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Research article

Real-life treatment persistence and treatment outcomes of Finnish patients with inflammatory bowel disease receiving vedolizumab as first-line biological treatment

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ABSTRACT

Purpose: To analyze treatment persistence and treatment outcomes of vedolizumab as first-line biological treatment in Crohn's disease (CD) and ulcerative colitis (UC) patients in a Finnish real-world setting.
Methods: Observational, retrospective, multi-center chart review study that included adult CD and UC patients initiating vedolizumab as first-line biological treatment between 2014 and 2020.
Results: The cohort consisted of 54 CD and 69 UC patients. At month 12, treatment persistence was 84.9 % in CD and 64.7 % in UC. Most vedolizumab discontinuations (CD, n = 11; UC, n = 26) were due to inefficacy. Discontinuations due to adverse events were rare (n < 5). Efficacy improvements were observed in treatment persistent patients at 12 months vs. baseline in the Harvey-Bradshaw Index (CD, 1.8 vs. 3.9, p = 0.001), Partial Mayo Score (UC, 1.0 vs. 4.9, p < 0.001), Physician's Global Assessment (CD, 0.9 vs. 1.8, p < 0.001; UC, 0.4 vs. 2.1, p < 0.001), along with positive endoscopic and biochemical outcomes. Clinical remission was 90.9 % vs. 63.0 % for CD, and 81.6 % vs. 12.3 % for UC, while corticosteroid use was 15.9 % vs. 53.7 % for CD, and 14.6 % vs. 92.8 % for UC at 12 months and baseline, respectively.
Conclusion: Vedolizumab was associated with improvements in efficacy, endoscopic activity, biochemical parameters, and decreased corticosteroid burden when used as a first-line biological treatment.

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1. Introduction

Crohn's disease (CD) and ulcerative colitis (UC) are inflammatory bowel diseases (IBDs) characterized by cycles of remission, relapse, and exacerbation of inflammation. The key symptoms include chronic abdominal pain, bloody diarrhea, weight loss, and fatigue [1]. IBD is a lifelong disease and has a significant, negative impact on the patient's quality of life [2]. The prevalence of IBD is increasing rapidly in all western countries, causing a significant burden of disease, which emphasizes the need for improved treatment strategies [3].

Vedolizumab is a gut-selective monoclonal antibody which reduces lymphocyte trafficking by targeting integrin $\alpha_4\beta_7$ [4]. It is indicated for the treatment of patients with moderate to severe CD, UC, or active chronic pouchitis. The efficacy and safety of vedolizumab have been well-established in randomized clinical trials and real-world evidence studies [5–12].

With an increasing number of treatment options for IBD, it is important to understand the efficacy and safety of these treatments in different patient groups and phases of treatment. Clinical trial data have suggested that biological-naive patients treated with vedolizumab achieve better treatment outcomes compared to anti-TNF (tumor necrosis factor) experienced patients [13,14]. The VARSITY trial showed that vedolizumab is superior in inducing clinical remission and endoscopic improvement with moderate-to-severe UC compared to adalimumab, and the effect was particularly evident among biological-naive patients [12]. A recent systematic review with meta-analysis found that CD and UC patients treated with vedolizumab have more favorable efficacy and safety outcomes in patients without previous exposure to biological treatment [15].

Despite existing evidence, supporting data on the real-world clinical benefit of vedolizumab in biological-naive patients in different populations and patient groups are essential for making informed clinical treatment choices. Therefore, we set out to analyze treatment persistence, treatment outcomes, and reasons for treatment discontinuation of vedolizumab as a first-line biological treatment in CD and UC patients in a real-world setting in Finland.

2. Material and methods

2.1. Study cohort and data collection

The study cohort included all adult ($\geq$18 years of age) patients with a diagnosis of CD (K50; The International Classification of Diseases, 10th revision) or UC (K51) who initiated vedolizumab as a first-line biological treatment between May 2014 and June 2020, in the five Finnish university hospital districts (Helsinki University Hospital, Tampere University Hospital, Turku University Hospital, Kuopio University Hospital, and Oulu University Hospital). Patients were followed-up from the first vedolizumab infusion (index date) until treatment discontinuation or end of follow-up. The baseline period was 12 months before the index date and the end of the study period was December 31, 2020. The induction phase was defined as $\leq$14 weeks and the maintenance phase as >14 weeks of treatment.

Vedolizumab was administered in routine care, and data were collected from the electronic health records by direct electronic retrieval and manual data collection by local gastroenterologists. Data on prescribed medications were collected from the Register for Reimbursed Drugs (The Social Insurance Institution of Finland).

2.2. Variables and outcome measures

The following information on demographics and clinical characteristics were collected at baseline: gender, diagnosis, age at diagnosis, age at vedolizumab start, height, weight, smoking status, selected comorbidities, extraintestinal manifestations, complications, and anatomic disease location and disease behavior according to the Montreal classification. The dates of vedolizumab administration were collected throughout the follow-up.

The primary outcome measure was treatment persistence 12 months post-vedolizumab initiation, defined as the time from initiation to discontinuation of therapy. Descriptive information on the reasons of discontinuation and the treatment choice after vedolizumab were collected for patients who discontinued vedolizumab during the study period. Reasons for treatment discontinuations were primary lack of response (no response during the 14 weeks of treatment as defined by the physician), secondary loss of response (loss of response after initial response as defined by the physician), adverse event, and other reasons (surgery, pregnancy, lost-to-follow-up, remissions, or other reported reasons). The assessment of clinical disease activity was based on Harvey-Bradshaw Index (HBI) in CD and Partial Mayo Score (pMS) in UC. Additionally, the Physician's Global Assessment (PGA) was used to evaluate disease activity in both CD and UC, with a PGA rating scale of: remission (0), mild (1), moderate (2), or severe (3) disease. Clinical response, remission (defined as HBI$\leq$4 in CD and as pMS<3 plus a combined stool frequency and rectal bleeding sub-score of $\leq$1 in UC), and steroid-free remission were determined according to standard criteria for those patients who persisted on vedolizumab and had both HBI and pMS recorded at the time point [16,17].

