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ORIGINAL ARTICLE

Real-World Outcomes of Patients Starting Intravenous and Transitioning to Subcutaneous Vedolizumab in Inflammatory Bowel Disease

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Abstract

Background Real-world data on starting intravenous (IV) vedolizumab (VDZ) and transitioning to subcutaneous (SC) treatment in inflammatory bowel disease (IBD) are scarce.

Aims To assess treatment outcomes of patients with IBD starting IV VDZ and switching to SC VDZ in routine clinical care.

Methods Adult patients with IBD switching from IV to SC VDZ treatment between 1 March 2020 and 31 December 2021 were identified from the Swedish IBD quality register. The primary outcome was SC VDZ persistence. Secondary outcomes included clinical remission, changes in quality of life (QoL) according to EuroQual 5-Dimensions 5-Levels (EQ-5D-5L) and the Short-Health Scale (SHS) and inflammatory markers, including faecal Calprotectin (FCP).

Results Altogether, 406 patients with IBD (Crohn's disease, $n=181$; ulcerative colitis, $n=225$) were identified. After a median follow-up of 30 months from starting IV VDZ treatment, the persistence rates were 98%(178/181) in Crohn's disease and 94% (211/225) in ulcerative colitis. Most patients (84%) transitioned during maintenance therapy, and the median follow-up from switch to SC VDZ was 10 months. Compared to baseline, statistically significant improvements were observed in all domains of the SHS, EQ-5D index value and visual analogue scale. Median (interquartile range) FCP concentrations (µg/g) decreased from 459 (185–1001) to 65 (26–227) in Crohn's disease ($n=45$; $p<0.001$) and from 646 (152–1450) to 49 (20–275) in ulcerative colitis ($n=58$; $p<0.001$).

Conclusion Initiating IV VDZ and switching to SC treatment was associated with high persistence rates and improvements in measures of QoL and FCP. These findings are reassuring for patients who start IV VDZ and switch to SC VDZ.

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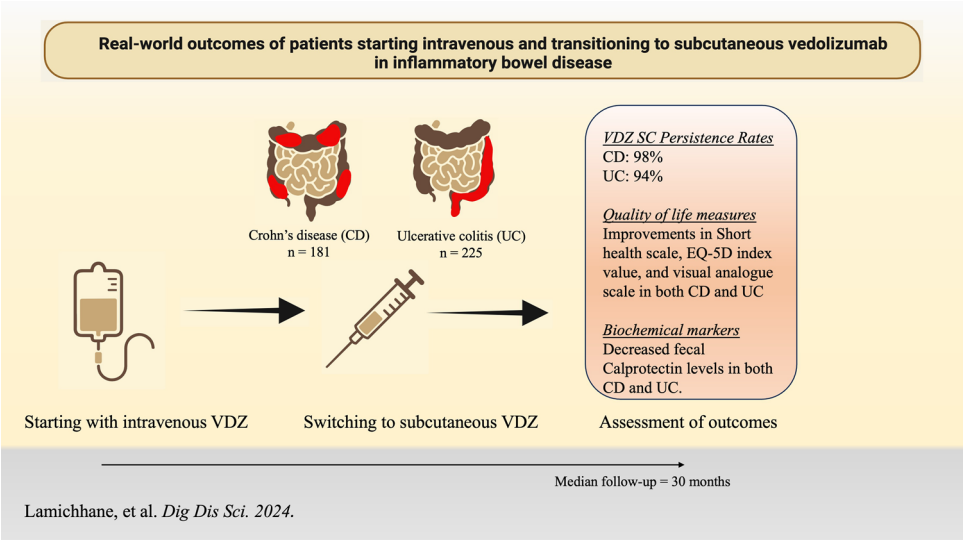
Graphical Abstract



Keywords Inflammatory bowel disease · Vedolizumab · Real-world data · Observational study

Abbreviations

CD	Crohn's disease
UC	Ulcerative colitis
CI	Confidence interval
FCP	Faecal Calprotectin
IQR	Interquartile range
IBD	Inflammatory bowel disease
HRQoL	Health-related quality of life
TNF	Tumor necrosis factor
SWIBREG	Swedish Inflammatory Bowel Disease Quality Register
EQ-5D-5L	EuroQual 5-Dimensions 5-Levels
SHS	Short-health scale
CRP	C-reactive protein
LOD	Lower limit of detection
PRO	Patient-reported outcomes

