Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Overview of post-hoc analyses

The following post-hoc analyses were conducted:

- The number and proportion of patients in the intention-to-treat (ITT) population with values for lactate dehydrogenase (LDH) ≤2 x upper limit of normal (ULN) was summarized by planned treatment for the first 5 study days. In case more than one LDH measurement was available for a single day, the largest value was taken for calculation (conservative approach). Proportions were calculated based on the number of patients in the ITT population. Missing LDH data for patients who had not dropped out were imputed using last-observation-carried-forward (LOCF).
- A Kaplan-Meier analysis was conducted to compare the time-to-normalization of Troponin (Tn) T or TnI values according to the planned treatment. Time-to-normalization is defined as time to first occurrence within normal reference range. The population at risk at baseline consisted of the patients in the ITT population with high baseline values (above ULN) in TnT or TnI (N=19 in the caplacizumab arm versus N=17 in the placebo arm).
- A similar analysis as for Troponin was conducted for creatinine and LDH. The number of patients in the ITT population with high baseline values (above ULN) in creatinine was N=11 in the caplacizumab arm and N=15 in the placebo arm. The number of patients in the ITT population with high baseline values (above ULN) in LDH was N=32 in the caplacizumab arm and N=32 in the placebo arm.
- The volume of PE and the number of PE days were summarized by actual treatment, based on the safety population. An overall summary and a summary by study period were included. The following study periods were defined: daily PE period on treatment, post-daily PE period on treatment, and overall study period including post-treatment period (until 1 month follow-up).

- The bleeding- and immune-related treatment-emergent adverse events (AEs) were selected from the clinical database by searching pre-specified preferred terms, and were listed together with their body system or organ class, start and end date, study period in which they occurred, seriousness, relation to therapy, and action taken.
- The safety outcomes were summarized by excluding recurrences of TTP (both exacerbations and relapses) as (serious) adverse events. As a result, the preferred term 'Thrombotic Thrombocytopenic Purpura' does not contain TTP recurrences. Other events like 'severe refractory TTP' etc were coded to the preferred term Thrombotic Thrombocytopenic Purpura.
- Finally, all available ADAMST13 activity data have been evaluated in relation with clinical remission or recurrent TTP disease up to the 12-month follow-up period (if available), to evaluate the potential of ADAMTS13 activity as biomarker for underlying disease activity. ADAMTS13 activity values <10% were considered as indicative for an active unresolved underlying autoimmune disorder. The time of occurrence of the exacerbation or relapse in a patient was correlated with the available ADAMTS13 activity data (profile) and study drug treatment duration. For relapse episodes, the following interpretation was applied: if a relapse event during the 1-month follow-up period was preceded by a continuous severe deficiency in ADAMTS13 activity (<10%) during the treatment period, the relapse event was considered as a relapse of the presenting TTP episode; if the relapse event during the 1-month follow-up or beyond was preceded by a normalization of ADAMTS13 activity during the 30 day post-PE treatment period (≥10% at least for the last measurement preceding treatment stop), then the relapse episode was considered as a *de novo* TTP relapse episode. For the evaluation of the predictive value of the marker the following ADAMTS13 activity data points were considered: the last available sampling point for ADAMTS13 activity before the end of the 30 day study drug

treatment period was used to correlate the underlying disease activity with the presence or absence of a relapse episode. For patients with exacerbations (which occurred variably during the 30 day study drug treatment period), no fixed visit was used to link ADAMTS13 activity with the exacerbation. If available, the ADAMTS13 activity value closest to the exacerbation was used for the data interpretation. All patients with available ADAMTS13 activity data were considered. Patients with missing data (e.g. no data during the treatment period) were excluded from the evaluation. Patient samples were measured for ADAMTS13 activity using the FRET-VWF73 assay.

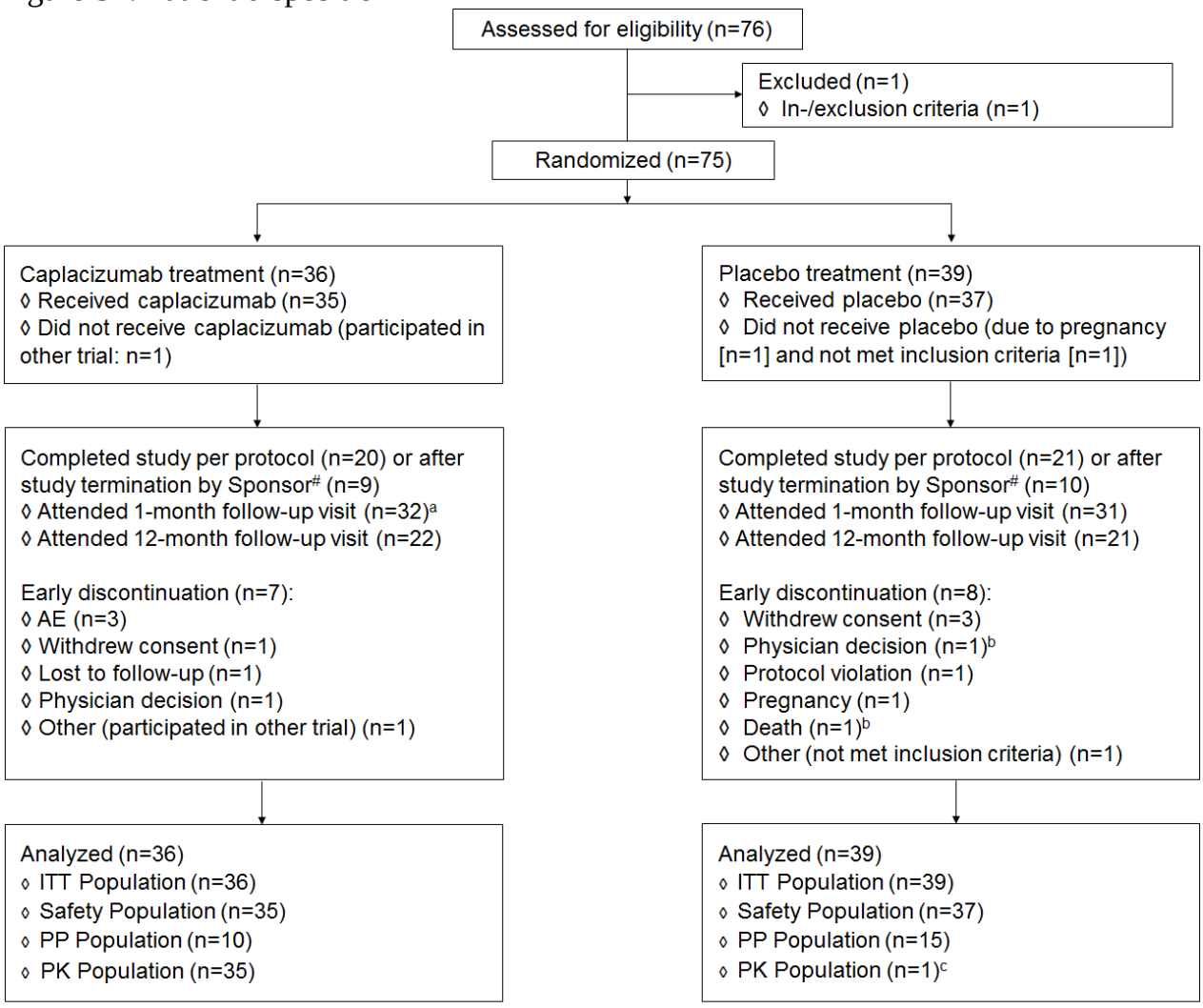
Methods for the determination of total drug and anti-drug antibody levels

