ORIGINAL PAPERS

Vedolizumab response in inflammatory bowel disease. Two years of follow-up

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ABSTRACT

Background: vedolizumab is an α4β7 integrin antagonist. The aim of this study was to evaluate the clinical response and remission rates with vedolizumab.

Methods: this was a retrospective study of inflammatory bowel disease (IBD) patients who received vedolizumab between 2016 and 2019. Response and remission rates were analyzed at three, six, 12, 18 and 24 months after induction.

Results: fifty-five patients were included. Clinical remission rates in CD and UC at three, six, 12, 18 and 24 months were 19.35 %, 26.67 %, 30.43 %, 30 %, 38.89 % and 29.17 %, 26.09 %, 19.05 %, 26.67 % and 20 %, respectively.

Conclusions: vedolizumab is effective for induction and maintenance of clinical remission, both in Crohn's disease and ulcerative colitis.

Keywords: Vedolizumab. Response. Remission.

INTRODUCTION

Vedolizumab is a fully humanized monoclonal IgG-1 antibody that selectively inhibits the interaction between α4β7 integrin and mucosal addressin cell adhesion molecule-1 (MAdCAM-1). Therefore preventing lymphocyte translocation from the blood into the inflamed gut tissue, which results in a reduction in local inflammation (1). In the GEMINI studies, vedolizumab proved to be effective as an induction and maintenance therapy in moderately to severely active ulcerative colitis (UC) and Crohn's disease (CD) (2,3). Immunogenicity for vedolizumab appears to be low (4) and it seems to have a favorable safety profile (5).

The primary aim of this study was to explore, according to the clinical practice, the response and remission rates to vedolizumab in our center after 24 months. The secondary aim was to assess whether there were any predictors of response to vedolizumab.

MATERIALS AND METHODS

Study design and patient population

A retrospective, single center, observational study was performed at the Hospital Universitario Virgen Macarena, Seville, Spain. Adult patients (≥ 18 years) with CD or UC receiving vedolizumab (first line or after previous biologic failure) between January 1st 2016 and July 1st 2019 were included.

Inclusion criteria were:

1. A confirmed diagnosis of CD or UC.
2. Patients who received at least a completed induction regimen of intravenous (IV) vedolizumab. The standard dosing regimen consisted in induction (300 mg IV at zero, two and six weeks), followed by maintenance (300 mg IV every eight weeks).

Outcomes and definitions

Response and remission definitions were based on the Harvey Bradshaw index (HBI) and Mayo scoring index (MSI). Clinical remission was considered when MSI was ≤ 2 and HBI was ≤ 4. Clinical response was defined as a decrease of at least two points in the HBI or MSI index from their previous score. Clinical response and remission were analyzed at three, six, 12, 18 and 24 months.

Data collection

Data of patients treated with vedolizumab from January 2016 to July 2019 were collected. All patients were followed in our inflammatory bowel disease (IBD) unit during the study

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period. An anonymous database was created that included demographic variables, smoking status, disease duration, disease phenotype, previous and concurrent IBD treatments at baseline and clinical measures of disease activity at vedolizumab induction and at months three, six, 12, 18, 24.

Statistical analysis

Baseline demographic characteristics were analyzed with standard descriptive statistics. For the analysis of quantitative variables, the non-parametric U Mann-Whitney test was used for the comparison of the groups. Statistical significance was considered when $p < 0.05$. The proportion of clinical responders to vedolizumab was compared at each time point using the Pearson's Chi-squared test. Univariate and multivariable logistic regression analyses were performed to evaluate predictors of clinical and objective remission at three, six, 12, 18 and 24 months. With regard to the response and remission rate analysis, patients who had adverse effects and those who had not yet completed follow-up were excluded. Therefore, the analysis included patients with treatment failure (including those requiring surgery).

