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A retrospective observational study of early experiences of vedolizumab treatment for inflammatory bowel disease in the UK

The REVIVE study

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Abstract

Results from clinical trials show that vedolizumab is an efficacious treatment for inflammatory bowel disease, namely Crohn's disease (CD) and ulcerative colitis (UC). However, there is limited evidence from real-world clinical practice, especially on early clinical experiences in the UK.

To describe real-world early experiences of vedolizumab to treat CD and UC in the UK.

A retrospective, chart review study of patients with CD or UC treated with vedolizumab across 5 UK hospitals. All eligible adults (≥18 years at initiation) with a diagnosis of CD and ≥14 weeks of data or UC and ≥10 weeks of data available following vedolizumab initiation were included.

Data were analyzed for 112 patients (CD: 66; UC: 46). Patients with CD had a median of 7.4 (interquartile range 5.7–9.4) months follow-up and patients with UC had a median of 7.4 (5.6–10.2) months follow-up post-vedolizumab initiation. Most patients, 80% (53/66) with CD and 89% (41/46) with UC, remained on vedolizumab treatment at the time of data collection. No new safety signals were identified during the study.

These results add to the body of evidence supporting vedolizumab as an effective and well-tolerated treatment for CD and UC in real-world clinical practice.

Abbreviations: AE = adverse event, CD = Crohn's disease, HBI = Harvey–Bradshaw index, IBD = inflammatory bowel disease, IQR = interquartile range, IRR = infusion-related reaction, SAE = serious adverse event, SCCAI = Simple Clinical Colitis Activity Index, TNFα = tumour necrosis factor-α, UC = ulcerative colitis.

Keywords: Crohn's disease, inflammatory bowel disease, tolerability, treatment effectiveness, treatment outcome, treatment persistence, ulcerative colitis, vedolizumab

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1. Introduction

The introduction of tumor necrosis factor-α (anti-TNFα) antagonists transformed the treatment of inflammatory bowel disease (IBD). However, approximately one-third of patients with IBD fail to respond (primary treatment failure).[1–4] Furthermore, over a third of patients who initially responded to treatment and subsequently discontinue treatment due to loss of response or intolerance,[1–4] with median time to loss of response in the real-world setting reported as between 53 and 99 weeks.[5] Anti-TNFα treatment can also be associated with adverse events (AEs) including infection, allergic reactions and possibly malignancy, which reflects the diverse role of TNFα in immune function.[2,6,7]

Vedolizumab is a biological therapy that has a different mode of action to anti-TNFαs and specifically targets the gut mucosa.[6,8] Vedolizumab was licensed in Europe in 2014 for the treatment of moderately to severely active Crohn's disease (CD) and ulcerative colitis (UC).[9] While positive results were reported from the GEMINI clinical trials,[10–12] evidence on early experiences of vedolizumab in the UK CD and UC population post-licensing is limited by small patient numbers and conducted in few centers, such as a study in 2 tertiary referral centers in London that included 50 patients across both diseases.[13] Information from the UK real-world setting is required as the characteristics and management of patients treated in routine clinical practice may differ from those of patients enrolled in the GEMINI trials.[10–12,14,15] Therefore, this study aimed to describe the real-world early experiences of vedolizumab in the UK to inform clinical practice and facilitate treatment decision making. It formed part of the REVIVE study—"A REtrospective UK chart review of early VedolIzumab experience: real-world effectiVEness and safety in IBD".

2. Methods

2.1. Study design and setting

A retrospective observational study was carried out in 5 UK secondary care centers. The study included relatively large centers with geographic representation across England and Scotland. Centers that were known to the study team to be early adopters of vedolizumab for treatment of CD and UC were selected in order to optimize both sample size and length of available follow-up.

2.2. Study population

Patients with a diagnosis of CD or UC and who have prescribed vedolizumab as part of routine clinical care were eligible for study participation. Patients were included in the study if they were aged ≥18 years at vedolizumab initiation, and with at least 14 or 10 weeks of follow-up history available in medical records post-initiation, respectively for CD and UC patients. Patients treated with vedolizumab as part of an interventional clinical trial and those not consenting to data collection were excluded. The study observation period was the period up to 24 months before vedolizumab initiation, and following vedolizumab initiation (patients were initiated on vedolizumab between November 2014 and April 2016) until data collection (May to July 2016).

