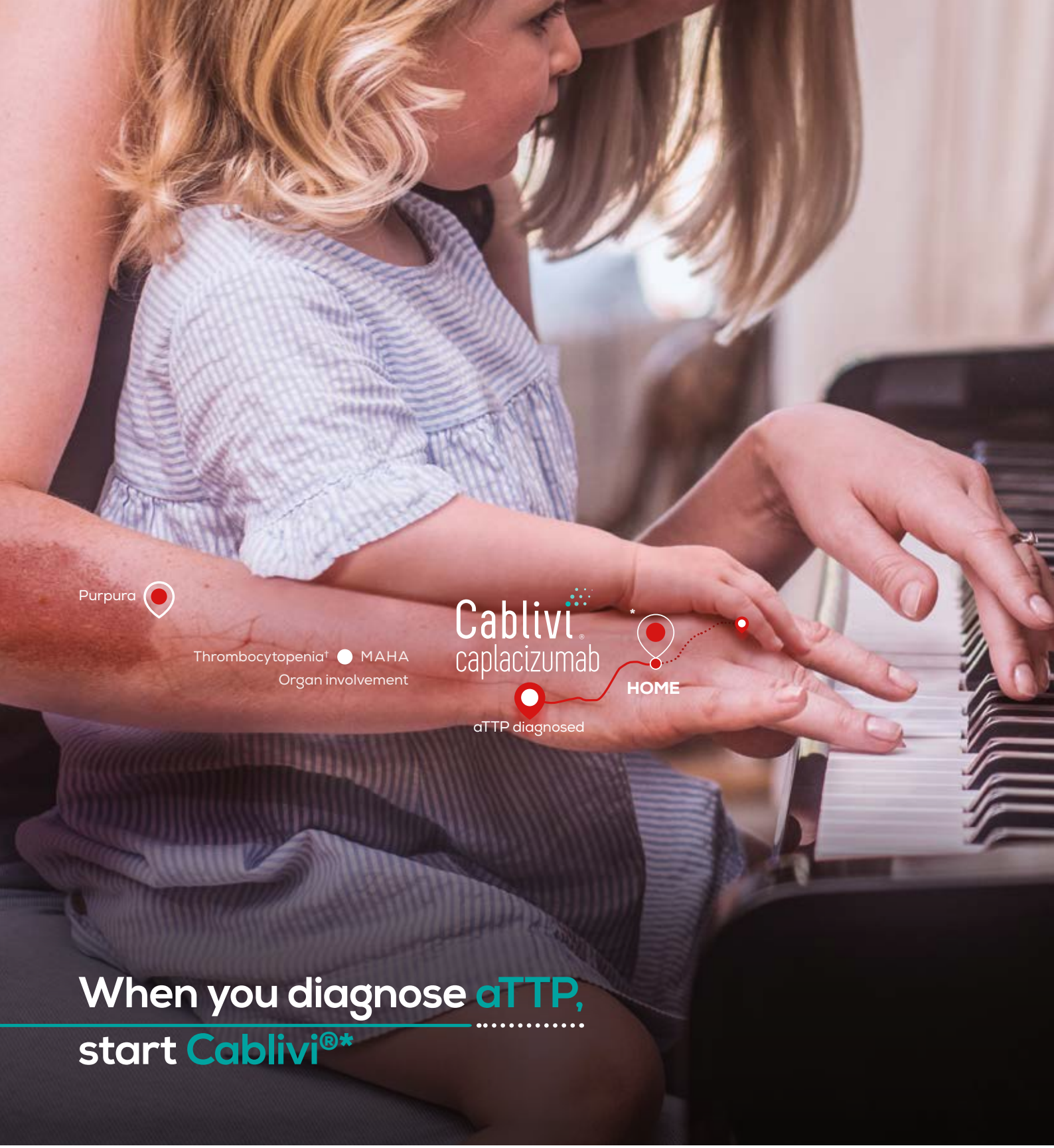


When you diagnose aTTP, start Cablivi®*

CABLIVI® provides protection from microthrombi within 24 hours of first treatment.[1]

aTTP = acquired Thrombotic Thrombocytopenic Purpura; MAHA = Microangiopathic Haemolytic Anaemia.

