ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

Section Editor: Stephen B. Hanauer, MD

Update on the Use of Vedolizumab in Patients With Crohn's Disease

Brian Bressler, MD, MS
Clinical Associate Professor of Medicine
Division of Gastroenterology
University of British Columbia
Vancouver, British Columbia, Canada

G&H Based on the research that has been conducted to date, how effective is vedolizumab for the treatment of Crohn's disease?

BB There is strong evidence in both clinical trial data and real-world data to support the important contribution that vedolizumab (Entyvio, Takeda) can have in patients with Crohn's disease. The most important measure that demonstrates that an agent can be effective in changing the natural history of Crohn's disease is likely the ability to heal the bowel, as defined by mucosal healing. Data from the VERSIFY study clearly show the ability of vedolizumab to heal the bowel, which gives clinicians confidence that the agent can be an important biologic to use in managing patients with Crohn's disease. The proportion of patients who achieve mucosal healing with vedolizumab appears to be similar to that seen with other agents as well.

Also demonstrating the value of vedolizumab are post hoc analyses from clinical trials. One of the most important post hoc analyses that has come out of the GEMINI program looked at how quickly vedolizumab can make patients start to feel better. Initially, there was some concern that it may take a little longer to produce a symptomatic response. When investigators went back and reviewed the diaries of biologic-naive patients, focusing on the patient-reported outcomes of abdominal pain and loose stool frequency, they found a statistically significant improvement compared with placebo as early as 2 weeks after therapy (ie, after the first infusion of vedolizumab, which was the first time that patients were being assessed). Thus, clinicians now know that vedolizumab can work quickly in biologic-naive patients.

An important recent real-world study is the EVOLVE study, which examined how effective vedolizumab is in comparison with an anti–tumor necrosis factor (TNF) agent when each is used as a patient's first biologic. This study, which looked at almost 1000 patients (approximately half of whom were on vedolizumab), included both Crohn's disease patients and ulcerative colitis patients. The study examined how likely patients were to do well if they started on vedolizumab compared with an anti-TNF agent, and was controlled, as best as a retrospective study could be, in terms of the severity of the disease itself. There were several important findings from this study. One was that, from an efficacy point of view, there did not appear to be a signal that either group did better. However, there was a statistically significant difference in safety profiles; biologic-naive patients who started on vedolizumab had a decreased likelihood of acquiring a serious infection compared with biologic-naive patients who started on an anti-TNF agent.

All of these points—the ability to heal the bowel in clinical trials, how quickly the drug works, and its safety profile in the real-world setting—demonstrate why vedolizumab should be an important consideration in the management options for Crohn's disease.

G&H Why did vedolizumab initially have a reputation for being slow to act in Crohn's disease?

BB Initially, vedolizumab had a reputation of being slow to act in Crohn's disease compared with how quickly it acts in ulcerative colitis or in comparison with other biologics in Crohn's disease. A possible reason for this reputation is that there are certain patients in whom vedolizumab indeed does take longer to act, and those are patients who have previously been exposed to an anti-TNF agent. However, the best position of vedolizumab in Crohn's disease is as the first biologic, and very good data are available showing that vedolizumab does, in fact, work quickly in those patients, which is why it is a good choice for them. The notion that vedolizumab is slow to act in biologic-naive patients is not supported by the literature.

… the best position of vedolizumab in Crohn's disease is as the first biologic, and very good data are available showing that vedolizumab does, in fact, work quickly in those patients …

G&H What are the longest follow-up data currently available on the use of vedolizumab in patients with Crohn's disease?

BB Long-term extension data have been published as far as 7 years, which is a long time period to look at how patients are doing. Likely the greatest value of long-term extension data mainly involves the safety profile of a drug. When studying patients for a long time, there is always a risk that there may be safety signals that were not initially appreciated. Reassuringly, that has not been the case with vedolizumab; despite following many patients for over 7 years in the long-term extension study from the GEMINI program, there have not been any new safety signals.

In terms of a real-world efficacy point of view, the EVOLVE study has followed patients up to over 2 years and has shown that vedolizumab is safer than an anti-TNF agent.

G&H Why else is the recent EVOLVE study important?

BB The EVOLVE study is important because it focused on a biologic-naive patient population, whereas many other real-world studies focus either mainly on biologic-exposed patients or a combination of biologic-exposed and biologic-naive patients. Where the value of vedolizumab can especially be appreciated is in biologic-naive patients.

In addition, it is well known that the expectation of how well vedolizumab would work is lower if used after an anti-TNF agent. The EVOLVE study showed that vedolizumab does not impact the effectiveness of a subsequent anti-TNF agent. This discovery is very important when thinking about the proper way to sequence biologics in inflammatory bowel disease.

G&H Does the gut selectivity of vedolizumab translate into safety benefits?