Introduction

Inflammatory bowel disease (IBD), comprising Crohn's disease and ulcerative colitis, is a progressive disease characterized by chronic inflammation of the gastrointestinal tract. The disease is associated with impaired quality of life (QoL), loss of work productivity, increased morbidity, and mortality [1–7]. To achieve and maintain remission with resolution of inflammation and restoration of QoL, patients often require long-term medical therapy. The introduction of biologics for the treatment of IBD has improved outcomes for many patients with the disease. Biologics are administered as intravenous (IV) infusions or as subcutaneous (SC) injections. Even though some patients perceive IV dosing with frequent interactions with healthcare providers as beneficial, many patients find SC administration more convenient [8]. Therefore, recently approved biological agents for the treatment of Crohn's disease and ulcerative colitis are administered as infusions only during the induction phase, and subcutaneous (SC) formulations are used during maintenance treatment.

IV vedolizumab (VDZ) is well established as an effective induction and maintenance therapy in IBD, and its use is also supported by numerous observational real-world studies [9–12]. Recently, the efficacy and safety of a SC formulation of VDZ were demonstrated in the VISIBLE 1 and VISIBLE 2 trials [13, 14]. In these phase III randomized controlled trials, patients with moderately to severely active Crohn's disease and ulcerative colitis who responded to induction therapy with two infusions of IV VDZ were switched to SC VDZ treatment. Based on the results of VISIBLE 1 and 2, SC VDZ was approved by the European Medicines Agency as maintenance therapy in adult patients with moderately to severely active Crohn's disease and ulcerative colitis in 2020. However, there remains a scarcity of real-world studies published as full-length papers that investigate patients switching from IV to SC VDZ [15–21]. It is important to note that these studies have primarily examined the period following the switch to SC VDZ and have not considered the IV treatment period.

To examine clinical outcomes of starting IV VDZ and switching to SC VDZ in IBD, we performed a nationwide

study using prospectively recorded data from the Swedish Inflammatory Bowel Disease Quality Register (SWIBREG).

Materials and Methods

Study Design and Setting

This study was a nationwide non-interventional cohort study assessing clinical outcomes in patients with IBD who started on IV VDZ and later switched to SC VDZ based on information in SWIBREG. At the end of 2021, Sweden had a population of 10.5 million [22]. The Swedish healthcare system is tax-funded and offers universal access, with prescription drugs provided free of charge above an annual threshold of SEK 2400 [approximately €230]. By using the unique Swedish personal identity number, assigned to all permanent Swedish residents, individuals can be followed until emigration or death, with virtually no loss to follow-up [23].

Data Source

The SWIBREG was started in 2005 and comprised > 55,000 patients with IBD in 2022, including > 85% of all patients with IBD treated with immunomodulators, biologics or surgery in Sweden [24]. The register holds prospectively recorded information on demographics, clinical characteristics, disease activity, treatments and QoL measures, i.e. the EuroQual 5-Dimensions 5-Levels (EQ-5D-5L) and the Short-Health Scale (SHS) [25]. Data on patient-reported outcomes (PROs) can be electronically recorded by patients, and information about inflammatory markers is automatically extracted from electronic health records or manually inserted by healthcare providers. The validity of diagnoses in the SWIBREG has been shown to be high [26].

Study Population

Patients with IBD who started VDZ treatment before 31 December 2021 were identified through SWIBREG. To be eligible for inclusion, patients had to have an established diagnosis of IBD, be over the age of 18 years and to have switched from IV to SC VDZ treatment before 31 December 2021. Patients were followed from the date of starting IV VDZ therapy to termination of the treatment, emigration, death or end of the study period, i.e., 25 February 2022. This was an observational study, and no predetermined dosing schedule was applied. The decision to transition from IV to SC treatment was at the discretion of the treating physicians.

