

TABLE 1. (Continued)

	UC with Noninflammatory Symptoms (n = 49)	Quiescent UC (n = 53)	<i>P</i> *	UC with Occult Inflammation (n = 27)	<i>P</i> *	Active UC (n = 43)	<i>P</i> *	<i>P</i> †
PHQ-15 somatization categories (%)								
Mild	1 (2.1)	19 (36.5)		12 (46.2)		2 (5.0)		
Low	11 (22.9)	18 (34.6)		9 (34.6)		11 (27.5)		
Medium	18 (37.5)	12 (23.1)		5 (19.2)		17 (42.5)		
High	18 (37.5)	3 (5.8)	<0.001	0 (0.0)	<0.001	10 (25.0)	0.59	<0.001
Mean SF-36 score (SD)								
Physical functioning	73.7 (24.9)	88.1 (17.8)	0.002	81.2 (24.8)	0.23	72.3 (27.0)	0.81	0.004
Role limitations physical health	42.8 (43.8)	86.8 (24.7)	<0.001	70.4 (40.5)	0.008	45.8 (44.5)	0.75	<0.001
Role limitations emotional problems	53.2 (44.9)	84.0 (33.3)	<0.001	88.9 (27.7)	<0.001	59.5 (43.9)	0.50	<0.001
Energy/fatigue	39.8 (22.1)	61.5 (19.9)	<0.001	55.5 (19.1)	0.005	39.6 (23.3)	0.98	<0.001
Emotional well- being	58.0 (23.6)	77.4 (16.3)	<0.001	77.5 (19.0)	<0.001	66.3 (20.1)	0.08	<0.001
Social functioning	59.9 (29.3)	85.4 (20.6)	<0.001	86.5 (19.0)	<0.001	56.3 (29.0)	0.56	<0.001
Pain	53.0 (27.0)	80.6 (19.1)	<0.001	83.1 (23.2)	<0.001	59.5 (21.0)	0.20	<0.001
General health	43.5 (20.4)	66.2 (22.2)	<0.001	66.6 (21.6)	<0.001	45.8 (24.1)	0.63	<0.001
Mean fecal calprotectin (SD)	90.3 (68.6)	79.3 (57.9)	0.39	774 (637)	<0.001	1536 (1284)	<0.001	<0.001

HADS, Hospital anxiety and depression scale; PHQ-15, Patient health questionnaire-15; SD, standard deviation; SF-36, 36 item short form health survey.

\*Independent samples t-test for continuous data, and  $\chi^2$  for comparison of categorical data vs. UC with true IBS.

†One way ANOVA for continuous data, and  $\chi^2$  for comparison of categorical data across all four groups.

defined cohort of patients with quiescent UC with ongoing GI symptoms. These symptoms, whether compatible with diagnostic criteria for IBS or not, are associated with poor psychological health and reduced quality of life.<sup>1,3</sup> This suggests that the ongoing debate as to whether such symptoms are the result of genuine coexistent functional disease is irrelevant. A preferable term may be GI symptoms in the absence of inflammation, and what is needed are management strategies for them.

David J. Gracie, BSc, MBChB,  
MRCP\*.<sup>†</sup>

Alexander C. Ford, MBChB, MD,  
FRCP\*.<sup>†</sup>

\*Leeds Gastroenterology Institute  
St. James's University Hospital  
Leeds, United Kingdom

<sup>†</sup>Leeds Institute of Biomedical and  
Clinical Sciences, University of Leeds  
Leeds, United Kingdom

## REFERENCES

1. Jonefjall B, Ohman L, Simren M, et al. IBS-like symptoms in patients with ulcerative colitis in deep remission are associated with increased levels of serum cytokines and poor psychological well-being. *Inflamm Bowel Dis*. 2016;22:2630–2640.
2. Gracie DJ, Williams CJ, Sood R, et al. Poor correlation between clinical disease activity and mucosal inflammation, and the role of psychological comorbidity, in inflammatory bowel disease. *Am J Gastroenterol*. 2016;111:541–551.
3. Gracie DJ, Williams CJ, Sood R, et al. Negative effects on psychological health and quality of life of genuine irritable bowel syndrome-type symptoms in patients with inflammatory bowel disease. *Clin Gastroenterol Hepatol*. [published online ahead of print May 14, 2016]. doi: 10.1016/j.cgh.2016.05.012.
4. Halpin SJ, Ford AC. Prevalence of symptoms meeting criteria for irritable bowel syndrome in inflammatory bowel disease: systematic review and meta-analysis. *Am J Gastroenterol*. 2012;107:1474–1482.

## Efficacy of Vedolizumab in Patients with Antibiotic and Anti-tumor Necrosis Alpha Refractory Pouchitis

### To the Editor:

Refractory pouchitis is a common cause of pouch failure, which may require surgical excision of the pouch or permanent diversion. Vedolizumab, a humanized immunoglobulin G1 monoclonal antibody to  $\alpha 4\beta 7$  integrin, has been shown to moderate gut lymphocyte trafficking with an efficacy in

The authors have no conflict of interest to disclose.

Copyright © 2016 Crohn's & Colitis Foundation of America, Inc.

DOI 10.1097/MIB.0000000000000992

Published online 7 December 2016.