2.3. Data collection

All potentially eligible patients were identified from hospital medical records. Patients provided written informed consent according to a protocol approved by the UK Health Research Authority (South Central–Oxford C) Research Ethics Committee (reference: 16/SC/0032; 15/01/2016). All procedures performed in studies involving human participants were in accordance with the ethical standards of the national research committee and with the 1964 Helsinki declaration and its later amendments.

Data were collected from hospital medical records on patient demographic and clinical characteristics (including age at vedolizumab initiation, IBD disease duration, comorbidities, prior IBD-related medication and surgery), vedolizumab treatment (including dosing, duration, reasons for discontinuation), concomitant IBD-medication, disease activity, and AEs.

2.4. Outcomes

The main outcomes of this study included persistence and duration of treatment. Disease activity is often poorly documented in medical records and a variety of measures are utilized in clinical practice. Since data on treatment persistence is generally available for all patients, vedolizumab treatment persistence was selected as a proxy for treatment effectiveness to account for inconsistent and poor recording of disease activity in medical records,[16] where patients showing clinical benefit and acceptable tolerability are expected to remain on treatment. Additional outcomes included clinical response and clinical remission at week 14 (CD) or 10 (UC) and safety profile.

Duration of treatment was taken as the time from vedolizumab initiation until data collection for patients with ongoing treatment. For patients discontinuing treatment, vedolizumab treatment duration was taken as the time from initiation until the discontinuation date recorded in the medical records or 56 days after the last vedolizumab infusion, whichever date was earliest. For the purposes of calculating vedolizumab persistence, patients remaining on treatment were censored at data collection.

Clinical response and clinical remission were analyzed (where data were available) at week 14 in patients with CD and at week 10 in patients with UC, which is consistent with the assessment points recommended in the Entyvio Summary of Product Characteristics.[17] Clinical response and remission were assessed in accordance with accepted standards widely used in IBD clinical trials. Clinical response was defined as a reduction of ≥3 points in the Harvey–Bradshaw Index (HBI) or an absolute HBI score ≤4 in patients with CD, and as a reduction of ≥3 points in Simple Clinical Colitis Activity Index (SCCAI) or an absolute SCCAI score ≤2 in patients with UC at follow-up compared with baseline. Clinical remission was defined as an HBI score ≤4 (CD) or an SCCAI score ≤2 (UC). AEs and serious AEs (SAEs) were recorded for up to 18 weeks (5 half-lives) following vedolizumab discontinuation. This data collection included AEs of special interest (nasopharyngitis, joint pain, infusion-related reactions [IRRs], gut-specific infections, skin rash) and any AE resulting in discontinuation of vedolizumab. Further details on the assessment of clinical outcomes are provided in the supplemental methods (see text, Supplemental Digital Content 1, http://links.lww.com/MD/C847).

2.5. Statistical analyses

Clinical response and remission were evaluated in the intention to treat population and in the subgroup of patients with active disease at baseline (defined as HBI ≥5 in patients with CD or SCCAI ≥3 in patients with UC). Pre-defined subgroup analyses were carried out according to anti-TNFα treatment status before

vedolizumab initiation (anti-TNFα naïve or anti-TNFα experienced). Categorical variables are presented as number (frequency). Quantitative variables are presented as mean (standard deviation; SD) or median (interquartile range [IQR], or range). Kaplan–Meier curves show the cumulative proportions of patients persistent on vedolizumab during follow-up, patients with ongoing treatment were censored on the date of data collection. Data were analyzed using Stata version 14 (StataCorp). No attempts were made to statistically account for missing data in analyses.