Data on age, sex, smoking status (defined as current smoker, previous smoker or never smoker), phenotypes of the Montreal classification [27], medical therapy and previous IBD-associated surgery at baseline, i.e. at initiation of VDZ treatment, were extracted from SWIBREG. Smoking status was defined as the last reported information on smoking before or at the initiation of VDZ treatment. In line with the recommendations by the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) II initiative [28], we used the two-item patient-reported outcome (PRO-2) to evaluate stool frequency and rectal bleeding in patients with ulcerative colitis and to assess daily loose stool frequency and abdominal pain score in Crohn's disease [29, 30]. Following STRIDE II, we extracted information on faecal calprotectin (FCP), C-reactive protein (CRP) and QoL measures from SWIBREG. To assess QoL, we used SHS and EQ-5D-5L. The SHS has been validated against the Inflammatory Bowel Disease Questionnaire (IBDQ) [31, 32] and assesses four self-reported dimensions of QoL, including symptom burden, functional status, disease-related worry, and general well-being. Each domain is scored from 0, no problem, to 5, worst imaginable state. The EQ-5D-5L captures the following five generic dimensions of HRQoL: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, separately rated from 1 (no problems) to 5 (severe problems) [33]. The responses are converted into a single number called the index value, where 1.0 represents the best possible well-being. The EQ5D-5L also comprises a visual analogue scale (VAS) that ranges from 0 to 100 to assess the current health state.

Outcomes

The primary outcome was the persistence rate of SC VDZ at the end of the study period. Reasons for termination of SC VDZ were reported by the treating physician using the termination criteria in SWIBREG, i.e., lack of or loss of response (termination because of primary non-response or secondary loss of response), intolerance or other reasons (e.g., patient's request and pregnancy). Secondary outcomes included clinical remission and corticosteroid-free clinical remission at last follow-up. Clinical remission was defined as a rectal bleeding score = 0 (no blood seen) and stool frequency score ≤ 1 (1–2 stools more than normal) in ulcerative colitis, and a stool frequency ≤ 3 and an abdominal pain score ≤ 1 (mild abdominal pain) in Crohn's disease. Corticosteroid-free was defined as the absence of exposure to systemic corticosteroids within the last 4 weeks. Other secondary outcomes included changes from baseline in CRP, FCP and health-related quality of life (HRQoL), as measured by the EQ-5D-5L index value and visual analogue scale, and also disease-related QoL, defined by the SHS. Data at baseline were included if collected within ± 4 weeks of the baseline visit, i.e., at initiation of IV VDZ treatment.

Statistical Analyses

Continuous variables are presented as median and interquartile range (IQR). A Kaplan–Meier curve was used to illustrate VDZ persistence from initiation of VDZ treatment. For clinical remission status at follow-up, we applied an intention-to-treat approach and reported remission rates were based on non-responder imputation, where missing data and discontinuation of SC VDZ were classified as treatment failure, regardless of the reason for discontinuation. Pairwise comparisons of FCP, CRP, and PROs, including symptoms, EQ-5D-5L and SHS, between baseline and last follow-up were performed using Wilcoxon matched-pairs signed-rank test and were restricted to patients who were still treated with SC VDZ. For clarity purposes, the number of individuals with valid data is reported in brackets for each analysis. For CRP and FCP levels below the lowest limit of detection (LOD), values were substituted with LOD/$\sqrt{2}$ [34]. To specifically examine changes in clinical measures during SC VDZ treatment, we repeated analyses but shifted the start of follow-up from initiation of IV VDZ treatment to date of switching to SC therapy. All tests were two-tailed, and p-values < 0.05 were considered statistically significant. STATA (Version 17).

Ethical Consideration

This study was approved by the Swedish Ethical review Authority (2014/375-31 and 2020-05060).

Results

Cohort of Patients Treated with Vedolizumab

We obtained data on 483 patients with IBD through SWIBREG. Patients with missing or inconsistent information on IBD subtype, no data on clinical characteristics and those who did not receive IV VDZ before SC VDZ were excluded. In total, 406 patients with IBD (Crohn's disease, $n = 181$; ulcerative colitis, $n = 225$), aged ≥ 18 years, starting IV VDZ therapy and transitioning from IV to SC VDZ treatment were included in the analyses. Basic demographics and clinical characteristics at the start of IV VDZ are presented in Table 1.