Endoscopic scoring was made using the Simple Endoscopic Score (SES-CD) for CD and the Mayo endoscopic score (MES) for UC [18,19]. Endoscopic healing was defined as SES-CD$\leq$2 in CD and MES$\leq$1 in UC. The following laboratory measures were electronically collected throughout the follow-up period: C-reactive protein (CRP), fecal calprotectin (fCal), B-hemoglobin (Hb), B-thrombocytes (TC), white blood cell count (WBC), and S-albumin. Moreover, information on vedolizumab trough concentrations and presence of vedolizumab anti-drug antibodies were retrieved. The vedolizumab trough concentration target was defined as >20 mg/ml during induction therapy and 5–15 mg/ml during maintenance therapy, according to the laboratory reference [20,21]. Data on the use of the following conventional pharmacotherapies were collected from the Register for Reimbursed Drugs: azathioprine, 6-mercaptopurine, methotrexate, 5-aminosalicylic acid, corticosteroids, and antibiotics.

2.3. Statistical analyses

Descriptive statistics were presented by number and proportion of patients for categorical variables, and by the mean, median, standard deviation (SD), and first and third quartiles (Q1, Q3) for continuous variables. Treatment persistence was estimated using the Kaplan-Meier method and presented as a proportion of patients continuing the treatment, discontinuation being the failure event. Normally distributed continuous variables were tested by unpaired *t*-test or one-way analysis of variance test and non-normally distributed variables by Kruskal Wallis test (Mann-Whitney *U* test for two groups). Changes in clinical, endoscopic, and biochemical outcomes were analyzed using a paired sample *t*-test or Wilcoxon Rank sum test. Statistical significance was considered when $p < 0.05$. Data were analyzed using R version 3.6.3 (https://www.r-project.org/).

3. Results

3.1. Patient characteristics

The study cohort consisted of 54 CD and 69 UC patients treated with vedolizumab as a first-line biological treatment (Table 1). A slightly higher proportion of patients in the CD cohort were female (51.9 %), whereas most patients in the UC cohort were male (63.3 %). The mean ages of CD and UC patients at the time of vedolizumab treatment initiation were 61.9 and 56.8 years, respectively. The mean time from diagnosis to start of vedolizumab treatment was 10.9 years in CD and 10.5 years in UC patients. The mean follow-up times were 25.5 (±15.2) and 19.8 (±16.6) months in CD and UC cohorts ($p = 0.018$), respectively.

According to the Montreal classification, there were equal numbers of CD patients with ileal (L1, 43.1 %) and ileocolonic (L3, 43.1 %) disease (Table 1). The predominant behavioral phenotype was non-stricturing, non-penetrating (B1, 43.4 %), followed by

Table 1
Baseline characteristics of patients diagnosed with Crohn's disease or ulcerative colitis and who initiated vedolizumab as a first-line biological treatment.

	Crohn's disease (n = 54)	Ulcerative colitis (n = 69)
Sex, n (%)		
Female	28 (51.9 %)	26 (36.7 %)
Male	26 (48.1 %)	43 (63.3 %)
Age (years), mean (SD)		
Age at diagnosis	51.3 (18.7)	45.8 (19.5)
Age at vedolizumab start	61.9 (13.5)	56.8 (17.1)
Time from diagnosis to vedolizumab start (years), mean (SD)	10.9 (13.0)	10.5 (11.2)
BMI, n (%)		
18–25	18 (36.0 %)	24 (42.9 %)
25–30	22 (44.0 %)	22 (39.3 %)
30–40	10 (20.0 %)	10 (17.9 %)
Missing n	<5	13
Smokers, n (%)		
Current	11 (20.8 %)	5 (8.2 %)
Former	21 (39.6 %)	22 (36.1 %)
Never Smoker	21 (39.6 %)	34 (55.7 %)
Missing n	<5	8
Surgery history, n (%)		
Yes	5 (9.3 %)	<5
No	48 (90.7 %)	58 (96.7 %)
Missing n	<5	9
HBI, mean (SD)	3.6 (2.6)	NA
Missing n	17	NA
pMS, mean (SD)	NA	4.9 (1.9)
Missing n	NA	<5
Montreal classification, n (%)		
A1: < 17 years	<5	NA
A2: 17–40 years	17 (31.1 %)	NA
A3: > 40 years	35 (66.0 %)	NA
L1: ileum	22 (43.1 %)	NA
L2: colon	7 (13.7 %)	NA
L3: ileocolon	22 (43.1 %)	NA
L4: upper gastrointestinal tract	<5	NA
B1: inflammatory	23 (43.4 %)	NA
B2: stricturing	21 (39.6 %)	NA
B3: penetrating	9 (17.0 %)	NA
p: perianal disease	<5	NA
E1: ulcerative proctitis	NA	<5
E2: left side ulcerative colitis	NA	26 (40.6 %)
E3: extensive colitis	NA	36 (56.3 %)

Abbreviations. BMI, Body mass index; HBI, Harvey-Bradshaw Index; NA, not applicable; pMS, partial Mayo score; SD, standard deviation.

stricturing (B2, 39.6 %) disease. Most UC patients had extensive colitis (56.3 %). The mean baseline HBI was 3.6 for the CD cohort, whereas the mean pMS was 4.9 for the UC cohort. Altogether, five CD patients and less than five UC patients had undergone intestinal surgery (including 2 patients with colectomy) before the index day.

The most common comorbidities were hypertension (CD, 44.4 %; UC, 30.4 %), cancer (CD, 37.0 %; UC, 34.8 %), other cardiac diagnosis (CD, 27.8 %; UC, 14.5 %), and type 2 diabetes (CD, 18.5 %; UC, 15.9 %) (Table 2). Most patients did not have extraintestinal manifestations (CD, 79.6 %; UC, 91.3 %) or complications (CD, 75.9 %; UC, 95.7 %). Obstruction (14.8 %) was the most common complication in CD.

3.2. Treatment persistence and reasons for discontinuation

Altogether, 92.6 % and 84.9 % of patients with CD persisted on vedolizumab treatment at months 6 and 12, respectively. In the UC cohort, 75.1 % of patients persisted on vedolizumab treatment at month 6 and 64.7 % at month 12. The CD cohort had a higher treatment persistence rate throughout the follow-up compared with the UC cohort ($p = 0.008$) (Fig. 1).