Total plasma caplacizumab concentration was quantified with a validated ELISA using an anti-caplacizumab monoclonal antibody capturing tool (internal clone, Ablynx). Human plasma samples were treated with acid to overcome target interference and subsequently neutralized. After incubation of these samples on the coated plates, bound caplacizumab was detected using a biotinylated anti-caplacizumab Nanobody (internal clone, Ablynx), followed by horse-radish-peroxidase labelled streptavidin (Dako) as secondary detection tool. The ELISA was developed with tetramethylbenzidine peroxide substrate solution, and optical density signal was measured at 450 nm.

Anti-drug antibody serum levels were evaluated by validated assays, using a screening-confirmation-titration assay approach. Serum samples were incubated overnight with a mixture of biotinylated and sulpho-tagged caplacizumab. The immune complexes were captured on a MA®96-well Streptavidin high bind plate (Meso Scale Discovery, Rockville, MD, USA) and the plate was read on the SECTOR Imager 2400 plate reader (MesoScale Discovery). Confirmation of Ab specificity was performed though drug displacement.

Supplementary Figures

Figure S1: Patient disposition



The Sponsor decided to terminate recruitment to the study due to persistent recruitment challenges with only 75 subjects of the planned 110 subjects randomized. Although recruitment was stopped, the study itself was not terminated at that point as all subjects randomized were to have the opportunity to complete study treatment and the 1-month post-study treatment follow-up period. The study itself therefore was completed when the last subject randomized reached the 1 month follow up visit. All subjects who had not yet reached the 1-month FU visit were to follow the protocol until that time point. For subjects still on study and who were already beyond the 1-month follow-up, sites were requested to perform an unscheduled visit to have one final visit, as well as to complete the End of Study page of the CRF.

[a] Two patients in the caplacizumab group attended the 12-month follow-up visit, but did not complete the study according to the End of Study CRF page

[b] Two patients in the placebo group died during the study. For one patient, death was the primary reason for premature patient discontinuation from the study. The other patient was discontinued 2 days before the patient died per physician decision.

[c] 12 samples from 1 placebo patient were unintentionally analyzed and reported. As expected, measured concentrations were below limit of quantification for these samples.

ITT population: The intent-to-treat population included all patients randomized, according to the randomized treatment assignment.

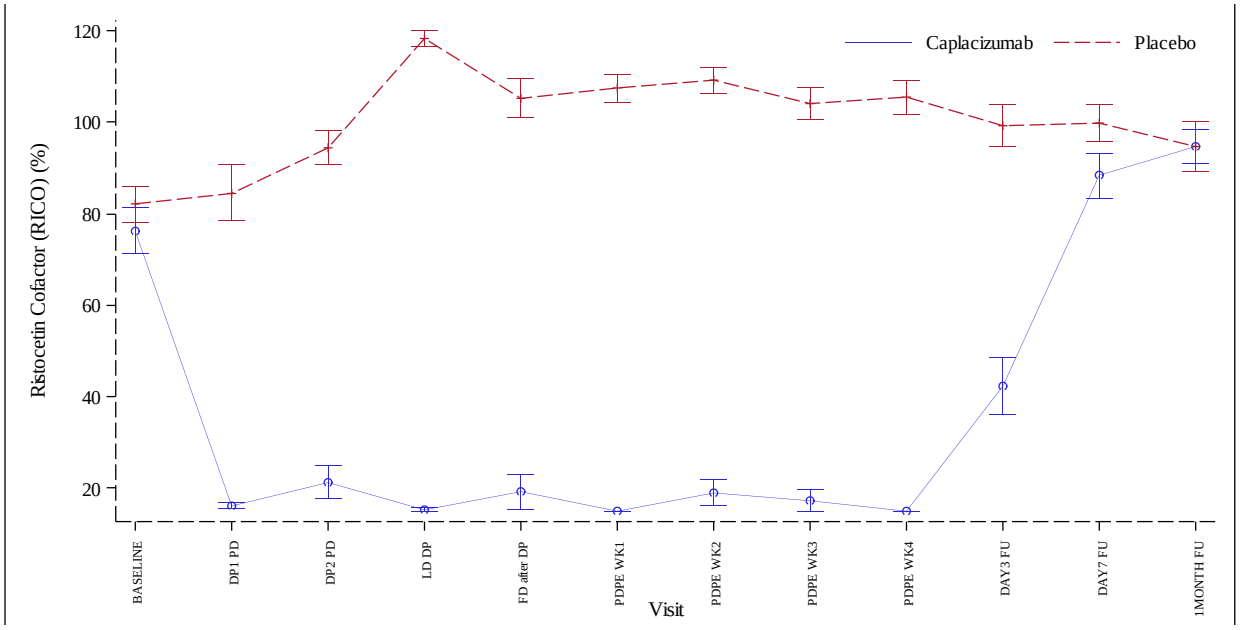
Safety population: The safety population included all patients who received at least one dose or partial dose of study drug, with treatment assignment designated according to actual treatment received.

