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## Safety of caplacizumab in patients without documented severe adamts13 deficiency during the hercules study

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**Objective:** To describe the safety of caplacizumab in patients enrolled in HERCULES for whom the diagnosis of aTTP was not confirmed based on documented severe ADAMTS13 deficiency.

**Methodology:** In HERCULES (NCT02553317), ADAMTS13 was measured at study baseline (following initial TPE), weekly following cessation of daily TPE during the treatment period, and twice during the follow-up period. Data from patients for whom the diagnosis of aTTP was not confirmed based on documented ADAMTS13 levels <10% were extracted and analyzed descriptively for efficacy and safety outcomes, with a focus on bleeding events.

**Results:** Overall, 7 patients in the placebo group (9.6%) and 13 patients in the caplacizumab group (18.1%) had a baseline ADAMTS13 ≥10%; of these, 4 and 9 patients, respectively, had a prior medical history of aTTP and/or ADAMTS13 values <10% at other time points during the study. This left 3 patients in the placebo group and 4 patients in the caplacizumab group for whom the diagnosis of aTTP could not be confirmed based on subsequent ADAMTS13 values or prior medical history, suggesting a diagnosis other than aTTP. Baseline ADAMTS13 levels were >60% for all patients and remained well above 10% throughout the study period. Possible alternative diagnoses included pancreatitis-induced TTP in 2 patients. One patient was reported as having 'thrombotic microangiopathy' and discontinued study drug treatment after 4 days (but continued daily TPE). The fourth patient had a report of 'megaloblastic anemia' and 'general adenopathies' and was withdrawn from the study due to a 'non-TTP diagnosis' after 2 days. The patients who continued daily TPE achieved a platelet count of $>150 \times 10^9$/L. Two patients experienced a moderate bleeding-related serious adverse event (SAE), 1 case of 'gastric ulcer hemorrhage' (considered unlikely related to study drug and recovered without intervention) and 1 case of epistaxis that led to study drug discontinuation (considered possibly related to study drug and recovered without intervention). Other mild bleeding-related non-serious adverse events (AEs) were reported in 1 patient: gingival bleeding (possibly related), ecchymosis (possibly related), and rectal hemorrhage (not/unlikely related). All events recovered spontaneously without intervention. Two other non-bleeding related SAEs were reported in 2 patients, both considered unrelated to study drug: 1 case of bacteremia and 1 case of cardiac tamponade.

**Conclusion:** The experience of caplacizumab in patients with a suspected non-aTTP diagnosis to date is limited, and so no definite conclusion can be drawn. Bleeding-related AEs were reported in 3 of the 4 patients; however, the type, nature and manageability of these events appear similar to those reported in the other patients in the study. Data first presented at American Society of Hematology annual meeting, December 7–10, 2019. Study sponsored by Sanofi.

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## Caplacizumab induces fast and durable platelet count responses with improved time to complete remission and recurrence-free survival in patients with acquired thrombotic thrombocytopenic purpura

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**Objective:** To characterize the durability of platelet count responses in the HERCULES trial.