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Prevention and treatment of VTE in patients with multiple myeloma

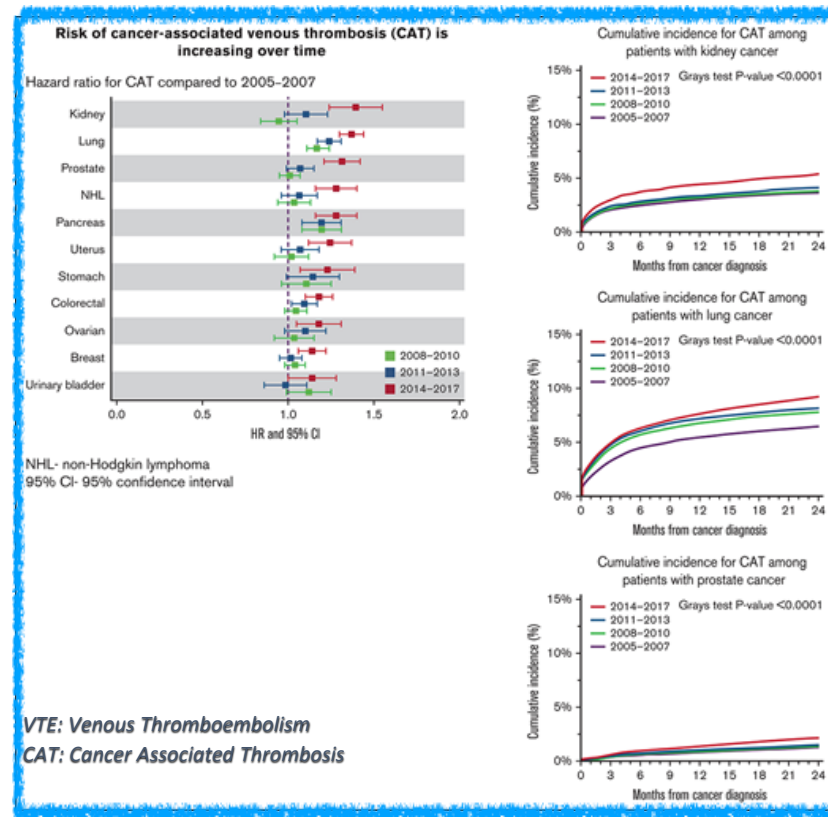
Grigoris GEROTZIAFAS

The burden of cancer associated thrombosis (CAT)

CAT is the second cause of death after cancer, itself

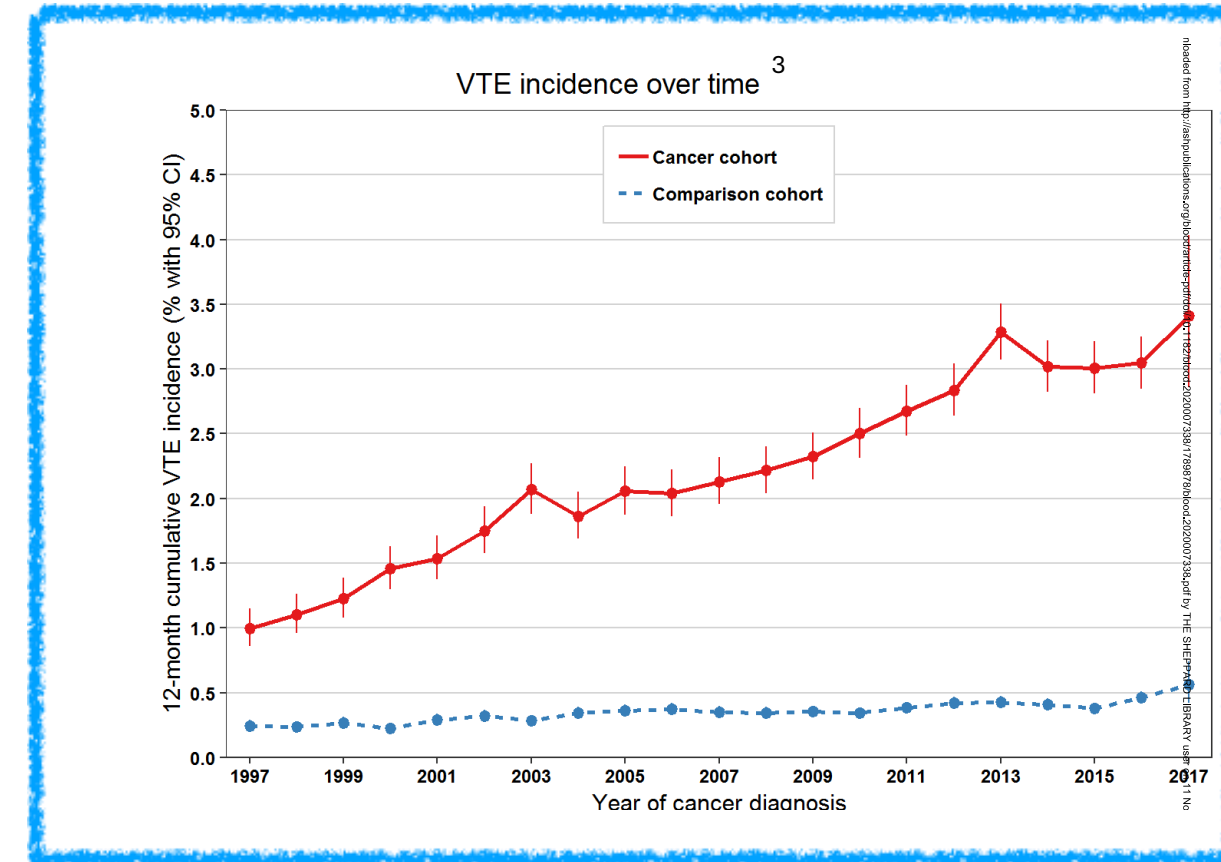
California Registry ¹

- ▲ 942,109 first primary cancer patients (2005-2017)
- ▲ 6.6% had a diagnosis of CAT
- ▲ 89 months follow up
- ▲ Incidence of CAT increased with stage
- ▲ Patients diagnosed with cancer more recently were at higher risk of CAT



International Agency for Research on Cancer (IARC)

Global cancer burden has risen to 19.3 million new cases and 10 million deaths in 2020 ²



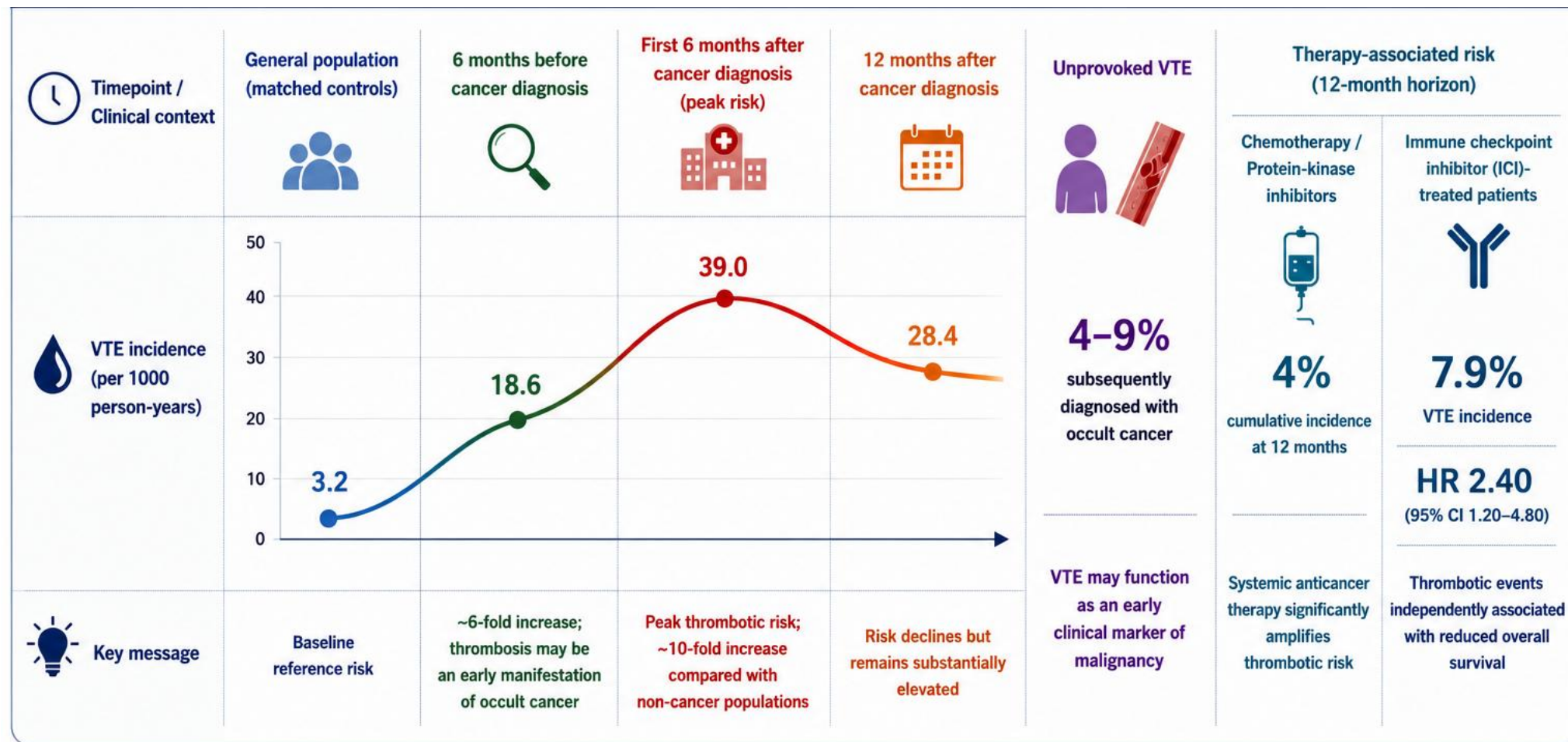
1. Mahajan A, Brunson A, Adesina O, Keegan THM, Wun T. The incidence of cancer-associated thrombosis is increasing over time. *Blood Adv* 2022;6(1):307-320.

2. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021;71(3):209-249

3. Mulder FI, Horvath-Puho E, van Es N, et al. Venous thromboembolism in cancer patients: a population-based cohort study. *Blood* 2021;137(14):1959-1969.

4. Khorana AA, et al. *J Thromb Haemost*. 2007;5:632-4.

Temporal evolution of cancer-associated thrombosis risk across the cancer care continuum



Cancer-associated thrombosis is a dynamic, longitudinal risk process that begins **before cancer diagnosis**, peaks during **early treatment**, and remains elevated **throughout the cancer care pathway**.

Economic burden of cancer-associated thrombosis (EU evidence)

Country	Population / setting	Time horizon	Key economic burden estimate(s)
 EU-28	All VTE (not cancer-specific; EU-wide context)	Annual	<p>€1.5–€13.2B/yr total VTE costs</p> <ul style="list-style-type: none"> • Hospital-associated: €1.0–€9.7B • Preventable: €0.5–€7.3B

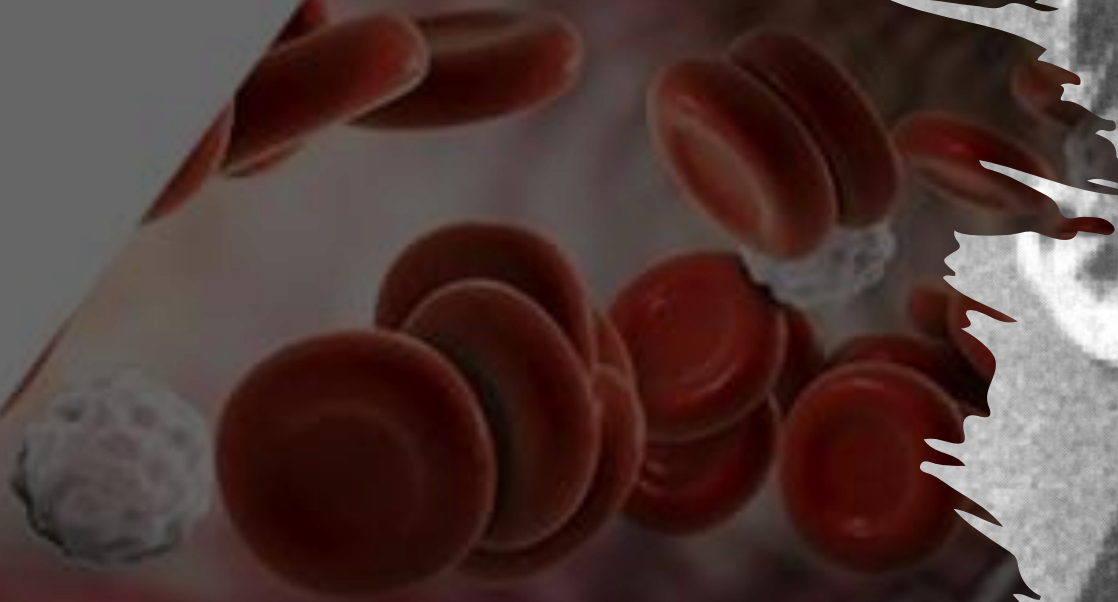
- ▶ €2- €3 in every €5 spent on VTE in the EU is spent on CAT
- ▶ 15%-20% of the patients with VTE are Oncological

 France	Hospitalized breast or prostate cancer patients with thromboembolic events	Per hospitalization	<p>With ≥1 recurrence:</p> <ul style="list-style-type: none"> • €5,545 (breast) • €5,692 (prostate)
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Cost intensity (country rows)

lower    higher

Alteration of blood constituents
(hypercoagulable state)



Blood stasis
(flow alterations)

Vascular lesion

CAT starts from the first guilty

🔥 Cancer cells induce thrombin generation and fibrin formation in their microenvironment

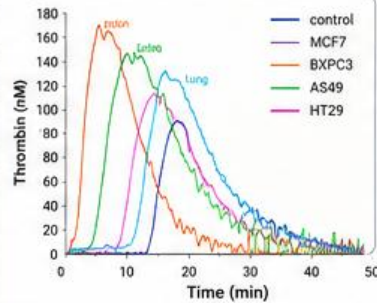
- 👹 survival
- 👹 proliferation
- 👹 protection
- 👹 migration



CANCER ASSOCIATED THROMBOSIS: THE FIRST GUILTY

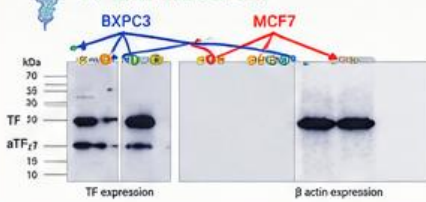
Multiple, converging mechanisms by which cancer cells promote thrombosis

1 TF-DEPENDENT CANCER CELL INDUCED HYPERCOAGUABILITY¹



Cancer cells express Tissue Factor (TF) that triggers thrombin generation and activates the coagulation cascade.

TF EXPRESSION



Unman. si CTRL (SCR_2b)
Unman. si TF (si_TF)
Reduced with siRNA knockdown confirms cancer cell-derived TF expression.

2 CANCER CELL INDUCED FIBRIN CLOT SHIELDS⁵



Cancer cells drive fibrin formation, creating a physical barrier.

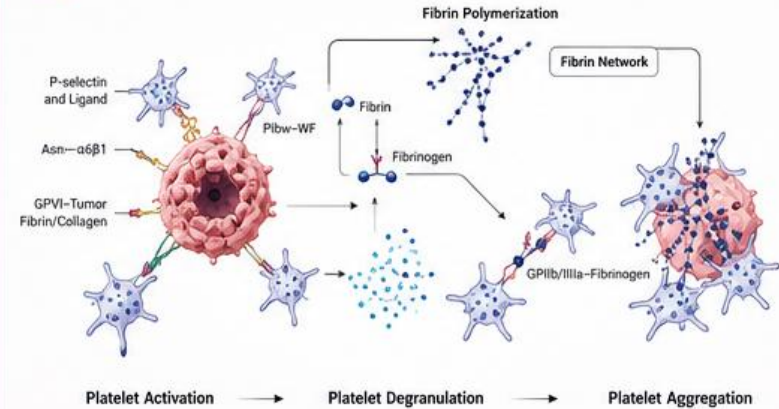


Fibrin shields tumor cells from immune surveillance and therapeutics.

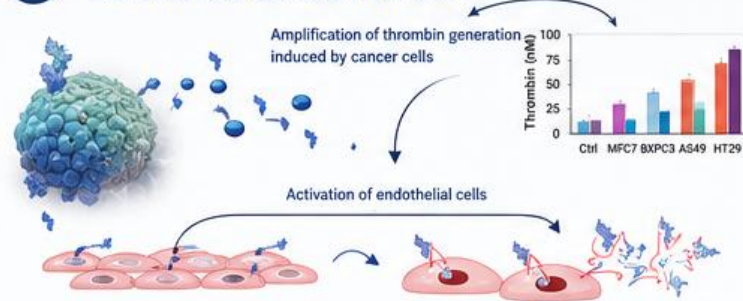


Facilitates survival, invasion, and metastasis.

3 CANCER CELL INDUCED PLATELET ACTIVATION

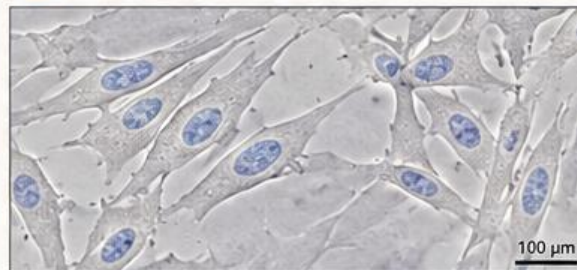


4 CANCER CELL INDUCED ENDOTHELIAL CELL ACTIVATION^{2,3}



Tissue Factor (TF) bearing Cancer Cell-derived EVs (TF-CaCe-EV) Intact Endothelial Cells
Activated TF-bearing Endothelial Cells Daughter generation TF-bearing Endothelial Cells

5 ACTIVATED ENDOTHELIAL CELLS BY CACE-dEV⁶



Upregulation of adhesion molecules (VCAM-1, ICAM-1, E-selectin)

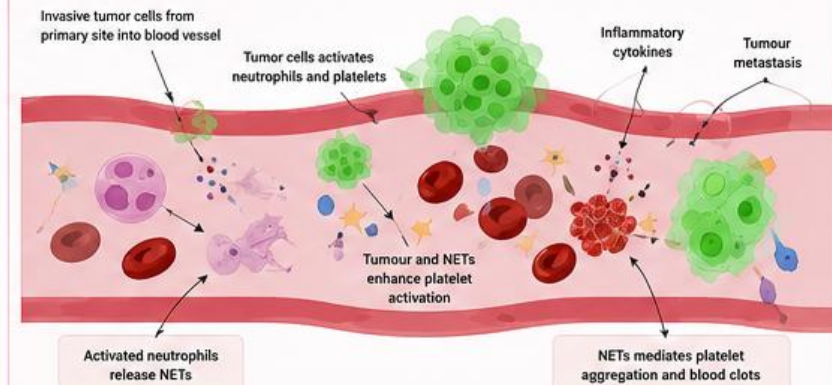


Procoagulant shift:
↑ TF, vWF, PAI-1
↓ Thrombomodulin



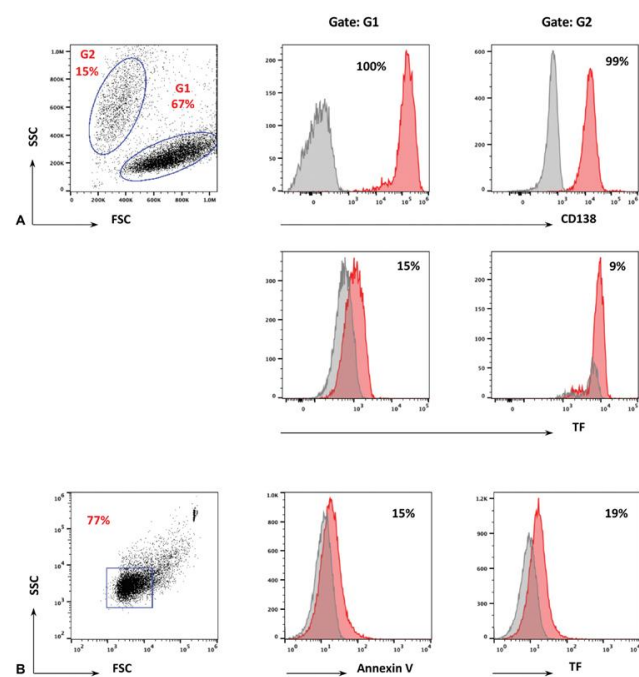
Promotes leukocyte adhesion and thrombus formation