PP population: The PP population included all randomized patients, according to the randomized treatment assignments, who had no major protocol deviations and satisfactorily completed the study.

PK population: The PK population consisted of all patients who received the study drug and for whom the primary PK data are considered to be sufficient and interpretable.

Figure S2: Pharmacodynamic Parameters – Time curve of Ristocetin Cofactor Activity (RICO) (A), von Willebrand Factor:Antigen (VWF:Ag) (B) and Factor VIII Chromogene (FVIII:C) (C). Data are expressed as Mean ± Standard Error (Safety Population)

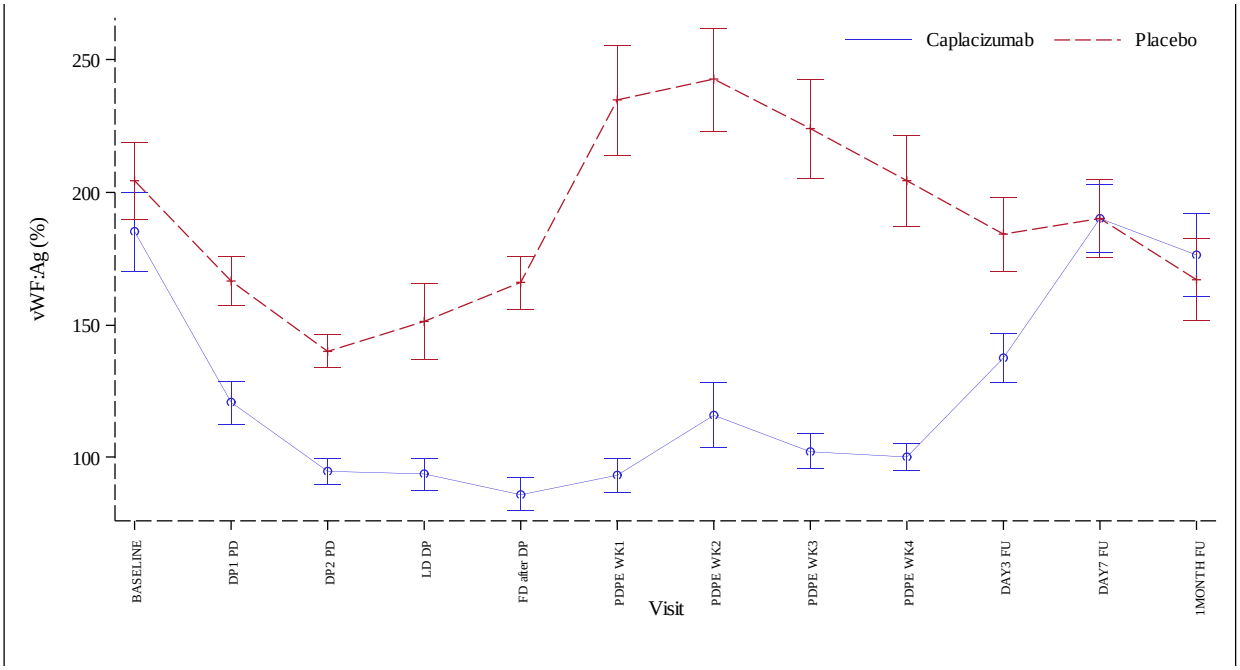
Panel A: Ristocetin Cofactor Activity (RICO)



<20% RICO represents the threshold for pharmacological activity of caplacizumab; values below lower limit of quantification (LLOQ) of 15% were set at LLOQ, values above upper limit of quantification (ULOQ) of 120% were set at ULOQ

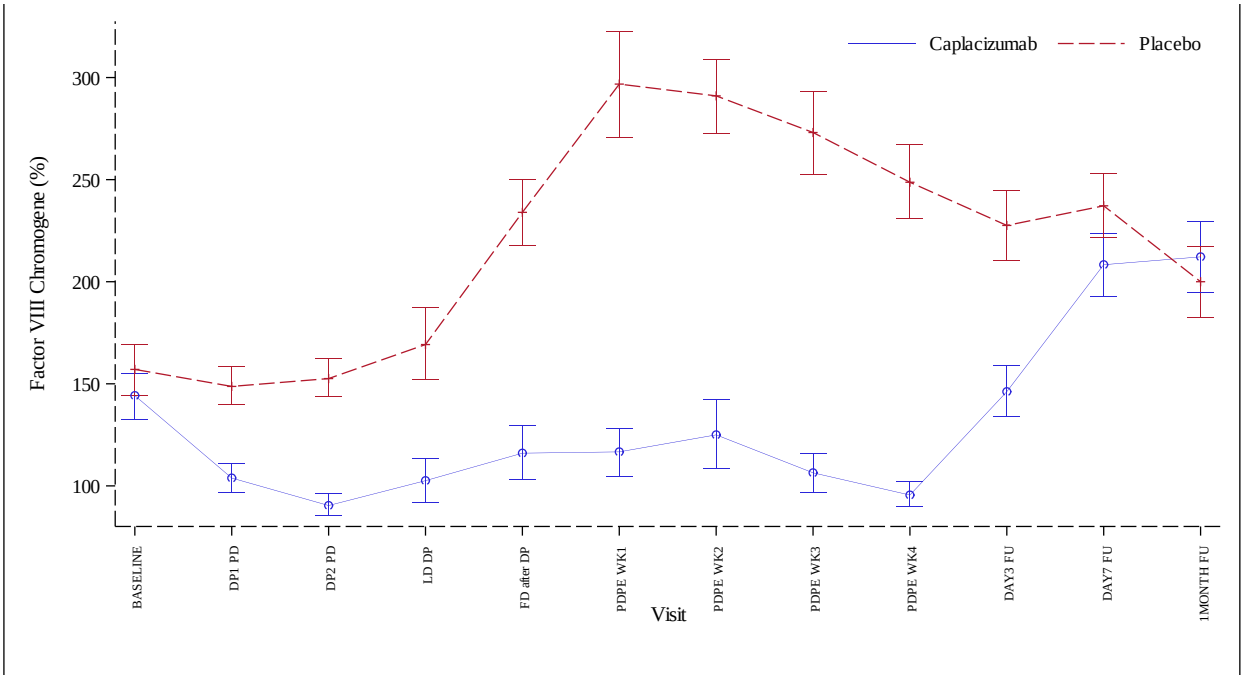
DP: Daily PE; PD: postdose; LD: Last Day; FD: First Day; PDPE: Post Daily PE; FU: Follow-up

