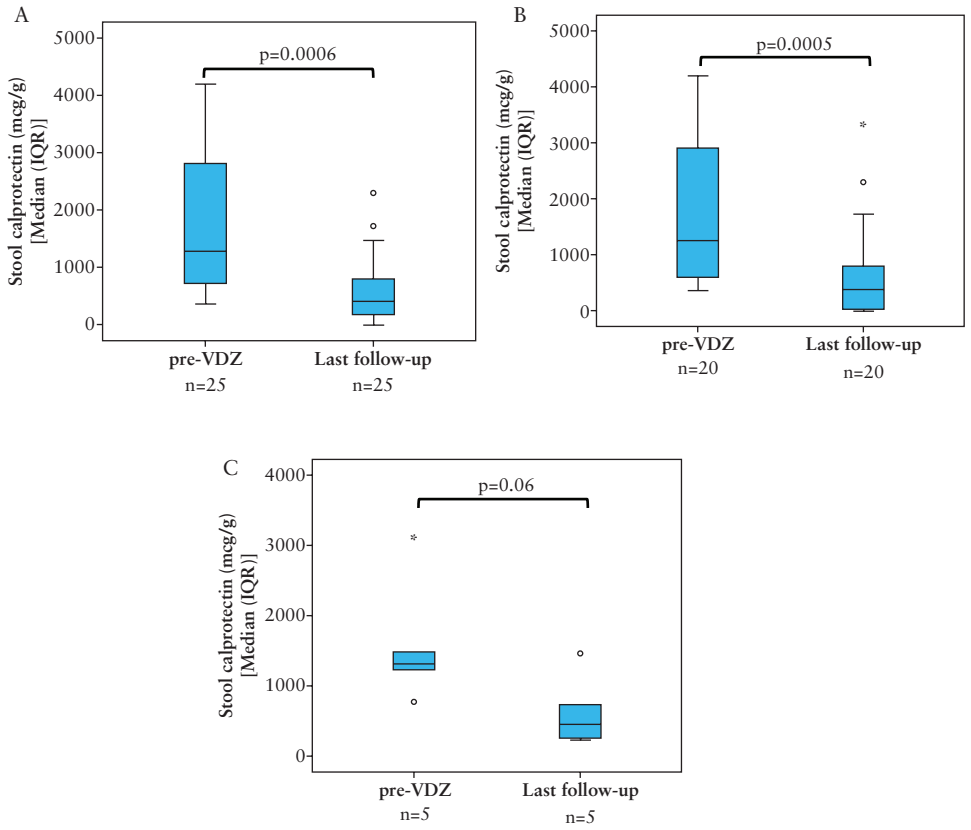

Figure 3. Change in stool calprotectin; all patients [a], ulcerative colitis/inflammatory bowel disease unclassified [UC/IBD-U [b], Crohn's disease [c]. Repeat measure at median 54 weeks (interquartile range [IQR] 22–54).

When comparing with adult data, 1-year clinical remission rates in the GEMINI 1 and 2 were 18% and 12%, respectively, lower than those seen in our study. A more accurate comparison would be with the GEMINI 3 study of TNF-refractory CD patients, in whom 27% achieved clinical remission by Week 10. Adult real-world cohorts report Week 14 CFR rates between 19% and 31% for CD and 19–36% for UC,[4–10] comparable to our data.

Consistent with our findings was the lack of serious adverse events associated with vedolizumab in either of these series. Nonetheless, Conrad *et al.* reported 29 adverse events in children, including upper respiratory tract infections, nausea, fatigue, headaches, nasopharyngitis, skin infections, and sinusitis.[12] Whereas GEMINI 1 revealed no difference in adverse events between vedolizumab and placebo,[1] GEMINI 2 demonstrated a higher incidence of nasopharyngitis with vedolizumab than with placebo [12.3% vs 8%].[2] The adult US VICTORY consortium of 212 patients reported enteric infections (five per 100 patient-year follow-up [PYF]), sinopulmonary infections [4.4 per 100 PYF] and arthralgia [3.1 per 100 PYF], among other less common adverse events.[9] Other real-life cohorts report infections from 0% to 25%, nasopharyngitis 0–23%, arthralgia 2–20%, and one report of anaphylaxis and rash.[4–8] Pruritis as an adverse event of vedolizumab had not been previously reported.

