Supplemental Table 1. Transient protocol of use for rituximab in immune-mediated TTP (translated).

Background		
The use of rituximab had been authorized in 2008 through a transient protocol of use for the treatment of "severe idiopathic thrombotic purpura (platelets < 30 000/ mm3) in patients with a contra-indication for or failure of corticosteroids and/or intravenous immunoglobulins and contra-indication to or failure of splenectomy. In 2014, a request for a transient protocol of use had been submitted for the indication of **autoimmune thrombotic thrombocytopenic purpura at the acute phase refractory to daily plasma exchange (TPE), as defined by the absence of significant improvement of platelet count at day 5 of the management despite daily TPE, and/or by a worsening of platelet count at TPE tapering, following the advice of the reference center**. Since then, the management of TTP has moved on, with new compounds that obtained a label in this indication (caplacizumab). The reference center for the management of thrombotic microangiopathies (CNR-MAT) requests now a transient protocol of use for rituximab in the following indications: "- Autoimmune TTP at the acute phase at diagnosis, in association with TPE, corticosteroids and caplacizumab; - Autoimmune TTP in clinical remission but with a persistently severe ADAMTS13 deficiency (preemptive treatment), to prevent clinical relapses."		
Question	The opinion of the advisory board is solicited on this demand of temporary protocol of use for the two following indications: - According to the provided documents, the advice of the working group on onco-hematology (WGOH) is requested regarding the benefit/risk balance of the use of rituximab frontline in the treatment of TTP at the acute phase in association to the standard treatment; - According to the provided documents, the advice of the working group on onco-hematology (WGOH) is requested regarding the benefit/risk balance of the use of rituximab as a preemptive strategy to avoid clinical relapses.	
Votes		**9**
Number of voting persons among the total number Number of favorable advices		**9** **9**
Number of advices against		
Number of abstentions		**0**
Answer to the question		
Main advices Minor advices	**Favorable advice**: the WGOH is unanimously favorable for this temporary protocol of use (9 votes "FOR"). A common indication for both indications formerly proposed as well as the exact posology must be finalized with the reference center (Dr COPPO)	
Proposed action:	**By**	**Schedule**

Supplemental Table 2. *Definition of outcomes*

Complete response	Full resolution of the neurologic manifestations (or stabilization of neurologic abnormalities in patients considered as having permanent sequels) and renal failure and recovery of normal platelet count (>150x10^3/mm^3) for at least two days.
Durable remission	Complete response with no further thrombocytopenia, renal failure or clinical worsening for more than 30 consecutive days from the first day of platelet count recovery. At this step, the episode is considered as ended.
Exacerbation	Initial treatment response but reappearance of clinical manifestations and/or thrombocytopenia (<100x10^3/mm^3 for at least 2 days) before durable remission (complete response with no further thrombocytopenia or clinical worsening for > 30 consecutive days of platelet count recovery)
Relapse	Reappearance of clinical features of iTTP (thrombocytopenia [<100x10^3/mm^3 for at least 2 days], associated or not with organ involvement) (i.e., a new episode of iTTP) after durable remission had been achieved.
Refractoriness	Platelet count after 4 days of standard intensive treatment less than double the initial, together with persistently elevated LDH levels.

Supplemental Table 3. Clinical features and treatment of patients on diagnosis treated without caplacizumab during the recruitment period of the triplet regimen cohort. Data of both cohorts were compared.

Characteristics	**iTTP patients (ADAMTS13 <10%) treated without caplacizumab (N=22)**	**P-value**
Age (y)	45 (35-56)	0.88
Female sex	15 (68%)	0.86
Weight (kg)	78 (65-100)	0.25
Body mass index	29 (23.3-33)	0.30
Ethnicity White African-West Indies Asian	 19 2 1	0.89
Ongoing antiplatelet agent/anticoagulation Antiplatelet agent Anticoagulant	2 (9%) 2 0	0.89
Relapse	8 (33.3%)	0.01
Cerebral involvement Headache Confusion Seizure Coma Focal deficiency	13 (59%) 5 7 0 0 4	0.86
Cardiac involvement	9 (41%)	0.83
Hemoglobin (g/dL)	9.3 (8-11.3)	0.28
Platelet count (x 10^3/mm^3)	18 (9.5-32)	0.17
LDH level xN (U/L)	3 (2.25-3)	0.20
Serum creatinine (µmol/L)	111 (66-158)	0.47
GFR (mL/min/1.73m^2) (MDRD)	90 (61-119)	0.41
Anti-ADAMTS13 antibodies (U/mL)	69 (46-100)	0.73
French Severity score: 0-2 3-4	 18 4	0.92
Immunosuppressive therapy -Corticosteroids -Rituximab Time between 1st infusion and 1st TPE	 15 (68%) 14 (63%) 5 (3-10)	 <0.01 <0.01 0.01
Other therapies Twice-daily TPE Cyclophosphamide Splenectomy Vincristine Bortezomib > 1 salvage therapy	1 1 0 0 0 0 0	0.02

