POST-NEW ORLEANS 2022
Novità dal Meeting della Società Americana di Ematologia

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Milano
Teatro Dal Verme
2-3-4 Febbraio 2023

LE MALATTIE TROMBOTICHE

Sergio Siragusa
PROMISE - UniPa

DICHIARAZIONE Sergio SIRAGUSA

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

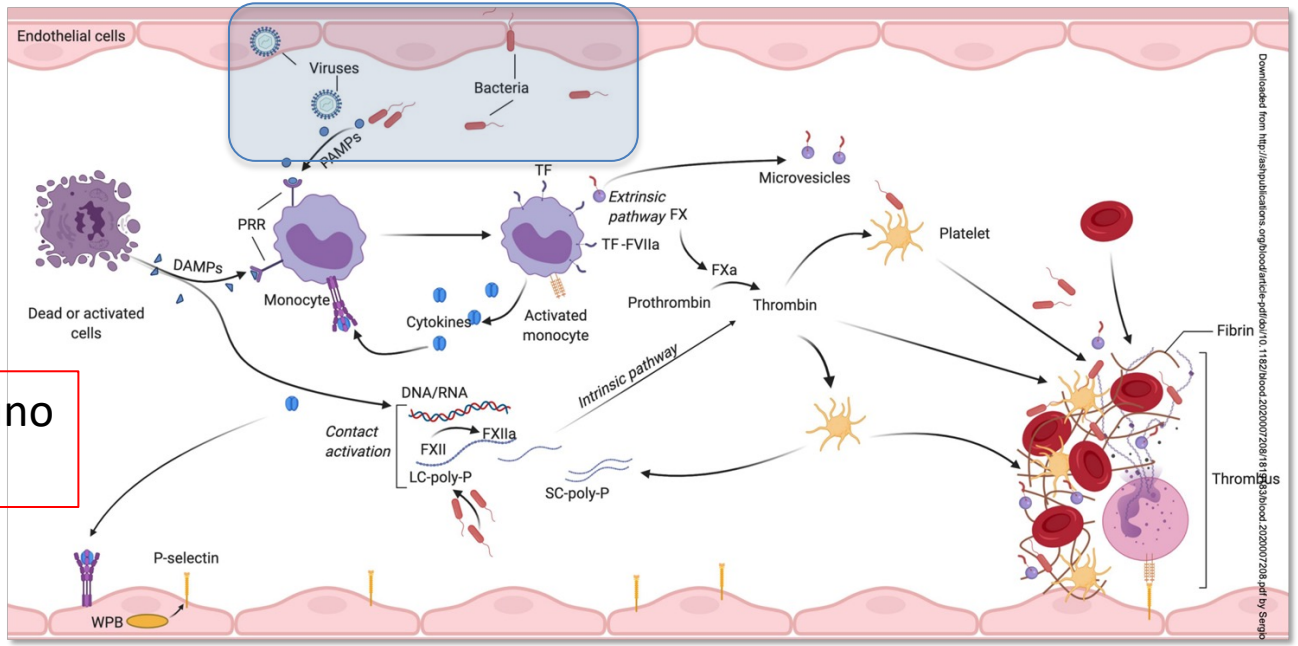
- Posizione di dipendente in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Consulenza ad aziende con interessi commerciali in campo sanitario **(NOVONORDISK, CSL, SOBI, TAKEDA)**
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario **(ROCHE, PFEIZER)**
- Partecipazione ad Advisory Board **(AMGEN, BAYER, NOVARTIS, JANSEEN, NOVONORDISK, CSL)**
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario **(NIENTE DA DICHIARARE)**
- Altro

Where are we going with thrombosis?

(proof of concept & clinically relevant)