In the CD cohort, vedolizumab was mostly discontinued due to secondary loss of response (46.2 % of discontinuations), followed by primary lack of response (38.5 %) (Table 3). In the UC cohort, primary lack of response was the most common reason for treatment discontinuation (68.8 %). Less than five patients (<4 %) discontinued vedolizumab due to adverse events. Events leading to treatment discontinuation included infection, hypersensitivity to vedolizumab, liver transplantation, and lymphoma. Altogether, 46.2 % of CD patients and 40.6 % of UC patients who discontinued vedolizumab switched to another biological treatment, most commonly to infliximab (50.0 % of CD and 76.9 % of UC patients).

3.3. Clinical effectiveness for persistent patients at month 12

Significant HBI ($\Delta HBI = -2.2$; $p = 0.001$) and PGA ($\Delta PGA = -0.9$; $p < 0.001$) improvements were observed from baseline to month 12 in treatment-persistent CD patients (Table 4). Similarly, there were significant changes in pMS ($\Delta pMS = -3.8$; $p < 0.001$) and PGA ($\Delta PGA = -1.6$; $p < 0.001$) from baseline to month 12 in the UC cohort. At month 12, 37.9 % of CD patients and 70.3 % of UC patients showed clinical response (Table 5). Clinical remission was observed in 90.9 % of CD patients and 81.6 % of UC patients at month 12. The corresponding remission rate was 63.0 % in the CD cohort and 12.3 % in the UC cohort at the baseline. A total of 26/30 CD patients and 27/31 UC patients in clinical remission had steroid-free remission 12 months after vedolizumab start.

Table 2
Comorbidities, extraintestinal manifestations, and complications in the study cohort.

	Crohn's disease (n = 54)	Ulcerative colitis (n = 69)
Comorbidities, n (%)		
Hypertension	24 (44.4 %)	21 (30.4 %)
Heart failure	5 (9.3 %)	<5
Coronary artery disease	6 (11.1 %)	5 (7.2 %)
Other cardiac diagnosis	15 (27.8 %)	10 (14.5 %)
Type 1 diabetes	0	<5
Type 2 diabetes	10 (18.5 %)	11 (15.9 %)
Psoriasis	0	<5
Arthritis or Ankylosing spondylitis	<5	0
Multiple sclerosis	<5	<5
History of tuberculosis	<5	0
Other serious infection	<5	<5
History of cancer	20 (37.0 %)	24 (34.8 %)
Chronic obstructive pulmonary disease	6 (11.1 %)	<5
No other diagnosis	0	0
Extraintestinal manifestations, n (%)		
Any	11 (20.4 %)	6 (8.7 %)
Arthralgia	<5	<5
Arthritis	<5	<5
Sacroiliitis	<5	<5
Pyoderma gangrenosum	0	0
Erythema nodosum	0	0
Episcleritis	0	0
Primary sclerosing cholangitis	<5	<5
No Extraintestinal manifestations	43 (79.6 %)	63 (91.3 %)
Complications, n (%)		
Fistula	<5	<5
Abscess	0	0
Obstruction	8 (14.8 %)	<5
No complications	41 (75.9 %)	66 (95.7 %)

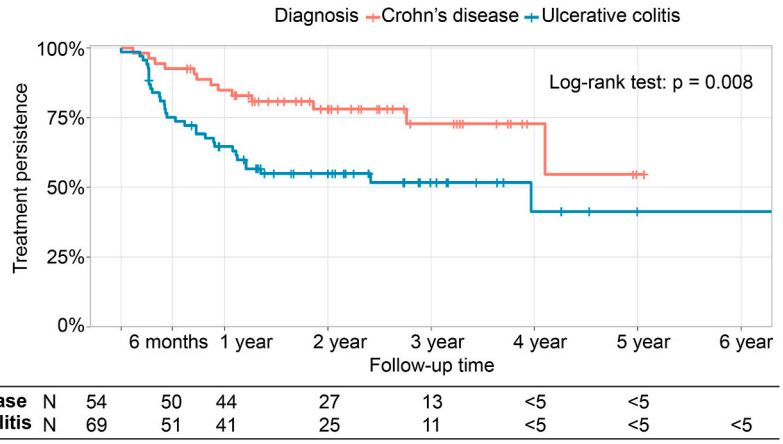

Fig. 1. Treatment persistence of vedolizumab as first-line biological treatment in CD and UC patients. Treatment persistence was estimated using the Kaplan-Meier method and presented as a proportion of patients continuing the treatment, discontinuation being the failure event.

Table 3
Reasons for vedolizumab discontinuation and treatment choice after the discontinuation.

	Crohn's disease (n = 13)	Ulcerative colitis (n = 32)
Reason of discontinuation, n (%)		
Discontinuation due to adverse event	<5	<5
Primary lack of response	5 (38.5 %)	22 (68.8 %)
Secondary loss of response	6 (46.2 %)	<5
Discontinuation due to other reason	<5	<5
Missing	0	0
Switch to another biological, n (%)		
No	7 (53.8 %)	19 (59.4 %)
Yes	6 (46.2 %)	13 (40.6 %)
Missing	0	0
Biological treatment after vedolizumab, n (%)		
Infliximab	<5	10 (76.9 %)
Adalimumab	0	<5
Golimumab	0	<5
Ustekinumab	<5	<5

3.4. Endoscopic outcomes for persistent patients at month 12

In the CD cohort, only six treatment-persistent patients had SES-CD scores available both at baseline and month 12. In these patients, there was a decrease in SES-CD during the 12-month follow-up (ΔSES-CD = −5.5; p = 0.05) (Table 4). Endoscopic healing was observed in 23.1 % (6/26) of CD patients who had endoscopic data available at baseline and in 50.0 % (6/12) of those patients at month 12. A significant decrease of the endoscopic Mayo score was observed in the UC cohort from baseline to month 12 (Δ_{MES} = −1.8, p < 0.001) (Table 4). Endoscopic healing was observed in 10.4 % (5/48) of UC patients having data available at baseline and 85.7 % (12/14) of patients at month 12.

3.5. Biochemical outcomes for persistent patients at month 12

There were significant improvements in median fecal calprotectin values from baseline to month 12 in both CD (Δ_{fCal} = −168.0 µg/g; p = 0.003) and UC (Δ_{fCal} = −387.0 µg/g; p = 0.026) cohorts (Table 4). In both CD and UC cohorts, the CRP values were within the reference range (<10 mg/l) throughout the first 12 months of follow-up and no significant changes were observed. Conversely, there were statistically significant changes in mean thrombocytes (Δ_{TC} = −23.2 E9/l, p = 0.010), hemoglobin (Δ_{Hb} = 3.6 g/l, p = 0.038), and white blood cell count (Δ_{WBC} = −2.0 E9/l, p = 0.002) in the UC cohort (Supplementary Tables 1 and 2).

