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Considerations for Creating a Protocol for Vedolizumab Infusions

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ABSTRACT

Vedolizumab (Entyvio, Takeda Pharmaceuticals America, Inc., Deerfield, IL) is one of several treatment options for the management of ulcerative colitis and Crohn's disease. It is a recombinant humanized anti −alpha-4-beta-7 integrin monoclonal antibody. This biologic immunotherapy is used in patients who have failed or achieved inadequate response to the different therapies currently available for these disease processes. Certain considerations include monitoring for tuberculosis, and the administration of immunizations before the initiation of therapy. A protocol for the safe administration of vedolizumab at New York University Center for Musculoskeletal Care Infusion Center is based on current prescribing guidelines.

Keywords: Entyvio, infusion, liver injury, progressive multifocal leukoencephalopathy, protocol, safety, vedolizumab

There are a variety of medication management options for the treatment of ulcerative colitis (UC) and Crohn's disease (CD). A large number of cases exist in which patients have failed or achieved inadequate responses to the different therapies currently available for these disease processes. Vedolizumab is a new biologic/immunotherapy infusion treatment recently added to many of the biologic immunotherapies infused at the Center for Musculoskeletal Care Infusion Center, New York University Medical Center, New York, NY.

Vedolizumab is a recombinant humanized anti−α4β7 integrin monoclonal antibody. It was produced in Chinese hamster ovary cells and binds to the human α4β7 integrin. Integrins are proteins involved in regulating cellular movement, including the migration of leukocytes to the gut.[1] It is specific to the intestinal tract because it binds to the α4β7 integrin, thereby blocking the interaction of the α4β7 integrin with mucosal addressin cell adhesion molecule -1. This then inhibits the migration of memory T-lymphocytes across the endothelium into inflamed gastrointestinal parenchymal tissue. Vedolizumab is indicated for patients with CD or UC who have an inadequate response to or a lost response to a tumor necrosis factor blocker or immunomodulator; or had an inadequate response to, were intolerant to, or showed dependence on corticosteroids.[2] It is also indicated in patients who were unable to achieve improved endoscopic appearance of mucosa or corticosteroid-free remission.[3]

Because vedolizumab was an eagerly awaited treatment option for the special populations of CD and UC patients aforementioned, our facility was looking forward to starting patients on this therapy. For reasons of patient safety and staff education, protocols are required for all biologics prescribed at our center. These protocols are initially developed by the nurse practitioners (NPs) of the infusion center. Information is gathered by reviewing evidence-based research, prescribing recommendations, and manufacturer's recommendations. A protocol is then developed and reviewed by the other NPs of the center. The draft is reviewed by the medical director of the infusion center and the head of the specialty that the drug is prescribed for (in this instance, the department head of gastroenterology). Occasionally, recommendations from a physician on staff who is doing research on the medication are also considered because he or she may be privy to postmarketing findings that may warrant consideration.

The review of the literature on vedolizumab revealed a number of considerations regarding therapy, including recommendations for tuberculosis

(Tb) screening, immunizations, and progressive multifocal leukoencephalopathy (PML) screening.

CONSIDERATIONS FOR TB SCREENING AND IMMUNIZATIONS

Because use may be associated with an increased risk for developing infections, patients should be tested for Tb before initiating treatment.[3] Those patients with a history of or active Tb may be referred to an infectious disease specialist for consultation and/or treatment. Along with Tb screening, patients should also be up-to-date with all immunizations recommended by the current immunization guidelines of the Centers for Disease Control and Prevention because patients will be immunosuppressed on therapy and more susceptible to infection.[4] Live vaccines may be administered if the benefits outweigh the risks, and non-live vaccines may be administered throughout the duration of treatment.[3]

CONSIDERATIONS FOR MONITORING FOR PML

PML is a rare occurrence. However, PML has a high risk of mortality, especially among immunosuppressed populations such as persons receiving vedolizumab. Given that natalizumab (Tysabri, Biogen Idec Inc., Cambridge, MA), a monoclonal antibody, is linked to the development of PML, it made sense to suspect that vedolizumab, another monoclonal antibody, might cause PML as well. It was found that natalizumab binds to $\alpha 4\beta 1$ and $\alpha 4\beta 7$ integrins. It is hypothesized that $\alpha 4\beta 1$ is widely expressed and critical for lymphocyte trafficking into the central nervous system and therefore thought to be responsible for the incidence of PML.[5] Vedolizumab does not bind to the $\alpha 4\beta 1$ integrin because it is only selective for the $\alpha 4\beta 7$ integrin.[6] In addition, there were no reported cases of PML with phase 3 clinical trials of vedolizumab.[7] After discussing these findings, we deemed PML screening was not necessary for treatment at our facility.

There is another hypothesis that the John Cunningham virus can be reactivated outside the central nervous system and possibly cross the blood-brain barrier causing PML. A longitudinal postmarketing research study, GEMINI, is currently being conducted on vedolizumab as mandated by the Food and Drug Administration. Screening considerations will be reconsidered if findings from the postmarketing study are significant.

CONSIDERATIONS FOR HEPATIC MONITORING

Four patients given vedolizumab during the GEMINI programme[5] developed acute hepatitis. Although causation could not clearly be established in these cases, similar reports of severe drug-induced liver injury have been reported with the use of Tysabri. Because the risk of hepatitis is less than 1% and all cases resolved without extended sequelae, our committee did not feel that a complete chemistry profile was warranted before initiating therapy. The patients are seen in office visits by their prescribing physicians who check their laboratory values before the initiation of infusion therapy. It is up to the discretion of the prescribing physicians to follow up on blood work during subsequent office visits. In addition, before each infusion, each patient undergoes a complete review of systems with the nurse assigned to him or her for that infusion. Findings of jaundice, icterus, fatigue, anorexia, dark urine, white-colored stool, myalgias, or arthralgias are brought to the attention of the covering NP for further evaluation.

PROTOCOL FOR ADMINISTERING VEDOLIZUMAB

Management of the Adult Patient Receiving Entyvio (Vedolizumab)

Supportive Data. The recommended adult dosage in UC and CD is 300 mg infused intravenously over approximately 30 minutes at 0, 2, and 6 weeks and then every 8 weeks thereafter.

Vedolizumab must be reconstituted in lyophilized powder with sterile water for injection (in a single-use 20-mL vial) and must be diluted in 250 mL sterile 0.9% sodium chloride injection before administration.

Vedolizumab must be administered within 4 hours of reconstitution and dilution.

Vedolizumab is contraindicated in patients with known hypersensitivity to vedolizumab.

Monitor patients for signs and symptoms of hypersensitivity during and after vedolizumab administration until clinically stable after completion of the infusion.

1. Infections: Vedolizumab is not recommended in patients with active, severe infections until infections are controlled. Consider withholding vedolizumab in patients who develop severe