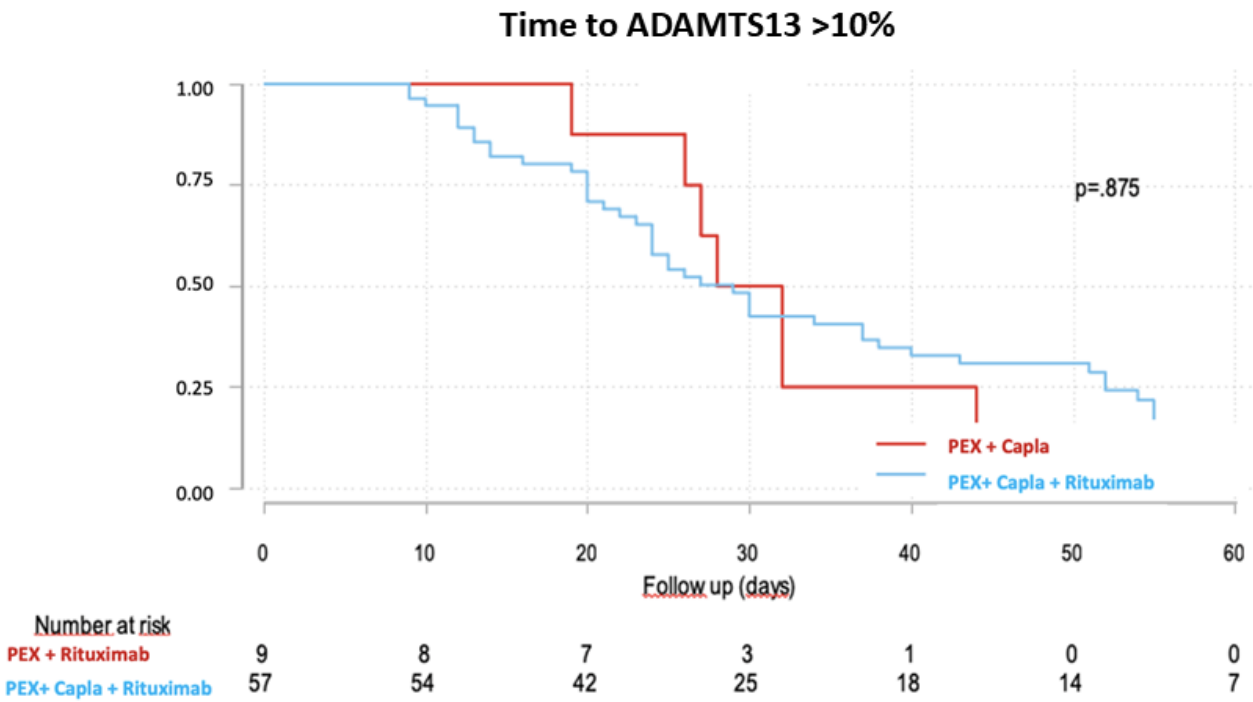

Supplementary Figure 1. Survival analysis. Time to ADAMTS13 >10% in patients treated with caplacizumab, with or without rituximab (n=66*). (It should be noted that all patients also received PEX and corticosteroids). *Missing values

Supplementary Table 1. Characteristics of the 8 patients who died during an acute episode†

Treated with caplacizumab	Patient number	Age (years) / Sex	Neurologic involvement	Cardiologic involvement	LDH ratio (patient/normal range)	Platelets (x 10^9/L) at first PEX	Time from first symptom to first PEX	Time from diagnosis to 1st PEX	Time from 1st PEX to death	Day from first PEX to 1st dose of caplacizumab	Clinical course and treatment	Ultimate cause of death
NO	**92**	54 /Male	Yes (Coma)	No	x 6	8	**UK**	0	<1 day	NA	Was only treated with 1 PEX procedure.	Brain death
NO	**98**	29 / Male	Yes (Seizures)	No	x 3.5	7	**UK**	1	12 hours	NA	Hospitalized with Status Epilepticus. Was only treated with 1 PEX procedure.	Refractory Status Epilepticus
NO	**101**	56 / Female	Yes (Low conscious level)	No	X 8	5	**3**	0	10 days	NA	Progression to coma. Refractory to PEX, corticosteroids, N-acetyl cysteine and rituximab (day 1).	Hypovolemic shock due to digestive bleeding
NO	**141**	58 / Female	Yes (Headache)	No	X 3	5	**3**	0	10 days	NA	Progression to myopericarditis and cerebellar ischemic stroke. Refractory to PEX and rituximab day 1 (2 doses).	Cardiogenic shock
NO	**148**	37 / Female	Yes (Seizures)	Yes (NSTEMI)	X 2	25	**UK**	0	12 hours	NA	Only 1 PEX procedure.	Cardiogenic shock
NO	**153**	36 / Male	Yes (Coma)	No	X 3.5	16	**4**	0	12 hours	NA	Only 1 PEX procedure.	Multiorgan failure
YES	**70**	43 / Female	Yes (Seizures)	Yes (troponin elevation)	x 5	**9**	**4**	0	5 days	1	Refractory TTP treatment: rituximab day 1 after PE 375 mg/m2/week. (1 dose), caplacizumab 10 mg/day, daily PEX.	Multiorgan failure. Intracranial bleeding
YES	**74**	61 / Male	Yes (Seizures)	Yes (troponin elevation)	x 12	**7**	**3**	0	10 days	1	Multifactorial encephalopathy. Refractory TTP to PEX, rituximab day 1 (2 doses), caplacizumab.	Multiorgan failure

