

## Answering Reviewers

- 1- *He had fallen from 55 kilograms to 43 kilograms during pouchitis. An upper endoscopy was done at the same time to evaluate diarrhea. It was normal and duodenal biopsy was negative for the presence of celiac disease. Serum antibodies for celiac disease including anti-gliadin antibodies, endomysial antibodies and anti-transglutaminase antibodies were negative. Therefore, gluten restricted diet was not given to the patient who was fed gluten. He gained weight almost 9 kilograms during vedolizumab treatment, and his quality of life is improved.*
- 2- *Effect of vedolizumab for treatment of pouchitis as review of literature was shown in Table. Vedolizumab selectively blocks gut lymphocyte trafficking by interacting with  $\alpha 4\beta 7$  heterodimer, is a monoclonal antibody (1). There are a severe infiltration of the mucosa by both innate and adaptive immune cells in active pouchitis. It was shown that an increased proportion of mucosal dendritic cells expressing integrin  $\alpha 7$  in patients with pouch inflammation (14). The integrin signaling in the pathogenesis of this clinical condition of pouchitis may possible pathogenic role. Therefore, blockade of  $\alpha 4\beta 7$  integrin with vedolizumab treatment might represent a promising therapeutic strategy for this clinical condition (14).*

**Table.** Effect of vedolizumab for treatment of pouchitis as review of literature

Country and Reference	Number of the patient	Age and gender	Features of inflammatory bowel disease	Outcomes
USA and reference 8	1	41 year-old female	She had pouchitis two years later ileal pouch–anal anastomosis (IPAA).	Improvement in clinical symptoms and decreased frequency of bowel movements to four to six per day without blood or mucus were reported with 6 weeks of vedolizumab treatment. There was no side effect.
Italy and reference 9	1	33 year-old man	33 year-old man with anti-TNF-refractory chronic pouchitis and concomitant primary sclerosing cholangitis (PSC).	3 months after ileostomy closure, chronic pouchitis occurred, refractory to antibiotics and anti-TNF. Thus, vedolizumab was started, leading to a marked improvement in clinical symptoms, which was maintained up at the end of follow up (week 34). There was no side effect.
Germany and reference 10	20	12 men, 8 female The median age was 22.5 year-old	All of the patients were pouchitis	Improvement of clinical symptoms and the Oresland score and the PDAI were reported significantly. There was no side effect.
Greece and reference 11	1	22 year-old female	She was first diagnosed with pouchitis 1 year after surgery time decided to administer infliximab followed	Vedolizumab was subsequently initiated, together with a single course of antibiotics, and the patient experienced improvement in clinical symptoms and laboratory results with no documented

			by adalimumab, both of which she discontinued after an early severe allergic reaction.	relapse since then. A new pouchoscopy at week 33 showed significant improvement.
USA and reference 12	12	9 female, 3 male the mean age 41 year-old	All of the patients had active pouchitis. Five patients (41.7%) used mesalamine, six (50.0%) took budesonide and four (33.3%) took prednisone prior to using vedolizumab. Eight (66.7%) had used anti-TNF agents prior to vedolizumab use.	Eight (66.7%) patients demonstrated significant reduction in mPDAI symptom subscores before and after vedolizumab therapy
Portugal and reference 13	1	20 year- old female	She was diagnosed with pouchitis and a severe symptomatic autoimmune hemolytic anemia one year later IPAA.	Patient reported symptoms improvement at week 12 and a pouchoscopy revealed only mucosal edema after 6 months of therapy. Her inflammatory markers and hemoglobin normalized on repeat testing, allowing steroid withdrawal.