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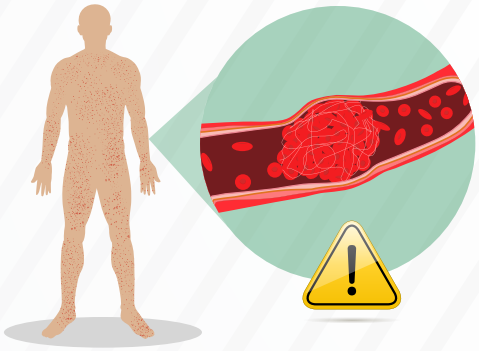
Insights into the Efficacy and Safety of Caplacizumab: Integrated Analysis of TITAN and HERCULES Trials

This infographic is intended for researchers and healthcare professionals and reflects the contents of the following article:

Peyvandi, F., Cataland, S., Scully, M., Coppo, P., Knoebl, P., Kremer Hovinga, J. A., ... & Callewaert, F. (2021). Caplacizumab Prevents Refractoriness and Mortality in Acquired Thrombotic Thrombocytopenic Purpura: Integrated Analysis. *Blood Advances, 5*(8), 2137–2141. https://doi.org/10.1182/bloodadvances.2020001834



Acquired thrombotic thrombocytopenic purpura (aTTP)

- aTTP is a rare, life-threatening immune-mediated thrombotic microangiopathy with a mortality rate of 8% to 20%
- aTTP therapy includes therapeutic plasma exchange (TPE) and immunosuppression
- Refractory disease occurs in up to 42% of patients and may lead to poor outcomes
- There remains a need for targeted, rapid-acting treatments to prevent early mortality and morbidity

An integrated analysis of TITAN (NCT01151423) and HERCULES (NCT02553317) trial findings to assess the efficacy and safety of caplacizumab, a monoclonal antibody used to manage aTTP

Study participants

Adult patients with an acute episode of aTTP diagnosed on the basis of clinical presentation (N = 220)

Treatment

- Participants were randomly assigned to receive caplacizumab or placebo in addition to TPE and immunosuppression
- Caplacizumab group (n = 108)
- Placebo group (n = 112)

Primary end point

Time-to-platelet-count response

Secondary efficacy end points

- Time to normalization of organ damage markers
- Number of TPE days
- Proportion of participants with TTP-related death, TTP recurrence, or ≥1 treatment-emergent major thromboembolic events (MTEs; assessed as a composite end point and as individual events)
- TTP recurrence (occurring ≤30 days after the end of daily TPE [exacerbation] or >30 days after the end of daily TPE [relapse]) during the blinded treatment period and the overall study period
- Refractory TTP

Statistical analysis

- Treatment groups were compared by using a two-sided log-rank test stratified by trial based on Kaplan-Meier analysis
- Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated by using a Cox proportional hazards regression model
- To compare treatment groups, a stratified Cochran-Mantel-Haenszel test was used as a stratification factor

Treatment efficacy of caplacizumab

Caplacizumab was associated with a significant reduction in the number of deaths (0 vs 4; $p < .05$) and incidence of refractory TTP (0 vs 8; $p < .01$) vs placebo during the treatment period

Caplacizumab significantly reduced the time-to-platelet-count normalization (HR, 1.65; 95% CI, 1.24–2.20; $p < .001$)

Caplacizumab reduced:

- Time to normalization of the organ damage marker lactate dehydrogenase (HR, 1.43; 95% CI, 1.04–1.96; $p = .03$)
- Induced a faster normalization of troponin (HR, 1.32; 95% CI, 0.86–2.04; $p = .29$)
- Serum creatinine (HR, 1.68; 95% CI, 0.89–3.15; $p = .14$)

There was a 33.3% reduction in the median number of TPE days with caplacizumab vs placebo (5.0 days [range, 1–35 days] vs 7.5 days [range, 2–46 days], respectively)

The composite end point of TTP-related death, exacerbation, or any treatment-emergent MTE was significantly reduced with caplacizumab compared with placebo (72.6% reduction; $p < .001$)

40.8%

Incidence of MTEs was numerically reduced by 40.8% with caplacizumab vs placebo (7.4% vs 12.5%)

84%

Caplacizumab was associated with an 84.0% reduction in the incidence of exacerbations during the blinded treatment period (6 vs 39 participants; $p < .001$)

Relapse of aTTP

- More relapses occurred with caplacizumab than with placebo (14 vs 0 participants)
- 13 of 14 relapses occurred within 10 days of stopping caplacizumab in participants with persistent levels of a disintegrin and metalloproteinase with a thrombospondin type 1 motif member 13 (ADAMTS13) <10%

Adverse events (AEs) associated with caplacizumab treatment

TPE-related treatment-emergent AEs (TEAEs) occurred in 40.6% (43 of 106) and 45.5% (50 of 110) in the caplacizumab and placebo groups, respectively

Serious TPE-related TEAEs occurred in 3.8% (4 of 106) in caplacizumab and 6.4% (7 of 110) in placebo group

Bleeding TEAEs were the most common AEs

Bleeding events were mainly mucocutaneous (epistaxis and gingival bleeding) and most occurrences were mild to moderate and self-limited

Severe TEAEs were uncommon; no new safety signals were identified

Key messages

- **Caplacizumab treatment prevents mortality and refractory disease and is generally well tolerated, with mild mucocutaneous bleeding as the main safety finding**
- **Integrated analysis, together with recent real-world evidence, further demonstrates that caplacizumab may address a serious unmet need in acute aTTP**

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