Table 1 Baseline demographics and clinical characteristics of patients starting intravenous vedolizumab

	Crohn's disease ($n = 181$)	Ulcerative colitis ($n = 225$)
Median age, years (IQR)	44.2 (30.5–60.3)	37.5 (28.0–57.4)
Sex female, *n* (%)	90 (49.7)	91 (40.4)
Median disease duration, years (IQR)	10 (4.7–22.5)	7.2 (2.6–14.7)
Current Smoker, *n* (%)	15 (8.3)	6 (2.7)
Location, n (%)		
Ileal, L1	45 (24.9)	
Colonic, L2	53 (29.3)	
Ileocolonic, L3	70 (38.7)	
Behavior, n (%)		
Inflammatory, B1	84 (46.4)	
Structuring, B2	44 (24.3)	
Penetrating, B3	15 (8.3)	
Perianal disease, *P*	24 (13.2)	
Extent, n (%)		
Proctitis, E1		29 (12.9)
Left-sided colitis, E2		62 (27.6)
Extensive colitis, E3		124 (55.1)
Previous surgery, n (%)	53 (29.3)	11 (4.9)
Previous medications, n (%)		
Anti-TNF	141 (77.9)	160 (71.1)
Ustekinumab	18 (9.9)	3 (1.3)
Tofacitinib	1 (0.5)	8 (3.6)
Concurrent medications, n (%)		
5ASA	5 (2.8)	25 (11.1)
Immunomodulators	23 (12.7)	27 (12.0)
Corticosteroids	24 (13.2)	45 (20.0)

Data were missing for location, $n = 13$; behavior, $n = 38$; extent, $n = 10$

5ASA 5-aminosalicylic acids

Persistence and Remission Rates

After a median (IQR) follow-up of 30 (16–51) months from initiation of IV VDZ, the SC VDZ persistence rates were 98% (178/181) in Crohn's disease and 94% (211/225) in ulcerative colitis (Fig. 1A, B). Reasons for termination of SC VDZ were lack/loss of response ($n = 9$), intolerance ($n = 2$), and other reasons, including patients' requests ($n = 6$).

Most patients (84%) transitioned from IV to SC VDZ during maintenance therapy, i.e., after > 14 weeks from initiation of IV VDZ treatment. As a result, the median follow-up from switching to SC VDZ was 10 (IQR 5–12) months. At last follow-up, clinical remission rates were 60% (109/181) in Crohn's disease and 56% (126/225) in ulcerative colitis. However, data on clinical remission status were missing for 20% (37/181) of the Crohn's disease patients and for 30% (68/225) of the ulcerative colitis patients. Of patients in clinical remission at last follow-up, 93% (101/109) with Crohn's disease and 95% (120/126) with ulcerative colitis were also in corticosteroid-free remission.