3. Results

3.1. Patient demographic and clinical characteristics at vedolizumab initiation

A total of 156 potentially eligible patients were identified and approached for consent; of these, 112 eligible patients provided written informed consent (72% of those approached) and were included in the study. As shown in Table 1, of the 112 patients included in the study, 66 patients were diagnosed with CD (mean age 42.4 [SD: 16.4] years, 27% male) and 46 patients with UC (mean age 42.5 years [SD: 18.0] years, 50% male). The mean duration of IBD at the time of treatment initiation was 13.8 years in patients with CD and 8.7 years in patients with UC. There were 16 patients who were anti-TNFα naïve at vedolizumab initiation (6 patients with CD and 10 patients with UC). The majority of patients with CD (71%, 47/66) and UC (72%, 33/46) had received 1 or more anti-TNFα therapies in the 2 years prior to vedolizumab initiation. At least 1 bowel, perianal or other surgical procedure considered to be related to IBD or associated complications in the 12 months prior to vedolizumab initiation was recorded for 12% (8/66) of patients with CD and 7% (3/46) of patients with UC.

3.2. Treatment persistence and reasons for discontinuation

In patients with CD (n = 66), the median duration of follow-up was 7.4 (IQR: 5.7–9.4) months and the median duration of vedolizumab treatment was 6.3 (IQR: 5.2–8.1) months. In patients with UC (n = 46), the median duration of follow-up was 7.4 (IQR: 5.6–10.2) months and the median duration of treatment was 7.1 (IQR: 5.4–9.3) months.

At data collection, 80% (53/66) of patients with CD and 89% (41/46) of patients with UC were persistent on vedolizumab. Persistence with vedolizumab is shown in Figure 1 as estimated cumulative proportions of patients who remained on treatment during follow-up. Based on the Kaplan–Meier curves, the proportions of patients with CD who were persistent on vedolizumab at week 14, 6 months, and 12 months were 95%, 83%, and 73%, respectively. In patients with UC, the proportions of patients persistent on vedolizumab at week 10, 6 months, and 12 months were 98%, 93%, and 85%, respectively. Median vedolizumab persistence had not been reached in patients with CD or UC at data collection.

Sixteen patients were anti-TNFα naïve at initiation, consisting of 6 patients with CD and 10 patients with UC. All of the 6 patients with CD and 9 of the patients with UC were persistent on vedolizumab at data collection (median follow-up 8.1 [IQR: 5.1–9.7] months and 6.4 [IQR: 5.4–9.0] months, respectively). In anti-TNFα experienced patients, 78% (47/60) of patients with CD and 89% (32/36) patients with UC were persistent on vedolizumab at data collection (median follow-up 7.4 [IQR: 5.7–9.4] months and 7.6 [IQR: 5.8–10.8] months, respectively).

Thirteen patients with CD (20%, 13/66) discontinued treatment, including 5 patients who discontinued before the week 14 infusion. The most commonly recorded reasons for discontinuation among patients with CD (not mutually exclusive) were lack of efficacy (54%, 7/13), loss of efficacy (8%, 1/13) and AEs (15%, 2/13). Five patients with UC discontinued vedolizumab (11%, 5/46), including 2 patients who discontinued before the week 14 infusion. The most commonly recorded reasons for discontinuation among patients with UC (not mutually exclusive) were lack of efficacy (80%, 4/5), loss of efficacy (20%, 1/5) and AEs (20%, 1/5).

3.3. Clinical response and clinical remission

A variety of measures were used to assess baseline disease activity, with HBI being the most commonly recorded in patients with CD (31/66 [47%]) and SCCAI being the most commonly recorded in patients with UC (18/46 [39%]). In patients with CD and recorded HBI disease activity assessments at baseline and follow-up, 79% (15/19) had a clinical response at week 14 and 68% (13/19) were in clinical remission. In patients with UC and recorded SCCAI assessments at baseline and follow-up, 92% (11/12) of patients had a clinical response at week 10 and 67% (8/12) were in clinical remission. In the subgroup of patients with active disease at baseline and with disease activity assessments at follow-up, 83% (10/12) of patients with CD had a clinical response at week 14 and 67% (8/12) were in clinical remission. In patients with UC, 88% (7/8) had a clinical response at week 10 and 50% (4/8) were in clinical remission.

