UNC INFLAMMATORY BOWEL DISEASE DRUG PROTOCOL

VEDOLIZUMAB (ENTYVIO)

TREATMENT PROTOCOL:

Vedolizumab is a humanized immunoglobulin G1 monoclonal antibody that targets $\alpha_4\beta_1$ integrin and blocks its interaction with the mucosal addressin call adhesion colecule-1 (MAdCAM-1) resulting in inhibition of inflammatory cells migration to the inflammation site. Vedolizumab is part of the anti-adhesion therapy class and is more gut specific compared to natalizumab, the other agent in this class. It has a half-life elimination time of 25 days

Current IBD indications for vedolizumab at UNC

Crohn's disease and ulcerative colitis:

Induction and maintenance therapy for adults with moderate-severe active Crohn's disease or ulcerative colitis who had inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator or had an inadequate response with, were intolerant, or demonstrated dependence on corticosteroids

Dosage and Route of Administration

- **Route of administration:** Intravenous (IV)
- **Form:** The drug comes as 300 mg lyophilized vedolizumab in a single-dose 20 ml vials. This will need to be reconstituted and diluted prior to administration
- **Dose and intervals:**
  - Induction: 300 mg at weeks 0, 2, and 6
  - Maintenance: 300 mg every 8 weeks

Time for Response

- Vedolizumab may take up to 14 weeks before it shows evidence of therapeutic benefits

Contraindications

- **Absolute:**
  - Known serious or severe hypersensitivity reaction to vedolizumab or any of its excipients
- **Relative/may use with caution*:**
  - Active systemic infection
  - Untreated chronic infections: latent TB and chronic hepatitis B
  - Progressive Multifocal Leukoencephalopathy (PML)†
  - Active current malignancy or history of cancer within 5 years‡

Administration and Safety Monitoring

Before initiation of therapy:

- Careful medical history to assess for any absolute and relative contraindications
- Evaluate immunization status and provide any indicated vaccines (influenza, pneumonia, hepatitis B, HPV)

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* While vedolizumab is considered gut-specific therapy, it has been associated with increased risk of infections, particularly upper respiratory and nasal mucosal infections. There has been also reports of serious infections such as anal abscesses, sepsis, tuberculosis, salmonella sepsis, listeria meningitis, giardiasis and CMV colitis. the FDA label advise:

1. Avoid starting vedolizumab in patients with active, severe infections until infection is controlled
2. Consider withholding vedolizumab in patients who develop severe infection while on therapy
3. Consider screening for tuberculosis prior to starting therapy

† PML caused by John Cunningham (JC) virus and has been reported in patients receiving natalizumab. To date, no cases have been reported with vedolizumab, likely due to the gut-selectivity. The FDA suggest to monitor patients for any new neurological symptoms (progressive weakness, clumsiness of limbs, vision disturbances, changes in thinking, memory, orientation, and personality) and if PML is suspected therapy should be discontinued. Routine screening for JC virus prior to initiation of therapy is not indicated

‡ Number of malignancies reported in the clinical trials is very small (0.4%) including colon cancer, transitional cell carcinoma, breast cancer, carcinoid tumor, and sq cell carcinoma. Since data about long term exposure is limited, it is suggested to follow similar precautions taken with other immunosuppressive/biologic therapies.

- Prior authorization: Email IBD nurse the patient's information
  - Anthea Darling, RN (Dr. Isaacs, Dr. Sartor, and Dr. Jain)
  - Laurie Powers, RN (Dr. Herfarth, Dr. Hansen)
  - Christina Womble, RN (Dr. Long, Dr. Sheikh)

- Pre-treatment laboratory evaluation:
  1. Screen for latent Tuberculosis (Quantiferon gold TB test or Tuberculin skin test + chest X-ray)
  2. Screen for chronic infections (HBs-Ag, HBs-Ab, HBc-Ab, HCV Ab, HIV testing)
  3. Baseline LFTs, albumin, CBC, renal function and CRP

Therapy administration:

- IBD nurse assists in placing treatment plan and arranging infusions

- *Pre-treatment:*

  1. Methylprednisolone sodium succinate (Solu-MEDROL) 40mg/ml injection: 20 mg IV once
  2. Cetirizine (Zyrtec) tablet 10 mg: 10 mg, oral once
  3. Acetaminophen (TYLENOL) tablet 650 mg, oral, once

- *Drug preparation:* 4.8 ml of sterile water is added to the vedolizumab vial using 21-25 gauge needle. The vial should be gently swirled for at least 15 seconds to allow the lyophilized powder to dissolve. The solution is then kept in room temperature for 20-30 minutes to allow for reconstitution and for any foam to settle[§]. The drug (5 ml, 300 mg) is withdrawn using 21-25 gauge needle and added to 250 ml of sterile 0.9% Sodium Chloride solution (infusion bag).

- *Drug administration:* infusion is administered over 30 minutes

- *Monitoring during infusion:* Vitals before starting therapy and at the end of infusion

[§] The vial should not be used if the drug product is not dissolved within 30 minutes

Laboratory monitoring while on therapy:

- Standing order can be placed as part of the therapy plan with every 1-2 infusion based on the provider's preferences
    1. CBC with differential, ALT, and creatinine with the first 3 infusions. Subsequent intervals per the treating physician
    2. CRP if clinically indicated

Special Considerations

- **Other safety considerations:**

    1. **Pregnancy and lactation:**

        a. Vedolizumab is pregnancy Category B- based on animal studies. It should be continued during pregnancy to avoid disease flares

        b. It can cross the placenta during the third trimester but with no evidence of adverse effects on the fetus. This is also based on animal studies. Given limited human data, live-attenuated vaccines should not be given to infants born to mothers receiving vedolizumab within the first 6 months of life.

        c. Breast feeding: It is unknown whether vedolizumab is detected in human milk. In animal studies, the drug was detected in the milk of lactating monkeys. FDA advised to exercise caution when administering vedolizumab to nursing mothers.

    2. **Immunizations:** Live vaccines may be administered with vedolizumab if the benefits outweigh the risks

    3. **Cancer risk:** only small number of malignancies reported in clinical trials (0.4%) including colon cancer, transitional cell carcinoma, breast cancer, carcinoid tumor, and sq cell carcinoma. However, given the lack of long term data and frequent concomitant immunosuppressive therapies, patients should be advised to comply with general cancer screening protocols: mammograms, annual pap smears, CRC/dysplasia surveillance and use protection against UV radiation (sunscreen)

Bibliography

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3. Hagan, M, Cross, RK. "Safety of vedolizumab in the treatment of Crohn's disease and ulcerative colitis." *Expert Opin Drug Saf.*, 2015: 1473-9.
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6. US Food and Drug Administration (FDA). *Prescribing information_Vedolizumab.* 2014. http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125476s000lbl.pdf (accessed February 8, 2016).