Cablivi® (caplacizumab-yhdp) – New orphan drug approval

- On February 6, 2019, the FDA announced the approval of Sanofi's Cablivi (caplacizumab-yhdp), for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy.

- Patients with aTTP develop extensive blood clots in the small blood vessels throughout the body. These clots can cut off oxygen and blood supply to the major organs and cause strokes and heart attacks that may lead to brain damage or death.

    - Patients can develop aTTP because of conditions such as cancer, HIV, pregnancy, lupus or infections, or after having surgery, bone marrow transplantation or chemotherapy.
    - In the U.S., aTTP affects < 2,000 adults each year.
    - Patients with aTTP can require treatment with daily plasma exchange.

- Cablivi is the first targeted treatment for aTTP and it works by targeting von Willebrand factor (vWF), a protein in the blood involved in hemostasis.

- The efficacy of Cablivi was established in HERCULES, a double-blind study in 145 adult patients with aTTP. Patients were randomized to either Cablivi or placebo. Patients in both groups received plasma exchange and immunosuppressive therapy. The primary endpoint was time to platelet count response (platelet count ≥ 150,000/μL followed by cessation of daily plasma exchange within 5 days).

    - Treatment with Cablivi in combination with plasma exchange and immunosuppression resulted in a significantly shorter time to platelet count response vs. plasma exchange and immunosuppression alone (Hazard Ratio = 1.55 [95% CI: 1.10, 2.20]; p = 0.01).
    - Cablivi also showed a significant reduction in a composite endpoint of aTTP-related death, recurrence of aTTP, or a major thromboembolic event during study drug treatment vs. placebo (12.7% vs. 49.3%; p < 0.0001).

- A warning and precaution of Cablivi is increased risk of bleeding.

- The most common adverse reactions (> 15%) with Cablivi use were epistaxis, headache, and gingival bleeding.

- Cablivi should be administered upon initiation of plasma exchange therapy and the recommended dose of Cablivi is as follows:

    - *First day of treatment*: 11 mg bolus intravenous injection at least 15 minutes prior to plasma exchange followed by an 11 mg subcutaneous (SC) injection after completion of plasma exchange on day 1.
    - *Subsequent days of treatment during daily plasma exchange*: 11 mg SC injection once daily following plasma exchange.
    - *Treatment after plasma exchange period*: 11 mg SC injection once daily continuing for 30 days following the last daily plasma exchange. If after initial treatment course, sign(s) of persistent underlying disease such as suppressed ADAMTS13 activity levels remain present, treatment may be extended for a maximum of 28 days.
    - Cablivi should be discontinued if the patient experiences more than 2 recurrences of aTTP, while on Cablivi.

- The estimated average cost for treating a typical aTTP episode with Cablivi is $270,000.

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- Sanofi will be launching Cablivi Patient Solutions, a comprehensive patient support program that will provide financial assistance to eligible patients.

- Sanofi plans to launch Cablivi in late 1st quarter 2019. Cablivi will be available as an 11 mg lyophilized powder in a single-dose vial.