3.6. Vedolizumab dosing frequency

In total, seven (13.0 %) CD patients and eight (11.6 %) UC patients had an additional infusion between weeks 9 and 11. In the maintenance phase, the median dosing interval was 56.0 days, which equals an 8-week dosing interval.

Table 4
Changes in the Harvey-Bradshaw Index, partial Mayo score physician's global assessment, endoscopic scores (SES-CD and MES), calprotectin, and C-reactive protein from baseline to month 12. Only treatment-persistent patients at month 12 (CD, n = 44; UC, n = 41) are included in the analyses.

	Baseline		12 months		12 months vs. baseline		
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	p-value
Crohn's Disease							
HBI	28	3.9 (2.5)	24	1.8 (2.0)	19	−2.2 (2.4)	**0.001**
Missing	16		20		25		
PGA	43	1.8 (0.7)	36	0.9 (0.8)	36	−0.9 (1.0)	**<0.001**
Missing	<5		8		8		
SES-CD	21	6.9 (5.3)	12	2.9 (2.7)	6	−5.5 (5.2)	**0.05**
Missing	23		32		38		
fCal (μg/g)	42	531.6 (525.3)	28	309.2 (294.5)	27	−275.4 (438.0)	**0.003**
Median (Q1, Q3)		332.0 (166.0, 721.8)		245.0 (67.5, 494.5)		−168.0 (−392.0, 15.5)	
Missing	<5		16		17		
CRP (mg/l)	39	6.9 (13.7)	43	6.7 (13.3)	39	0.4 (19.7)	0.908
Missing	<5		<5		<5		
Ulcerative colitis							
pMS	39	4.9 (1.9)	38	1.0 (1.0)	37	−3.8 (2.3)	**<0.001**
Missing	<5		<5		<5		
PGA	41	2.1 (0.6)	38	0.4 (0.6)	38	−1.6 (0.8)	**<0.001**
Missing	0		<5		<5		
MES	30	2.2 (0.7)	14	0.7 (0.9)	12	−1.8 (1.1)	**<0.001**
Missing	11		27		29		
fCal (μg/g)	37	1661.8 (2019.9)	28	492.6 (1123.9)	24	−1213.9 (2503.1)	**0.026**
Median (Q1, Q3)		883.0 (307.0, 2150.0)		115.5 (16.8, 328.8)		−387.0 (−1481.8, −27.8)	
Missing	<5		13		17		
CRP (mg/l)	30	4.6 (5.6)	38	6.5 (23.0)	28	4.6 (26.6)	0.365
Missing	11		<5		13		

Abbreviations. CRP, C-reactive protein; fCal, fecal calprotectin; HBI, Harvey-Bradshaw Index; MES, Mayo endoscopic score; PGA, physician's global assessment; pMS, partial Mayo score; SD, standard deviation; SES-CD, simple endoscopic score.

Table 5
The number and proportion of treatment-persistent CD and UC patients with a clinical response, remission, and steroid-free remission at baseline, month 6, and month 12.

Treatment outcome	Crohn's disease			Ulcerative colitis		
	Baseline (n = 54)	6 months (n = 50)	12 months (n = 44)	Baseline (n = 69)	6 months (n = 51)	12 months (n = 41)
Clinical response, n (%)	NA	10 (34.5 %)	11 (37.9 %)	NA	19 (55.9 %)	26 (70.3 %)
Patients with outcome available, n (%)	NA	29 (58.0 %)	29 (65.9 %)	NA	30 (58.8 %)	7 (90.2 %)
Endoscopic healing, n (%)	6 (23.1 %)	<5	6 (50.0 %)	5 (10.4 %)	6 (75.0 %)	12 (85.7 %)
Patients with outcome available, n (%)	34 (63.0 %)	5 (10.0 %)	12 (27.3 %)	48 (69.6 %)	8 (15.7 %)	14 (34.1 %)
Clinical remission n (%)	29 (63.0 %)	31 (96.9 %)	30 (90.9 %)	8 (12.3 %)	24 (75.0 %)	31 (81.6 %)
Patients with outcome available, n (%)	46 (85.1 %)	32 (64.0 %)	33 (75.0 %)	65 (94.2 %)	32 (62.7 %)	38 (92.7 %)
Steroid-free remission, n (%)	12 (26.1 %)	22 (68.8 %)	26 (78.8 %)	<5	14 (43.8 %)	27 (71.1 %)
Patients with outcome available, n (%)	46 (26.1 %)	32 (64.0 %)	33 (75.0 %)	65 (94.2 %)	32 (62.7 %)	38 (92.7 %)

Abbreviations. NA, not applicable.

3.7. Vedolizumab trough concentrations and anti-drug antibodies

In the induction phase, the mean vedolizumab trough concentrations were 32.5 mg/ml in CD (n = 11) and 25.0 mg/ml in UC (n = 14) patients. The trough level was below the threshold (20 mg/ml) in one (1/11; 9.1 %) CD patient and seven (7/14; 50.0 %) UC patients. During the maintenance treatment, the mean trough concentrations in CD and UC cohorts were 13.7 mg/ml (n = 28) and 21.6 mg/ml (n = 21), respectively. Altogether, five CD patients (5/28; 17.9 %) and less than five UC patients had vedolizumab concentrations below the target level (5 mg/ml) during the maintenance phase. Anti-drug antibodies were not identified in any of the patients.

3.8. Concomitant treatments

The proportion of patients using corticosteroids, 5-aminosalicylic acid, methotrexate, antibiotics, 6-mercaptopurine, or

azathioprine during the first year of follow-up is shown in Table 6. Most patients in both CD (53.7 %) and UC (92.8 %) cohorts used corticosteroids at baseline, but there was a marked reduction in corticosteroid use during the first 12 months of vedolizumab treatment. In the CD cohort, only 18.0 % of treatment-persistent patients used corticosteroids at month 6 and 15.9 % at month 12. In the UC cohort, the proportion of treatment-persistent patients using corticosteroids at month 6 was 45.1 % and 14.6 % at month 12.