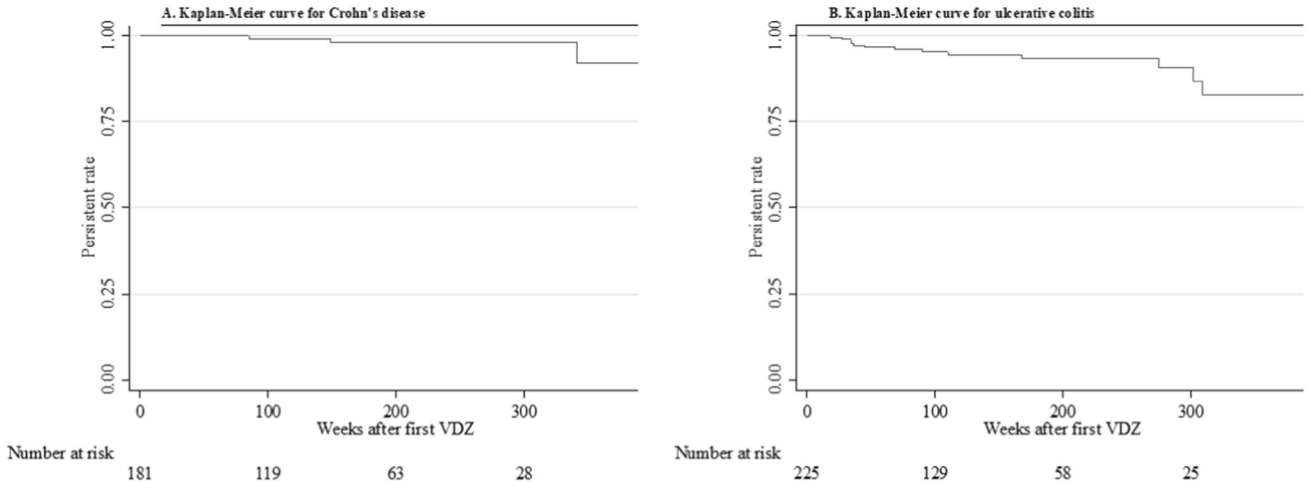


Fig. 1 Kaplan–Meier curve illustrating subcutaneous vedolizumab (VDZ) persistence from initiation of intravenous VDZ treatment in **A** 181 patients with Crohn's disease and **B** 225 patients with ulcerative colitis transitioning from IV to SC VDZ treatment

Biochemical and Quality of Life Outcomes

Of the patients with information about FCP both at baseline and last follow-up, the median (IQR) FCP (µg/g) levels decreased from 459 (185–1001) to 65 (26–227) in Crohn's disease ($n = 45$, $p < 0.001$) and from 646 (152–1450) to 49 (20–275) in ulcerative colitis ($n = 58$, $p < 0.001$). In patients with Crohn's disease, a marginally significant change in median (IQR) CRP concentration (g/L) was observed between baseline [4.0 (2.0–6.8)] and last follow-up [3.2 (1.0–4.7), $p = 0.049$, $n = 47$], whilst CRP decreased from 3.8 (1.0–5.0) to 2.2 (1.0–4.0) in patients with ulcerative colitis ($p = 0.02$, $n = 48$). Compared to baseline, statistically significant improvements were observed in all four domains of the SHS, EQ-5D index value and EQ-5D visual analogue scale, both in patients with Crohn's disease and ulcerative colitis (Table 2).

Table 2 Health-related (EQ-5D-5L) and disease-related (SHS) quality of life outcomes at baseline, i.e., at the start of VDZ treatment, and at last follow-up in patients with Crohn's disease and ulcerative colitis

	Crohn's disease				Ulcerative colitis			
	n	Baseline median (IQR)	Last follow-up median (IQR)	Sign-rank test *p*-value	*n*	Baseline median (IQR)	Last follow-up median (IQR)	Sign-rank test *p*-value
Short-Health Scale								
Bowel symptoms	108	2 (1–3)	1 (0–1)	< 0.001	121	2 (1–3)	1 (0–1)	< 0.001
Activities of daily living	111	2 (1–3)	1 (0–2)	< 0.001	123	2 (1–3)	1 (0–1)	< 0.001
Worry	108	2 (1–3)	1 (0–2)	< 0.001	122	2 (1–3)	1 (1–2)	< 0.001
General well-being	107	2 (1–2)	1 (1–2)	< 0.001	121	2 (1–2)	1 (1–2)	< 0.001
EQ-5D-5L								
Mobility	53	1 (1–1)	1 (1–1)	0.728	47	1 (1–1)	1 (1–1)	0.249
Self-Care	53	1 (1–1)	1 (1–1)	0.642	47	1 (1–1)	1 (1–1)	0.58
Usual Activities	53	1 (1–2)	2 (1–3)	0.036	47	2 (1–2)	1 (1–2)	< 0.001
Pain/Discomfort	53	2 (1–3)	2 (1–2)	< 0.001	47	2 (2–3)	2 (1–2)	0.01
Anxiety/Depression	53	2 (1–3)	1 (1–2)	0.005	47	2 (2–3)	1 (1–2)	0.001
EQ5D index value	53	0.8 (0.7–0.9)	0.8 (0.8–0.1)	0.004	47	0.7 (0.7–0.8)	0.9 (0.7–1)	< 0.001
Visual analogue scale	51	70 (50–80)	80 (61–90)	< 0.001	43	70 (50–80)	80 (70–90)	< 0.001