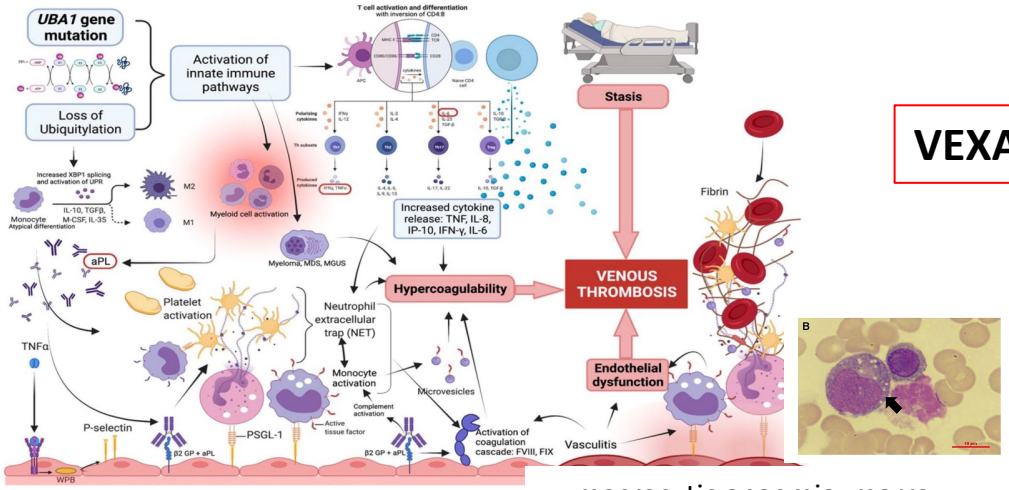
How cancer/activated cells may affect coagulation

Cancer/chemo/immuno therapy



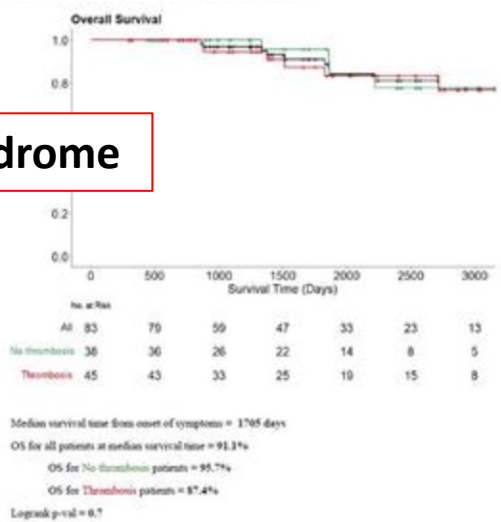
What is new at ASH-2022 about thrombosis in haematological malignancies

Proof of concepts: VTE in pre-cancers conditions and/or high bleeding risk



macrocytic anaemia, marrow dysplasia, vacuolisation in myeloid cells and thrombosis