4. Discussion

In this real-life, retrospective, observational study we observed high treatment persistence and remission rates, as well as positive clinical, biochemical, and endoscopic treatment outcomes of vedolizumab in a Finnish cohort of biological-naive patients with CD or UC. The results also indicate that vedolizumab has a major corticosteroid-sparing effect and good tolerability in this patient population.

In this study cohort of 123 biological-naive IBD patients, the mean age was higher than in our earlier study (FINVEDO), in which data on patients receiving vedolizumab from any treatment line was collected (CD, 61.9 vs. 40.3 years; UC, 56.8 vs. 37.5 years) [22]. Over one-third of patients had a history of cancer, and cardiovascular disorders were common at baseline. According to recent evidence, the incidence of IBD is increasing especially among the elderly in Finland [23]. These are more fragile patients with a history of co-existing cancer and increased risk for infections due to immunosuppression. Thus, there is an increasing need for treatments with minimal impact on systemic immunosuppression. These patients are not eligible for systemic cytokine therapy, and similar to earlier studies, the presence of comorbidities, especially cancer, and older age were likely among the main reasons for choosing vedolizumab as the first-line biological in this cohort [15,24,25].

High treatment persistence rates were observed in this cohort. At month 6, 92.6 % of CD patients and 75.1 % of UC patients persisted on vedolizumab treatment, while at month 12, treatment persistence was 84.9 % in the CD and 64.7 % in the UC cohort. These are higher rates than the ones reported earlier for Italian (CD, 55.7 %; UC, 50.0 %) and Australian first-line vedolizumab CD patients (CD, 78.6 %) [24,26]. Bressler and colleagues reported a similar vedolizumab treatment persistence rate of 84.0 % in CD as observed in this study, but a higher treatment persistence of 82.3 % in UC at month 12 in biological-naive patients from Canada, Greece, and the USA [27]. Similarly, Bokemeyer et al. (83 %), Dotti et al. (89.3 %), and Sablich et al. (78 %) reported higher treatment persistence rates at month 12 in biological-naive German, Brazilian, and Italian UC patients [28–30].

After two years of follow-up, lower treatment persistence rates were reported for CD (Bressler et al., 67.2 %; Pudippedi et al., 66.4 %), but higher treatment persistence rates were observed in UC patients (Bressler et al., 76.3 %; Bokemeyer et al., 71 %) compared to what was observed in this study (CD, 78.0 %; UC, 54.9 %) [26–28]. Less than five patients in the total study cohort discontinued treatment due to adverse events, which indicates good tolerability and safety of vedolizumab in real-life clinical practice, in line with previous observations [24,29–31].

We observed statistically significant improvements in clinical indices and calprotectin during the first year of follow-up among treatment-persistent IBD patients. Additionally, a significant decrease in the Mayo endoscopic score was observed from baseline to month 12 in the UC cohort, but the low availability of SES-CD scores at baseline and at month 12 limited the possibilities to analyze endoscopic outcomes in CD. At month 12, 50 % of treatment-persistent CD patients and 85.7 % of treatment-persistent UC patients who had endoscopic data available achieved endoscopic healing. These results of positive clinical, biochemical, and endoscopic outcomes are in line with the earlier evidence from other biological-naive study cohorts in real-world settings [15,24,26,27,30,31].

At month 12, 78.8 % of treatment-persistent CD patients were in steroid-free remission. At month 6, higher remission (96.9 % vs. 41.8 %) and steroid-free remission (68.8 % vs. 36.5 %) rates were observed for CD patients in this study compared with the Finnish study of unselected vedolizumab patients [22]. The CD cohorts for both studies had different characteristics at baseline. Our earlier FINVEDO study had a CD cohort with a more complicated disease course than the CD cohort we describe here, which may contribute to the higher clinical remission and steroid-free remission rates observed. Our observation is in line with earlier reports indicating that biological-naive patients may have better treatment outcomes compared to anti-TNF-experienced patients [13,14].

In the UC cohort, remission and steroid-free remission were observed in 81.6 % and 71.1 % of patients at month 12, respectively. A similar remission rate for UC patients at 6 months was observed in this study compared to the previous Finnish study (75 % vs. 73.3 %), but for steroid-free remission, lower rates (43.8 % vs. 65.1 %) were observed. Our observations at 6 months are closer to the steroid-free remission rate of 30 % reported in a systematic review [15]. Our results are in agreement with the clinical remission rate of 75 % reported in a German study, and close to a steroid-free remission rate of 60.7 % reported in a similar vedolizumab first-line Italian

Table 6
Proportion of treatment-persistent CD and UC patients using conventional treatments at baseline and during the follow-up.

	Crohn's disease			Ulcerative colitis		
	Baseline	6 months	12 months	Baseline	6 months	12 months
	(n = 54)	(n = 50)	(n = 44)	(n = 69)	(n = 51)	(n = 41)
Concomitant medications, n (%)						
Corticosteroids	29 (53.7 %)	9 (18.0 %)	7 (15.9 %)	64 (92.8 %)	23 (45.1 %)	6 (14.6 %)
5-aminosalicylic acid	5 (9.3 %)	0 (0.0 %)	0 (0.0 %)	22 (31.9 %)	<5	0 (0.0 %)
Methotrexate	13 (24.1 %)	<5	0 (0.0 %)	<5	<5	<5
6- mercaptopurine or Azathioprine	27 (50.0 %)	5 (10.0 %)	<5	41 (59.5 %)	6 (11.8 %)	<5
Antibiotics	15 (27.8 %)	7 (14.0 %)	<5	16 (23.2 %)	<5	<5

study [24,29].

A high steroid-free remission of 94 % at the end of follow-up in biological-naive UC patients who used steroids at baseline was reported for the same German UC cohort [29].

In this study, the UC cohort had lower treatment persistence, remission, and steroid-free remission rates than the CD cohort. Such differences have also been previously reported for treatment persistence by Macaluso et al. and Moens et al. [24,32]. Our observations suggest that patients in the UC cohort had a more complicated disease course than patients in the CD cohort. The disease activity in the UC cohort was moderate even if over 90 % of patients used corticosteroids at baseline (vs. 54 % in the CD cohort). Furthermore, 12 % of UC patients were in remission at baseline compared to over 60 % in the CD cohort.