6 DIRECT ENDOTHELIAL CELL ACTIVATION/ INFLAMMATION BY THE TUMOR

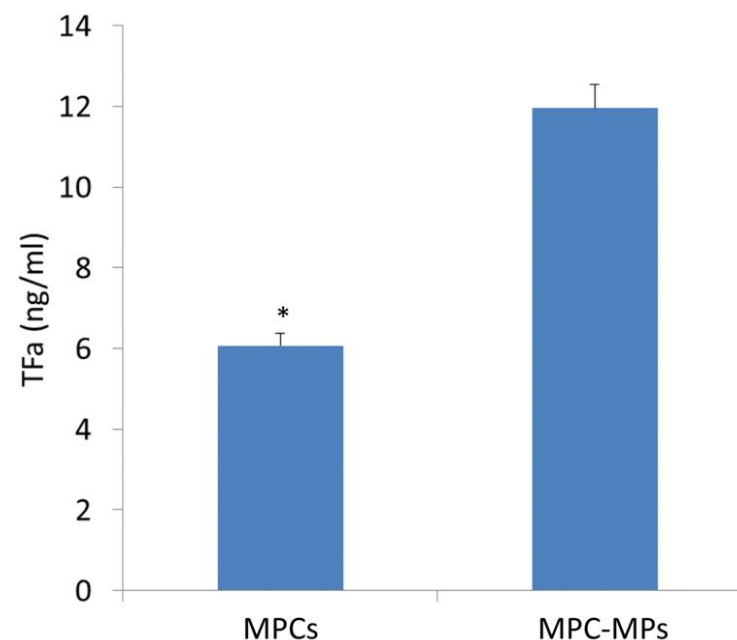


Procoagulant properties of myeloma plasma cells

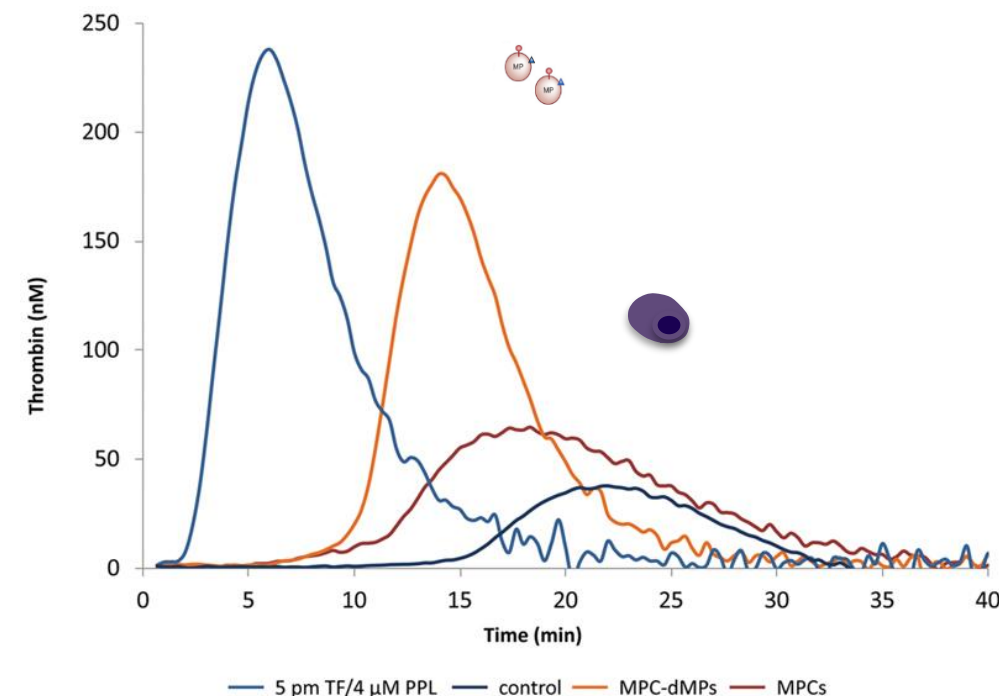
TF expression in MPC



Dissemination of TF activity



















Thrombin generation induced by MPC and MPC-dMPs



TF: Tissue Factor
PPL: procoagulant phospholipids
MPC: Myeloma Plasma Cells

Somatic mutations in cancer cells and CAT risk

Mutation	Cancer type(s)	Risk estimate (Hazard ratio)
 KRAS	Various, colorectal	1.3–2.5
 Ki-67 high	Breast	2.2 -3.5
 EGFR	NSCLC, glioblastoma	0.97 – 2.19
 PTEN	Glioblastoma	1.1–1.8 (NS)
 IDH1	Glioma	0.05–0.26
 ALK	NSCLC	1.97
 ROS1	NSCLC	1.29 (NS)
 CDKN2A/B	Various	1.4–1.8
 STK11	Various	1.6–2.1
 MET	Various	1.83
 KEAP1	Various	1.8–2.5
 CTNNB1	Various	1.7–2.7
 TP53	Various	1.85
 ERBB2	Various	1.72
 COAGULOME (TF, PAI-2, PAI-1, uPA, uPAR, tPA)	Various	1.3 - 2.5
 CHIP (Clonal hematopoiesis of indeterminate potential)	-	1.5 – 4.2

 High risk;  Intermediate risk;  Protective

Marchetti et al. *Cancers (Basel)*. 2025;20;17:2712. Lanting et al. *Curr Opin Hematol*. 2025 May 1;32(3):138-145.
Zon et al. *Blood*. 2024;144:2149-2154.; Saidak et al. *Cancer Immunol Immunother*. 2021;70:923-933.

ROADMAP-CAT: Hypercoagulability in newly diagnosed treatment-naïve patients with **Multiple Myeloma** or Lung Adenocarcinoma (LAC)

Mechanism	Alterations of hypercoagulability biomarkers at diagnosis (vs Healthy Subjects)	Implication
Cellular activation	<ul style="list-style-type: none"> ↑ Tissue factor activity (MM & LAC) ↑ Heparanase ↓ Thrombomodulin ↑ TFPI 	Endothelial cell activation drives procoagulant shift
Thrombin generation	<ul style="list-style-type: none"> Prolonged lag-time ↓ Thrombin peak (esp. LAC) ↓ MRI (MM) ↓ ETP (MM) 	Dysregulated and less efficient thrombin burst reflecting TFPI and TM release by activated endothelial cells
Procoagulant phospholipids & platelets	<ul style="list-style-type: none"> Shortened PPL clotting time ↑ P-selectin 	Platelet activation and microparticle-driven coagulation
Coagulation factors	<ul style="list-style-type: none"> ↑ FVIIa preserved FV & AT 	TF pathway activation with preserved natural inhibitors
Fibrin turnover	<ul style="list-style-type: none"> ↑ FM (MM & LAC) ↑ D-dimers 	<ul style="list-style-type: none"> Ongoing fibrin formation Fibrin degradation

AT: antithrombin; **ETP:** endogenous thrombin potential; **FM:** fibrin monomers; **FV:** factor V; **FVIIa:** activated factor VII; **LAC:** lung adenocarcinoma; **MM:** Multiple myeloma; **MRI:** mean rate index of thrombin generation propagation phase; **PPL:** procoagulant phospholipids; **TFa:** tissue factor activity; **TFPI:** tissue factor pathway inhibitor

Syrigos et al Oncologist. 2018;23:1372-1381.
Fotiou et al. Blood Cancer Journal. 2018;8:102

ROADMAP-CAT: Hypercoagulability in newly diagnosed treatment-naïve patients with **Multiple Myeloma** or Lung Adenocarcinoma

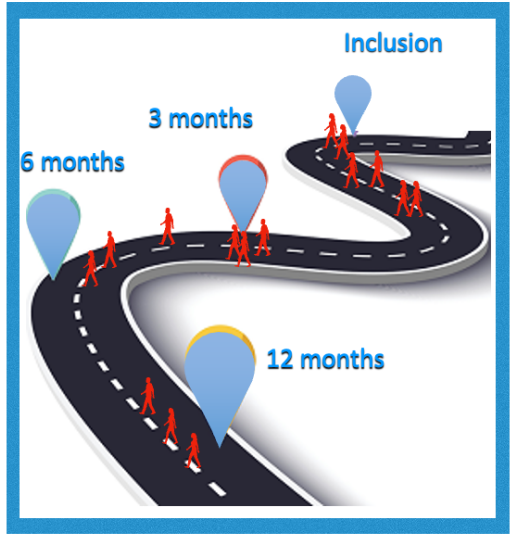


ROADMAP-MM-CAT

PROspective Risk Assessment and bioMARKers of hypercoagulability for the identification of patients with Multiple Myeloma at risk for Cancer-Associated Thrombosis


144 NDMM


12 months VTE incidence: 10.4% (n=15)



Type of prophylaxis	n of events
No	6
ASA	6
LMWH	3

The rate of VTE did not differ significantly between patients who received thromboprophylaxis and those who did not.