* In conjunction with plasma exchange (PEX) and immunosuppression.
† Severe thrombocytopenia (typically <30 x 10^9/L).

Fighting complex diseases
with groundbreaking therapies.

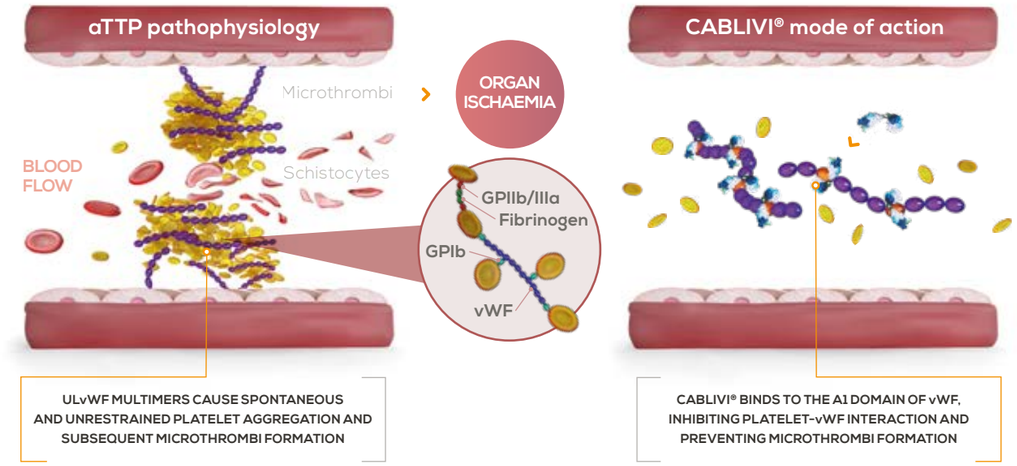
SANOFI GENZYME

CABLIVI®: AN INNOVATIVE TREATMENT FOR aTTP[1–3]

Historical therapies for aTTP do not immediately act on platelet adhesion, leaving patients at risk of thrombotic complications.[4,5]

CABLIVI® targets the A1 domain of von Willebrand Factor (vWF) and completely suppresses vWF binding to platelets within 24 hours of treatment initiation.[1]

FIGURE 1: CABLIVI® in the treatment pathway



ADAMTS13 = a disintegrin and metalloproteinase with thrombospondin motifs 13; GP = Glycoprotein; ULvWF = ultra large von Willebrand Factor; vWF = von Willebrand Factor

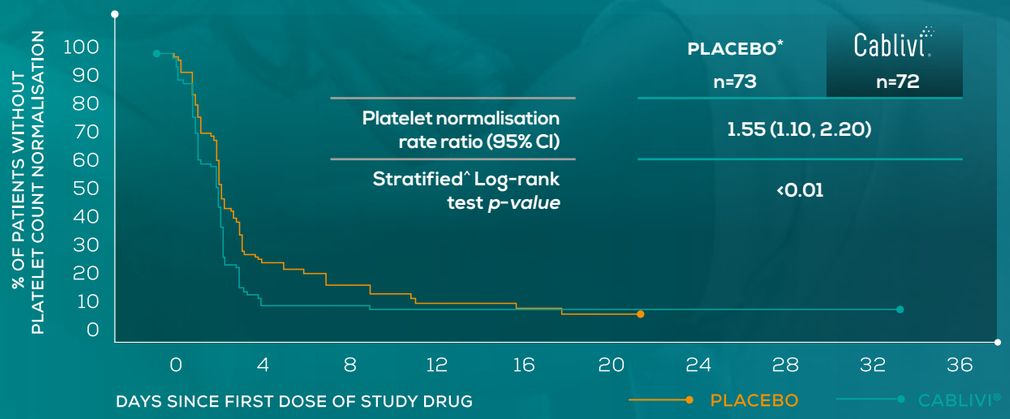
Adapted from Holz 2012.[3]

CABLIVI® PREVENTS THE ULTRA LARGE vWF-MEDIATED PLATELET ADHESION AND SUBSEQUENT ACCUMULATION OF MICROTHROMBI, WHICH LEADS TO THE ORGAN AND TISSUE DAMAGE AND SEVERE THROMBOCYTOPENIA SEEN IN aTTP.[2]

CABLIVI® EFFICACY: PRIMARY ENDPOINT – TIME TO PLATELET COUNT RESPONSE

Treatment with CABLIVI®* resulted in a statistically significant reduction in time to platelet count response ($p<0.01$).[6]

FIGURE 2: Time to platelet count response^ (HERCULES).