Based on the dosing frequency observed, vedolizumab was used according to the summary of product characteristics [33]. The proportion of patients who reached the target therapeutic concentration of vedolizumab during induction and maintenance therapies was similar in this cohort to that reported earlier [21]. Based on a recent meta-analysis, patients with UC who achieve endoscopic and clinical remission have significantly higher vedolizumab trough concentrations during maintenance therapy [34]. However, a similar effect was not observed in patients with CD. Therefore, the therapeutic significance of vedolizumab trough level measurements in real-life clinical practice remains unclear [21,34].

A major reduction in corticosteroid use was observed during the first 12 months of vedolizumab treatment in both patient groups. Both indications had a similar proportion of patients using corticosteroids at month 12 but tapering off was faster in the CD cohort. Also, other concomitant treatments were discontinued during the follow-up, preventing patients from possible immunosuppression-related harm.

The key limitations of this study were both potential variations in data recording and incomplete recording of variables for some patients. Some analyses were limited by the small number of patients with available data variables. In addition, this study only included patients who had vedolizumab as the first-line biological treatment, without any comparator group of either conventional therapy or other biologics. Despite the differences in healthcare systems and treatment practices between different countries, this study provides important additional information on the use of vedolizumab in biological-naive patients.

In conclusion, here we have shown further evidence that vedolizumab has high treatment persistence and positive treatment outcomes when used as the first-line biological treatment. The low number of discontinuations due to adverse events suggests good tolerability in real-life clinical practice. Importantly, vedolizumab seems to have a significant positive impact on corticosteroid burden. These results support existing evidence demonstrating that vedolizumab is a valuable treatment option for biological-naive IBD patients.

Data availability statement

Has data associated with your study been deposited into a publicly available repository?

Answer: No. The authors do not have permission to share data. According to the Finnish legislation, access to individual-level data is restricted only to individuals named in the study permit. The study protocol is available upon request from the corresponding author.

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Ethics approval statement

This study was reviewed and approved by the Finnish Data Permit Authority, Findata, with the approval number: THL/6750/14.02.00/2020.

Informed consent was not required for this study because according to the Finnish legislation (Act on the Secondary Use of Health and Social Data (552/2019) by the Ministry of Social Affairs and Health), the patients included in the study cohort were not contacted, and the study did not affect the treatment of the patients.

Review and/or approval by an ethics committee was not needed for this study because according to the Finnish legislation (Act on the Secondary Use of Health and Social Data (552/2019) by the Ministry of Social Affairs and Health), the patients included in the study cohort were not contacted, and the study did not affect the treatment of the patients. The study was conducted in accordance with the Helsinki Declaration of 1975, Good Pharmacoepidemiology Practices, and Data Protection Directive.

Previous presentations

Abstract + Poster at the 18th Congress of ECCO; Copenhagen, Denmark; 1–4 March 2023.

CRediT authorship contribution statement

Tero Ylisaukko-oja: Writing – original draft, Methodology, Conceptualization. **Clas-Göran af Björkesten:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Anja Eberl:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Heikki Nuutinen:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Airi Jussila:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Pauliina Molander:** Writing – review & editing,

Methodology, Data curation, Conceptualization. **Ritva Koskela:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Timo Blomster:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Markku Pajala:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Tuire Ilus:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Paula Haiko:** Writing – review & editing, Funding acquisition, Conceptualization. **Bianca Kovac:** Writing – review & editing, Funding acquisition. **Saija Silvola:** Writing – review & editing, Funding acquisition, Conceptualization. **Sarah Smith:** Writing – review & editing, Project administration, Methodology, Data curation. **Jari Jokelainen:** Formal analysis. **Taina Sipponen:** Writing – review & editing, Methodology, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Tero Ylisaukko-oja reports financial support was provided by MedEngine Oy. Sarah Smith reports financial support was provided by MedEngine Oy. Jari Jokelainen reports financial support was provided by MedEngine Oy. Paula Haiko reports financial support was provided by Takeda Oy. Anja Eberl reports was provided by Janssen-Cilag SAS. Clas-Göran af Björkesten reports financial support was provided by AbbVie Inc. Clas-Göran af Björkesten reports financial support was provided by Bristol Myers Squibb Co. Clas-Göran af Björkesten reports financial support was provided by Janssen Pharmaceuticals Inc. Clas-Göran af Björkesten reports financial support was provided by Merck Sharp & Dohme Corp. Clas-Göran af Björkesten reports financial support was provided by Pfizer Inc. Clas-Göran af Björkesten reports financial support was provided by Takeda Oy. Clas-Göran af Björkesten reports financial support was provided by Mylan Pharmaceuticals Inc. Clas-Göran af Björkesten reports financial support was provided by Ferring Pharmaceuticals Inc. Clas-Göran af Björkesten reports financial support was provided by Vifor (International) AG. Heikki Nuutinen reports financial support was provided by Takeda Oy. Pauliina Molander reports financial support was provided by AbbVie Oy. Pauliina Molander reports financial support was provided by Bristol Myers Squibb Co. Pauliina Molander reports financial support was provided by Gilead Sciences. Pauliina Molander reports financial support was provided by Janssen-Cilag SAS. Pauliina Molander reports financial support was provided by Orion Corporation. Pauliina Molander reports financial support was provided by Pfizer. Pauliina Molander reports financial support was provided by Sandoz Inc. Pauliina Molander reports financial support was provided by Takeda Oy. Pauliina Molander reports financial support was provided by Tillotts Pharma AG. Pauliina Molander reports financial support was provided by Viatris. Ritva Koskela reports financial support was provided by Pfizer Inc. Ritva Koskela reports financial support was provided by Vifor (International) AG. Ritva Koskela reports financial support was provided by Janssen Pharmaceuticals Inc. Ritva Koskela reports financial support was provided by Takeda Oy. Ritva Koskela reports financial support was provided by Ferring Pharmaceuticals Inc. Taina Sipponen reports financial support was provided by AbbVie Oy. Taina Sipponen reports financial support was provided by Bristol Myers Squibb Co. Taina Sipponen reports financial support was provided by Pfizer. Taina Sipponen reports financial support was provided by Takeda Oy. Taina Sipponen reports financial support was provided by Celltrion, Inc. Taina Sipponen reports financial support was provided by Janssen-Cilag SAS. Tero Ylisaukko-oja reports a relationship with MedEngine Oy that includes: equity or stocks.