 VTE

 no VTE

ROADMAP-LA-CAT

PROspective Risk Assessment and bioMARKers of hypercoagulability for the identification of patients with Lung Adenocarcinoma at risk for Cancer-Associated Thrombosis

150 NDMM

12 months VTE incidence: 8%



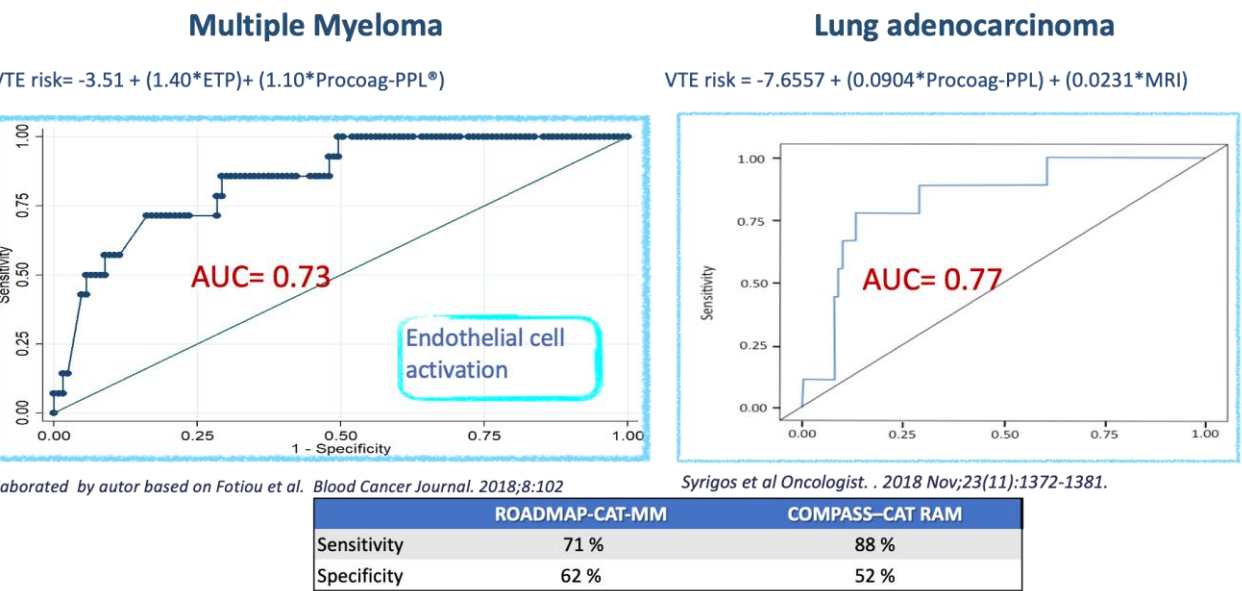
NDMM: newly diagnosed multiple myeloma
VTE: venous thromboembolism

MM: Multiple Myeloma
LA: Lung Adenocarcinoma
CAT: Cancer Associated Thrombosis
VTE: Venous ThromboEmbolism

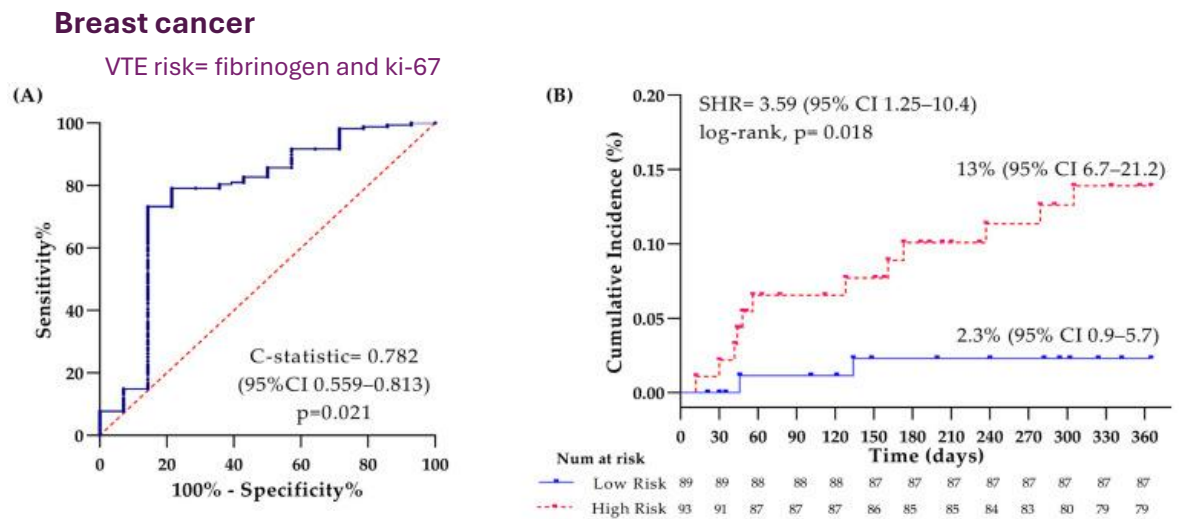
Syrigos et al Oncologist. 2018;23:1372-1381.
Fotiou et al. Blood Cancer Journal. 2018;8:102

Hypercoagulability biomarkers for personalized CAT- RAM

ROADMAP-CAT



HYPERCAN

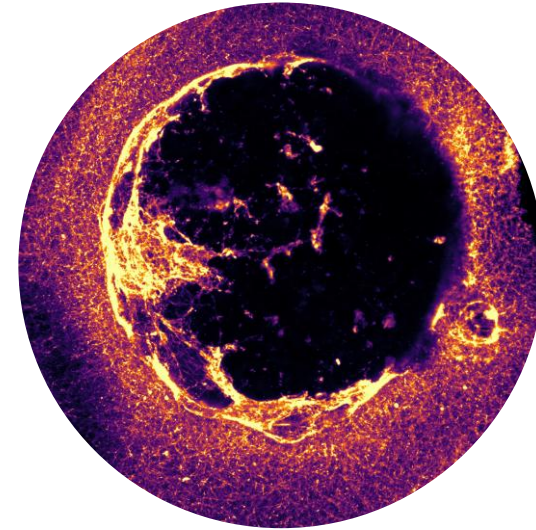


CAT: Cancer Associated Thrombosis
VTE: Venous ThromboEmbolism

Marchetti et al. Cancers (Basel). 2025 Aug 20;17(16):2712.
Syrgios et al Oncologist. 2018;23:1372-1381.
Fotiou et al. Blood Cancer Journal. 2018;8:102

Cancer-Associated Thrombosis

- a) Treatment complication
- b) Accident
- c) Hazard
- d) **Hallmark of cancer**



- Hypercoagulability is linked with the procoagulant fingerprint of cancer cells
- Biomarkers of hypercoagulability are predictors of CAT
- **4TS:** Tumor - Type of cancer – Time since diagnosis – Stage – Treatment type
- + intrinsic risk factors
- ***CAT is associated with high risk of recurrence and bleeding***
- ***CAT is associated with reduced survival***
- ***CAT is preventable ... if we apply guidelines***