Panel B: von Willebrand Factor:Antigen (VWF:Ag)



DP: Daily PE; PD: postdose; LD: Last Day; FD: First Day; PDPE: Post Daily PE; FU: Follow-up

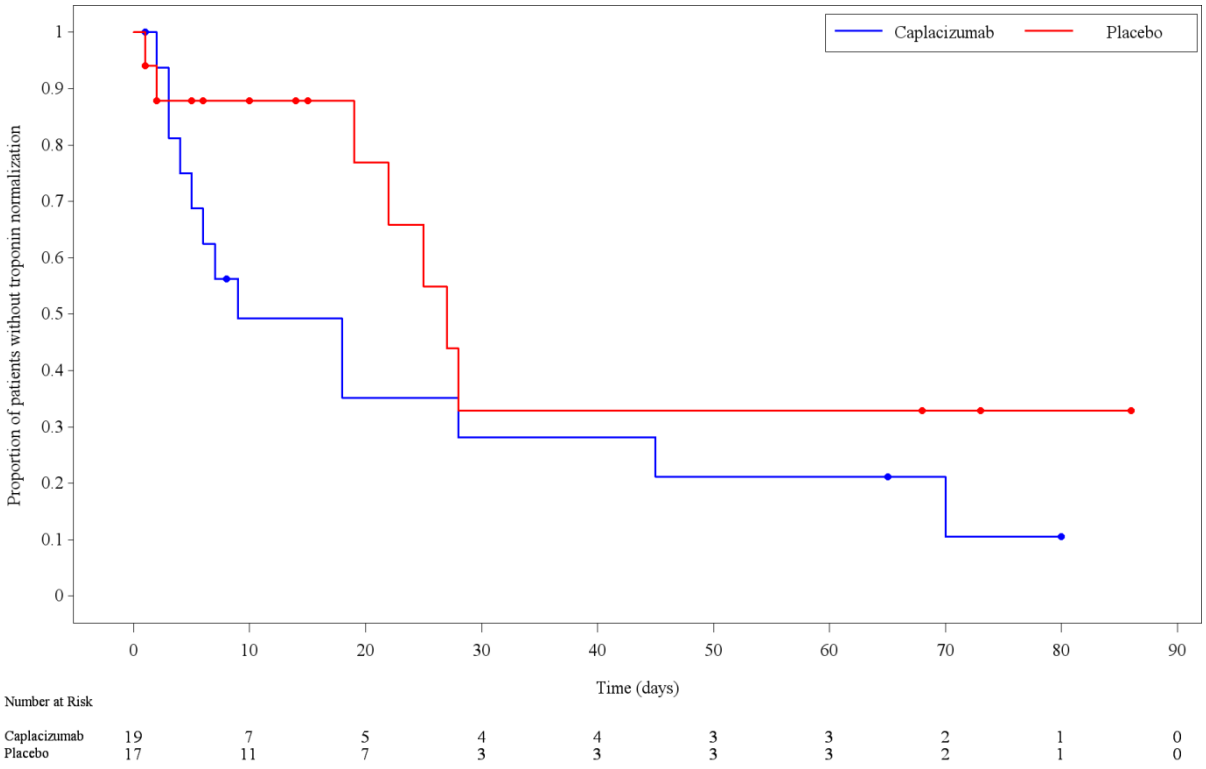
Panel C: Factor VIII Chromogene



Values below lower limit of quantification (LLOQ) of 3% were set at LLOQ

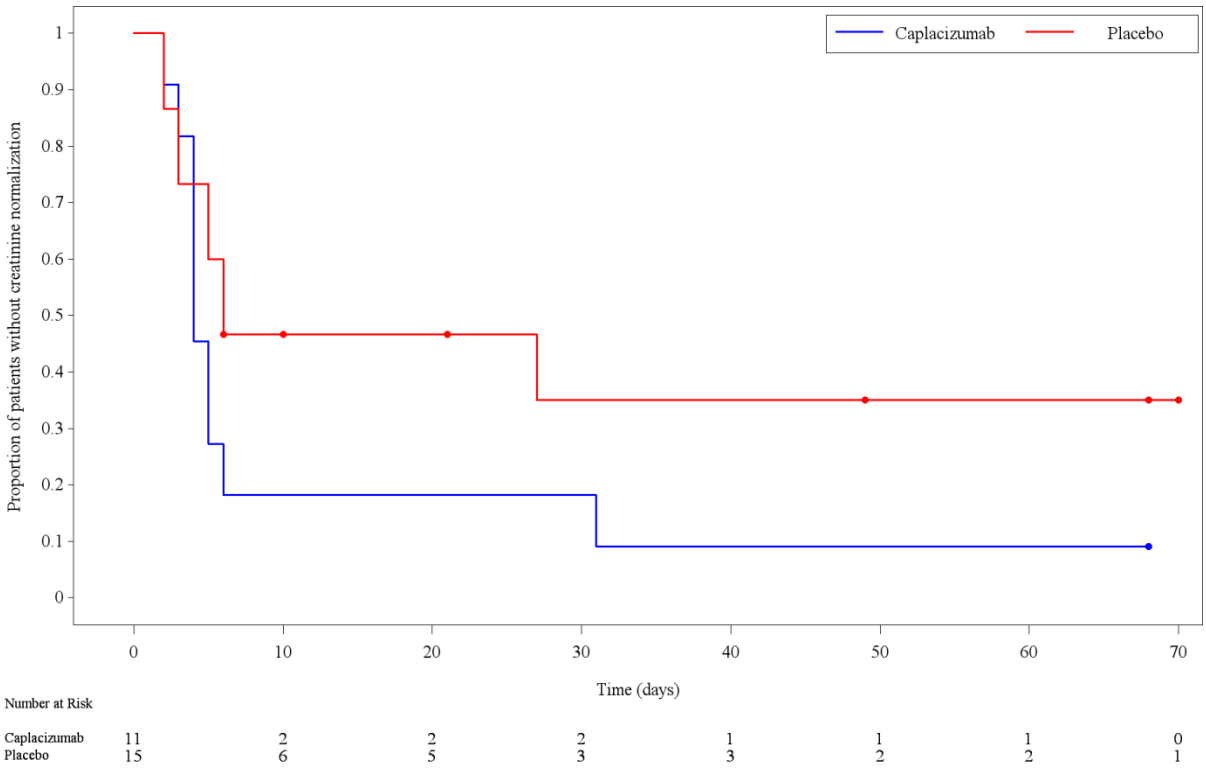
DP: Daily PE; PD: postdose; LD: Last Day; FD: First Day; PDPE: Post Daily PE; FU: Follow-up

Figure S3: Time to Troponin T or I normalization (A), creatinine (B) and LDH (C) curves for patients with abnormal high levels at baseline (Intention-to-treat (ITT) Population).