EQ-5D-5L EuroQual 5-Dimensions 5-Levels, *SHS* Short-Health Scale

Biochemical Changes After Switching from IV to SC VDZ

To specifically examine drug persistence after transitioning to SC VDZ treatment, we depicted VDZ persistence from the date of a switch to SC VDZ in patients with Crohn's disease and ulcerative colitis (Fig. 2A, B). The median follow-up from the date of switch from IV to SC VDZ was 10 months. Correspondingly, we compared concentrations of FCP and CRP between date of switching to SC VDZ (±4 weeks) and last follow-up. In patients with Crohn's disease, no statistically significant changes in median (IQR) FCP (µg/g) levels were observed between date of switching to SC VDZ [111 (41–278)] and last follow-up [60 (29–278)] ($p=0.23$, $n=36$) or in median (IQR) CRP (g/L) concentrations [3.0 (1.1–8.8)] vs [4.0 (1.4–8.9)] ($p=0.75$, $n=33$). Also, in patients with ulcerative colitis, no statistically significant changes in median (IQR) FCP (µg/g) levels were identified from date of switch [43(25–101)] to last follow-up [33 (25–84)] ($p=0.26$, $n=31$) or in median (IQR) CRP (g/L) concentrations, [1.6 (0.8–3.2)] vs [2.0 (0.9–4.0 g/L)] ($p=1.0$, $n=29$).

Discussion

This nationwide real-world study used data from the Swedish IBD quality register (SWIBREG) and examined drug persistence rates and clinical outcomes in a large cohort of patients with IBD who started on IV VDZ and later switched to SC VDZ treatment. High SC VDZ persistence rates were observed in patients with Crohn's disease (98%) and ulcerative colitis (94%) after a median follow-up of 30 months from the start of IV VDZ treatment. These rates were associated with improvements in health-related and disease-related QoL measures. Decreased levels of FCP were observed in both Crohn's disease and ulcerative colitis, and CRP concentrations were also lower in ulcerative colitis.

The efficacy of SC VDZ in patients with Crohn's disease and ulcerative colitis was demonstrated in the VISIBLE I and II trials. In these trials, patients with a clinical response to two infusions of IV VDZ switched to SC treatment. At 52 weeks after the first infusion, SC VDZ continuation rates were 73% in Crohn's disease and 61% in ulcerative colitis. These rates cannot be directly compared with our VDZ SC persistent rates of 98% in Crohn's disease and 94% in ulcerative colitis since switching was not compulsory in Sweden but performed at the discretion of the treating physician. Some patients may refuse to switch to SC therapy due to fear of loss of efficacy, a more spaced-out medical follow-up, increased frequency of administration, and self-administered injection [35] and these patients were excluded from our study. Most of our patients transitioned from IV to SC VDZ during maintenance treatment, further supporting the hypothesis that our study population represented a selected group of patients who benefited from VDZ therapy. Also, we used wide eligibility criteria reflecting clinical practice, whereas the inclusion of patients in VISIBLE I and II was limited to selected and homogenous groups of patients. Different treatment patterns and combinations with other therapies may also have influenced the results. While the protocols strictly regulated the dosing of VDZ and prohibited initiation of additional drugs in the two randomized control trials, treatments may have varied depending on individual