RESULTS

Baseline patient characteristics

Fifty-five patients (31 CD, 24 UC) were included in the study. Figure 1 summarizes the patient flowchart of the study and demographics are summarized in table 1; 83.9 % (26/31) of the patients with CD and 100 % of the patients with CU had received anti-TNFα therapies prior to initiating vedolizumab. Most of the patients had received two different anti-TNFα therapies (46.2 % CD, 62.5 % UC). The main reason for the onset of vedolizumab was the lack of response to previous treatments (64.5 % CD, 95.8 % UC), followed by adverse effects to previous therapy (19.4 % CD, 4.2 % CU). In addition, 12.9 % started vedolizumab as a first line therapy due to concomitant diseases.

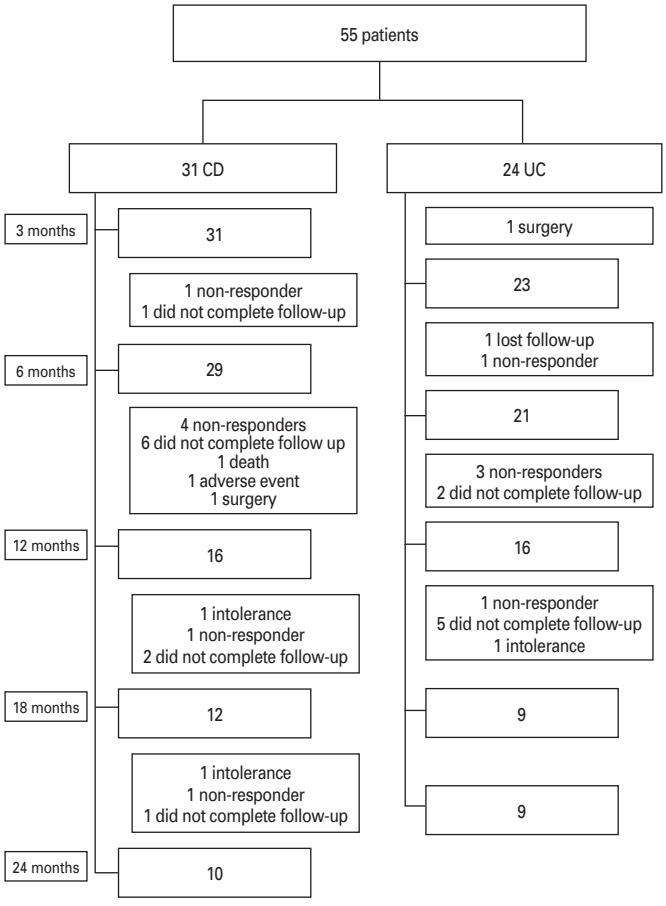

Fig. 1. *Study flowchart.*

Table 1. *Baseline patient demographics*

		Crohn's disease (n = 31)	Ulcerative colitis (n = 24)
Gender (n, %)			
Men		8 (25.8)	13 (54.2)
Women		23 (74.2)	11 (45.8)
Age (mean ± SD)		41.7 ± 12.9	41.4 ± 14.9
Smoking status (n, %)			
Smokers		9 (29)	1 (4.2)
Non smokers		17 (54.8)	21 (87.5)
Ex-smoker		5 (16.1)	2 (8.3)
Montreal (n, %)	Age	A1: 8 (25.8) A2: 16 (51.6) A3: 7 (22.6)	
	Location	L1: 6 (19.4) L2: 12 (38.7) L3: 12 (38.7) L3+L4: 1 (3.2)	E1: 5 (20.8) E2: 14 (58.3) E3: 5 (20.8)
	Behavior	B1: 13 (41.9) B2: 10 (32.3) B3: 8 (25.8)	S1: 7 (29.2) S2: 10 (41.7) S3: 7 (29.2)
Basal Harvey Bradshaw index (mean ± SD)		7.81 ± 2.02	--
Basal Mayo scoring index (mean ± SD)		--	6,42 ± 2.3
Perianal disease (n, %)		11 (35.5)	1 (4.2)
Extraintestinal manifestations (n, %)		17 (54.8)	8 (33.3)
Previous anti-TNF treatment		26 (83.9)	24 (100)
Infliximab		1 (3.8)	5 (20.8)
Adalimumab		6 (23.1)	1 (4.2)
IFX y ADA		12 (46.2)	15 (62.5)
IFX, ADA and golimumab		1 (3.8)	3 (12.5)
IFX, ADA and certolizumab		5 (19.2)	0 (0)
ADA and certolizumab		1 (3.8)	0 (0)
Concomitant treatment			
AZT		2 (6.5)	5 (20.8)
MTX		4 (12.9)	3 (12.5)
Corticosteroids		22 (71)	16 (66.7)