Adapted from Scully *et al.* 2019.[6]
CI = confidence interval.

PATIENTS TREATED WITH CABLIVI®, IN CONJUNCTION WITH PEX AND IMMUNOSUPPRESSION, ARE 55% MORE LIKELY TO ACHIEVE PLATELET COUNT RESPONSE AT ANY GIVEN TIME POINT, VS. PATIENTS TREATED WITH PEX AND IMMUNOSUPPRESSION ALONE ($p<0.01$).[6]

CI = confidence interval
PEX = plasma exchange
^ Platelet count response was defined as initial platelet count ≥150x10^9/L with subsequent stop of daily PEX within 5 days.
* In conjunction with plasma exchange (PEX) and immunosuppression.

CABLIVI® EFFICACY: SECONDARY ENDPOINTS

There were no deaths in the CABLIVI® plus PEX and immunosuppression group, and 3 deaths in the placebo plus PEX and immunosuppression group.[2]

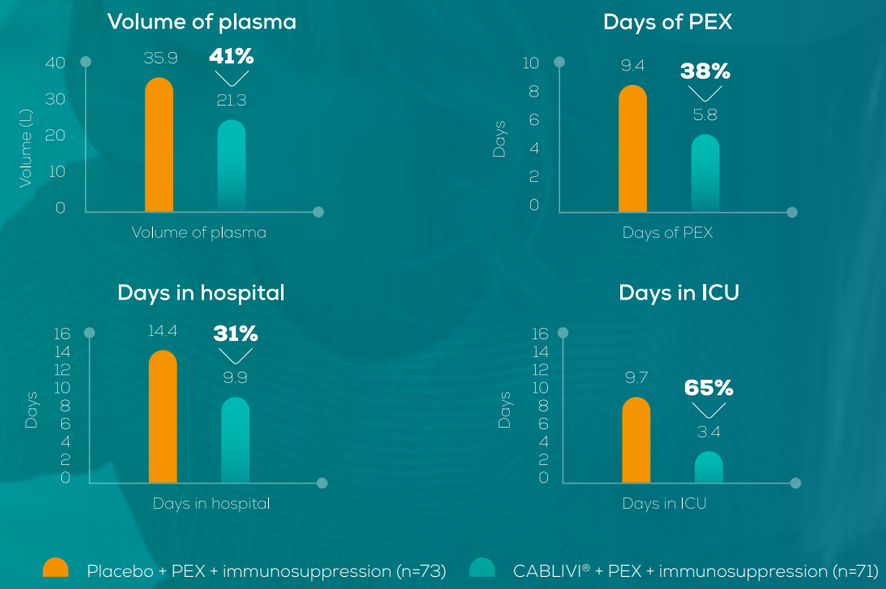
TABLE 1: aTTP-related death, aTTP recurrence, or a major thromboembolic event during the study drug treatment period.[6]

Number of subjects (%)	PLACEBO* n=73	Cablivi.* n=72†	
Total number of subjects with at least one of the events[$]	36 (49.3)	9 (12.7)	*p-value* <0.0001
aTTP-related death[‡]	3 (4.1)	0	
Recurrence of aTTP[#] (exacerbation)	28 (38.4)	3 (4.2)	
At least one treatment emergent major thromboembolic event[‡‡]	6 (8.2)	6 (8.5)	
aTTP recurrence[$$]	28 (38)	9 (12)	*p-value* <0.001
During the study drug treatment period[¶]	28 (38)	3 (4)	
During the follow-up period (relapses)[##]	0	6 (8)[‡]	
Refractory aTTP[$$$]	3 (4)	0	*p-value* 0.057

CABLIVI® EFFICACY: HEALTHCARE RESOURCE UTILISATION

In the HERCULES study, CABLIVI®* reduced volume and duration of PEX and time spent in hospital vs. PEX and immunosppression alone.[2]