VEXAS Syndrome



– *Blood (2022) 140 (Supplement 1): 2788–2789*

D-dimer and risk of VTE in acute adult leukemia

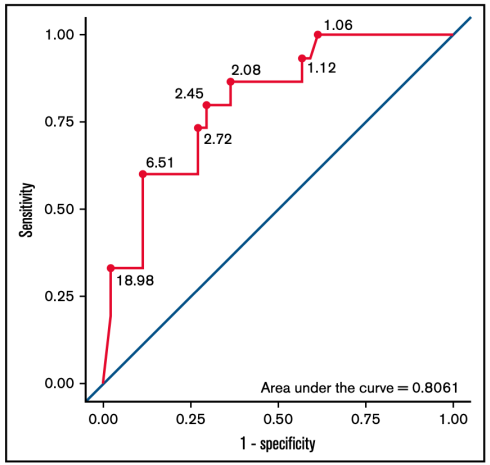


Figure 2. **ROC curve of D-dimer for predicting arterial or venous thrombosis.**

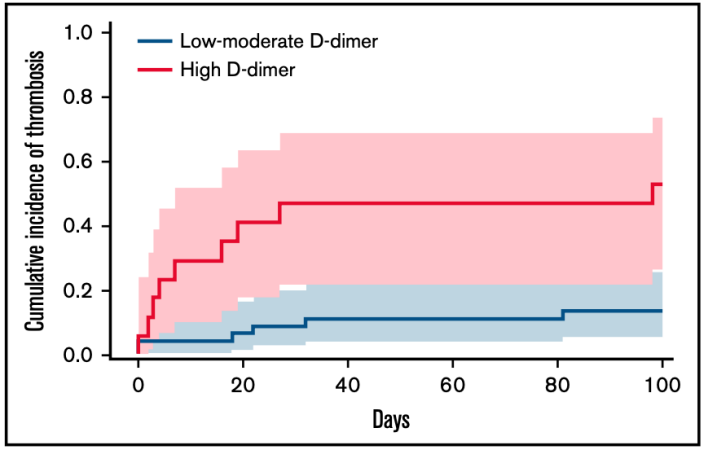
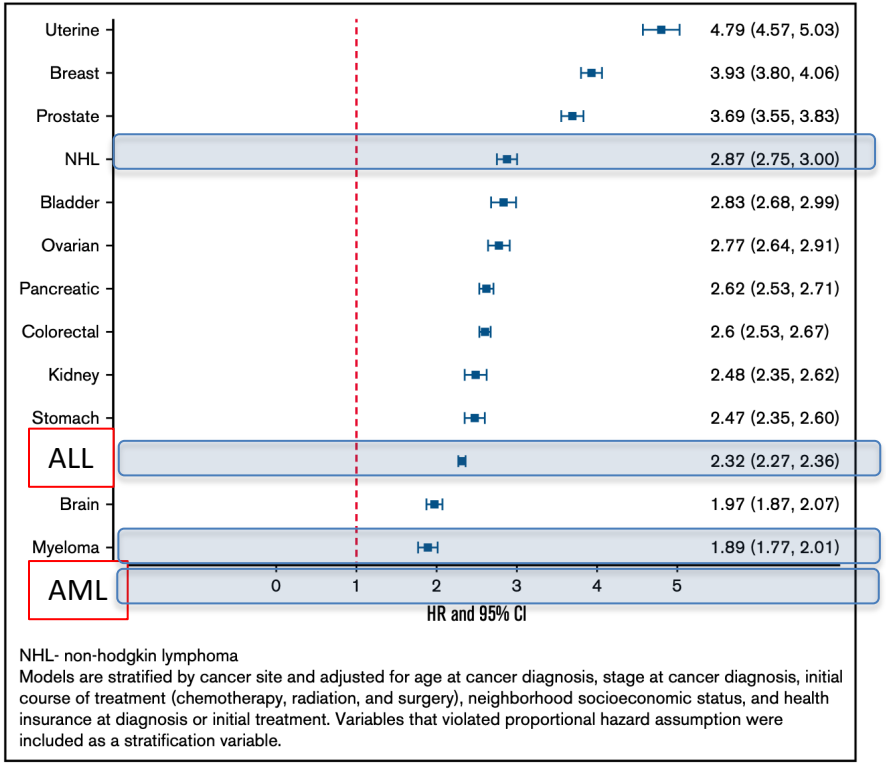


Figure 1. Cumulative incidence at 100 days of venous or arterial thrombosis stratified for D-dimer levels. Cumulative incidence and 95% CIs (indicated by shaded areas) of arterial or venous thrombosis throughout 100-day follow-up, stratified for index D-dimer levels. The dashed red line represents high D-dimer levels (≥4 μg/mL), and the solid blue line indicates low to moderate D-dimer levels (<4 μg/mL).

Anderson DR et al. BloodAdv 2022;6:5146-5151

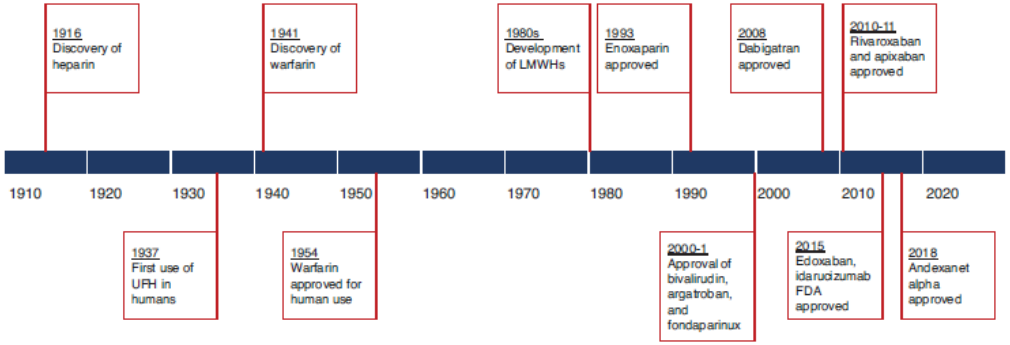
Proven: Incidence of thrombosis in haematological neoplasms



NHL- non-hodgkin lymphoma
Models are stratified by cancer site and adjusted for age at cancer diagnosis, stage at cancer diagnosis, initial course of treatment (chemotherapy, radiation, and surgery), neighborhood socioeconomic status, and health insurance at diagnosis or initial treatment. Variables that violated proportional hazard assumption were included as a stratification variable.