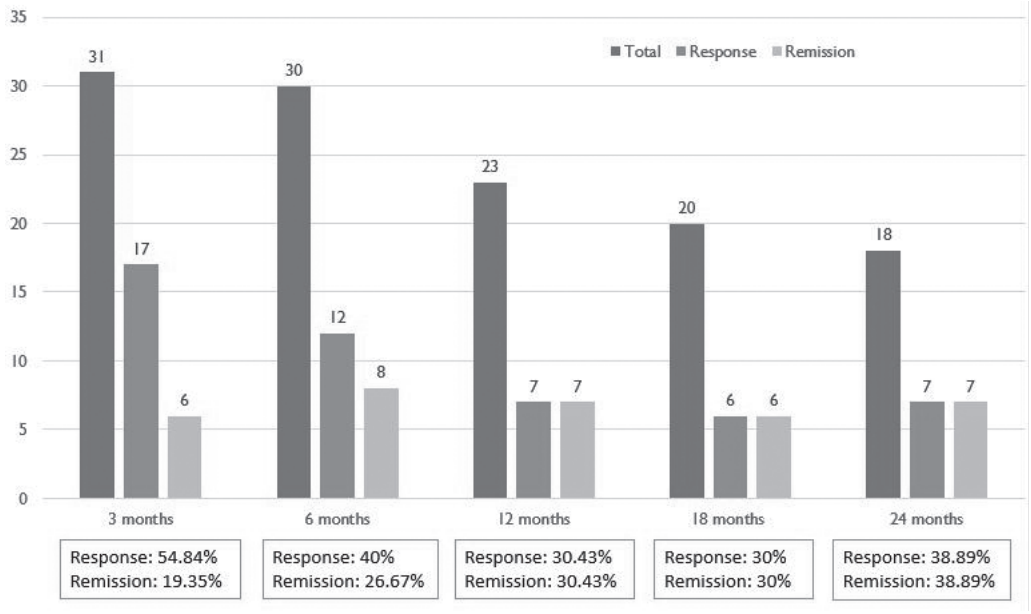

Fig. 2. *Clinical response and remission rates in CD.*

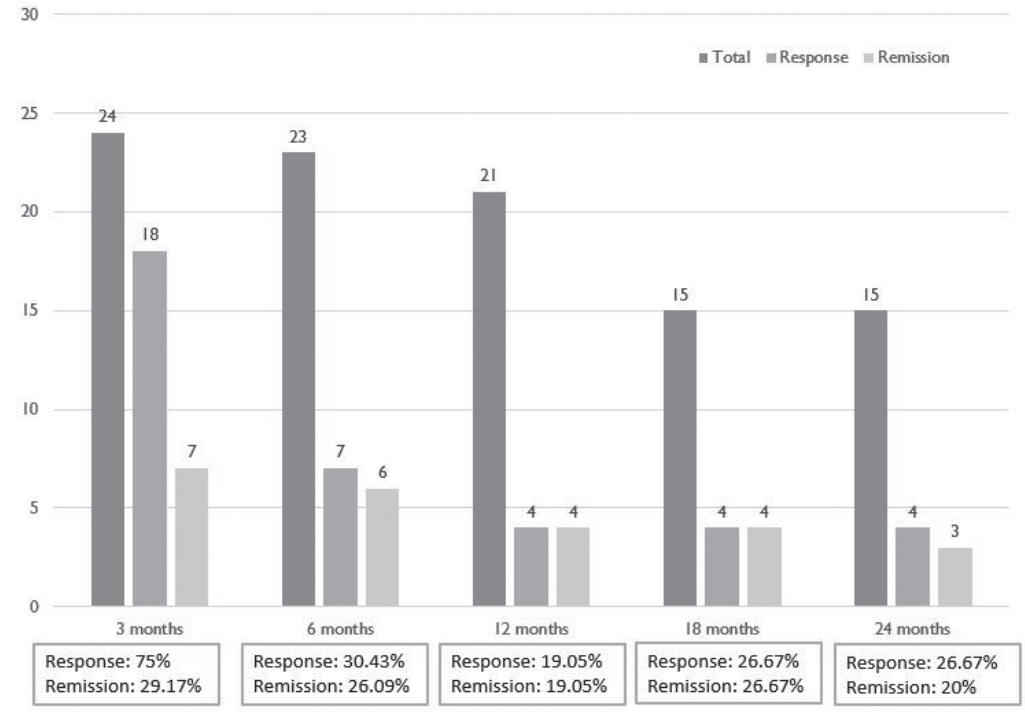

Fig. 3. *Clinical response and remission rates in UC.*

Clinical response and remission

Clinical response and remission rates to vedolizumab therapy in CD and UC are summarized in figures 1 and 2. Overall, there was a decrease in the Harvey-Bradshaw and Mayo index values compared to baseline at three, six, 12, 18 and 24 months ($p < 0.05$), as well as a decrease in C-reactive protein. Nine patients (6 CD, 3 UC) required a 4th dose of vedolizumab at week 10. Nine patients (29 %) with CD required intensification of vedolizumab.

Predictors of clinical and objective remission with vedolizumab

In the multivariate analysis, no relationship was observed with age, smoking, type of disease or previous anti-TNF and higher response rates. At 12 months, higher response and remission rates were observed in females (81.8 %, $p = 0.039$), while 87.5 % of patients with CD treated with corticosteroids did not respond at six months.

Safety profile of vedolizumab

Five patients (3 CD, 2 CU) experienced an adverse event, four required suspension. One patient presented abdominal pain and vomiting, two patients (1 CD, 1 UC) had skin lesions and the remaining two experienced headaches and joint pain. One patient (CD) died during follow-up due to a respiratory failure, as a consequence of a nephrotic syndrome in the context of a secondary amyloidosis.

DISCUSSION