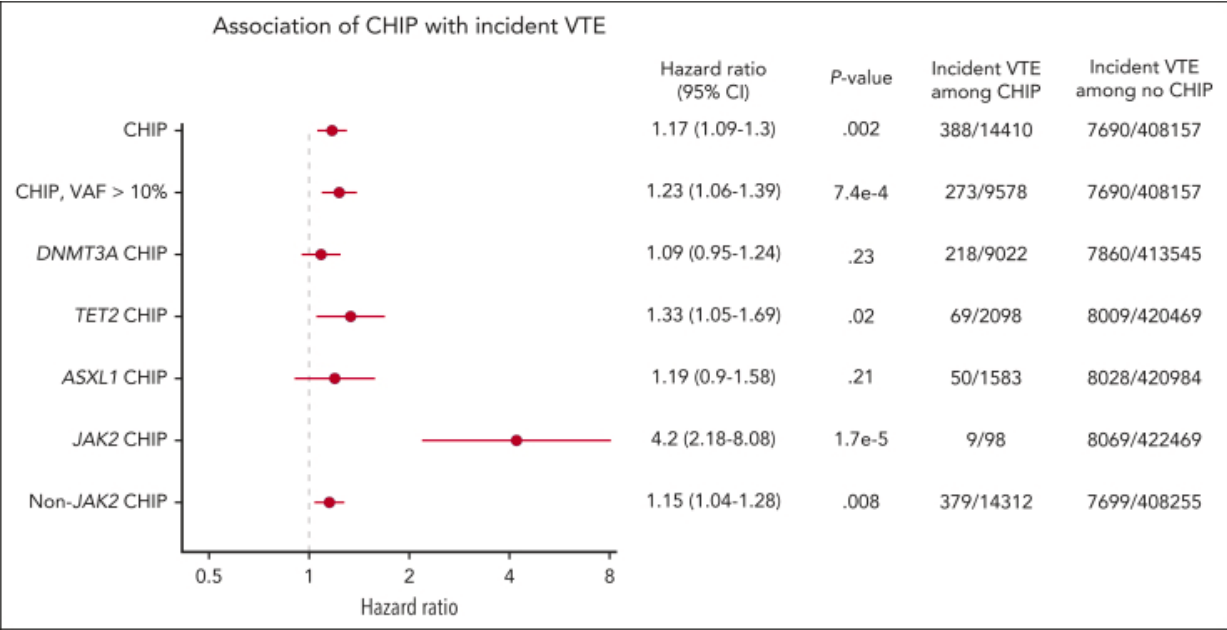


Mutations Polymorphisms CHIPS and CAT

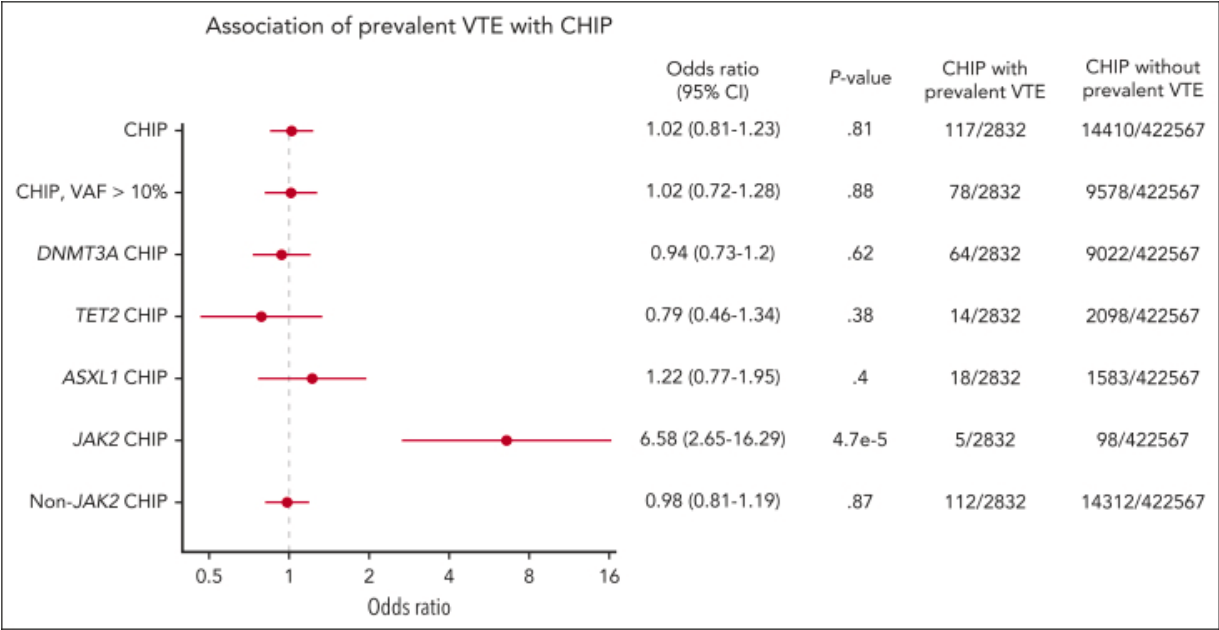



Clonal hematopoiesis of indetermined potential and risk of VTE

Incidence of VTE in individuals with and without CHIP



Prevalence of CHIP in individuals with and without VTE





Targeted Anticancer Treatment and CAT



Myeloma Regimens — VTE & Arterial Thrombosis Rates

Regimen	Drug class	VTE %	Risk	Art. %	Risk	Key comment / source
IMiD-based regimens						
Thalidomide mono	IMiD	3–6%	Mod	~1%	Mod	Without prophylaxis; lower risk than combination
Thal + Dex (TD)	IMiD	15–26%	High	2–4%	Mod	Highest VTE risk of all IMiD regimens; dex amplifier
MPT (melphalan + pred + thal)	IMiD	12–20%	High	2–3%	Mod	IFM 99-06; thromboprophylaxis mandatory
Len + Dex (Rd)	IMiD	8–15%	High	1–3%	Mod	FIRST trial; risk highest in first 6 months
MPR (melphal + pred + len)	IMiD	5–10%	Mod	1–2%	Low	MM-015; aspirin prophylaxis used
Pom + Dex (PomDex)	IMiD	3–8%	Mod	1–2%	Low	MM-003; lower VTE than lenalidomide combos
Proteasome inhibitor (PI)–based regimens						
Bortezomib mono / VD	PI	2–5%	Low	2–5%	Mod	↑ arterial events vs IMiD; vasc. endothelial toxicity
VMP (bort + melphal + pred)	PI	2–4%	Low	3–5%	Mod	VISTA; arterial events signal; neuropathy-related immobility
VRd (bort + len + dex)	PI + IMiD	6–12%	Mod	2–4%	Mod	SWOG S0777; additive thrombotic risk; LMWH preferred
Carfilzomib mono / Kd	PI	3–6%	Low	5–15%	High	ENDEAVOR, ASPIRE; cardiotoxicity: HTN, HF, ATE signal
KRd (carfilz + len + dex)	PI + IMiD	8–14%	High	6–12%	High	ASPIRE; highest combined thromboembolic burden
Ixazomib + len + dex (IRd)	PI + IMiD	5–10%	Mod	2–4%	Mod	TOURMALINE-MM1; oral PI; similar profile to VRd

Low (<5%)

Moderate (5–10%)

High (10–20%)

Art. = arterial thrombosis · Without prophylaxis unless stated · Rates from landmark RCTs and pooled analyses

Myeloma Regimens — VTE & Arterial Thrombosis Rates

Regimen	Drug class	VTE %	Risk	Art. %	Risk	Key comment / source
Monoclonal antibody (mAb)–based regimens						
Daratumumab + Rd (DRd)	mAb + IMiD	5–8%	Mod	1–3%	Low	POLLUX; mAb does not independently ↑ VTE
Daratumumab + VMP (DVMP)	mAb + PI	2–4%	Low	2–4%	Mod	ALCYONE; PI-driven arterial risk preserved
Daratumumab + VRd (DVRd)	mAb + PI + IMiD	7–12%	Mod	3–6%	Mod	PERSEUS; triplet backbone drives thromboembolic risk
Isatuximab + KRd (Isa-KRd)	mAb + PI + IMiD	8–14%	High	5–10%	High	IKEMA; carfilzomib drives arterial risk
Elotuzumab + Rd (ERd)	mAb + IMiD	4–7%	Low	1–2%	Low	ELOQUENT-2; favourable thrombotic profile
Novel / cellular agents						
Belantamab mafodotin	ADC	1–3%	Low	1–2%	Low	DREAMM-2; limited data; ocular toxicity predominates
Teclistamab / Talquetamab	BiTE / TCE	2–5%	Low	1–3%	Low	MajesTEC-1/MonumenTAL-1; CRS may trigger coagulopathy
BCMA CAR-T (ide-cel / cilta-cel)	CAR-T	3–7%	Low	1–4%	Low	KarMMa / CARTITUDE-1; CRS-associated coagulation activation

Low (<5%)

Moderate (5–10%)

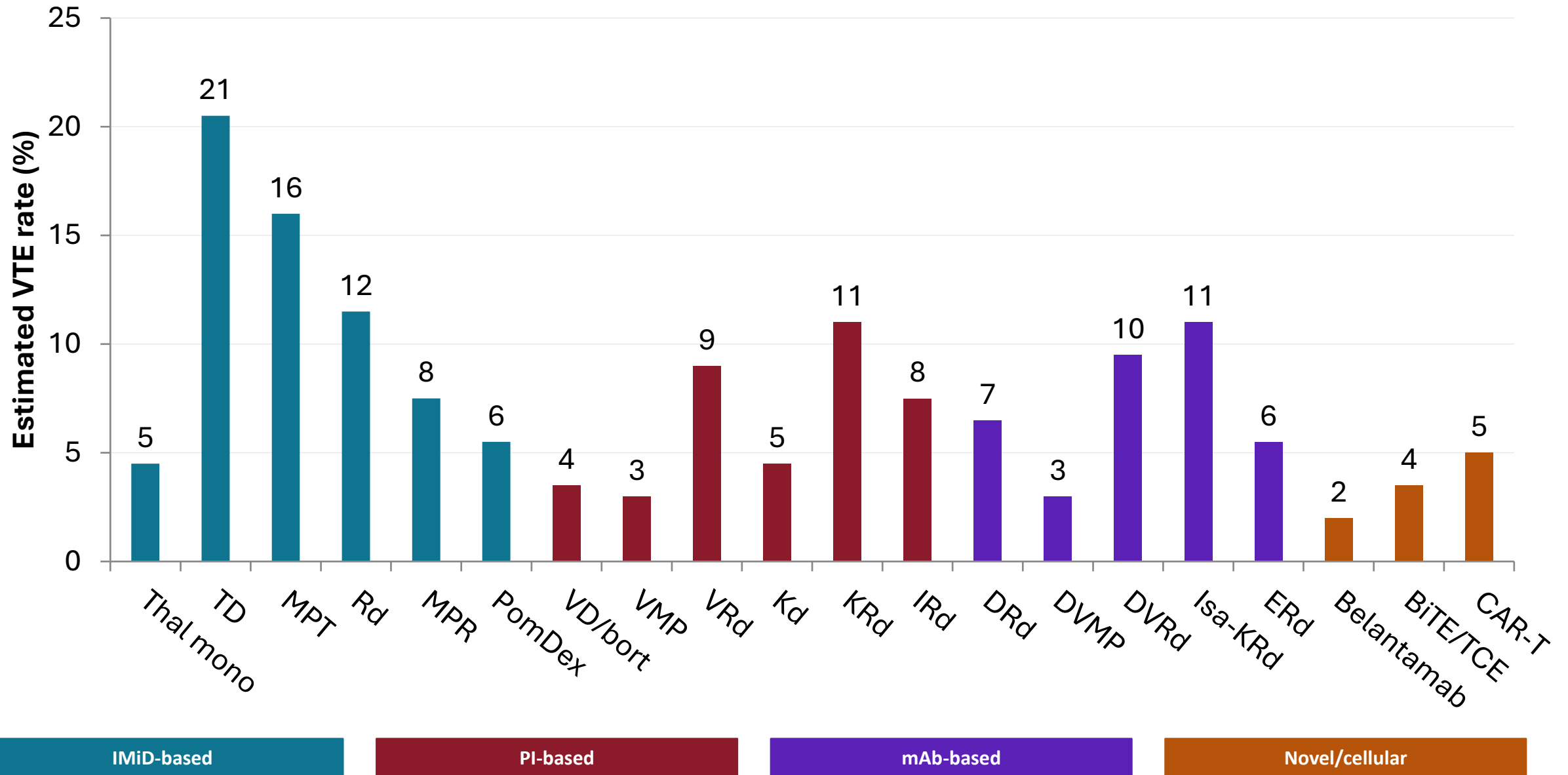
High (10–20%)