3.4. Vedolizumab safety

AEs were reported in 35% (23/66) of patients with CD and 26% (12/46) of patients with UC. Two SAEs were reported in patients with CD (Table 2): 1 SAE was an anaphylactoid reaction on concomitant mercaptopurine which occurred on the second infusion. The infusion was stopped and the patient discontinued vedolizumab. The second SAE was vomiting. One SAE was reported in a patient with CD, which was vomiting and diarrhea. AEs of special interest were reported in 15 patients with CD and 8 patients with UC. These included 1 case of nasopharyngitis in a patient with CD. IRRs were reported in only 1 patient with CD and 1 patient with UC.

4. Discussion

The results from this multi-center study on early experiences in real-world clinical practice in the UK suggest that vedolizumab is an effective and well-tolerated treatment for CD and UC in adults. Our results are broadly consistent with the GEMINI trials[12,18,19] and previous observational studies.[15,20] The demographic and clinical characteristics of the study sample were comparable with previous non-interventional studies that investigated vedolizumab treatment outcomes.[13–17,19]

After a median follow-up of 7.4 months post-initiation, at least 80% of patients persisted on vedolizumab treatment. Although a relatively short follow up period is reported in this study, the results are encouraging for persistence during the early maintenance phase for both CD and UC patients, including patients who were anti-TNFα naïve at initiation.

Table 1

Patient demographic and clinical characteristics at vedolizumab initiation.

	Crohn's disease (n = 66)	Ulcerative colitis (n = 46)
Age, years (mean [SD])	42.4 (16.4)	42.5 (18.0)
Males, n (%)	18 (27%)	23 (50%)
Duration of IBD, years (mean [SD])	13.8 (8.9)	8.7 (9.2)
Smoking history, n (%)		
Current	8 (12%)	3 (7%)
Ex-	12 (18%)	8 (17%)
Never	15 (23%)	15 (33%)
Not known	31 (47%)	20 (43%)
Body Mass Index, kg/m^2 (mean [SD])	24.1 (4.6)	24.3 (8.1)
Comorbidities, n (%)		
None	18 (27%)	21 (46%)
Extra Intestinal manifestations*	14 (21%)	1 (2%)
Autoimmune disorders	8 (12%)	3 (7%)
Osteoporosis	10 (15%)	2 (4%)
Arthralgias	6 (9%)	1 (2%)
Infections	1 (2%)	2 (4%)
Other	28 (42%)	21 (46%)
Disease location (CD)†		
L1: Ileal	12 (18%)	–
L2: Colonic	24 (36%)	–
L3: Ileocolonic	22 (33%)	–
L1L4: (Ileal and upper disease)	2 (3%)	–
L4-Isolated upper disease	2 (3%)	–
Not known	4 (6%)	–
Disease location (UC)		
All of colon	–	4 (9%)
Left side of colon	–	12 (26%)
Rectum and sigmoid colon only	–	19 (41%)
Proximal to the splenic flexure	–	1 (2%)
Proximal to the splenic flexure and left side of colon	–	1 (2%)
Rectum only	–	1 (2%)
Other	–	3 (7%)
Not known	–	2 (4%)
Disease behaviour (CD)†		
Non-stricturing, non-penetrating	26 (39%)	–
Stricturing	20 (30%)	–
Penetrating	2 (3%)	–
Penetrating and stricturing	3 (5%)	–
Penetrating and perianal disease	1 (2%)	–
Penetrating, stricturing and perianal disease	1 (2%)	–
Stricturing and perianal disease	1 (2%)	–
Not known	12 (18%)	–
Anti-TNFα naïve, n (%)	6 (9%)	10 (22%)
IBD-related therapy in previous 2 years, n (%)		
≥1 Aminosalicylate	13 (20%)	40 (87%)
≥1 Corticosteroid	43 (65%)	42 (91%)
≥1 Immunomodulator	49 (74%)	33 (72%)
Lines of anti-TNFα 0‡	19 (29%)	13 (28%)
1	37 (56%)	27 (59%)
2	10 (15%)	6 (13%)
UC/CD related surgical procedures in previous 12 months§, n (%)		
0	58 (88%)	43 (93%)
1	5 (8%)	3 (7%)
2	1 (2%)	0 (0%)
3	2 (3%)	0 (0%)
Concomitant corticosteroids at initiation, n (%)	16 (24%)	26 (57%)
Concomitant immunomodulators at initiation, n (%)	17 (26%)	11 (24%)

CD = Crohn's disease, IBD = inflammatory bowel disease, SD = standard deviation, TNFα = tumour necrosis factor-α, UC = ulcerative colitis.

