Supplementary Online Content

Vincent JL, Francois B, Zabolotskikh I, et al. Effect of a recombinant human soluble thrombomodulin on mortality in patients with sepsis-associated coagulopathy: the SCARLET randomized clinical trial. *JAMA*. doi:10.1001/jama.2019.5358.

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

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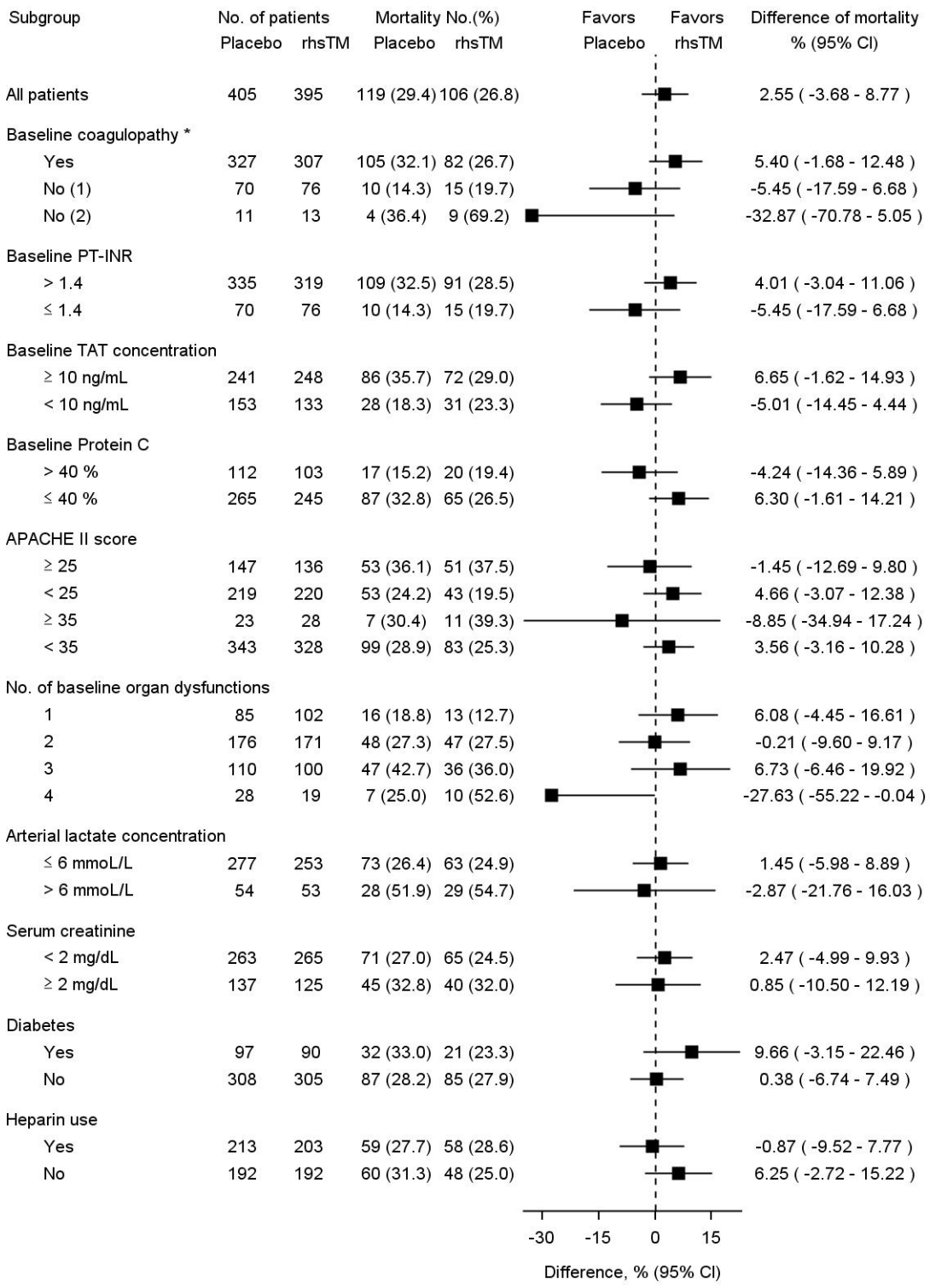
eFigure 1. Subgroup analysis of 28-day mortality rate stratified by baseline characteristics



*Yes: PT-INR >1.40 and platelet count >30 × 10^9/L; No (1): PT-INR ≤1.40; No (2): platelet count ≤30 × 10^9/L; 4 patients had both INR ≤ 1.4 and platelet count ≤ 30 × 10^9/L; rhsTM: recombinant human soluble thrombomodulin