Arterial signal

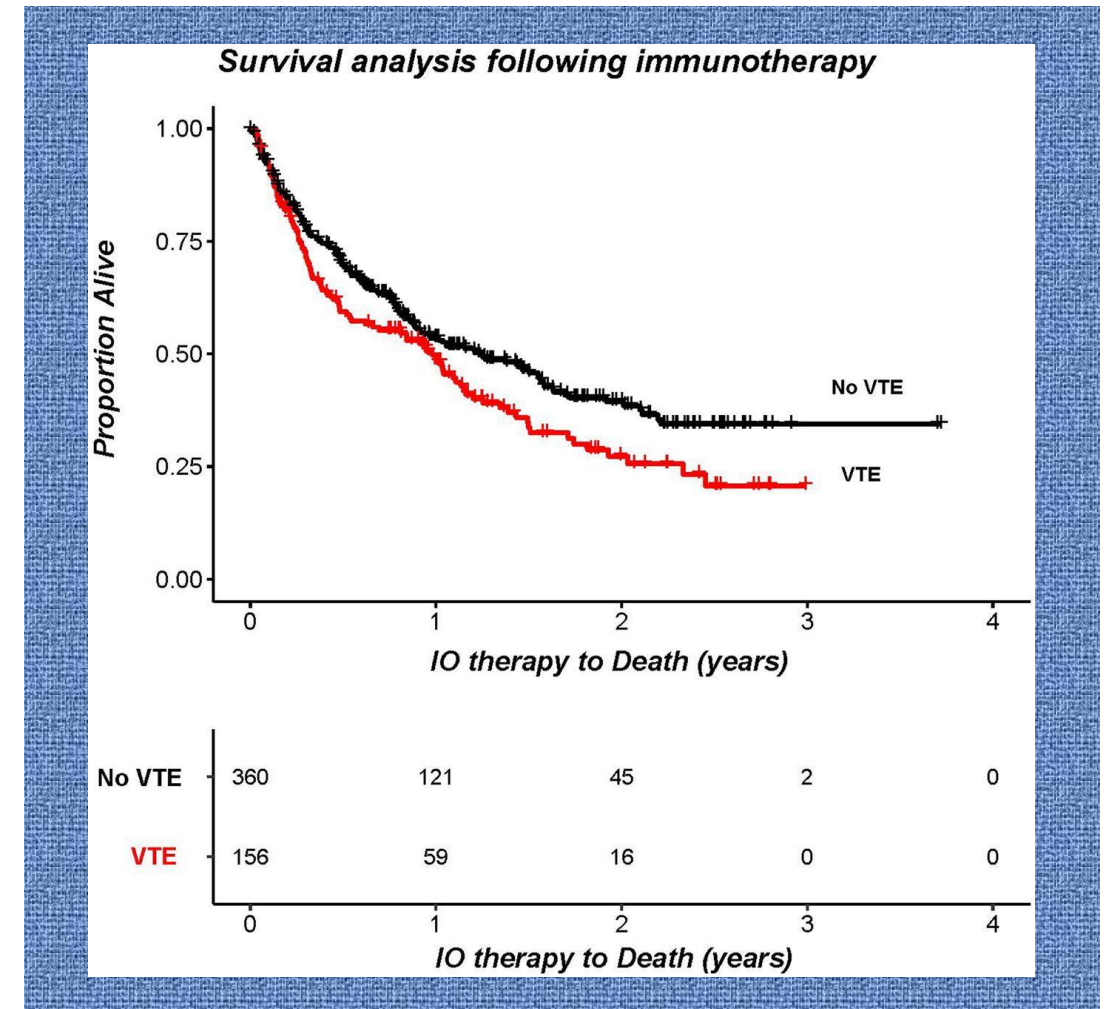
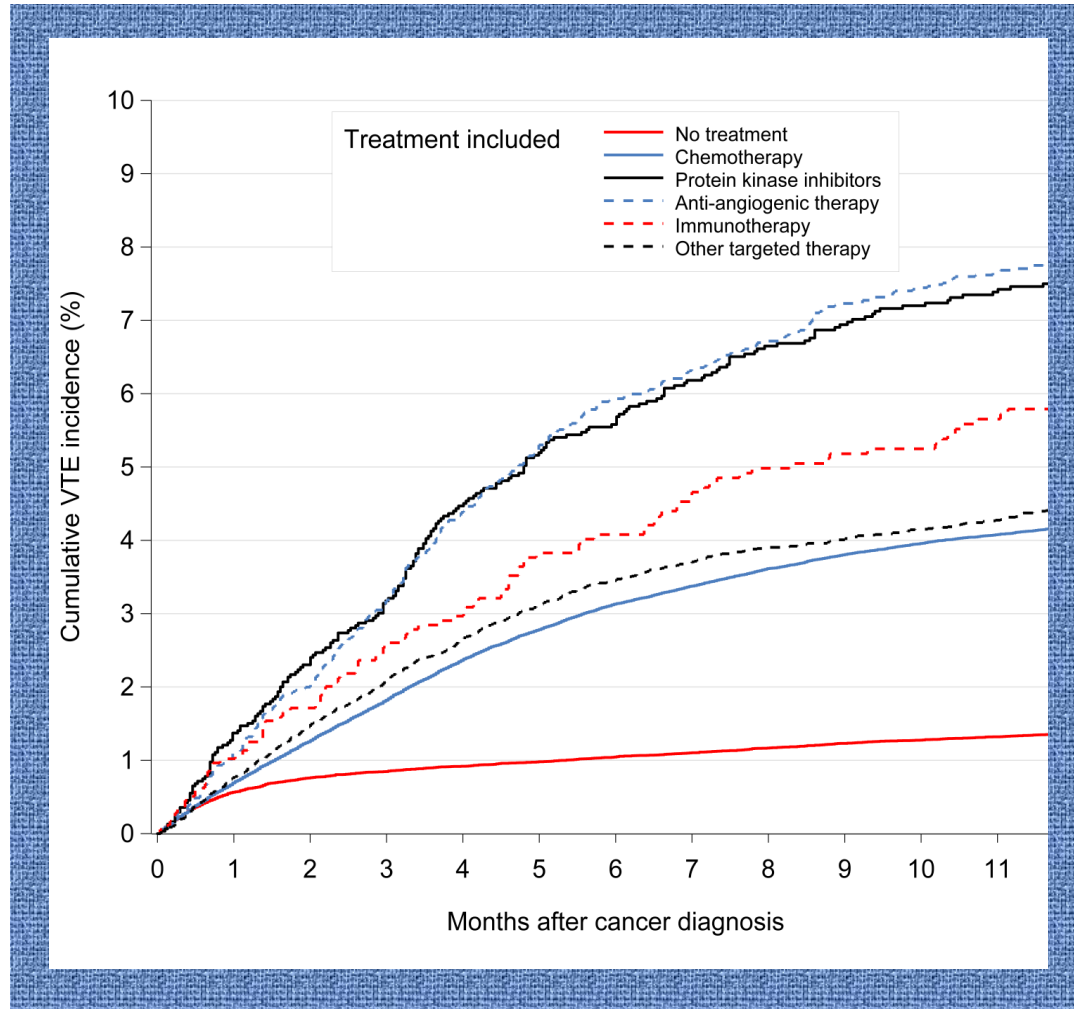
ADC = antibody–drug conjugate · BiTE/TCE = T-cell engager · CAR-T = chimeric antigen receptor T cell · CRS = cytokine release syndrome

Rates are approximations; heterogeneity across trials is substantial. Arterial event reporting is inconsistent across studies — data should be interpreted with caution.

Comparative VTE Rates by Regimen



Targeted Anticancer Therapies and risk of CAT Comparison with conventional Chemotherapy



Immunotherapy and CAT

229 Patients treated with Immunotherapy

VTEs occurred in 18 of 229 patients = 7.9%

Symptomatic VTE = 13 of 18 (72.2%) → **worse OS for symptomatic VTE (3.6 vs 19.1 m (p= 0.001))**

Multivariable cox regression analysis symptomatic VTEs independently associated with worse OS (HR 2.40 (95%CI: 1.20 - 4.80), p=0.01)

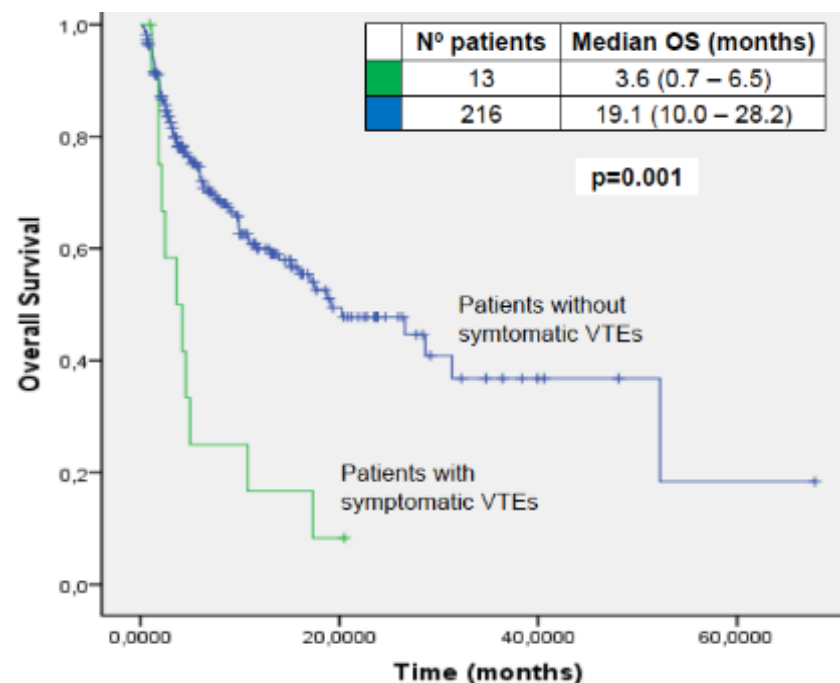
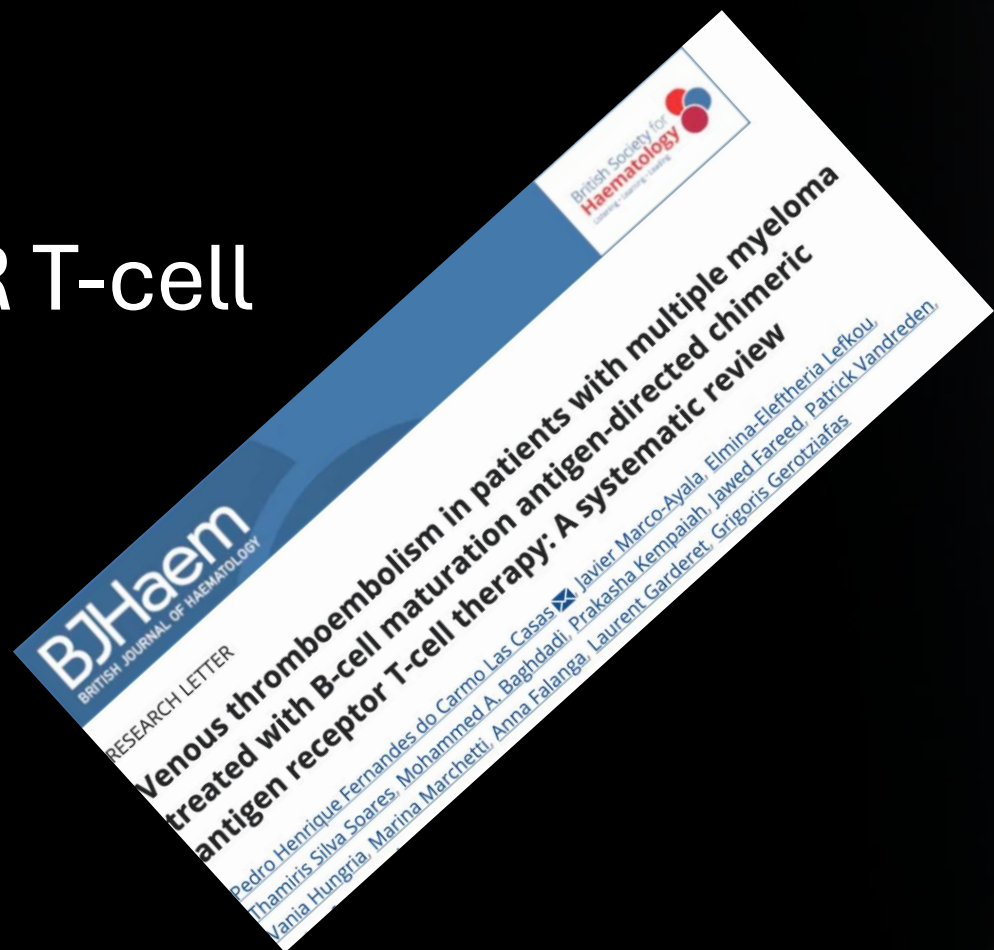


