

New England Journal of Medicine publishes positive results of the pivotal trial of Cablivi® (caplacizumab) for rare blood clotting disorder

- * HERCULES Phase 3 trial met its primary endpoint, demonstrating that treatment with Cablivi resulted in a significantly faster time to platelet count response in patients with acquired thrombotic thrombocytopenic purpura (aTTP) when administered in conjunction with plasma exchange and immunosuppression
- * Cablivi was associated with a significant reduction in aTTP-related death, recurrence, or at least one major thromboembolic event while patients were on treatment, the study's first key secondary endpoint
- * Cablivi was approved by the European Commission in August 2018

PARIS – January 9, 2019 - *The New England Journal of Medicine (NEJM)* today published positive results of the Phase 3 trial of Cablivi® (caplacizumab) in adults with acquired thrombotic thrombocytopenic purpura (aTTP).

aTTP is a rare, life-threatening autoimmune blood disorder characterized by extensive clot formation in small blood vessels throughout the body, leading to severe thrombocytopenia (very low platelet count), microangiopathic hemolytic anemia (loss of red blood cells through destruction), ischemia (restricted blood supply to parts of the body) and widespread organ damage, especially in the brain and heart.

The current treatment for aTTP consists of daily plasma exchange, in which a patient's blood plasma is removed and replaced with donor plasma, and immunosuppression. Even with currently available treatments, patients continue to be at risk of developing acute blood clotting conditions, such as stroke and heart attack, as well as recurrence of disease.

Key findings of the HERCULES Phase 3 study of Cablivi include:

- On the primary endpoint, Cablivi significantly reduced the time to platelet count normalization ($p=0.01$). At any given time point during the study, patients receiving Cablivi were 1.55 times more likely to achieve normal platelet counts than patients on placebo.
- Treatment with Cablivi was associated with a 74 percent reduction in aTTP-related death, recurrence of aTTP, or at least one major thromboembolic event compared with placebo ($p<0.001$).

- During the overall study period, patients receiving Cablivi experienced a significantly lower number of aTTP recurrences (67 percent reduction) compared to placebo ($p < 0.001$).
- Refractory disease developed in 0 patients in the Cablivi group versus 3 patients in the placebo group, although this did not reach statistical significance ($p = 0.06$).
- Normalization of three organ-damage markers (lactate dehydrogenase, cardiac troponin I, and serum creatinine) occurred sooner in patients who received caplacizumab versus placebo (p not tested for significance due to hierarchical statistical testing).
- Results showed a clinically meaningful reduction in the use of plasma exchange in patients treated with Cablivi (average 5.8 days; 38 percent reduction) versus placebo (9.4 days), as well as a shorter stay in the intensive care unit (65 percent reduction) and hospital (31 percent reduction).

Cablivi demonstrated a safety profile consistent with what has been previously reported and in line with its mechanism of action; this included an increased risk of bleeding. The most frequently reported bleeding-related adverse events were epistaxis and gingival bleeding.

“aTTP is a life-threatening disease, and the current treatment options do not fully halt the extensive clot formation in small blood vessels throughout the body, leaving patients at risk for significant morbidity and early death,” said Marie Scully, M.D, professor of hematology at University College London Hospitals, and lead author of the HERCULES study. *“These results demonstrate that Cablivi has the potential to address a major unmet medical need and to help those facing the potentially devastating consequences of this disorder.”*

HERCULES is a Phase 3 randomized, double-blind, placebo-controlled study of Cablivi in patients with aTTP. In the study, 145 patients were randomly assigned to Cablivi or placebo in conjunction with plasma exchange and immunosuppression.

About Cablivi® (caplacizumab)

Cablivi is an anti-vWF Nanobody, which inhibits the interaction between ultra-large von Willebrand Factor (vWF) multimers and platelets and, therefore, stops the formation and accumulation of the micro-clots that cause the thrombocytopenia, tissue ischemia, and organ dysfunction in aTTP. Cablivi was developed by Ablynx, a Sanofi company.

Cablivi was approved by the European Commission in August 2018 for the treatment of adults experiencing an episode of aTTP. It is the first therapeutic specifically indicated for the treatment of aTTP.

Additionally, the U.S. Food and Drug Administration (FDA) has accepted for priority review the Biologics License Application for Cablivi for treatment of patients 18 years of age and older experiencing an episode of aTTP. The target action date for the FDA decision is February 6, 2019.

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

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