* Excluding primary sclerosing cholangitis.

† Data were reclassified according to Montreal scores.

‡ patients may have received TNFi therapy more than 2 years before vedolizumab initiation.

§ IBD-related surgical procedures in patients with CD included bowel resection, partial colectomy, defunctioning loop colostomy, laparotomy and Hartmaan's, abscess drainage, examination under anaesthesia and anal biopsies, anal dilation, and incisional hernia repair; IBD-related surgical procedures in patients with UC included liver transplant [related to UC], examination under anaesthesia and inguinal hernia repair.

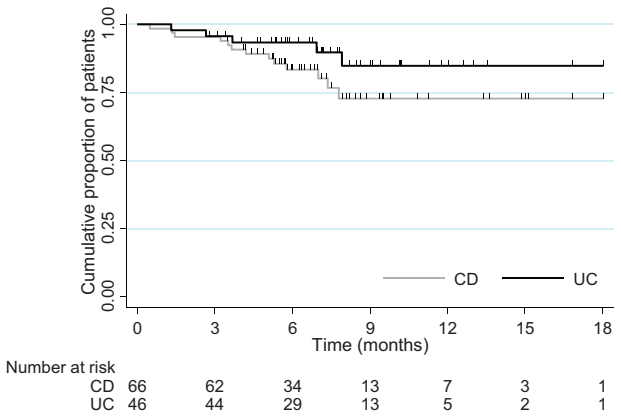

Figure 1. Cumulative proportion of patients persistent on vedolizumab during follow-up stratified by inflammatory bowel disease indication. Marks represent censored patients.

As anticipated, recording of disease activity in medical records at the time points of interest (baseline, as well as week 14 in patients with CD and week 10 in patients with UC) was limited. This finding reflects those from the 2016 UK IBD Audit which found that only 31% of adult patients with IBD had disease activity recorded in their medical records within 3 months of starting a new biologic,[21] suggesting a variety of real-world patient-level and service-level factors contribute to low levels of recording of disease severity. As limited disease activity data were available, and only for a proportion of patients in this study, interpretation of the results on clinical response and remission must be made with caution. The supplemental table (see table, Supplemental Digital Content 2, http://links.lww.com/MD/C847) summarizes the responses observed in our study with the current published real-life experience of vedolizumab.[13,15,20,22–24] Until assessment and recording of disease activity as part of routine care are improved, retrospective studies like ours that rely on medical records will not be able to comprehensively determine the impact of vedolizumab treatment on clinical response or remission on the IBD population in the real-world. While this type of real-world evidence have less internal validity compared with a formal registration study demonstrating efficacy, many patients are excluded from these studies[14] and real-world data is crucial to demonstrate clinical effectiveness in the whole cohort of patients exposed to a treatment.

In this study, 20% of patients with CD and 11% of patients with UC discontinued vedolizumab, with lack of efficacy as the most commonly recorded reason. Less than half of patients who discontinued treatment did so before the week 14 infusion. No new safety signals were identified in this study and few SAEs were observed, which reflect published evidence from clinical trial and real-world settings.[10–12,15,20,22–24,25] Similarly, IRRs were reported in only 2% of patients with CD and UC, respectively, which corresponds to findings from other observational studies.[15,22–24]

Although the sample size was relatively small, this study presents results of early vedolizumab use in the UK from a geographically representative group of hospitals. Results are provided for patients initiated on vedolizumab shortly after the drug became available in the UK before which alternative treatment options for many of these patients were not available. In the future, patients are likely to be initiated on vedolizumab sooner in the course of their disease and therefore results presented in this early cohort may differ from findings in future UK clinical practice. Studies to provide evidence on longer-term effectiveness are underway[26] and will add to the body of real-world evidence on appropriate uses of vedolizumab in the real-world setting.