Pivotal studies have shown vedolizumab to be effective and safe, both for induction and maintenance in patients with IBD (2,3). CD patients treated with vedolizumab present clinical remission rates of around 19 % at three months, shown both in a real-world cohort in Canada (6), a prospective German study (7) and the present study (19.35 %). In UC, clinical remission rates at three months range between 23 and 51 % (6-12). Specifically, we report rates of 29.17 % in our study. The variance may be due to different inclusion criteria and definitions of active disease, remission and response, which may cause differences in the severity of the disease between each population. For instance, Kotze reported a clinical remission rate of 51 % in UC. This study included 54 % of UC patients with a previous biologic failure, compared to 100 % in our study.

At 12 months, clinical remission rates of 30.43 % in CD were observed in our study. This rate is slightly higher than that reported by Kotze (6), but somewhat lower than those reported in the GEMINI trial (3) and VICTORY consortium trial (12). The differences with the GEMINI trial may be due to the proportion of patients who had received prior anti-TNF therapy, which was limited to 50 %. Lower remission rates were found in UC patients than that reported in the literature (2,6,13,14), both at 12 and 18 weeks. The larger number of patients in this study compared to ours may explain this difference.

Subgroup analyses of GEMINI 2 showed higher clinical remission rates in males, younger patients and CD patients with a shorter disease duration (5). However, higher response and remission rates were observed in females only at 12 months compared to males. Besides, previous studies suggest that prior treatment with corticosteroid is associated with a lack of clinical remission (11,15). This is consistent with our results, as patients with concomitant treatment with corticosteroids were less likely to achieve clinical remission at six months.