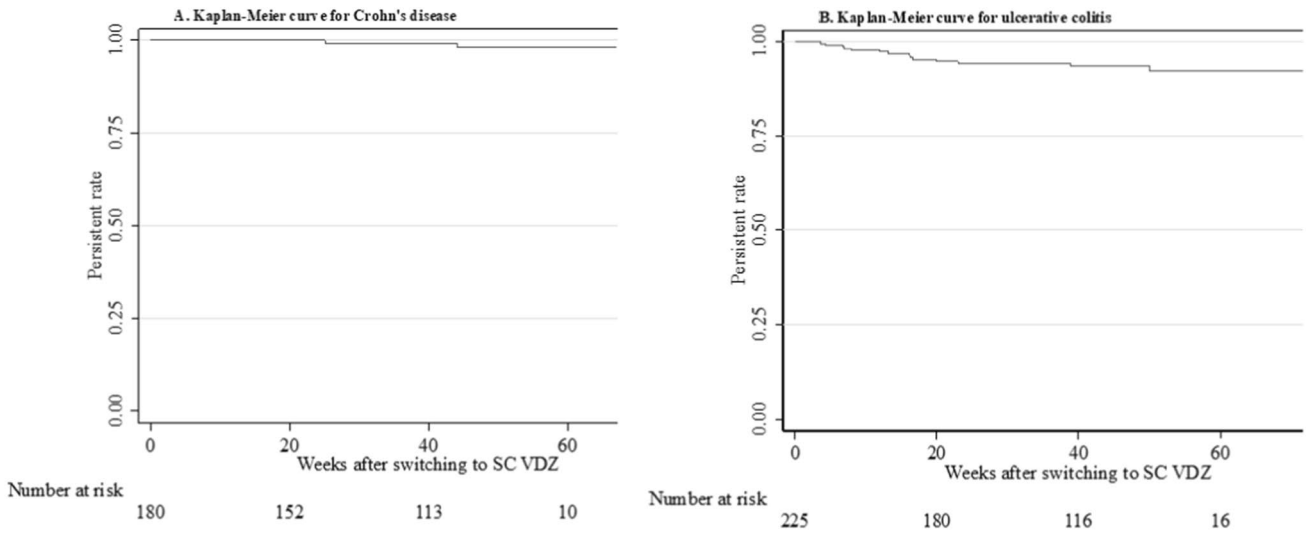


Fig. 2 Kaplan–Meier curve illustrating subcutaneous vedolizumab (VDZ) persistence from the date of switch from intravenous VDZ to subcutaneous VDZ treatment in A) 181 patients with Crohn's disease and B) 225 patients with ulcerative colitis

patient characteristics and decisions by treating physicians in our nationwide cohort.

Since the first real-world full-length paper by Ventress et al. reporting discontinuation rates of SC VDZ in British patients with IBD [17], additional cohorts have been published from Croatia, Italy, the Netherlands, Norway, Sweden, and the United Kingdom [15, 16, 18–21]. Compared with our cohort of 406 patients, these cohorts were considerably smaller, except for a recent British study with 563 participants [21]. Unlike our nationwide cohort, the majority of previous studies reported data from single centers [15–17, 19]. Most of the participants (85%) in the study by Ventress et al. had been treated with IV VDZ for at least 4 months, and the SC VDZ persistence rate was 92% 12 weeks after transitioning from IV to SC treatment [17]. The Dutch dataset was established by merging data from the Amsterdam UMC and a cohort of patients with IBD from nine other centers in the Netherlands [18]. Most patients switched from IV VDZ to SC VDZ during maintenance therapy, as the median period before switching was 20 months. After a median follow-up of 27 weeks from switching, 88% of patients were still treated with SC VDZ. Even though the period of IV VDZ treatment was comparable to our study, patient populations differed. We obtained secondary-care data from almost all Swedish IBD centers, whereas nearly all Dutch patients (92%) were treated at tertiary referral centers. This difference may explain why we observed a numerically higher SC VDZ persistence rate (96%) in patients with IBD after a median follow-up of 10 months from switching to SC treatment. Similar to our results, Bergqvist et al. reported high persistence rates for the 89 patients switching to SC VDZ at a single center in southern Sweden [15]. Only 4% of patients had discontinued SC VDZ after 6 months from switching to SC therapy, and 12% after 12 months. Some of the patients in the Swedish single-center study may even have been included in our cohort since we obtained data from the Swedish IBD quality register.

The observed SC VDZ persistence rates in our cohort were linked to increasing clinical remission rates, improvements in measures of HRQoL (EQ5D-5L) and disease-related QoL (SHS), and also in inflammatory markers, i.e., FCP and in ulcerative colitis also CRP. Of patients in clinical remission at last follow-up, most were also in corticosteroid-free remission. Restoration of QoL is regarded as one of the most important long-term treatment targets for patients with IBD, whereas normalization of CRP, decreasing FCP to an acceptable range and clinical remission have been recognized as medium-term targets [28]. Of the previously reported real-world cohorts, QoL has only been addressed in the single-center cohorts from Sweden and Norway [15, 19], and the recent multicentre study from the UK [21], where patients were included when switching from IV to SC VDZ. During follow-up, no changes in the SHS composite score or separate SHS items were observed in the Swedish study, the EQ5D-5L in the Norwegian cohort or in the IBD control scores in the British cohort. In contrast to these previous single-center studies, we examined associations of the entire VDZ treatment episode, i.e., from the start of IV VDZ treatment to the last follow-up, in patients transitioning from IV VDZ to SC VDZ. The difference in study design probably explains why we observed improvements in FCP, whereas this has not been reported in previous studies [15, 17, 18, 20, 21]. This assumption is supported by the fact that we did not observe any changes in FCP or CRP when we repeated the analyses and used time period since switching to SC VDZ as the underlying time scale.