Table 2: Multivariable analysis.		Overall Survival		
Variables	Hazard ratio	95% CI	p	
Sex	0.96	0.61 – 1.50	0.87	
Age	0.98	0.96 – 1.00	0.08	
Race	0.81	0.10 – 6.11	0.84	
Smoking history	1.01	0.64 – 1.58	0.95	
History of VTEs	2.07	0.86 – 4.95	0.10	
Combination immunotherapy	0.54	0.24 – 1.21	0.13	
Immunotherapy & bevacizumab	0.68	0.06 – 6.78	0.74	
Immunotherapy & chemotherapy	0.48	0.14 – 1.59	0.23	
Immunotherapy & tyrosine kinase inhibitors	0.34	0.04 – 2.64	0.74	
Symptomatic VTEs	2.40	1.20 – 4.80	0.01	

CAR T-cell and CAT



Incidence and Localization of VTE in MM Patients Treated with Ide-cel or Cilta-cel

Key clinical trials vs standard of care · without prophylaxis unless stated



Trial	Type of trial	n	Therapy	VTE events No. (%)	VTE type	Prophylaxis for VTE in protocol	Median follow up (months)
KarMMa-1	Phase I/IIb	128	Ide-Cel	2 (1.6%)	1 PE 1 DVT	NA	13.3
KarMMa-3	RCT	254	Ide-Cel	3 (1.2%)	DVT	Per institution	18.6
			SoC ^a	0	—	All patients on pomalidomide / lenalidomide should use. Drug choice per institution	19.6
CARTITUDE-1	Phase I/IIb	132	Cilta-cel	4 (4.1%)	3 DVT 1 PE	Low-dose aspirin may be continued. Per institution	12.4
CARTITUDE-1 Japan	Phase I/IIb	9	Cilta-cel	1 (11%)	1 PE	NA	8.5
CARTITUDE-2	Phase I/IIb	20	Cilta-cel	0	—	NA	11.3
CARTITUDE-4	RCT	208	Cilta-cel	1 (0.5%)	PE	Strongly recommended during bridging. No type specified. Per institution	15.9
		211	SoC (DaraPD/PVd)	6 (2.8%)	4 PE 2 DVT	Strongly recommended. Drug choice per institution	15.9

Abbreviations: DVT, deep vein thrombosis; MM, multiple myeloma; NA, not available; PE, pulmonary embolism; RCT, randomised controlled trial; SoC, standard of care; VTE, venous thromboembolism; F/U, follow-up.

^a According to investigator's discretion: daratumumab, pomalidomide and dexamethasone; daratumumab, bortezomib and dexamethasone; ixazomib, lenalidomide and dexamethasone; carfilzomib and dexamethasone; or elotuzumab, pomalidomide and dexamethasone.

VTE in Patients Treated with BCMA-directed CAR T-cell Therapy or Standard of Care

Comparison of VTE incidence across included studies — statistical analysis



CAR-T cell treatment	VTE events / n	Comparator SoC	VTE events / n	OR (95% CI)	p value
Ide-cel	5 / 1605	Cilta-cel	5 / 938	0.58 (0.17–2.02)	0.5132
Ide-cel	5 / 1605	SoC (Total)	6 / 343	0.18 (0.06–0.61)	0.0047
Cilta-cel	5 / 938	SoC (Total)	6 / 343	0.30 (0.10–0.96)	0.0424
Ide-cel	5 / 1605	SoC (Poma-based)	6 / 211	0.11 (0.01–0.35)	0.0006
Cilta-cel	5 / 938	SoC (Poma-based)	6 / 211	0.18 (0.06–0.61)	0.0073

Interpretation

- OR < 1 significantly → Both ide-cel and cilta-cel confer markedly lower VTE risk vs SoC (Total and Poma-based comparators)
- OR = 0.58 (ns) → No significant difference in VTE rate between ide-cel and cilta-cel directly
- Strongest effect vs Poma-based SoC: ide-cel OR 0.11 (p = 0.0006); cilta-cel OR 0.18 (p = 0.0073) — reflects high VTE burden of pomalidomide backbone

Abbreviations: BCMA, B-cell maturation antigen; CAR, chimeric antigen receptor; OR, odds ratio; Poma, pomalidomide; SoC, standard of care; VTE, venous thromboembolism.

Bold OR values and red p values indicate statistical significance (p < 0.05).

VTE after CAR T-cell therapy in Multiple Myeloma patients



Reported **VTE incidence is low**, but **likely underestimated**, especially in **real-world** studies.



When thrombotic events are **actively sought and systematically documented**, VTE rates appear **similar to those expected** in relapsed/refractory MM patients receiving **standard thromboprophylaxis**.



The main gap is **methodology**: inconsistent surveillance, variable definitions, and incomplete reporting.



These data support the need for **more rigorous assessment and reporting** of thrombotic complications after CAR T-cell therapy—
not definitive conclusions about **thrombotic safety** or **prophylaxis adequacy**.



Prevention and treatment of venous thromboembolism in patients with multiple myeloma: Clinical practice guidelines on behalf of the European Myeloma Network












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VTE risk assessment tools for patients with myeloma



Parameter	IMPEDE-VTE	SAVED	PRISM	IMWG (2008)
Year Developed	2019	2019	2024–2025	2008
Target Population	All newly diagnosed MM	MM receiving IMiDs	Contemporary MM population	MM receiving IMiDs
Model Type	Weighted score	Weighted score	Multivariable prediction model	Expert consensus algorithm
Previous VTE	✓ (+3)	✓ (+3)	✓	✓
Obesity / BMI	✓ (BMI ≥25)	—	✓	✓
Age	—	Age ≥80 (+1)	✓	✓
Central Venous Catheter	✓ (+2)	—	✓	✓
Recent Surgery	✓ (+2)	Surgery within 90 days (+2)	✓	✓
Pelvic/Hip/Femur Fracture	✓ (+4)	—	✓	✓
Erythropoietin Use	✓ (+1)	—	✓	✓
Doxorubicin	✓ (+3)	—	✓	Major risk factor
High-Dose Dexamethasone	✓ (+4)	✓ (+1)	✓	Major risk factor
IMiD Exposure	✓ (+4)	Core component	✓	Core component
Race/Ethnicity	Asian race (−3)	Asian race (+3)	—	—
Comorbidities	Limited	Limited	Extensive	Included qualitatively
Renal Dysfunction	—	—	✓	✓
Performance Status	—	—	✓	✓
Disease Characteristics	Limited	Limited	Extensive	Limited
Risk Categories	Low / Intermediate / High	Low / High	Low / Intermediate / High	Low / High
Score Range	−3 to ≥15	0–5	Variable	Qualitative
Validation	Extensive external validation	External validation	Emerging validation	No formal validation
Predictive Performance	AUC ≈ 0.65–0.68	AUC ≈ 0.60–0.63	AUC ≈ 0.70–0.75*	Not reported
Current EMN Position	Preferred RAM	Alternative RAM	Investigational	Historical model
Clinical Utility	Current standard	Simple bedside tool	Precision thrombosis approach	Historical reference

Comparison of VTE risk assessment models for patients with myeloma

DOMAIN	 1. SAVED SCORE (Validation Study)	 2. IMPEDE VTE SCORE (IMiD-Treated MM)	 3. VTE-PREDICT MM SCORE (Newly Diagnosed MM)	 4. EXPERT OPINION (Consensus)
 Population used for development	N = 4446 MM pts	N = 2397 MM pts on IMiDs	N = 783 newly diagnosed MM pts	Expert opinion consensus
 Study design	Retrospective	Retrospective	Retrospective	Not applicable
 C-index (discrimination)	0.65 (derivation), 0.63 (validation)	0.61	0.67	Not applicable
 External validation	Yes (external cohort of 1747 patients)	Yes (validated in 1181 patients)	Yes	Not applicable
 Sensitivity / Specificity	Sensitivity: ~71%, Specificity: ~52%	Sensitivity: ~72%, Specificity: ~48%	Sensitivity: ~77%, Specificity: ~57%	Not applicable
 Risk categories (Score)	Low (≤ 3), Intermediate (4–7), High (≥ 8)	Low (≤ 1), High (≥ 2)	Low (0), Intermediate (1–6), High (≥ 7)	Low (0–1), High (> 1)
 Limitations	<ul style="list-style-type: none">Derived retrospectivelyNo daratumumab/carf-based therapiesLimited in modern regimens	<ul style="list-style-type: none">Applies only to IMiD usersDeveloped before anti-CD38 therapiesModest PPV	<ul style="list-style-type: none">Includes metaphase cytogenetics (not widely available)Moderate PPVLimited generalizability	<ul style="list-style-type: none">SubjectiveNot validatedLacks granularity and risk score weighting