FIGURE 3: PEX parameters, duration of ICU stay and overall hospitalisation.[6]



- **CABLIVI®* LEADS TO A 74% REDUCTION IN THE COMPOSITE ENDPOINT VS. PEX AND IMMUNOSUPPRESSION ALONE (*p*<0.0001).[6]**
- **CABLIVI®* LEADS TO A 67% REDUCTION IN EXACERBATIONS OR RELAPSES VS. PEX AND IMMUNOSUPPRESSION ALONE (*p*<0.001).[6]**
- **IN THE HERCULES STUDY, NO PATIENTS TREATED WITH CABLIVI®* WERE REFRACTORY TO TREATMENT.[6]**

CONSIDERABLY REDUCED THERAPY EFFORT WITH CABLIVI®[6]

* In conjunction with plasma exchange (PEX) and immunosuppression.

† % based on 71 subjects entering the study drug treatment period.

$ Patients could have more than 1 event.

‡ Adjudicated by a blinded independent committee.

Recurrence: thrombocytopenia after initial recovery of platelet count, requiring re-initiation of daily PEX.

$$ Recurrence (the occurrence of either an exacerbation or relapse): recurrent thrombocytopenia after initial recovery of platelet count, requiring re-initiation of daily PEX.

‡‡ ADAMTS13 activity levels were <10% at the end of the study drug treatment period in all of these patients.

¶ Exacerbation: recurrent thrombocytopenia after initial recovery of platelet count (platelet count ≥150×10^9/L with subsequent stop of daily PEX within 5 days), requiring re-initiation of daily PEX, occurring during the first 30-day post-daily PEX period.[6]

Relapse: recurrent thrombocytopenia after initial recovery of platelet count requiring re-initiation of daily PEX, occurring after the 30-day post-daily PEX period.[6,$]

$$$ Refractory TTP: an absence of platelet count doubling after 4 days of standard treatment and LDH > ULN (definition based on Benhamou *et al.* 2015).[7]

Volume of plasma, days of PEX and days in hospital evaluated in 73 placebo plus PEX and immunosuppression patients and 71 CABLIVI®* patients.[2,6]

Days in ICU evaluated in 27 placebo plus PEX and immunosuppression patients and 28 CABLIVI®* patients.[2,6]

ICU = intensive care unit

* In conjunction with plasma exchange (PEX) and immunosuppression.

CABLIVI®: SAFETY PROFILE

In some cases, bleeding events were serious and required medical attention; however, most were self-limited and all resolved.[2,†]

TABLE 2: Overall safety profile of CABLIVI®.[6]

Number of subjects (%) with	PLACEBO* n=73	Cablivi* n=71
At least one TEAE	66 (90.3)	68 (95.8)
At least one TEAE leading to study drug discontinuation	9 (12.3)	5 (7.0)
At least one SAE	12 (16.4)	23 (32.4)
At least one SAE leading to death	3 (4.1)	1 (1.4)[$]

CABLIVI®* HAS A FAVOURABLE SAFETY PROFILE WITH MUCOCUTANEOUS BLEEDING (EPISTAXIS AND GINGIVAL BLEEDING) AS THE MOST FREQUENTLY REPORTED BLEEDING-RELATED AE AND NO TREATMENT-RELATED DEATHS.[2]

TEAE = treatment-emergent adverse event, SAE = serious adverse event.

* In conjunction with PEX and immunosuppression.

[$] One patient died in the CABLIVI® group during the treatment-free follow-up period. The cause of death was cerebral ischaemia and was adjudicated as TTP related but assessed by the investigator as unrelated to treatment.[6]

† In case of active, clinically significant bleeding, treatment with CABLIVI® should be interrupted. If needed, the use of von Willebrand Factor concentrate could be considered to correct haemostasis. CABLIVI® should only be restarted upon the advice of a healthcare professional experienced in the management of thrombotic microangiopathies.[2]

Cablivi caplacizumab

REFERENCES AND PRESCRIBING INFORMATION

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2. CABLIVI® Professional Information, www.swissmedicinfo.ch
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6. Scully M, *et al.* Caplacizumab Treatment for Acquired Thrombotic Thrombocytopenic Purpura. N Engl J Med. 2019;380:335–46.
7. Benhamou Y, *et al.* Cardiac troponin-I on diagnosis predicts early death and refractoriness in acquired thrombotic thrombocytopenic purpura. Experience of the French Thrombotic Microangiopathies Reference Center. J Thromb Haemost. 2015;13(2):293–302.

