Category :**Hematology: Other**

A153 - ***Caplacizumab rapidly inhibits VWF–platelet interaction: pharmacodynamic data from healthy volunteers and patients with aTTP***

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Introduction:

Caplacizumab targets the A1 domain of von Willebrand factor (VWF) and inhibits VWF–platelet interaction. In clinical trials in patients with acquired thrombotic thrombocytopenic purpura (aTTP), the 10 mg dosing regimen of caplacizumab completely blocked VWF-mediated platelet adhesion within 24 hours. The aim of this study was to further characterize the speed of action of caplacizumab.

Methods:

VWF activity data (ristocetin cofactor [RICO] assay) from a Phase 1 study with caplacizumab in healthy White and Japanese volunteers (single intravenous [IV] or subcutaneous [SC] 10 mg dose; n=16 per group), and from the Phase 2 TITAN study in a subset of patients (n=12) with RICO sampling at 5–10 minutes, 3–6 hours, and 8–24 hours after the IV loading dose, were included in this analysis. RICO inhibition to <20% reflects full neutralization of VWF–platelet binding by caplacizumab. Informed consent was obtained from all study participants.

Results:

Complete inhibition of RICO activity was achieved in 15/16 healthy subjects (94%) at 1 hour after caplacizumab IV dosing, and in all participants at 3 hours after dosing (**Table**). With the 10 mg SC dose, RICO activity <20% was achieved in half of subjects (8/16) after 1 hour and in all subjects after 3 hours. RICO remained suppressed for 24 hours in 30/32 volunteers after a single IV or SC dose and started to recover thereafter.

In TITAN, Day 1 RICO activity values were available for 11/12 patients; 8/11 (72.7%) achieved RICO <20% within 5–10 minutes after the first IV loading dose, and the remaining 3 patients (27.3%) after 3–6 hours. In 8/12 patients with available data, RICO remained <20% at 8–24 hours after the IV loading dose.

Conclusion:

Caplacizumab, through its IV loading dose, induces rapid and sustained inhibition of VWF–platelet interaction, starting within minutes in most patients, which is essential in a life-threatening disease like aTTP. This study and editorial support funded by Ablynx, a Sanofi company. Previously presented at 29th ISTH Congress.

Table:

Analysis time point at Day 1, n (%)	10 mg IV White (n=8)	10 mg IV Japanese (n=8)	10 mg SC White (n=8)	10 mg SC Japanese (n=8)
1 hour post-dose: RICO <20% / RICO ≥20%	7 (87.5) / 1 (12.5)	8 (100.0) / 0	4 (50.0) / 4 (50.0)	4 (50.0) / 4 (50.0)
3 hours post-dose: RICO <20% / RICO ≥20%	8 (100.0) / 0	8 (100.0) / 0	8 (100.0) / 0	8 (100.0) / 0
24 hours post-dose: RICO <20% / RICO ≥20%	6 (75.0) / 2 (25.0)	8 (100.0) / 0	8 (100.0) / 0	8 (100.0) / 0
48 hours post-dose: RICO <20% / RICO ≥20%	1 (12.5) / 7 (87.5)	0 / 8 (100.0)	5 (62.5) / 3 (37.5)	6 (75.0) / 2 (25.0)

72 hours post-dose: RICO <20% / RICO ≥20%	0 / 8 (100.0)	0 / 8 (100.0)	0 / 8 (100.0)	0 / 8 (100.0)

Effect of caplacizumab on RICO activity in the healthy volunteer study. IV, intravenous; RICO, ristocetin cofactor; SC, subcutaneous. RICO activity was ≥20% in all healthy volunteers at baseline.