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POSTER ABSTRACTS

331.THROMBOTIC MICROANGIOPATHIES/THROMBOCYTOPENIAS AND COVID-19-RELATED THROMBOTIC/VASCULAR DISORDERS: CLINICAL AND EPIDEMIOLOGICAL

Management of Immune Thrombotic Thrombocytopenic Purpura without Therapeutic Plasma Exchange: Analysis of Efficacy and Safety Data

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Background:
Immune thrombotic thrombocytopenic purpura (iTTP) is a rare, life-threatening autoimmune disorder caused by ADAMTS13 deficiency. Caplacizumab, an anti-VWF nanobody, is approved for iTTP treatment, reducing the need for therapeutic plasma exchange (TPE) and improving platelet recovery and survival.

Methods:
We conducted a retrospective study on 42 acute iTTP cases in Austria and Germany, treated with a modified regimen aimed at avoiding TPE if platelet count increased post-first caplacizumab dose. An extensive efficacy and safety analysis of this approach was performed, in comparison with a control group of 59 patients with iTTP, receiving frontline caplacizumab treatment with TPE and immunosuppression (standard of care, SOC). The main outcome was time to platelet count normalization. Secondary outcomes included clinical response, exacerbation, refractory iTTP, and iTTP-related deaths. Retrospective safety assessments with evaluation of treatment emergent adverse events (TEAE) were performed in both cohorts.

Results:
The median time to platelet count normalization was similar between the two cohorts (3 and 4 days; P = 0.31, see Figure 1). There were no significant differences in clinical response, exacerbations, refractoriness, or iTTP-related deaths (see Table 1). Four patients did not respond to the first dose of caplacizumab, and TPE was initiated. Cytomegalovirus infection, HIV/hepatitis B co-infection, and ovarian teratoma may have hindered immediate treatment response. Platelet count doubling and median platelet count change after first caplacizumab dose were unaffected by TPE. The median time to LDH normalization was 11 days in the TPE-free cohort.
During overall follow-up at least one adverse event (TEAE) was observed in 11 patients (26.2%) in the TPE-free group and 15 patients (25.4%) in the SOC group (excluding adverse events of iTTP that were evaluated as outcome parameters) (see Table 1). There was one TTP-related death reported in the SOC group (1.7%). The cause of death in this patient was cerebral ischemia due to multiple strokes.
Serious adverse events associated with therapeutic plasma exchange were observed in 3 patients (5.1%) exclusively in the SOC cohort. These included (1) in-hospital cardiac arrest (IHCA), (2) generalized seizure and supraventricular tachycardia and (3) a transfusion reaction with hypotension, rigors, pruritus and exanthema.
Bleeding complications were reported without a significant difference and mainly comprised gingival bleeding and epistaxis. Two patients in the TPE-free cohort (4.8%) experienced major bleeding events, namely subdural hematoma requiring surgical intervention and gastrointestinal bleeding with mass transfusion. Spontaneous subdural hematoma occurred in one patient after 20 days of caplacizumab treatment. Gastrointestinal bleeding from a colon diverticulum occurred in another patient after a clinical response and resulted in a significant drop in hemoglobin and thrombocytes. Gastrointestinal bleeding worsened with concomitant factor XIII deficiency, which was reconstituted intravenously in addition to mass transfusion.

Conclusion:

Caplacizumab and immunosuppression, without TPE, rapidly controlled microvascular thrombosis and achieved a sustained clinical response in iTTP. The efficacy was similar to the control group, which received SOC.
Standard iTTP treatment with TPE may lead to a prolonged hospital stay, including admission to the ICU, multiple sessions of daily TPE with associated risks, and the associated costs of plasma, equipment, nursing care, and medical supervision. The number of patients experiencing critical adverse events was comparable between groups. Bearing all restrictions of a retrospective cohort in mind, we did not identify a critical safety signal for TPE-free iTTP-treatment. However, TPE itself resulted in three life-threatening adverse events in the SOC cohort, including an in-hospital cardiac arrest.
In conclusion, omitting TPE appears to be a viable choice for acute iTTP management that may reduce treatment burden without compromising patient outcomes or safety.

Disclosures Kühne: *Alexion:* Honoraria. **Knoebl:** *Roche:* Honoraria; *Shire/Takeda:* Honoraria; *CLS Behring:* Honoraria; *Novo-Nordisk:* Honoraria; *Ablynx/Sanofi:* Honoraria; *Alexion:* Honoraria. **Eller:** *Alexion:* Honoraria; *Sanofi-Genzyme:* Honoraria. **Brinkkoetter:** *Vifor CSL*: Honoraria; *Bayer:* Honoraria; *Alexion:* Honoraria; *Travere:* Honoraria; *Roche:* Honoraria; *Novartis:* Honoraria; *AstraZeneca:* Honoraria; *Sanofi-Genzyme:* Honoraria, Research Funding. **Voelker:** *Alexion:* Honoraria; *Sanofi-Genzyme:* Honoraria; *Bayer:* Honoraria; *GC Biopharma:* Honoraria; *AstraZeneca:* Honoraria.

Table 1. Outcome parameters and safety analysis of the TPE-free and SOC cohorts treated with frontline caplacizumab.*

Parameter	TPE-free cohort (n=42)	SOC cohort (n=59)	P Value
Primary outcome			
Median time to platelet count normalization – days (range; IQR)	3 (1-12; 2-4)	4 (2-27; 3-5)	0.31
Key secondary outcomes			
Patients achieving a clinical response without requiring TPE – no. (%)	38 (90.5)		
Patients achieving a clinical response – no. (%)	41 (97.6)	57 (96.6)	
Patients with a clinical exacerbation – no. (%)	2 (4.8)	9 (15.3)	
Patients refractory to therapy – no. (%)	0 (0)	1 (1.7)	
TTP-related death – no. (%)	0 (0)	1 (1.7)	
Other secondary outcomes			
Median change in platelet count after first dose of caplacizumab (IQR), x10E9/l	16 (7-26)	16 (4-35)	
Median time to recovery of ADAMTS13 activity to ≥20% after treatment initiation – days (IQR)	25 (13-33)	37 (19-51)	0.01
Patients without confirmed recovery of ADAMTS13 activity to ≥20% at end of follow-up – no. (%)	4 (9.5)	10 (16.9)	
Days in hospital Median (IQR)	11 (5-18)	14 (9-21)	0.03
Patients admitted to ICU – no. (%) Data missing – no. (%)	6 (14.3) 7 (16.7)	42 (71.2) 8 (13.6)	<0.001
Days on ICU, if admitted Median (IQR)	4 (2-4)	4 (2-6)	
Adverse events			
Patients with at least one adverse event during overall follow-up period – no. (%)	11 (26.2)	15 (25.4)	
TPE-related adverse events – no. (%)	0 (0)	3 (5.1)	
Any bleeding – no. (%)	5 (11.9)	2 (3.4)	
Major bleeding according to ISTH – no. (%)	2 (4.8)	0 (0)	

* There were no significant differences between the two cohorts in the parameters listed in this table except as noted.

Figure 1. Time to platelet count normalization after the first caplacizumab administration. Symbols indicate censored data. P value is 0.31 according to log rank test.

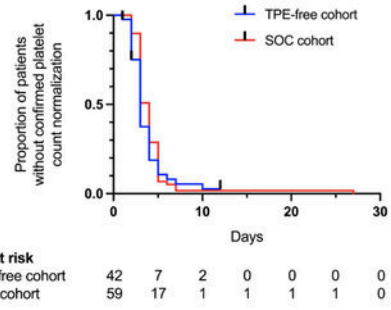

Figure 1

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