Effectiveness of Vedolizumab in Patients with Inflammatory Bowel Disease and Concomitant Primary Sclerosing Cholangitis

Priscila Santiago MD; Anthony Robateau, MD; Rachel Lopdrup, MD; Manuel Braga Neto, MD, PhD; Laura Raffals, MD, MS; John Eaton, MD; Guilherme Piovezani Ramos, MD; Edward V. Loftus, Jr., MD.
Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN.

ABSTRACT

BACKGROUND
Patients with concomitant primary sclerosing cholangitis (PSC) and inflammatory bowel disease (IBD) have higher expression of mucosal addressin cell adhesion molecule 1 (MAdCAM-1) in both liver and intestines. MADCAM-1 interacts with α4β7 integrin to allow access of lymphocytes to the intestinal mucosa and is inhibited by vedolizumab (VDZ). Although VDZ has not been shown to slow progression of PSC, little is known about its impact in intestinal inflammation of PSC-IBD patients.

OBJECTIVE
We aimed to report the effectiveness of VDZ in controlling intestinal inflammation in a large PSC-IBD cohort.

METHODS
We conducted a retrospective review of patients with PSC-IBD treated with VDZ from January 2009 to January 2019. Data were abstracted at baseline, and at 6 and 12 months after initiation of VDZ. Outcomes of interest included: clinical response, radiologic response and healing, endoscopic response, mucosal healing, and histologic healing.

RESULTS
A total of 108 patients with PSC-IBD treated with VDZ were identified. The majority were male (66%). The most common IBD subtype was ulcerative colitis (UC) (61.1%). Over three quarters of the cohort (79.6%) had previously failed other biologic therapy (Table 1). Median duration of VDZ therapy was 17.5 months (Table 2). Clinical response was 72.6% at 6 months and 77.1% at 1 year. Endoscopic response was noted in 47.1% and 58.1% of the cases at 6 months and 1 year, respectively. Radiologic response at 6 months and 1 year was 32.4% and 38.9%, respectively. Radiology healing at 6 months and 1 year was 16.2% and 18.2%, respectively. Histologic healing at 6 months was 6.7% and 18.8% at 1 year. Colectomy while on vedolizumab occurred in 15% of the patients.

CONCLUSIONS
VDZ is effective in the management of intestinal inflammation in patients with PSC-IBD, with clinical and endoscopic outcomes at 1-year follow-up comparable to current clinical trials in non-PSC patients. Further studies comparing outcomes of PSC-IBD patients on VDZ to other biologic therapies are needed.

OBJECTIVES

- We aimed to report the effectiveness of vedolizumab (VDZ) in controlling intestinal inflammation in a large PSC-IBD cohort.

METHODS

- Retrospective review of patients with PSC-IBD treated with vedolizumab from January 2009 to January 2019.
- Demographic, clinical, endoscopic, and radiologic data were abstracted at baseline, and at 6 and 12 months after initiation of VDZ.
- Outcomes of interest: clinical response, radiologic response and healing, endoscopic response, mucosal healing, and histologic healing.

RESULTS

- 108 patients with PSC-IBD treated with VDZ.
- The most common IBD subtype was ulcerative colitis (61.1%).
- 80% had previously failed biologics.
- Clinical response: 72.6% and 77.1% at 6 and 12 months, respectively.
- Endoscopic response: 47.1% and 58.1% at 6 and 12 months, respectively.

RESULTS

TABLE 1 – BASELINE CHARACTERISTICS

Patient demographics	N = (108)
Male, n (%)	72 (66.7)
Median age, years (range)	45 (19-83)
Median disease duration, years (range)	8 (0-50)
Prior use of other biologics, n (%)	86 (79.6)
Combination therapy while on VDZ, n (%)	
Thiopurine/6MP/azathioprine	18 (17.3)
MTX	1 (1.0)
IBD Subtype, n (%)	
CD	36 (33.3)
UC	66 (61.1)
IC	6 (5.6)
CD Location, n (%)	
Terminal ileum	0/34 (0)
Colon	4/34 (11.8)
Ileocolonic	29/34 (85.3)
Upper GI	1/34 (2.9)
Perianal disease, n (%)	9 (8.8)
CD phenotype, n (%)	
Inflammatory	16/36 (44.4)
Stricturing	14/36 (38.9)
Penetrating	6/36 (16.7)
UC extension, n (%)	
Proctitis	3/64 (4.7)
Left-sided colitis	2/64 (3.1)
Pancolitis	59/64 (92.2)
Bowel resection before VDZ, n (%)	45 (55.6)
History of Liver Transplant, n (%)	33 (30.6)

TABLE 2 – OUTCOMES WITH VEDOLIZUMAB

VDZ outcomes	N = 108
Median duration of therapy, months (range)	17.5 (2.0-66.0)
Drug dose frequency, n (%)	
Every 8 weeks	79 (73.1)
Every 6 weeks	7 (6.5)
Every 4 weeks	22 (20.4)
VDZ discontinued indefinitely, n (%)	46 (43.0)
Clinical response at 6 months, n (%)	74/102 (72.6)
Clinical response at 1 year, n (%)	64/83 (77.1)
Endoscopic response at 6 months, n (%)	24/51 (47.1)
Endoscopic healing at 6 months, n (%)	8/55 (14.5)
Endoscopic response at 1 year, n (%)	25/43 (58.1)
Endoscopic healing at 1 year, n (%)	12/46 (26.1)
Radiologic response at 6 months, n (%)	11/34 (32.4)
Radiologic healing at 6 months, n (%)	6/37 (16.2)
Radiologic response at 1 year, n (%)	7/18 (38.9)
Radiologic healing at 1 year, n (%)	4/22 (18.2)
Histologic healing at 6 months, n (%)	3/45 (6.7)
Histologic healing at 1 year, n (%)	9/48 (18.8)
Colectomy on VDZ, n (%)	16/108 (15.0)

DISCUSSION

- We described the real world-efficacy of VDZ in gut outcomes of a large retrospective cohort of well-established PSC-IBD patients.

CONCLUSIONS

- VDZ is effective in the management of intestinal inflammation in patients with PSC-IBD.
- Clinical and endoscopic outcomes at 1-year follow-up are comparable to currently available clinical trials in non-PSC patients.
- Further studies comparing outcomes of PSC-IBD patients on VDZ to other biologic therapies are needed.

REFERENCES

1. Tse CS, Loftus EV Jr, Raffals LE, et al. Effects of vedolizumab, adalimumab and infliximab on biliary inflammation in individuals with primary sclerosing cholangitis and inflammatory bowel disease. Aliment Pharmacol Ther 2018;48:190-195.
2. Christensen B, Micic D, et al. Vedolizumab in patients with concurrent primary sclerosing cholangitis and inflammatory bowel disease does not improve liver biochemistry but is safe and effective for the bowel disease. Aliment Pharmacol Ther. 2018 Mar;47(6):753-762.
3. Lynch KD, International Primary Sclerosing Cholangitis Study Group (IPSCSG), Levy C. Effects of Vedolizumab in Patients With Primary Sclerosing Cholangitis and Inflammatory Bowel Diseases. Clin Gastroenterol Hepatol. 2020 Jan;18(1):179-187.e6.