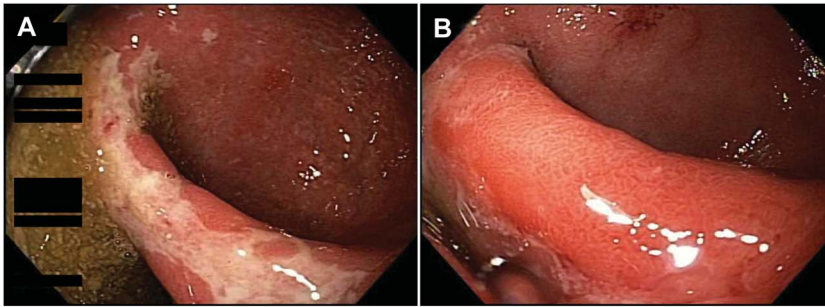


FIGURE 1. A, Patient 4 pouch endoscopy while on adalimumab therapy for 9 months reveals active pouchitis with ulceration, edema, exudate, and PDAI endoscopic subscore of 5. B, Patient 4 pouch endoscopy after 3 months of vedolizumab therapy reveals mucosa with mild edema, no ulceration, and endoscopic subscore of 1.

treatment of both Crohn's disease and ulcerative colitis (UC).<sup>1,2</sup> Although tumor necrosis factor  $\alpha$  inhibitors have been reported to be effective as treatment for pouchitis,<sup>3</sup> there are no data regarding the use of vedolizumab in refractory pouchitis and it is not labeled for this use. We report a small case series of 4 patients treated with vedolizumab for antibiotic and anti-tumor necrosis factor refractory pouchitis. Four patients were identified as having refractory pouchitis and underwent pouch endoscopy before and after 3 months of therapy with vedolizumab during the period 2015 to 2016.

Patient 1, a 54-year-old man, had undergone colectomy and ileal pouch–anal anastomosis in 2000 for medically refractory UC. He suffered from ankylosing spondylitis and chronic pouchitis. He had been treated serially with antibiotics, budesonide, infliximab, methotrexate, and adalimumab in combination with hyperbaric oxygen therapy. Pouchoscopy before initiation revealed confluent ulceration with the Pouchitis Disease Activity Index (PDAI) endoscopic subscore of 4. Endoscopy 4 months after the initiation of vedolizumab therapy revealed visual improvement, with few small ulcers noted, with a PDAI endoscopic subscore of 3. He experienced improvement in clinical symptoms and has avoided surgical resection of his pouch but does require maintenance

therapy budesonide. Patient 2, a 54-year-old woman, underwent colectomy and ileal pouch–anal anastomosis in 1991 for medically refractory UC. She developed recurrent stricture at the pouch inlet and afferent limb and pouchitis. Treatment included surgical stricturoplasty, followed by antibiotics, thiopurines, mesalamine, intravenous immunoglobulin therapy, fecal microbiota transplant, and adalimumab. Despite these treatments, she continued to have symptoms of diarrhea and pain. Pouch endoscopy revealed chronic pouchitis with edema and loss of vascular pattern consistent with a PDAI subscore of 5, along with cuffitis, and ulcerated strictures in the neoterminal ileum. She underwent pouchoscopy 4 months after initiating therapy with vedolizumab, which revealed improvement in pouchitis with normal appearing mucosa and PDAI endoscopic subscore of 1 but ongoing ulceration at cuff and inlet. Symptom improvement was reported for both pain and diarrhea. Patient 3, a 54-year-old woman after restorative proctocolectomy for refractory UC in 2012, had required pouch redo surgery in 2014 for severe pouch dysfunction. She suffered from diarrhea requiring intravenous hydration despite use of antibiotics, infliximab with azathioprine, and mesalamine. Her pouchoscopy revealed pouchitis and ileitis with a PDAI score of 3. Pouch endoscopy 4 months after the

initiation of vedolizumab revealed improved mucosa of the pouch with PDAI score of 1. She noted improvement in symptoms of diarrhea. Patient 4 was a 53-year-old woman who had undergone total abdominal proctocolectomy and pouch construction in 2004 for UC complicated by *Clostridium difficile* infection. She had suffered from chronic pouchitis despite treatment with antibiotics, entocort, methotrexate, and adalimumab. Pouch endoscopy while on adalimumab revealed marked ulceration with pouchitis score of 5 (Fig. 1A). After 3 months of vedolizumab, repeat pouchoscopy revealed resolution of ulceration with score of 1 (Fig. 1B). She noted reduction in symptoms of diarrhea, with mild symptoms of arthralgia.

In summary, we present 4 cases of patients with refractory pouchitis who after 3 months of open-label vedolizumab therapy were noted to have improved symptoms and measurable improvement in the endoscopic appearance of the pouch. We speculate that the gut-specific immune modulation mediated by vedolizumab results in these notable responses to therapy. This warrants further study to validate the use of this medication in antibiotic and anti-tumor necrosis factor  $\alpha$  refractory pouchitis, along with better understanding of the mechanism of this form of pouch dysfunction.

**Jessica Philpott, MD, PhD**

**Jean Ashburn, MD**

**Bo Shen, MD**

Departments of Gastroenterology  
and Colorectal Surgery, The Cleveland  
Clinic, Cleveland, Ohio

## REFERENCES

1. 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.
2. Sandborn WJ, Feagan BG, Rutgeerts P, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med*. 2013;369:711–721.
3. Herfarth HH, Long MD, Isaacs KL. Use of biologics in pouchitis: a systematic review. *J Clin Gastroenterol*. 2015;49:647–654.