BB We always expected that it would, and the EVOLVE study proved that. A focused approach to impacting the gastrointestinal tract immune system, as vedolizumab works, has now been proven to be a safer and effective way to manage inflammatory bowel disease.

G&H Over the years of vedolizumab use, what have been the most common adverse events that may occur?

BB Vedolizumab is generally a well-tolerated drug. There have been reports of infusion reactions, but they are very uncommon. Some patients have complained of headaches when starting treatment, and some patients have complained of fatigue. It is difficult to determine whether particular adverse events can be attributed to vedolizumab; however, adverse-event data from treatment and comparator groups do not appear to have significant differences.

G&H Based on all of the study data available thus far, which patients with Crohn's disease are the most appropriate candidates for treatment with vedolizumab?

BB Patients with Crohn's disease who are most appropriate for vedolizumab treatment are those who have never been on a biologic before; that is the best time to use vedolizumab. Another group is patients with Crohn's disease who do not have other conditions that would benefit from more systemic immune suppression. For example, in a patient with Crohn's disease who has psoriasis, using a drug that is not as selective as vedolizumab, such as an anti-TNF agent or an anti–interleukin 12/23 agent, might treat both conditions at the same time.

G&H Should vedolizumab be avoided in any patients with Crohn's disease?

BB As described in the product monograph, there are certain scenarios in which clinicians should hold or not start vedolizumab. For example, if a patient has an allergic reaction, he or she should not continue the therapy. An example of someone who should not be considered for vedolizumab therapy is a hospitalized patient whose Crohn's disease is refractory to intravenous corticosteroids.

G&H How might vedolizumab treatment be optimized for patients with Crohn's disease?

BB One way it may be possible to optimize vedolizumab treatment is by giving an extra dose during induction, which certain centers, including my own, consider doing. Thus, in patients whose disease does not respond appropriately after the week 6 dose, my colleagues and I administer a week 10 dose (1 extra dose). In addition, there has been a good deal of research on whether treatment should be intensified from every 8 weeks to every 4 weeks when there is a loss of response. This might be a way to recapture response or optimize it in a patient with Crohn's disease who is doing well on vedolizumab but, in the opinion of the clinician or the patient, not well enough.

As the immunogenicity of vedolizumab is lower than that of other Crohn's disease drugs, the added value of an immunomodulator is not thought to be an important consideration.

G&H What are the next steps in research involving the use of vedolizumab in patients with Crohn's disease?

BB Likely the next step in research overall is understanding how to better achieve response or remission in a larger proportion of patients. In addition, there has been much discussion about combining the therapies that are currently available. Vedolizumab appears to be a natural choice because of its safety profile. There are many different combinations being considered right now, and there is currently some research underway to try to understand whether combining vedolizumab with other biologics could increase the proportion of patients whose Crohn's disease would improve. For example, there is currently ongoing a single-arm study examining patients with high-risk Crohn's disease who are being treated with vedolizumab, adalimumab, and methotrexate, with adalimumab being stopped after induction. However, none of this research on combination therapy has been published or reported yet.

Disclosures

Dr Bressler has served as an advisor/speaker for Pfizer, Merck, Ferring, Janssen, AbbVie, Takeda, Celgene, Genentech, and Novartis; has served as an advisor/consultant to Amgen, Allergan, AMT, Fresenius Kabi, Gilead, Protagonist, Sandoz, Alimentiv, Iterative Scopes, Mylan, and BMS; has received research support from Janssen, AbbVie, Takeda, Atlantic Pharmaceuticals, GSK, BMS, Amgen, Genentech, Merck, RedHill Biopharma, BI, Qu Biologics, Celgene, and Alvine; and has had stock options in Qu Biologics.

Suggested Reading

Bressler B, Yarur A, Silverberg MS, et al. Vedolizumab and anti-TNFα real-world outcomes in biologic-naïve inflammatory bowel disease patients: results from the EVOLVE study [published online March 31, 2021]. *J Crohns Colitis*. doi:10.1093/ecco-jcc/jjab058.

Danese S, Sandborn WJ, Colombel JF, et al. Endoscopic, radiologic, and histologic healing with vedolizumab in patients with active Crohn's disease. *Gastroenterology*. 2019;157(4):1007-1018.e7.

Feagan BG, Lasch K, Lissoos T, et al. Rapid response to vedolizumab therapy in biologic-naive patients with inflammatory bowel diseases. *Clin Gastroenterol Hepatol*. 2019;17(1):130-138.e7.

Loftus EV Jr, Feagan BG, Panaccione R, et al. Long-term safety of vedolizumab for inflammatory bowel disease. *Aliment Pharmacol Ther*. 2020;52(8):1353-1365.

Sandborn WJ, Feagan BG, Rutgeerts P, et al; GEMINI 2 Study Group. Vedolizumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med*. 2013;369(8):711-721.

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(3):618-627.e3.