Panel A: Time to first Troponin T or I normalization



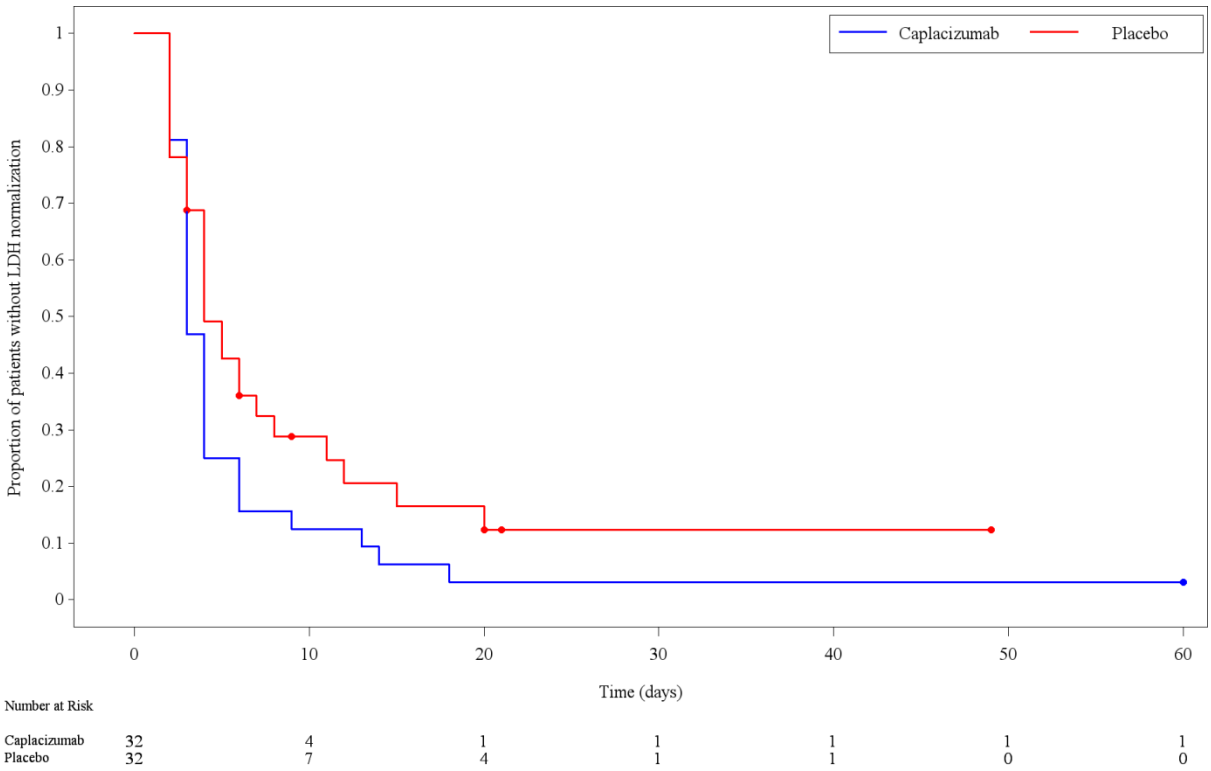
Censored observations are represented by a dot. Any patient still at risk at 1 month FU is censored.

Panel B: Time to first creatinine normalization



Censored observations are represented by a dot. Any patient still at risk at 1 month FU is censored.

Panel C: Time to first LDH normalization



Censored observations are represented by a dot. Any patient still at risk at 1 month FU is censored.