Cablivi 10mg powder and solvent for the preparation of a solution for injection: AI: Caplacizumab 10mg. **I:** Treatment of adults suffering from an episode of acquired thrombotic thrombocytopenic purpura aTTP in conjunction with plasmapheresis and immunosuppression. **D:** Initial dose 10mg i.v. prior to plasmapheresis; subsequent doses 10mg s.c. after completion of every plasmapheresis, then 10mg s. c. daily for up to 30 days after finishing the daily plasmapheresis treatment. A forgotten dose can be made up for within the next 12 hours. **Contraindication:** Oversensitivity. **Cautionary measures:** No data available for children and adolescents or on patients with severe liver dysfunction. An adjustment of the dose or particular cautionary measures may be necessary with older patients. In the case of active clinically relevant bleeding, treatment should be discontinued. Patients with coagulopathy must be closely monitored. Discontinue therapy at least 7 days before planned operations or dental interventions and inform the surgeon. In emergency operations the use of a von Willebrand factor concentrate can be considered. **Interaction:** platelet aggregation inhibitors, anticoagulants, low molecular weight heparin: due to potentially raised risk of haemorrhage, careful consideration and close monitoring. **Side effects:** Epistaxis, headaches, bleeding, tiredness, urticaria, fever. **P:** 1 vial with 10mg powder and 1 pre-filled syringe with solvent. **Med. class:** B. **MAH:** sanofi-aventis (suisse) sa, 1214 Vernier. (GZCH.CAPL.19.08.0136(1)) **Updated:** October 2019. For further information please see the prescribing information at www.swissmedicinfo.ch.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See the "Undesirable effects" section for advice on the reporting of adverse reactions.

WHEN YOU DIAGNOSE aTTP, START CABLIVI®*

CABLIVI®'S INNOVATIVE MODE OF ACTION

CABLIVI® is a humanised nanobody that binds to von Willebrand Factor and thereby suppresses its ability to adhere to platelets within 24 hours of first treatment.[1,2,6]

CABLIVI®'S EFFICACY

In patients treated with CABLIVI® in conjunction with PEX and immunosuppression vs. PEX and immunosuppression alone:[2,6]

55% more likely to achieve platelet count response at any given point in time ($p<0.01$)

74% reduction in the proportion of patients experienting aTTP-related deaths, exacerbation of aTTP or major thromboembolic events ($p<0.0001$)†

41% reduction of the plasma volume

38% reduction of the duration of PEX

31% reduction of days spent in hospital

65% reduction of days spent in ICU

CABLIVI®'S SAFETY PROFILE

CABLIVI® has a favourable safety profile with mucocutaneous bleeding (epistaxis and gingival bleeding) as the most frequently reported bleeding-related adverse event and no treatment-related deaths.[2,6]

CABLIVI® IS THE FIRST DRUG INDICATED FOR THE TREATMENT OF ADULTS EXPERIENCING AN EPISODE OF ACQUIRED THROMBOTIC THROMBOCYTOPENIC PURPURA (aTTP), IN CONJUNCTION WITH PLASMA EXCHANGE (PEX) AND IMMUNOSUPPRESSION.[2,#]

* In conjunction with plasma exchange (PEX) and immunosuppression.

\# CABLIVI® has been evaluated in 131 patients in total.[1,2,6]

† Composite endpoint: patients experienced at least one of the events. aTTP-related death (CABLIVI® 0/72; placebo 3/73), exacerbation of aTTP (CABLIVI® 3/72; placebo 28/73) or major thromboembolic event (CABLIVI® 6/72; placebo 6/73).[2,6]

§ Volume of plasma (CABLIVI® 35.93L; placebo 21.33L), duration of PEX (CABLIVI® 5.8 days; placebo 9.4 days), days in hospital (CABLIVI® 9.9; placebo 14.4) and days in ICU (CABLIVI® 3.4; placebo 9.7).[2,6]

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Cablivi
caplacizumab

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