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Appendix A. Supplementary data

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Abbreviations list

BMI	Body mass index
CD	Crohn's Disease
CRP	C-reactive protein
CS	Corticosteroids
fCal	Fecal calprotectin
Hb	B-hemoglobin
HBI	Harvey-Bradshaw Index
IBD	Inflammatory Bowel Disease
MES	Mayo endoscopic score
NA	Not applicable
PGA	Physician's Global Assessment
pMS	Partial Mayo Score
Q1	First quartile
Q3	Third quartile
SD	Standard deviation

SES-CD	Simple Endoscopic Score
TC	B-thrombocytes
TNF	Tumor necrosis factor
UC	Ulcerative colitis
WBC	White blood cell count

References

[1] C. Abraham, J.H. Cho, Inflammatory bowel disease, N. Engl. J. Med. 361 (2009) 2066–2078, https://doi.org/10.1056/NEJMra0804647.
[2] S.R. Knowles, L.A. Graff, H. Wilding, C. Hewitt, L. Keefer, A. Mikocka-Walus, Quality of life in inflammatory bowel disease: a systematic review and meta-analyses-Part I, Inflamm. Bowel Dis. 24 (2018) 742–751, https://doi.org/10.1093/ibd/izx100.
[3] G.G. Kaplan, The global burden of IBD: from 2015 to 2025, Nat. Rev. Gastroenterol. Hepatol. 12 (2015) 720–727, https://doi.org/10.1038/nrgastro.2015.150.
[4] T. Wyant, E. Fedyk, B. Abhyankar, An overview of the mechanism of action of the monoclonal antibody vedolizumab, J Crohns Colitis 10 (2016) 1437–1444, https://doi.org/10.1093/ecco-jcc/jjw092.
[5] S. Schreiber, A. Dignass, L. Peyrin-Biroulet, G. Hather, D. Demuth, M. Mosli, et al., Systematic review with meta-analysis: real-world effectiveness and safety of vedolizumab in patients with inflammatory bowel disease, J. Gastroenterol. 53 (2018) 1048–1064, https://doi.org/10.1007/s00535-018-1480-0.
[6] T. Engel, B. Ungar, D.E. Yung, S. Ben-Horin, R. Eliakim, U. Kopylov, Vedolizumab in IBD-lessons from real-world experience; A systematic review and pooled analysis, J Crohns Colitis 12 (2018) 245–257, https://doi.org/10.1093/ecco-jcc/jjx143.
[7] B.G. Feagan, P. Rutgeerts, B.E. Sands, S. Hanauer, J.-F. Colombel, W.J. Sandborn, et al., Vedolizumab as induction and maintenance therapy for ulcerative colitis, N. Engl. J. Med. 369 (2013) 699–710, https://doi.org/10.1056/NEJMoa1215734.
[8] W.J. Sandborn, B.G. Feagan, P. Rutgeerts, S. Hanauer, J.-F. Colombel, B.E. Sands, et al., Vedolizumab as induction and maintenance therapy for Crohn's disease, N. Engl. J. Med. 369 (2013) 711–721, https://doi.org/10.1056/NEJMoa1215739.
[9] W.J. Sandborn, F. Baert, S. Danese, Ž. Krznarić, T. Kobayashi, X. Yao, et al., Efficacy and safety of vedolizumab subcutaneous formulation in a randomized trial of patients with ulcerative colitis, Gastroenterology 158 (2020) 562–572.e12, https://doi.org/10.1053/j.gastro.2019.08.027.
[10] S. Vermeire, G. D'Haens, F. Baert, S. Danese, T. Kobayashi, E.V. Loftus Jr., et al., Efficacy and safety of subcutaneous vedolizumab in patients with moderately to severely active Crohn's disease: results from the VISIBLE 2 randomised trial, J Crohns Colitis 16 (2022) 27–38, https://doi.org/10.1093/ecco-jcc/jjab133.
[11] B.E. Sands, B.G. Feagan, P. Rutgeerts, J.-F. Colombel, W.J. Sandborn, R. Sy, et al., Effects of vedolizumab induction therapy for patients with Crohn's disease in whom tumor necrosis factor antagonist treatment failed, Gastroenterology 147 (2014) 618–627.e3, https://doi.org/10.1053/j.gastro.2014.05.008.
[12] B.E. Sands, L. Peyrin-Biroulet, E.V. Loftus, S. Danese, J.-F. Colombel, M. Törüner, et al., Vedolizumab versus adalimumab for moderate-to-severe ulcerative colitis, N. Engl. J. Med. 381 (2019) 1215–1226, https://doi.org/10.1056/NEJMoa1905725.
[13] B.G. Feagan, K. Lasch, T. Lissoos, C. Cao, A.M. Wojtowicz, J.M. Khalid, et al., Rapid response to vedolizumab therapy in biologic-naive patients with inflammatory bowel diseases, Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc 17 (2019) 130–138.e7, https://doi.org/10.1016/j.cgh.2018.05.026.
[14] B.E. Sands, W.J. Sandborn, G. Van Assche, M. Lukas, J. Xu, A. James, et al., Vedolizumab as induction and maintenance therapy for Crohn's disease in patients naïve to or who have failed tumor necrosis factor antagonist therapy, Inflamm. Bowel Dis. 23 (2017) 97–106, https://doi.org/10.1097/MIB.0000000000000979.
[15] M. Attauabi, G.R. Madsen, F. Bendtsen, J.B. Seidelin, J. Burisch, Vedolizumab as the first line of biologic therapy for ulcerative colitis and Crohn's disease - a systematic review with meta-analysis, Dig Liver Dis Off J Ital Soc Gastroenterol Ital Assoc Study Liver 54 (2022) 1168–1178, https://doi.org/10.1016/j.dld.2021.11.014.
[16] W.J. Sandborn, B.G. Feagan, S.B. Hanauer, H. Lochs, R. Löfberg, R. Modigliani, et al., A review of activity indices and efficacy endpoints for clinical trials of medical therapy in adults with Crohn's disease, Gastroenterology 122 (2002) 512–530, https://doi.org/10.1053/gast.2002.31072.
[17] G. D'Haens, W.J. Sandborn, B.G. Feagan, K. Geboes, S.B. Hanauer, E.J. Irvine, et al., A review of activity indices and efficacy end points for clinical trials of medical therapy in adults with ulcerative colitis, Gastroenterology 132 (2007) 763–786, https://doi.org/10.1053/j.gastro.2006.12.038.
[18] M. Daperno, G. D'Haens, G. Van Assche, F. Baert, P. Bulois, V. Maunoury, et al., Development and validation of a new, simplified endoscopic activity score for Crohn's disease: the SES-CD, Gastrointest. Endosc. 60 (2004) 505–512, https://doi.org/10.1016/s0016-5107(04)01878-4.
[19] K.W. Schroeder, W.J. Tremaine, D.M. Ilstrup, Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study, N. Engl. J. Med. 317 (1987) 1625–1629, https://doi.org/10.1056/NEJM198712243172603.
[20] M.P. Sparrow, K. Papamichael, M.G. Ward, P. Riviere, D. Laharie, S. Paul, et al., Therapeutic drug monitoring of biologics during induction to prevent primary non-response, J Crohns Colitis 14 (2020) 542–556, https://doi.org/10.1093/ecco-jcc/jjz162.
[21] S. Kolehmainen, T. Ylisaukko-oja, J. Jokelainen, M. Koivusalo, T.S. Jokiranta, T. Sipponen, Benefit of measuring vedolizumab concentrations in inflammatory bowel disease patients in a real-world setting, Scand. J. Gastroenterol. 56 (2021) 906–913, https://doi.org/10.1080/00365521.2021.1938206.
[22] T. Ylisaukko-Oja, J. Aaltonen, H. Nuutinen, T. Blomster, A. Jussila, M. Pajala, et al., High treatment persistence rate and significant endoscopic healing among real-life patients treated with vedolizumab - a Finnish Nationwide Inflammatory Bowel Disease Cohort Study (FINVEDO), Scand. J. Gastroenterol. 53 (2018) 158–167, https://doi.org/10.1080/00365521.2017.1416160.
[23] K. Kontola, P. Oksanen, H. Huhtala, A. Jussila, Increasing incidence of inflammatory bowel disease with greatest change among the elderly: a nationwide study in Finland, 2000-2020, J Crohns Colitis (2022) jjac177, https://doi.org/10.1093/ecco-jcc/jjac177.
[24] F.S. Macaluso, W. Fries, S. Renna, A. Viola, M. Muscianisi, M. Cappello, et al., Effectiveness and safety of vedolizumab in biologically naïve patients: a real-world multi-centre study, United Eur Gastroenterol J 8 (2020) 1045–1055, https://doi.org/10.1177/2050640620948802.
[25] R. di Giuseppe, S. Plachta-Danielzik, W. Mohl, M. Hoffstadt, T. Krause, B. Bokemeyer, et al., Profile of patients with inflammatory bowel disease in conjunction with unmet needs and decision-making for choosing a new biologic therapy: a baseline analysis of the VEDOIBD-Study, Int. J. Colorectal Dis. 36 (2021) 2445–2453, https://doi.org/10.1007/s00384-021-03943-5.
[26] A. Pudipeddi, Y. Ko, S. Paramsothy, R.W. Leong, Vedolizumab has longer persistence than infliximab as a first-line biological agent but not as a second-line biological agent in moderate-to-severe ulcerative colitis: real-world registry data from the Persistence Australian National IBD Cohort (PANIC) study, Ther Adv Gastroenterol 15 (2022) 17562848221080792, https://doi.org/10.1177/17562848221080793.
[27] B. Bressler, A. Yarur, M.S. Silverberg, M. Bassel, E. Bellaguarda, C. Fourment, et al., Vedolizumab and anti-tumour necrosis factor α real-world outcomes in biologic-naïve inflammatory bowel disease patients: results from the EVOLVE study, J Crohns Colitis 15 (2021) 1694–1706, https://doi.org/10.1093/ecco-jcc/jjab058.
[28] Bokemeyer B, Plachta-Danielzik S, di Giuseppe R, Efken P, Mohl W, Krause T, et al. Real-world effectiveness of vedolizumab compared to anti-TNF agents in biologic-naïve patients with ulcerative colitis: A two-year propensity-score-adjusted analysis from the prospective, observational VEDOIBD-study. Aliment. Pharmacol. Ther. n.d.;n/a. https://doi.org/10.1111/apt.17616.
[29] R. Sablich, M.T. Urbano, M. Scarpa, F. Scognamiglio, A. Paviotti, E. Savarino, Vedolizumab is superior to infliximab in biologic naïve patients with ulcerative colitis, Sci. Rep. 13 (2023) 1816, https://doi.org/10.1038/s41598-023-28907-3.
[30] A.Z. Dotti, E.G. Vilela, J.M.F. Chebli, L.A. Chebli, D.O. Magro, F. Steinwurz, et al., P586 vedolizumab in mild to moderate Crohn's disease patients naïve to biological therapy: a multicentric observational study, J Crohns Colitis 17 (2023) i714–i715, https://doi.org/10.1093/ecco-jcc/jjac190.0716.