Supplementary Tables

Table S1: Overview of eligibility criteria

Inclusion criteria
1. Patient 18 years of age or older (adults) or aged 12 to < 18 years (adolescents)
2. Male or female patient, willing to accept an acceptable contraceptive regimen.
3. Patient with a clinical diagnosis of TTP.
4. Patient requiring PE (one single PE session prior to randomization into the study was allowed).
5. Patient accessible to follow-up.
6. Patient able to provide signed and dated informed consent and assent (if applicable, for adolescents).
Exclusion criteria
1. Patient with a platelet count greater than or equal to 100000/µL.
2. Patient with a severe active infection indicated by sepsis (requirement for pressors with or without positive blood cultures).
3. Patient with clinical evidence of enteric infection with Escherichia coli 0157 or related organism.
4. Patient with anti-phospholipid syndrome.
5. Patient with a diagnosis of disseminated intravascular coagulation (DIC).
6. Patient who is pregnant or breast-feeding.
7. Patient with hematopoietic stem cell or bone marrow transplantation-associated thrombotic microangiopathy.
8. Patient with known congenital TTP.
9. Patient with active bleeding or high risk of bleeding.
10. Patient with uncontrolled arterial hypertension.

11. Patient receiving known chronic treatment with anticoagulant treatment that could not be stopped safely, including but not limited to: o Vitamin K antagonists o Heparin or low molecular weight heparin (LMWH) o Non-acetyl salicylic acid non-steroidal anti-inflammatory molecules.
12. Patient with a severe or life-threatening clinical condition other than TTP that would impair participation in the study.
13. Patients with malignancies resulting in a life expectation of less than 3 months.
14. Patients with known or suspected bone marrow carcinosis.
15. Patients who could not comply with study protocol requirements and procedures.
16. Patient with a known hypersensitivity to the active substance or to excipients of the study drug.
17. Patient with severe liver impairment, corresponding to grade 3 toxicity defined by the Common Terminology Criteria for Adverse Events (CTCAE) scale. For the key liver parameters, this is defined as follows: o Bilirubin >3 x upper limit of normal (ULN) (needed to differentiate isolated increase in indirect bilirubin due to haemolysis, this was not an exclusion parameter but disease-related) o Alanine transaminase (ALT)/aspartate transaminase (AST) >5 x ULN o Alkaline phosphatase (AP) >5 x ULN o Gamma glutamyl transpeptidase (GGT) >5 x ULN.
18. Patient with severe chronic renal impairment, as defined by glomerular filtration rate <30 mL/min.

Table S2: Demographics, baseline characteristics of patients and TTP therapy

	Caplacizumab	Placebo	Total
Demographics (ITT population)			
	Caplacizumab N=36	Placebo N=39	Total N=75
Age (years)			
Mean (SD)	40.6 (12.7)	42.5 (13.2)	41.6 (12.9)
Min-Max	19-72	21-67	19-72
Gender, n (%)			
Male	12 (33.3)	19 (48.7)	31 (41.3)
Female	24 (66.7)	20 (51.3)	44 (58.7)
Ethnicity/ Race, n (%)			
Caucasian	32 (88.9)	34 (87.2)	66 (88.0)
Black	4 (11.1)	5 (12.8)	9 (12.0)
Baseline BMI (kg/m^2)	n=25	n=37	n=62
Mean (SD)	28.7 (9.1)	29.3 (6.7)	29.1 (7.7)
Min-Max	16.2-50.7	19.4-45.7	16.2-50.7
Baseline Disease Characteristics (ITT population)			
	Caplacizumab N=36	Placebo N=39	Total N=75
Initial Episode or Recurrent, n (%)			
Initial	24 (66.7)	27 (69.2)	51 (68.0)
Recurrent	12 (33.3)	12 (30.8)	24 (32.0)
PE Prior to Randomization, n (%)			

No	34 (94.4)	35 (89.7)	69 (92.0)
Yes	2 (5.6)	4 (10.3)	6 (8.0)
Platelets (10^9/L)	n=35	n=37	n=72
Mean (SD)	21.1 (18.2)	28.0 (20.0)	24.6 (19.3)
Min-Max	2-70	5-84	2-84
LDH (U/L)	n=34	n=35	n=69
Mean (SD)	1277 (853)	1270 (939)	1274 (891)
Min-Max	239.5-3874.0	247.0-4703.0	239.5-4703.0
ADAMTS13 activity, n (%)			
<10%	28 (77.8)	30 (76.9)	58 (77.3)
≥10%	2 (5.6)	6 (15.4)	8 (10.7)
Missing	6 (16.7)	3 (7.7)	9 (12.0)
ADAMTS13 Functional Inhibitors (BU/mL), n (%)[a]			
< 0.5	6 (16.7)	6 (15.4)	12 (16.0)
≥0.5 and ≤ 2	15 (41.7)	9 (23.1)	24 (32.0)
> 2	5 (13.9)	8 (20.5)	13 (17.3)
>> 2	4 (11.1)	7 (17.9)	11 (14.7)
Missing	6 (16.7)	9 (23.1)	15 (20.0)
VWF:Ag (%)	n=23	n=27	n=50
Mean (SD)	180.3 (78.2)	189.6 (74.3)	185.3 (75.4)
Min-Max	99.0-420.0	107.9-434.0	99.0-434.0
TTP therapy (ITT population)			
	Caplacizumab N=36	Placebo N=39	Total N=75

PE tapering, n (%)	11 (30.6)	11 (28.2)	22 (29.3)
Corticosteroids during daily PE, n (%)	32 (88.9)	36 (92.3)	68 (90.7)
Rituximab during daily PE, n (%)*	2 (5.6)[b]	9 (23.1)[b]	11 (14.7)
Duration of exposure to study drug (days), Mean (SD) (safety population)	n=35	n=37	n=72
Mean (SD)	37.9 (15.0)	39.2 (18.6)	38.6 (16.9)
Min-Max	3-77	2-90	2-90

Baseline was defined as prior to first administration of study drug.

ITT (intention-to-treat) population: all randomized patients, according to randomized treatment assignment including 3 patients that did not receive study drug.

Safety population: all patients receiving study drug (either caplacizumab or placebo)

n = number of patients with data available; % = percentage based on N (number of patients within analysis population).