Abbreviations: LDH: lactate dehydrogenase. GFR: Glomerular Filtration Rate. MDRD Modification of Diet in Renal Disease. TPE: therapeutic plasma exchange. ADAMTS13: A Disintegrin And Metalloproteinase with ThromboSpondin-1 motifs, 13rd member. Data are given as median (25th-75th percentile) for quantitative variables and as n (%) for qualitative variables. Severe ADAMTS13 activity was defined as an activity <10% (normal range for ADAMTS13 activity: 50%-100%). The positivity threshold for anti-ADAMTS13 immunoglobulin G (IgG) was 12 U/mL, according to the manufacturer's instructions (Technoclone®). Cardiac involvement was defined as an increase of troponin and/or electrocardiographic abnormalities. Patients at high risk of early death of iTTP were defined by a French severity score ≥3 (cerebral involvement: yes=1 / no=0, LDH: >10xU.LN=1 / ≤10xULN=0, age: >60 years=2 / >40 and ≤60 years=1 / ≤40 years=0) [1].

Reference

1. Benhamou Y, Assie C, Boelle PY, et al. Development and validation of a predictive model for death in acquired severe ADAMTS13 deficiency-associated idiopathic thrombotic thrombocytopenic purpura: the French TMA Reference Center experience. Haematologica 2012;97(8):1181-6.

Supplemental Table 4. Maximum platelet count reached in the 19 patients of the triplet regimen cohort who developed thrombocytosis

Patient #	Platelet count (x $10^3/mm^3$)
2876	481
2797	484
2793	497
2859	508
2802	517
2764	524
2757	526
2806	526
2801	528
2747	540
2786	576
2739	582
2883	607
2831	658
2885	682
2622	691
2742	741
2777	742
2761	949

Appendix

The members of the Reference Center for Thrombotic Microangiopathies (CNR-MAT) are: Augusto Jean-François (Service de Néphrologie, dialyse et transplantation ; CHU Larrey, Angers); Azoulay Elie (Service de Réanimation Médicale, Hôpital Saint-Louis, Paris); Barbay Virginie (Laboratoire d'Hématologie, CHU Charles Nicolle, Rouen); Benhamou Ygal (Service de Médecine Interne, CHU Charles Nicolle, Rouen); Bordessoule Dominique (Service d'Hématologie, Hôpital Dupuytren, Limoges); Charasse Christophe (Service de Néphrologie, Centre Hospitalier de Saint-Brieuc); Charvet-Rumpler Anne (Service d'Hématologie, CHU de Dijon) ; Chauveau Dominique (Service de Néphrologie et Immunologie Clinique, CHU Rangueil, Toulouse); Choukroun Gabriel (Service de Néphrologie, Hôpital Sud, Amiens); Coindre Jean-Philippe (Service de Néphrologie, CH Le Mans); Coppo Paul (Service d'Hématologie, Hôpital Saint-Antoine, Paris); Corre Elise (Service d'Hématologie, Hôpital Saint-Antoine, Paris); Delmas Yahsou (Service de Néphrologie, CHU de Bordeaux, Bordeaux); Deschenes Georges (Service de Néphrologie Pédiatrique, Hôpital Robert Debré, Paris); Devidas Alain (Service d'Hématologie, Hôpital Sud-Francilien, Corbeil-Essonnes); Dossier Antoine (Service de Néphrologie, Hôpital Bichat, Paris); Fain Olivier (Service de Médecine Interne, Hôpital Saint-Antoine, Paris); Fakhouri Fadi (Service de Néphrologie, CHU Hôtel-Dieu, Nantes) ; Frémeaux-Bacchi Véronique (Laboratoire d'Immunologie, Hôpital Européen Georges Pompidou, Paris); Galicier Lionel (Service d'Immunopathologie, Hôpital Saint-Louis, Paris); Grangé Steven (Service de Réanimation Médicale, CHU Charles Nicolle, Rouen) ; Guidet Bertrand (Service de Réanimation Médicale, Hôpital Saint-Antoine, Paris); Halimi Jean-Michel (Service de Néphrologie Pédiatrique, Hôpital Bretonneau, Tours); Hamidou Mohamed (Service de Médecine Interne, Hôtel-Dieu, Nantes); Herbrecht Raoul (service d'Oncologie et d'Hématologie, Hôpital de Hautepierre, Strasbourg); Hié Miguel (Service de Médecine Interne, Groupe Hospitalier Pitié-Salpétrière, Paris) ; Jacobs Frédéric (Service de Réanimation Médicale, Hôpital Antoine Béclère, Clamart); Joly Bérangère (Service d'Hématologie Biologique, Hôpital Lariboisière, Paris) ; Kanouni Tarik (Unité d'Hémaphrèse, Service d'Hématologie, CHU de Montpellier) ; Kaplanski Gilles (Service de Médecine Interne, Hôpital la Conception, Marseille) ; Lautrette Alexandre (Hôpital

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