[31] U. Helwig, M. Mross, S. Schubert, H. Hartmann, A. Brandes, D. Stein, et al., Real-world clinical effectiveness and safety of vedolizumab and anti-tumor necrosis factor alpha treatment in ulcerative colitis and Crohn's disease patients: a German retrospective chart review, BMC Gastroenterol. 20 (2020) 211, https://doi.org/10.1186/s12876-020-01332-w.
[32] A. Moens, B. Verstockt, D. Alsoud, J. Sabino, M. Ferrante, S. Vermeire, Translating results from VARSITY to real world: adalimumab vs vedolizumab as first-line biological in moderate to severe IBD, Inflamm. Bowel Dis. 28 (2022) 1135–1142, https://doi.org/10.1093/ibd/izab257.
[33] EMA. Entyvio, Eur Med Agency, 2018. https://www.ema.europa.eu/en/medicines/human/EPAR/entyvio. (Accessed 27 April 2022).
[34] S. Singh, P.S. Dulai, N. Vande Casteele, R. Battat, M. Fumery, B.S. Boland, et al., Systematic review with meta-analysis: association between vedolizumab trough concentration and clinical outcomes in patients with inflammatory bowel diseases, Aliment. Pharmacol. Ther. 50 (2019) 848–857, https://doi.org/10.1111/apt.15484.