Retrospective data collection from patient medical records was used in this study and therefore analyses were affected by the quality and completeness of original data entry. For example, data were missing for some patient characteristics such as disease location. As described earlier, there were limited data recorded on disease activity assessments, which restricted analyses of clinical response and remission. While few AEs were reported in this study, it is acknowledged that recording of AE data in medical records may be incomplete. However, it is expected that SAEs and IRRs would be captured and the number of these events identified in this study were low.

Table 2

Vedolizumab adverse events, serious adverse events and adverse events of special interest.

Adverse events*	Crohn's disease (n = 66)	Ulcerative colitis (n = 46)
AE	23/66 (35%)	12/46 (26%)
SAE†	2/66 (3%)	1/46 (2%)
AE of special interest	15/66 (23%)	8/46 (17%)
Joint pain	11 (17%)	5 (11%)
Skin rash	2 (3%)	1 (2%)
Infusion-related reactions	1 (2%)	1 (2%)
Nasopharyngitis	1 (2%)	0 (0%)
Gut specific infections	1 (2%)	0 (0%)
AE leading to discontinuation‡	2 (3%)	1 (2%)

AE = adverse event, SAE = serious adverse event.
* Not mutually exclusive.
† SAE in CD: anaphylaxis (n = 1), vomiting (n = 1); SAE in UC: vomiting and diarrhoea (n = 1).
‡ AE leading to discontinuation in patients with CD included "anaphylaxis" (SAE), "low mood post-infusion"; AE leading to discontinuation in patients with UC was "vomiting and diarrhoea leading to hospitalisation" (SAE).

5. Conclusion

This study demonstrated effective treatment of IBD with vedolizumab in real-world practice in the UK, as indicated by high rates of persistence with treatment and promising response and remission rates for patients with recorded disease activity data. No new safety signals were identified. These findings support the ongoing use of vedolizumab to treat CD and UC.

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Author contributions

FG performed the statistical analyses. FC, DG, SL, SS, GO, AR, FG, DD, SM, PMI were involved in the conception or design of the study; and acquisition, analysis or interpretation of the data; and drafting the article or revising it critically for important

intellectual content; and final approval of the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and reported.

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References

[1] Gisbert JP, Marín AC, McNicholl AG, et al. Systematic review with meta-analysis: the efficacy of a second anti-TNF in patients with inflammatory bowel disease whose previous anti-TNF treatment has failed. Aliment Pharmacol Ther 2015;41:613–23.

[2] Petkau JM, Eksteen B. Selective biologics for ulcerative colitis and Crohn's disease—clinical utility of vedolizumab. Biol Targets Ther 2016;10:33–52.

[3] Roda G, Jharap B, Neeraj N, et al. Loss of response to anti-TNFs: definition, epidemiology, and management. Clin Transl Gastroenterol 2016;7:e135doi: 10.1038/ctg.2015.63.

[4] Allez M, Karmiris K, Louis E, et al. Report of the ECCO pathogenesis workshop on anti-TNF therapy failures in inflammatory bowel diseases: definitions, frequency and pharmacological aspects. J Crohns Colitis 2010;4:355–66.

[5] Ma C, Evaschesen CJ, Gracias G, et al. Inflammatory bowel disease patients are frequently nonadherent to scheduled induction and maintenance infliximab therapy: a Canadian cohort study. Can J Gastroenterol Hepatol 2015;29:309–14.

[6] Krupka N, Baumgart DC. Designing biologic selectivity for inflammatory bowel disease—role of vedolizumab. Drug Des Devel Ther 2014; 9:147–54.

[7] Ali T, Kaitha S, Mahmood S, et al. Clinical use of anti-TNF therapy and increased risk of infections. Drug Healthc Patient Saf 2013;5:79–99.

