A Newly Approved Treatment for a Rare Blood Clotting Disorder

On February 6, 2019, the FDA approved caplacizumab-yhdp (Cablivi—Ablynx), an injection drug therapy specifically indicated for the treatment of adults with acquired thrombotic thrombocytopenic purpura (aTTP). It is explicitly used in combination with plasma exchange and immunosuppressive therapy. The HERCULES trial demonstrated caplacizumab's efficacy in aTTP treatment and led to its FDA approval. In this double-blind, controlled trial, 145 patients with aTTP were randomized to receive either caplacizumab (10 mg intravenous loading bolus followed by 10 mg subcutaneously daily) or placebo during plasma exchange and for 30 days thereafter. The primary outcome was the time to normalization of platelet count, with discontinuation of daily plasma exchange within 5 days thereafter. The results showed that the median time to normalization was shorter with caplacizumab than with placebo (2.69 days versus 2.88 days). The authors also concluded that treatment with caplacizumab in patients with aTTP resulted in a lower incidence of a composite of aTTP-related death, recurrence of aTTP, or a thromboembolic event during the treatment period. In addition, this treatment had a lower rate of recurrence of aTTP during the trial than placebo. Adverse effects reported in the trial included epistaxis, gingival hemorrhage, and headache.

aTTP is an immune-mediated deficiency of the von Willebrand factor (vWF). Cleaving protease ADAMTS13 allows for unrestrained adhesion of vWF multimers to platelets and microthrombosis. This results in thrombocytopenia, hemolytic anemia, and tissue ischemia. Caplacizumab is a vWF-directed antibody fragment that targets the A1-domain of vWF, inhibiting the interaction between vWF and platelets. This reduces both vWF-mediated platelet adhesion and consumption. The manufacturer recommends initial dosing of 11 mg intravenously at least 15 minutes prior to plasma exchange, followed by 11 mg subcutaneously after completion of plasma exchange on day one. Subsequent dosing during daily plasma exchange should be 11 mg subcutaneously once daily. If a patient experiences more than two recurrences of aTTP during therapy, caplacizumab should be discontinued. Common adverse events reported include gingival hemorrhage, headache, epistaxis, paresthesia, fatigue, urticaria, fever, and bleeding complications (58%). Due to the high frequency of bleeding risk, it is highly advised to monitor patients closely for bleeding when administering caplacizumab in patients who concomitantly take anticoagulants.

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Olivia Rockwell, PharmD/MBA Candidate