Our study has several limitations. Firstly, the number of patients is reduced. Secondly, it is a retrospective and single-center study. However, preliminary information was obtained that may act as a starting point for future evaluations of the impact of vedolizumab in IBD patients.

In conclusion, treatment with vedolizumab is effective for induction and maintenance of clinical remission in patients with IBD who have not responded to or tolerated anti-TNF treatment.

REFERENCES

1. Scribano ML. Vedolizumab for inflammatory bowel disease: from randomized controlled trials to real-life evidence. World J Gastroenterol 2018;24(23):2457-67. DOI: 10.3748/wjg.v24.i23.2457
2. Feagan BG, Rutgeerts P, Sands BE, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. N Engl J Med 2013;369(8):699-710. DOI: 10.1056/NEJMoa1215734
3. Sandborn WJ, Feagan BG, Rutgeerts P, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. N Engl J Med 2013;369(8):711-21. DOI: 10.1056/NEJMoa1215739
4. Shim HH, Chan PW, Chuah SW, et al. A review of vedolizumab and ustekinumab for the treatment of inflammatory bowel diseases. JGH Open 2018;2(5):223-34. DOI: 10.1002/jgh3.12065
5. Barré A, Colombel JF, Ungaro R. Review article: predictors of response to vedolizumab and ustekinumab in inflammatory bowel disease. Aliment Pharmacol Ther 2018;47(7):896-905. DOI: 10.1111/apt.14550
6. Kotze PG, Ma C, Almutairdi A, et al. Real-world clinical, endoscopic and radiographic efficacy of vedolizumab for the treatment of inflammatory bowel disease. Aliment Pharmacol Ther 2018;48(6):626-37. DOI: 10.1111/apt.14919
7. Baumgart DC, Bokemeyer B, Drabik A, et al. Vedolizumab induction therapy for inflammatory bowel disease in clinical practice - A nationwide consecutive German cohort study. Aliment Pharmacol Ther 2016;43(10):1090-102. DOI: 10.1111/apt.13594
8. Chaparro M, Garre A, Ricart E, et al. Short and long-term effectiveness and safety of vedolizumab in inflammatory bowel disease: results from the ENEIDA registry. Aliment Pharmacol Ther 2018;48(8):839-51. DOI: 10.1111/apt.14930
9. Kopylov U, Ron Y, Avni-Biron I, et al. Efficacy and safety of vedolizumab for induction of remission in inflammatory bowel disease - The Israeli real-world experience. Inflamm Bowel Dis 2017;23(3):404-8. DOI: 10.1097/MIB.0000000000001039
10. 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(12):2879-85. DOI: 10.1097/MIB.0000000000000561
11. Amiot A, Grimaud JC, Peyrin-Biroulet L, et al. Effectiveness and safety of vedolizumab induction therapy for patients with inflammatory bowel disease. Clin Gastroenterol Hepatol 2016;14(11):1593-601.e2.
12. 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(8):1147-55. DOI: 10.1038/ajg.2016.236
13. Tursi A, Mocci G, Faggiani R, et al. Vedolizumab is effective and safe in real-life treatment of inflammatory bowel diseases outpatients: a multicenter, observational study in primary inflammatory bowel disease centers. Eur J Intern Med 2019;66:85-91. DOI: 10.1016/j.ejim.2019.06.006
14. Allegretti JR, Barnes EL, Stevens B, et al. Predictors of clinical response and remission at 1 year among a multicenter cohort of patients with inflammatory bowel disease treated with vedolizumab. Dig Dis Sci 2017;62(6):1590-6. DOI: 10.1007/s10620-017-4549-3
15. Stallmach A, Langbein C, Atreya R, et al. Vedolizumab provides clinical benefit over 1 year in patients with active inflammatory bowel disease - A prospective multicenter observational study. Aliment Pharmacol Ther 2016;44(11-12):1199-212 DOI: 10.1111/apt.13813