Anjlee Mahajan et al. BloodAdv 2022;6:307-320

The future: Development of new anticoagulants (in cancer)



FXI-FXII Inhibitors

	Mechanism of action	Route of administration	Onset of action	Half-life	Administration frequency	Renal excretion	Metabolism by CYP	Potential for food and drug interactions
DNA aptamers: 11.16, 12.7, and FELIAP	Bind over large surface areas on a target protein and block specific macromolecular interactions	IV or SC	Rapid (minutes to hours)	Short (minutes to hours)	Daily	No	No	No
ASOs: IONIS FXI-Rx (ISIS 416858) and fesomersen	Inhibit the biosynthesis of FXI	SC	Slow (weeks)	Long (weeks)	Once weekly to once monthly	No	No	No
Antibodies								
Abelacimab (MAA868)	Binds to the catalytic domain of FXI and locks it in the inactive zymogen confor-mation, preventing its activation by FXII/thrombin	IV or SC	Rapid (hours)	Long (weeks)	Once monthly	No	No	No
Osocimab (BAY 1213790)	Binds next to the active site of FXIa and inhibits the activation of factor IX	IV or SC	Rapid (hours)	Long (30–44 days)	Once monthly	No	No	No
Xisomab (AB023)	Inhibits FXIIa-mediated activation of FXI but not FXI activation by thrombin	IV	Rapid (hours)	Days to weeks, half-life increases with high doses	Once monthly	No	No	No
Garadacimab (CSL312)	Binds to the catalytic domain of FXIIa and inhibits its protease activity	IV or SC	Rapid (hours)	Long (weeks)	Once monthly	No	No	No
Small molecules								
Milvexian (BMS-986177/ JNJ-70033093)	Active site-directed inhibitor of FXI	Oral	Rapid (minutes to hours) Saturable absorption with doses ≥300 mg	Short (terminal half-life 8.3–13.8 hours)	Once or twice daily	Yes, <20%	Yes	Yes
Asundexian (BAY 2433334)	Active site-directed inhibitor of FXI	Oral	Rapid (minutes to hours)	Short (terminal half-life 15.8–17.8 hours)	Once daily	Yes, <15%	Yes	Yes

O. Cohen et al. Hematology 2022;495-505

Mitigating the risk of venous thromboembolism in patients with multiple myeloma receiving immunomodulatory-based therapy

Fahrettin Covut[1] and Kristen M. Sanfilippo[2,3]

[1]Division of Hematology and Oncology, Washington University School of Medicine, St Louis, MO; [2]Division of Hematology, Washington University School of Medicine, St Louis, MO; [3]Division of Hematology/Oncology St Louis Veterans Administration Medical Center, St Louis, MO

Graded recommendations

1. Thromboprophylaxis should be strongly considered in patients with MM assessed as high risk for VTE, especially newly diagnosed patients receiving IMiD-based combination therapies. (Strong recommendation, moderate certainty in evidence about effects)
2. The SAVED, IMPEDE VTE, and PRISM scores are validated clinical tools that can quantify risk of VTE in newly diagnosed patients with MM. (Conditional recommendation, moderate certainty of evidence about effects)
3. If available, patients should be enrolled in clinical trials evaluating risk-assigned thromboprophylaxis strategies in patients with MM.

Thrombosis questions from the inpatient wards

George Goshua,[1] Pavan K. Bendapudi,[2] and Alfred Ian Lee[1]

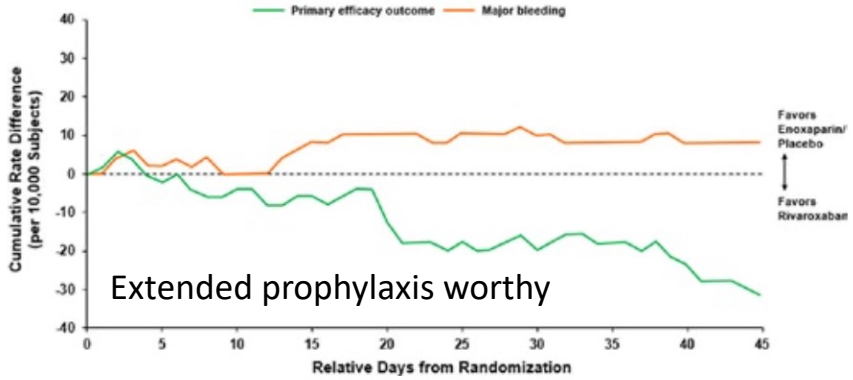
[1]Section of Hematology, Yale School of Medicine, New Haven, CT, and [2]Division of Hematology, Blood Transfusion Service, Massachusetts General Hospital; Division of Hemostasis and Thrombosis, Beth Israel Deaconess Medical Center; and Harvard Medical School, Boston, MA