[8] Cherry LN, Yunker NS, Lambert ER, et al. Vedolizumab: an α4β7 integrin antagonist for ulcerative colitis and Crohn's disease. Ther Adv Chronic Dis 2015;6:224–33.

[9] European Medicines Agency. Entyvio EMA Authorisation: EMEA/H/C/002782. 2014. Available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002782/human_med_001751.jsp&mid=WC0b01ac058001d124. Accessed December 12, 2017.

[10] Feagan BG, Rutgeerts P, Sands BE, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. N Engl J Med 2013;369:699–710.

[11] Sandborn WJ, Feagan BG, Rutgeerts P, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. N Engl J Med 2013;369:711–21.

[12] Sands BE, Feagan BG, Rutgeerts P, et al. Effects of vedolizumab induction therapy for patients with Crohn's disease in whom tumor necrosis factor antagonist treatment failed. Gastroenterology 2014; 147:618–27.

[13] Samaan MA, Pavlidis P, Johnston E, et al. Vedolizumab: early experience and medium-term outcomes from two UK tertiary IBD centres. Frontline Gastroenterol 2017;8:196–202.

[14] Ha C, Ullman TA, Siegel CA, et al. Patients enrolled in randomized controlled trials do not represent the inflammatory bowel disease patient population. Clin Gastroenterol Hepatol 2012;10:1002–7.

[15] Dulai PS, Singh S, Jiang X, et al. The real-world effectiveness and safety of vedolizumab for moderate-severe Crohn's disease: results from the US VICTORY Consortium. Am J Gastroenterol 2016;111:1147–55.

[16] Osterman MT, Haynes K, Delzell E, et al. Comparative effectiveness of infliximab and adalimumab for Crohn's disease. Clin Gastroenterol Hepatol 2014;12:811–7.

[17] EMC. Entyvio 300 mg powder for concentrate for solution for infusion: Summary of Product Characteristics 2015. Available at: https://www.medicines.org.uk/emc/medicine/28980. Accessed December 12, 2017.

[18] Feagan BG, Rubin DT, Danese S, et al. Efficacy of vedolizumab induction and maintenance therapy in patients with ulcerative colitis, regardless of prior exposure to TNF antagonists. Clin Gastroenterol Hepatol 2017;15:229–39.

[19] Sands BE, Sandborn WJ, Van Assche G, 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 2017;23:97–106.

[20] Baumgart DC, Bokemeyer B, Drabik A, et al. Vedolizumab Germany Consortium. Vedolizumab induction therapy for inflammatory bowel disease in clinical practice–a nationwide consecutive German cohort study. Aliment Pharmacol Ther 2016;43:1090–102.

[21] Royal College of Physicians. National clinical audit of biological therapies: annual report. UK inflammatory bowel disease (IBD) audit 2016. London, Royal College of Physicians, 2016. Available at: https://www.rcplondon.ac.uk/projects/outputs/national-clinical-audit-biologicaltherapies-annual-report-2016. Accessed December 12, 2017.

[22] Shelton E, Allegretti JR, Stevens B, et al. Efficacy of vedolizumab as induction therapy in refractory IBD patients: a multicenter cohort. Inflamm Bowel Dis 2015;21:2879–85.

[23] Amiot A, Grimaud J-C, Peyrin-Biroulet L, et al. Effectiveness and safety of vedolizumab induction therapy for patients with inflammatory bowel disease. Clin Gastroenterol Hepatol 2016;14:1593–601.

[24] Vivio EE, Kanuri N, Gilbertsen JJ, et al. Vedolizumab effectiveness and safety over the first year of use in an IBD clinical practice. J Crohns Colitis 2016;10:402–9.

[25] Colombel J-F, Sands BE, Rutgeerts P, et al. The safety of vedolizumab for ulcerative colitis and Crohn's disease. Gut 2017;66:839–51.

[26] ClinicalTrials.gov. Entyvio (Vedolizumab) Long Term Safety Study 2016. Available at: https://clinicaltrials.gov/ct2/show/NCT02674308?term=vedolizumab+PASS&rank=1. Accessed December 12, 2017.