* There were no significant differences in the listed demographics or baseline characteristics between the study groups except for Rituximab during daily PE ($P<0.05$).

[a] ADAMTS13 Functional Inhibitors > 2 BU/mL when residual ADAMTS13 activity was between 11-25%, and >> 2 BU/mL when residual ADAMTS13 activity was 10% or less. Inhibitor titers of at least 0.5 BU/mL were considered as positive.

[b] Imbalance between caplacizumab and placebo group is a possible site effect as one site used rituximab as part of standard of care as of Day 2 of daily PE and this site recruited 7 patients, 5 of whom were randomized to placebo.

Table S3: Efficacy endpoints (Intention-to-treat (ITT) Population)

Primary endpoint: Kaplan-Meier analysis of time to confirmed platelet response		
	Caplacizumab N=36	Placebo N=39
Overall		
Censored patients at 30 days, n (%)[a]	5 (13.9)	11 (28.2)
Patients with confirmed platelet response, n (%)[a]	31 (86.1)	28 (71.8)
One PE session prior to randomization		
Censored patients at 30 days, n (%)[a]	0	0
Patients with confirmed platelet response, n (%)[a]	2 (5.6)	4 (10.3)
Median (95% CI)	2.44 (1.92-2.97)	4.31 (2.91-5.68)
25th percentile (95% CI)	1.92 (1.92-2.97)	3.37 (2.91-4.79)
75th percentile (95% CI)	2.97 (1.92-2.97)	5.23 (2.91-5.68)
No PE session prior to randomization		
Censored patients at 30 days, n (%)[a]	5 (13.9)	11 (28.2)
Patients with confirmed platelet response, n (%)[a]	29 (80.6)	24 (61.5)
Median (95% CI)	3.00 (2.74-3.88)	4.92 (3.21-6.59)
25th percentile (95% CI)	2.72 (1.76-2.85)	3.01 (1.92-4.36)
75th percentile (95% CI)	4.31 (3.41-7.31)	11.37 (5.89-DNE)
	HR (95% CI)[b]	p-value[c]

Caplacizumab vs. Placebo	2.197 (1.278-3.778)	0.005	
Secondary endpoints			
	Caplacizumab N=36	Placebo N=39	Total N=75
Exacerbations of TTP within 30 days of last day of initial daily PE			
Exacerbations of TTP[d] Number of patients, n (%)	3 (8.3)	11 (28.2)	14 (18.7)
Relapse of TTP			
Relapse during 1-month follow-up period[e] Number of patients, n (%)	8 (22.2)	0	8 (10.7)
Relapse during 12-month follow-up period Number of patients, n (%)	11 (30.6)	3 (7.7)	14 (18.7)
Complete remission[f] following initial daily PE			
Overall Number of patients, n (%)	29 (80.6)	18 (46.2)	47 (62.7)
Summary of plasma exchange data			
During daily PE period Number of PE days Mean (SD) Min-Max Total volume of PE administered (L) Mean (SD)	 5.9 (2.4) 3-15 19.9 (8.2)	 7.9 (6.4) 2-35 28.3 (21.4)	 6.9 (5.0) 2-35 24.3 (16.9)

Min-Max	5.0-44.8	7.1-103.8	5.0-103.8
During overall study drug treatment period			
Number of PE days			
Mean (SD)	7.7 (4.7)	11.7 (8.5)	9.7 (7.1)
Min-Max	3-21	2-43	2-43
Total volume of PE administered (L)			
Mean (SD)	25.8 (15.6)	41.8 (31.2)	34.2 (26.1)
Min-Max	5.0-75.3	7.4-127.8	5.0-127.8
Up to 1-month follow-up			
Number of PE days			
Mean (SD)	10.2 (6.6)	11.7 (8.5)	11.0 (7.6)
Min-Max	4-29	2-43	2-43
Total volume of PE administered (L)			
Mean (SD)	36.0 (25.9)	41.8 (31.2)	39.0 (28.7)
Min-Max	5.0-109.3	7.4-127.8	5.0-127.8

N = number of patients in population; n = number of patients with the observation; % = percentage based on N; CI = Confidence Interval; DNE = Does Not Exist (due to small number of events); PE = plasma exchange.

ITT (intention-to-treat) population: all randomized patients, according to randomized treatment assignment including 3 patients that did not receive study drug.

[a] n = number of patients with data available; % = percentage based on N (number of patients within analysis population).

[b] Hazard ratio is based on a stratified Cox proportional hazards regression model with One PE Session Prior to Randomization (Yes/No) as a covariate.

[c] p-value from stratified log-rank test (1-sided log-rank test to assess superiority at 2.5% significance level) is based on an analysis stratified for presence/absence of one PE session prior to randomization. An observation was censored if it did not meet the defined time interval of 30 days after first study drug administration.

[d] Exacerbation is defined as recurrent thrombocytopenia following a response and requiring a re-initiation of daily PE treatment after ≥ 1 day but ≤ 30 days after last daily PE

[e] Relapse is defined as *de novo* event of TTP that occurs later than 30 days after last daily PE.

[f] Complete remission after initial daily PE is defined as confirmed platelet response and absence of exacerbation.

Table S4: Pharmacokinetic (PK) Concentrations (ng/mL) (Mean ± Standard Error) reported for each visit (PK Population)

Visit	N*	Mean ± SE
Baseline	33	100.0 ± 0
DP Day 1 5-10 min PD	32	1765.9 ± 185.0
DP Day 1 3-6 h PD	31	450.4 ± 36.2
DP Day 1 8-24 h PD	34	562.0 ± 36.8
DP Day 2 predose	24	288.0 ± 24.0
DP Day 2 1-6 h PD	35	415.8 ± 24.8
DP Day 2 6-12 h PD	32	570.7 ± 52.2
DP Day 2 18-24 h PD	35	489.3 ± 32.5
LD DP predose	25	348.4 ± 38.3
FD after DP	24	521.9 ± 31.5
PDPE Week 1	31	490.6 ± 36.1
PDPE Week 2	29	524.9 ± 39.4
PDPE Week 3	30	499.6 ± 35.1
PDPE Week 4	25	503.4 ± 31.2
Day 3 FU	30	346.7 ± 25.4
Day 7 FU	28	162.3 ± 20.2
1 month FU	29	100.0 ± 0

*Number of patients in the PK population with available PK data for the visit

PK population: all patients who received the study drug and for whom the primary PK data are considered to be sufficient and interpretable.