	With platelet transfusions
Platelet count ≥50 000/μL	Full-dose anticoagulation • LMWH (eg, enoxaparin 1 mg/kg twice daily or 1.5 mg/kg once daily) • DOAC (eg, apixaban 5 mg twice daily or rivaroxaban 20 mg once daily)
Platelet count <50 000/μL	Full-dose anticoagulation • LMWH • DOAC Transfuse platelets to raise platelet count ≥50 000/μL
	No platelet transfusions
Platelet count ≥50 000/μL	Full-dose anticoagulation • LMWH • DOAC
Platelet count 25 000-50 000/μL	Half-dose anticoagulation • LMWH (eg, enoxaparin 0.5 mg/kg twice daily or 0.75 mg/kg once daily) • DOAC (eg, apixaban 2.5 mg twice daily or rivaroxaban 10 mg once daily)
Platelet count <25 000/μL	No anticoagulation

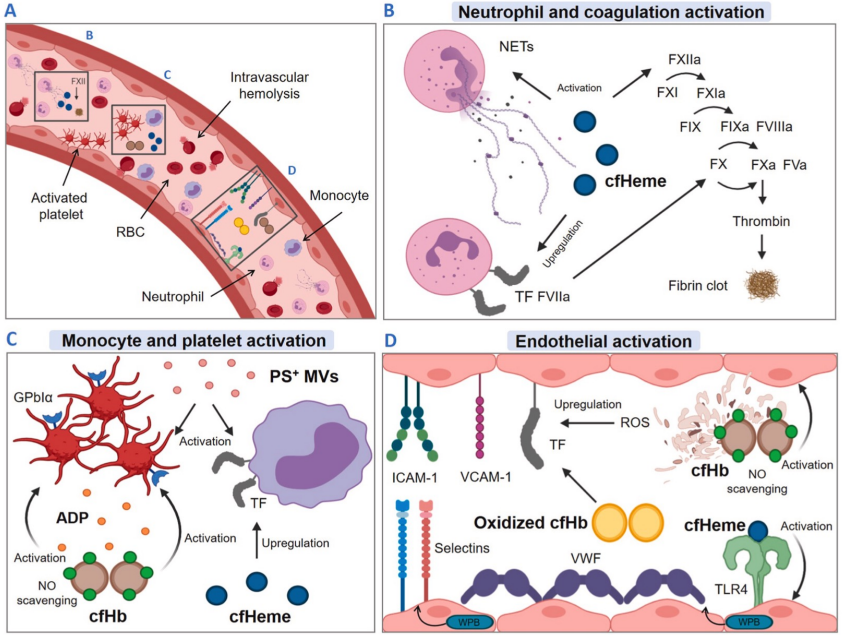
To prophylax or not, and how much and how long? Controversies in VTE prevention for medical inpatients, including COVID-19 inpatients

Alex C. Spyropoulos

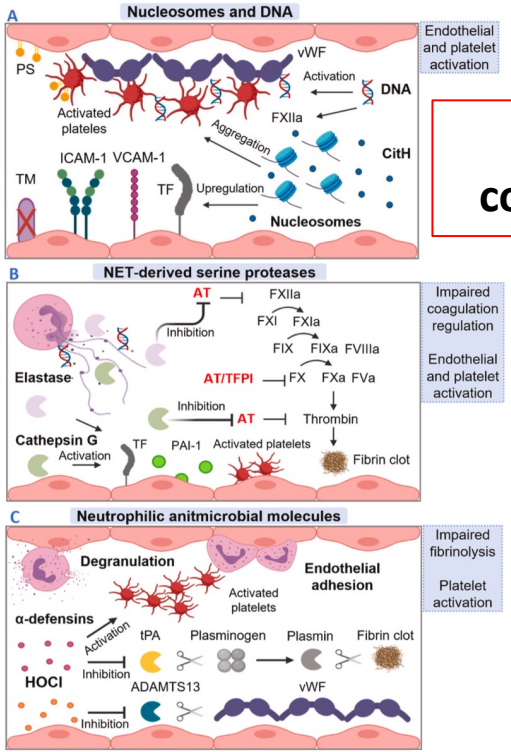
Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY; Institute of Health Systems Science, Feinstein Institutes for Medical Research, Manhasset, NY; and Anticoagulation and Clinical Thrombosis Services at Northwell Health, Lenox Hill Hospital, New York, NY