† All patients were treated with corticosteroids as of the first day after PE

LDH: Lactate dehydrogenase; NA: not available; NSTEMI: non-ST-elevation myocardial infarction; PEX: plasma exchange; TTP: Thrombotic Thrombocytopenic Purpura; UK: Unknown.

Supplementary Table 2. Time to platelet normalization (>150x10^9/L) in patients treated with caplacizumab as initial treatment

Caplacizumab as initial treatment	**Time in days** Mean ± SD Median (IQR)	**p-value**
0-3 days (N=30)	6.93 ± 11.5 4 (3-5)	**0.003**
4-6 days (N=9)	12.2 ± 20.0 5 (5-9)	
≥7 days (N=4)	18.3 ± 13.8 14.5 (10-26.5)	

IQR: interquartile range; SD: standard deviation

31 (70%) patients received caplacizumab at 0-3 days (1 was missing for time to platelet normalization), 9 (20%) at 4-6 days and 4 (9%) at 7 or more days from diagnosis

Supplementary Table 3. Multivariate analysis of factors related to length of hospitalization and number of plasma exchanges

Factors related to length of hospitalization	**Coefficient**	**SE**	**t**	**p>ltl**	**95%CI**
Constant	25.94	6.90	3.76	**0.000**	12.03;39.85
Age	0.14	0.11	1.24	0.218	-0.08; 0.36
Platelets ≥10	-4.29	2.93	-1.46	0.148	-10.11; 1.55
Hemoglobin ≥8	-7.51	2.85	-2.63	**0.010**	-13.17; -1.84
LDH ≥1000	2.50	2.45	1.02	0.310	-2.36; 7.35
Cardiovascular manifestations	-2.89	2.97	-0.97	0.334	-8.78; 3.01
Neurological manifestations	-7.01	2.95	-2.38	**0.019**	-12.86; -1.17
Caplacizumab within 0-3 days	-11.22	2.83	-3.96	**0.000**	-16.87; -5.58
Rituximab	4.97	2.81	1.77	0.081	-0.62; 10.56
Factors related to number of PEX	**Coefficient**	**SE**	**t**	**p>ltl**	**95%CI**
Constant	13.39	5.51	2.43	**0.017**	2.48; 24.29
Age	0.20	0.09	2.23	**0.027**	0.023; 0.38
Platelets ≥10	-3.25	2.67	-1.22	0.226	-8.53; 2.03
Hemoglobin ≥8	-3.02	2.58	-1.17	0.244	-8.12; 2.09
LDH ≥1000	1.44	2.17	0.66	0.508	-2.85; 5.74
Cardiovascular manifestations	-3.07	2.77	-1.11	0.270	-8.57; 2.43
Neurological manifestations	-6.74	2.82	-2.39	**0.018**	-12.30; -1.17
Caplacizumab within 0-3 days	-7.49	2.63	-2.84	**0.005**	-12.71; -2.27
Rituximab	5.93	2.61	2.27	**0.025**	0.77; 11.10

CI: confidence interval; LDH: lactate dehydrogenase; PEX: plasma exchanges; SE: standard error.

Supplementary Table 4. Number of iTTP patients treated with caplacizumab with adverse events

	iTTP patients treated with caplacizumab (N=77)
Adverse events	28 (36%)
Bleeding events	*16 (21%)*
Gingivorrhagia	15 (19%)
Metrorrhagia	8 (10%)
Non-bleeding events	*15 (19%)*
Thrombocytosis	15 (19%)
Serious adverse events	**0 (0%)**
Deaths	**0 (0%)**

iTTP: Immune Thrombotic Thrombocytopenic Purpura