In addition to representing the second largest cohort of patients switching from IV to SC VDZ, other strengths of this study include the prospective nationwide multicenter design, where decisions to switch from IV to SC VDZ treatment were made according to clinical practice. Collectively, these measures enabled us to capture the real-world clinical effectiveness of IV followed by SC VDZ and enhance the generalizability of our findings. However, it is important to acknowledge that reported remission rates at last follow-up probably may underestimate the true rates since we applied an intention-to-treat approach and classified missing data and discontinuation of SC VDZ as treatment failure, regardless of the reason for discontinuation. On the other hand, the observed high SC VDZ persistence rates may indicate that physicians selectively picked patients in deep remission on IV VDZ when switching patients to SC VDZ. Even though examined in the British multicenter cohort [21], this may suggest that comparisons with patients who remain on IV VDZ treatment can be challenging to interpret due to confounding factors.

Given the observational nature of the study, assessments of PRO, inflammatory markers and endoscopy were not compulsory during follow-up. Therefore, there may have been reporting bias by individual physicians or nurses, which could have influenced the number of patients with reported outcome measures during follow-up. The use of different FCP and CRP assays challenges the possibility of comparing results from measurements across Sweden, since different assays have various cut-offs for limits of detection and inter-assay differences in FCP exist. Therefore, we only performed pairwise comparisons and compared levels at the last follow-up to baseline. The absence of data on vedolizumab levels further limited the study. Lastly, due to the relatively low number of events, we were likely to lack the necessary statistical power to explore possible predictors of drug persistence. These limitations should be taken into account when interpreting findings.

In conclusion, our findings provide further support for switching from IV to SC treatment with VDZ. The observed associations between this treatment strategy and long-term

drug persistence rates and improvements in measures of QoL and FCP are reassuring for patients with IBD who are candidates for switching to SC VDZ therapy.

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Author's contributions Guarantor: CE and JH had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: CE and JH. Acquisition of data: JH. Drafting of the manuscript: NL, NM, CE and JH. Statistical analysis: NL, CE and JH. Interpretation of data, and critical revision of the manuscript for important intellectual content: All authors.

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Data availability No additional data are available due to Swedish regulations.

Declarations

Conflict of interest NL, NM, and VB have nothing to declare. *N–P* E is an employee at Takeda. OO has been PI on projects at Karolinska Institutet, partly financed by investigator-initiated grants from Janssen and Ferring, and Karolinska Institutet has received fees for lectures and participation on advisory boards from Janssen, Ferring, Takeda, and Pfizer. OO also reports a grant from Pfizer in the context of a national safety monitoring program. JFL has coordinated a study on behalf of the Swedish IBD quality register (SWIBREG), which received funding from Janssen. HH has served as a speaker, consultant or advisory board member: AbbVie, Janssen, Pfizer, Takeda, Tillotts Pharma, Vifor Pharma, and received grant support from Ferring and Tillotts Pharma. JM has served as a speaker, consultant or advisory board member for AbbVie, Bayer, BMS, Hospira, Janssen, MSD, Pfizer, Sandoz, Takeda, and UCB, and has received grant support from AbbVie, Calpro AS, Fresenius Kabi, Pfizer, SVAR Life Science, and Takeda. CE reports grant support/lecture fee/advisory board from Takeda, Janssen Cilag, Pfizer, Abbvie. JH has served as speaker, consultant and/or advisory board member for AbbVie, Aqilion, BMS, Celgene, Celltrion, Ferring, Galapagos, Gilead, Hospira, Janssen, MEDA, Medivir, MSD, Novartis, Pfizer, Prometheus Laboratories Inc, Sandoz, Shire, Takeda, Thermo Fisher Scientific, Tillotts Pharma, and Vifor Pharma. JH also has received grant support from Janssen, MSD and Takeda.

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