Values below lower limit of quantification (LLOQ) of 100 ng/mL were set at LLOQ.

DP: Daily PE; PD: postdose; LD: Last Day; FD: First Day; PDPE: Post Daily PE; FU: Follow-up

Table S5: Number and Proportion of Patients in with Lactate Dehydrogenase (LDH) Values ≤2 x the Upper Limit of Normal by Study Day (Intention-to-treat (ITT) Population)

n (%)	Caplacizumab N=36	Placebo N=39
Analysis Relative Day		
1	11 (30.6)	9 (23.1)
2	28 (77.8)	20 (51.3)
3	33 (91.7)	29 (74.4)
4	34 (94.4)	34 (87.2)
5	34 (94.4)	34 (87.2)

N=number of patients in the population of interest; n=number of patients with LDH ≤ 2 x the ULN; ULN=upper limit of the normal range

Table S6: Treatment-emergent adverse events (AEs) reported for at least 5 patients per treatment arm (Safety Population)

System Organ Class Preferred Term	Caplacizumab N=35 n (%)	Placebo N=37 n (%)	Total N=72 n (%)
Patients with any AE	34 (97.1)	37 (100)	71 (98.6)
Blood and lymphatic system disorders[a]	**7 (20.0)**	**12 (32.4)**	**19 (26.4)**
Anemia[b]	3 (8.6)	8 (21.6)	11 (15.3)
Cardiac disorders	**9 (25.7)**	**8 (21.6)**	**17 (23.6)**
Eye disorders	**7 (20.0)**	**5 (13.5)**	**12 (16.7)**
Gastrointestinal disorders	**22 (62.9)**	**25 (67.6)**	**47 (65.3)**
Nausea	10 (28.6)	11 (29.7)	21 (29.2)
Vomiting	7 (20.0)	8 (21.6)	15 (20.8)
Diarrhoea	6 (17.1)	3 (8.1)	9 (12.5)
Constipation	7 (20.0)	10 (27.0)	17 (23.6)
Gingival bleeding	5 (14.3)	2 (5.4)	7 (9.7)
Abdominal pain	2 (5.7)	5 (13.5)	7 (9.7)
General disorders and administration site conditions	**21 (60.0)**	**22 (59.5)**	**43 (59.7)**
Fatigue	6 (17.1)	5 (13.5)	11 (15.3)
Pyrexia	6 (17.1)	6 (16.2)	12 (16.7)
Asthenia	1 (2.9)	6 (16.2)	7 (9.7)
Infections and infestations	**16 (45.7)**	**13 (35.1)**	**29 (40.3)**
Urinary tract infection	5 (14.3)	0	5 (6.9)
Injury, poisoning and procedural complications	**7 (20.0)**	**7 (18.9)**	**14 (19.4)**

Investigations	**11 (31.4)**	**14 (37.8)**	**25 (34.7)**
Metabolism and nutrition disorders	**15 (42.9)**	**16 (43.2)**	**31 (43.1)**
Hypokalemia	9 (25.7)	8 (21.6)	17 (23.6)
Hyperglycemia	2 (5.7)	5 (13.5)	7 (9.7)
Musculoskeletal and connective tissue disorders	**17 (48.6)**	**16 (43.2)**	**33 (45.8)**
Myalgia	7 (20.0)	1 (2.7)	8 (11.1)
Pain in extremity	5 (14.3)	8 (21.6)	13 (18.1)
Muscle spasms	4 (11.4)	5 (13.5)	9 (12.5)
Arthralgia	3 (8.6)	8 (21.6)	11 (15.3)
Nervous system disorders	**21 (60.0)**	**23 (62.2)**	**44 (61.1)**
Headache	12 (34.3)	10 (27.0)	22 (30.6)
Paraesthesia	8 (22.9)	8 (21.6)	16 (22.2)
Dizziness	8 (22.9)	3 (8.1)	11 (15.3)
Psychiatric disorders	**14 (40.0)**	**17 (45.9)**	**31 (43.1)**
Insomnia	5 (14.3)	5 (13.5)	10 (13.9)
Anxiety	4 (11.4)	5 (13.5)	9 (12.5)
Agitation	3 (8.6)	5 (13.5)	8 (11.1)
Reproductive system and breast disorders	**5 (14.3)**	**3 (8.1)**	**8 (11.1)**
Respiratory, thoracic and mediastinal disorders	**18 (51.4)**	**15 (40.5)**	**33 (45.8)**
Epistaxis	11 (31.4)	4 (10.8)	15 (20.8)
Dyspnoea	5 (14.3)	4 (10.8)	9 (12.5)
Cough	5 (14.3)	2 (5.4)	7 (9.7)

Skin and subcutaneous tissue disorders	**15 (42.9)**	**9 (24.3)**	**24 (33.3)**
Vascular disorders	**13 (37.1)**	**15 (40.5)**	**28 (38.9)**
Hypertension	5 (14.3)	6 (16.2)	11 (15.3)

AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA version 15.0 or higher).

SOC = System Organ Class; AE = Adverse Event

N = number of patients in population; n = number of patients with events; % = percentage of n based on N

[a] Relapse of TTP and exacerbation of TTP, although originally captured as adverse events, were not included as (Serious)AE under this system organ class (preferred term: thrombotic thrombocytopenic purpura), but are discussed as secondary efficacy outcomes and reported in manuscript Table 2 – Efficacy endpoints.

[b] Relapse of anemia, exacerbation of anemia, … were coded to anemia