Within the paediatric population, responses to IBD treatment differ between older children and those with early-onset or very early-onset IBD.[20] In our cohort dosing was based on adult recommended dose with non-standardised, weight-based modifications in younger children. Since children weighing less than 30 kg are best dosed by body surface area [BSA],[21] until formal dosing guidance is available it is reasonable to dose children with the equivalent of 300 mg/1.73m^2 [ie 175 mg/BSA], and those over 40 kg as adults.

Our cohort did not show superiority of combination therapy over monotherapy with vedolizumab; however, this analysis is limited by the small sample size and limited follow-up. This comparative analysis was not specifically presented in the two previous paediatric case series. Shelton *et al.* did not find any benefit of combination therapy over sole vedolizumab in their adult cohort, but noted that the sample size may have been too small to detect a difference.[4]

Considering the small sample size and the lack of comparison group, we found that shortening infusion interval from 8 to 4 weeks led to improved effect in 3/7 [43%]. This is supported by recent pharmacokinetic data demonstrating significant correlation between higher vedolizumab drug levels and clinical response in IBD patients.[22–24]

In our cohort we did not demonstrate any disease features associated with better response, including age at diagnosis, disease location or extent, or disease duration. However, this needs to be re-assessed in larger studies.

Our study is limited by its retrospective nature and hence a lack of standardised treatment regimens and concomitant therapies, as well as endoscopic evaluation in only some patients. Despite being the largest cohort to date, the cohort is still limited in size. Response rates are difficult to relate solely to vedolizumab effect, since variable use of induction corticosteroids and nutritional therapy obviously contribute to clinical response. Since vedolizumab in paediatric IBD is limited to off-label use, our cohort was represented entirely by patients failing conventional therapies. Previous anti-TNF failure may be associated with lower remission rates than anti-TNF naïve

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patients; however, results from studies assessing these differences are conflicting.[4,8,9,25–27]

Our study presents encouraging data that vedolizumab is safe and effective in paediatric UC, and to a lesser extent also in CD. Although it might seem that combination therapy is not required, a larger focused study is required to address this question with certainty. Clinicians should be aware of possible adverse events related to the upper respiratory and nasopharygeal regions with vedolizumab. We show preliminary data suggesting that shortening infusion interval to 4 weeks may improve effectiveness in some patients. The currently enrolling prospective multicentre VEDOKIDS cohort study will further define the role of vedolizumab in paediatric IBD and will provide trough drug monitoring data to predict the success and required dosing in children.

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This was an investigator-initiated study with no external funding provided. All data were generated as part of routine clinical practice and were analysed independently for the purpose of this study.

Conflict of Interest

OL received travel grants from Ferring and Takeda. AL received research grants, honoraria, and travel grants, or participated in advisory boards or activities organised by MSD, Janssen, Abbvie and Abbott, Falk, Takeda, and Nestle. JCE received research support from MSD and advisory board honoraria from AbbVie and Janssen. LdR received consultation fees, research grants, or honoraria from Shire, Merck, Janssen, Abbvie, and Pfizer. FR received consultation fees from Takeda. AR recived from the advisory board of Abbvie. HHU declares industrial project collaboration with Eli Lilly and UCB Pharma. CP received travel grants from Abbvie and MSD, and participated in advisory boards organised by MSD and Abbvie. KLK received consultation fees from Ferring and Tilllotts Pharma and advisory board honoraria from Abbvie and MSD. JB received sponsorship from Abbvie and MSD. DT received consultation fees, research grants, royalties, or honoraria from Janssen, Pfizer, Hospital for Sick Children, Ferring, MegaPharm, AstraZeneca, Abbvie, Takeda, Rafa, Boehringer Ingelheim, Biogen, Atlantic Health, and Shire. AA, RS, NS, VMW, DS, SC, CJ, TdM, JMdC, LR, and MF declare no conflict of interest.

Author Contributions

Authors have made substantial contributions to the following: the concept and design of the study: OL, DT; acquisition of data: OL, AA, AL, JE, LdR, FR, NS, RS, VW, AR, HU, CP, KLK, CJ, SC, DS, TdM, JMdC, LR, JB, DT; analysis and interpretation of data: OL, MF, DT; drafting the article: OL, DT; critical review and approval of draft: all authors.

Supplementary Data

Supplementary data are available at *ECCO-JCC* online.

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