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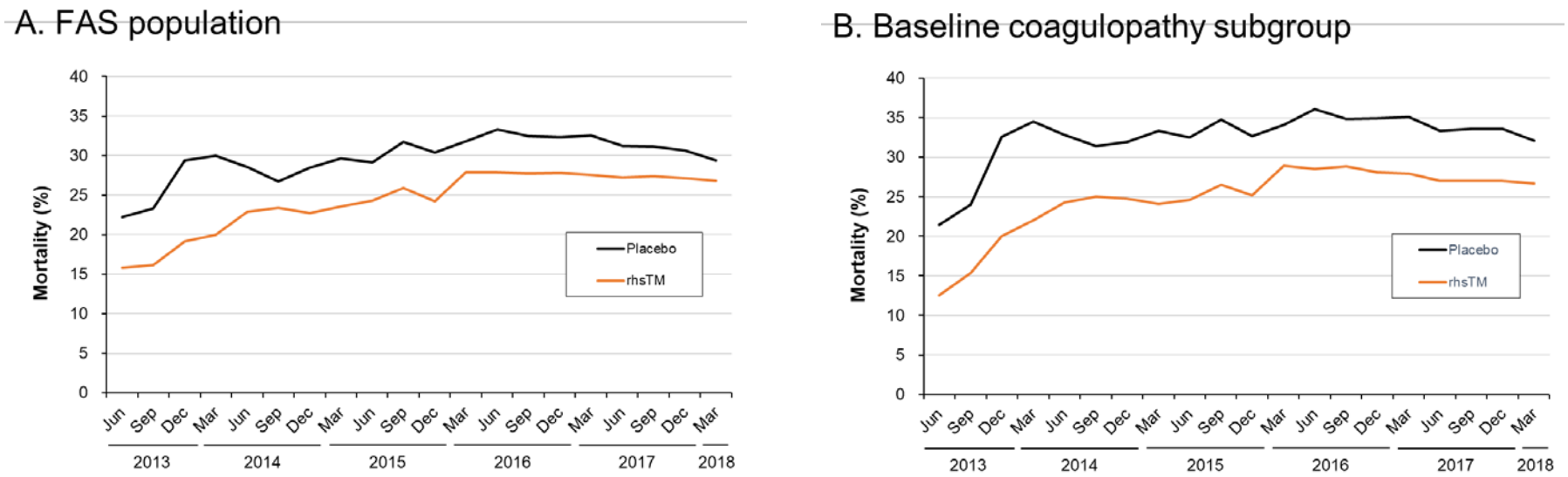
eFigure 2. Transition of 28-day mortality rate through the trial for the 2 treatment arms in the full analysis set (FAS) population (panel A) and in the baseline coagulopathy subgroup (panel B).



The cumulative 28-day mortality rate by 3 month-moving during 5 years (April 2013 to March 2018) of data from 5.5 years (October 2012 to March 2018) for the 2 treatment arms is shown. Subgroup (B) was defined post hoc as patients (n=634) with baseline PT-INR >1.4 and platelet count >30 × 10^9/L. rhsTM: recombinant human soluble thrombomodulin

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eTable 1. Treatment-emergent adverse events (TEAEs), defined as any adverse event following exposure to study treatment, in the safety population

	rhsTM	Placebo	Total
	(N=396)	(N=404)	(N=800)
Safety Assessment	**n (%)**	**n (%)**	**n (%)**
Any TEAE	377 (95.2)	377 (93.3)	754 (94.3)
Any TESAE	206 (52.0)	202 (50.0)	408 (51.0)
Any TEAE resulting in death	108 (27.3)	119 (29.5)	227 (28.4)
Any TEAE leading to permanent discontinuation of study drug	47 (11.9)	41 (10.1)	88 (11.0)
Any study drug-related TEAE	113 (28.5)	108 (26.7)	221 (27.6)
TEAE by maximum severity			
Mild	56 (14.1)	55 (13.6)	111 (13.9)
Moderate	82 (20.7)	86 (21.3)	168 (21.0)
Severe	78 (19.7)	71 (17.6)	149 (18.6)
Potentially life-threatening	161 (40.7)	165 (40.8)	326 (40.8)

TESAE, treatment-emergent serious adverse event; rhsTM: recombinant human soluble thrombomodulin

eTable 2. Treatment-emergent serious major bleeding events (TE-SMBEs)

	rhsTM (n=396)	Placebo (n=404)
Adverse event assessment	**n (%)**	**n (%)**
Total number of TE-SMBE	23	18
Number of subjects with at least one TE-SMBE	23 (5.8)	16 (4.0)
Blood and lymphatic system	0	1
Disseminated intravascular coagulation	0	1
Endocrine	1	0
Adrenal hemorrhage	1	0
Gastrointestinal	5	2
Gastrointestinal hemorrhage	0	1
Gastrointestinal ulcer hemorrhage	1	0
Intra-abdominal hematoma	1	0
Mesenteric hemorrhage	1	0
Rectal hemorrhage	0	1
Retroperitoneal hematoma	1	0
Retroperitoneal hemorrhage	1	0
General and administration site	0	1
Catheter site hemorrhage	0	1
Infections and infestations	0	1
Endocarditis	0	1
Injury, poisoning and procedural complications	8	4
Post procedural hemorrhage	6	2
Procedural hemorrhage	1	0
Wound hemorrhage	1	2
Investigations	0	1
Hemoglobin decreased	0	1
Metabolism and nutrition	0	1
Hypovolemia	0	1
Musculoskeletal and connective tissue	0	1
Compartment syndrome	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	1
Tumor hemorrhage	0	1
Nervous system	2	1
Cerebral hemorrhage	1	1
Hemorrhage intracranial	1	0
Respiratory, thoracic and mediastinal	3	2
Epistaxis	2	0
Hemoptysis	1	2
Vascular	4	2
Arterial hemorrhage	0	1
Extremity necrosis	0	1
Hemorrhage	1	0
Hemorrhagic shock	3	0

A major bleeding event was defined as any intracranial hemorrhage, any life-threatening bleeding, or bleeding event classified as serious by the investigator, with administration of at least 1440 mL [typically 6 units] of packed red blood cells over 2 consecutive days; rhsTM: recombinant human soluble thrombomodulin