What is new at ASH-2022 about thrombosis in non-cancer haematological patients



Haemolysis and coagulation activation



Neutrophils and coagulation activation

Blood Reviews 50 (2021) 100834

THROMBOSIS AND HEMOSTASIS

Comment on Fassel et al, page 2221

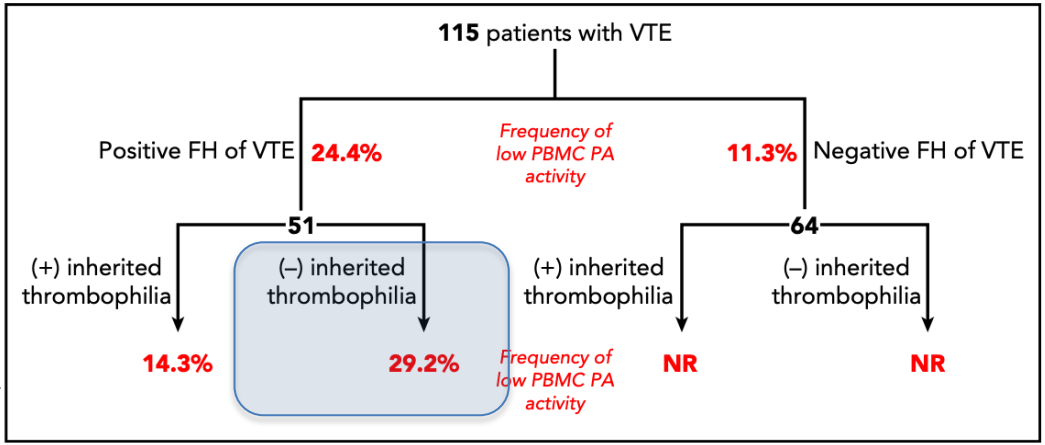
A novel "vascular" thrombophilia

Ravi K. Alluri and Keith R. McCrae | Cleveland Clinic

Annexin A2 is expressed in many cell types, including endothelial cells, monocytes, macrophages, trophoblasts, and tumor cells. annexin A2 increases the catalytic efficiency of t-PA–mediated plasminogen activation by 60-fold; in the context of endothelial cells, this leads to increased vascular wall fibrinolytic activity.

Annexin-2 deficiency -> high risk for thrombosis (obstetric complications?)

Annexin-2 increase -> DIC, hyperfibronolysis (APL), cancer burden



Deficient plasminogen activation in peripheral blood mononuclear cells (PBMCs) by measuring Annexin-2 (reduction)

Fassel H et al. Blood. 2021;137(16):2221-2230

EVIDENCE-BASED MINIREVIEW

Should caplacizumab be used routinely in unselected patients with immune thrombotic thrombocytopenic purpura?

George Goshua[1,2] and Pavan K. Bendapudi[3–5]

[1]Section of Hematology, Yale University School of Medicine, New Haven, CT; [2]Department of Health Policy and Management, Harvard T. H. Chan School of Public Health, Boston, MA; [3]Division of Hematology and Blood Transfusion Service, Massachusetts General Hospital, Boston, MA; [4]Division of Hemostasis and Thrombosis, Beth Israel Deaconess Medical Center, Boston, MA; and [5]Harvard Medical School, Boston, MA

Parameter	Caplacizumab observational experience A[14]	Caplacizu observati experien				
Number of subjects	60	90				
Mortality per episode (%)	1.7	1.1				
Number of TPE sessions	9 (2–41)[a]	5 (4–7)	7 (5–14)	8.5 (6–12.5)	10.2[b]	15 (8–23)
Hospital LOS (days)	18 (5–79)[a]	13 (9–19)	12 (8–24)	12 (9–15)	12 (4–53)[c]	12 (8–20)

We believe that the available **data do not support the routine use of caplacizumab** in unselected patients with iTTP (grade IB). Major outcomes of clinical concern such as mortality and cardiovascular and neurological events are not significantly reduced by caplacizumab.

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