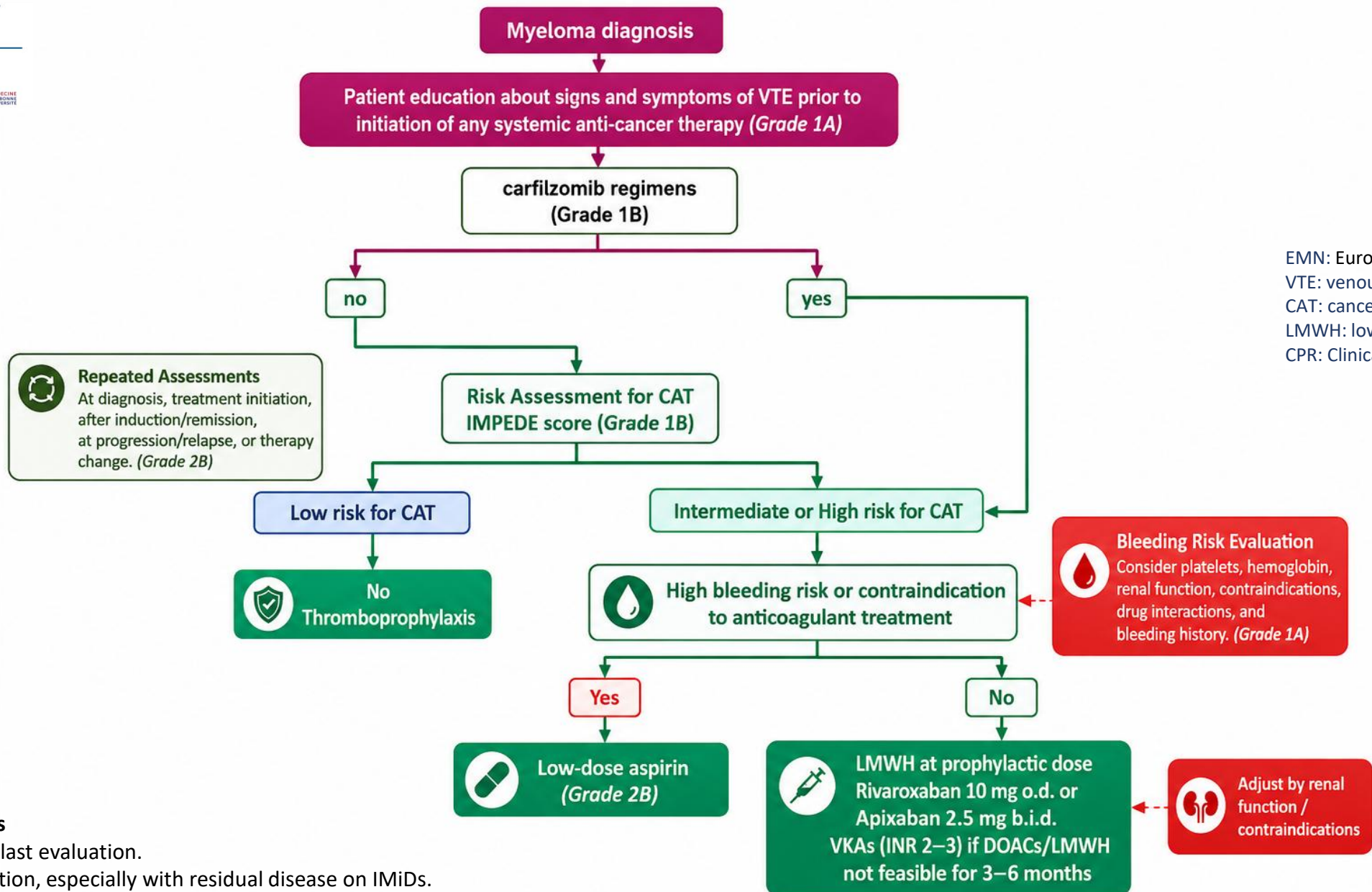


KEY TAKE-HOME MESSAGE:

All existing VTE risk models in MM show moderate discrimination (C-index ~0.6–0.7) with varying validation strengths and important limitations, underscoring the need for updated models reflecting modern therapies.

Abbreviations: VTE, venous thromboembolism; MM, multiple myeloma; IMiD, immunomodulatory drug; PPV, positive predictive value; pts, patients.

Prevention of VTE in patients with multiple myeloma



EMN: European Myeloma Network
VTE: venous thromboembolism
CAT: cancer associated thrombosis
LMWH: low molecular weight heparin
CPR: Clinical Prediction Rule

Duration of Prophylaxis
At least 6 months from last evaluation.
Avoid early discontinuation, especially with residual disease on IMiDs.
Maintenance: case-by-case adjustment with IMPEDE score and QoL assessment.

Thromboprophylaxis in acute medically ill patients with MM

Key Principle

- Patients with **multiple myeloma (MM)** and **acute medical illness (including COVID-19)**
- Benefit **equally** from standard thromboprophylaxis for acutely ill medical patients
- Should follow the **most recent guideline recommendations**

Recommendation

- **Administer prophylactic doses of:**
 - **LMWH** (*Grade 1A*)
 - **Fondaparinux** (*Grade 1A*)
- **Applicable to:**
 - Hospitalized patients
 - Outpatients receiving care in **primary healthcare settings**
 - Patients managed **at home**

Recommended therapeutic protocols for CAT treatment

LMWH

Acute phase

Secondary prevention

DOAC

Acute phase

Secondary prevention

Rivaroxaban 15 mg b.i.d. x 3 weeks

Rivaroxaban 20 mg o.d.

Apixaban 10 mg b.i.d. x 5 days

Apixaban 5 mg b.i.d. → 2.5 mg b.i.d.

LMWH x 5 days and then edoxaban 60 mg daily

Treatment of VTE in hematological patients. ESMO and EMN guidelines

CAT
symptomatic or incidental

Assess bleeding risk before therapy
Does the patient present with at least one of the following risk factors?

Recurrent or life-threatening VTE during IMiD/carfilzomib regimens → Individualized decisions (response, severity, risk profile) (Grade 2C)

renal insufficiency
platelets <50 G/L
anemia
drug interactions
(Grade 1A)

Yes

No

Acute phase
5 – 10 days

LMWH (Grade 1A)
Severe renal insufficiency; CrCl <30 mL/min → UFH with anti-Xa monitoring (Grade 1A)

LMWH (1A)
Apixaban (1A)
Edoxaban (1A)
Rivaroxaban (1A)

Long-term phase
3-6 months

LMWH (I, A)

LMWH (1A)
Apixaban (1A)
Edoxaban (1A)
Rivaroxaban (1A)

Duration:
Minimum **6 months** (Grade 1A).
Extend beyond 6 months if **active MM** (NDMM, relapse/progression, no remission) (Grade 1A)
Extend during **ongoing IMiD or carfilzomib therapy* (Grade 1A)
Decision based on **VTE recurrence vs bleeding risk** → refer to thrombosis specialist (Grade 2B)
Extended prevention (>6 months): Reduced-dose apixaban (2.5 mg bid) preferred over full dose (Grade 1B)

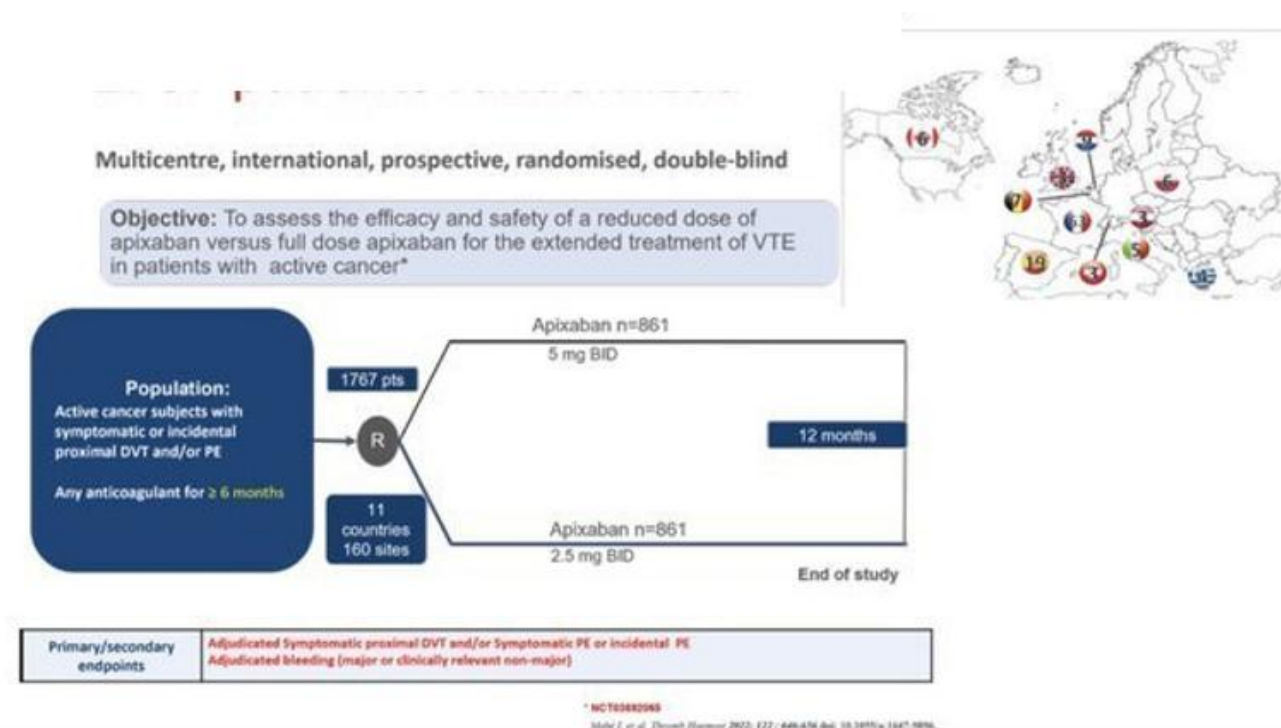
LMWH (III, B)

LMWH (1A)
Apixaban (1A)
Edoxaban (1A)
Rivaroxaban (1A)

API-CAT trial: Extended Reduced-Dose Apixaban for CAT

Study design

- **Randomized**, double-blind, noninferiority trial
- **1 766 patients** with active cancer and proximal deep-vein thrombosis or pulmonary embolism who had completed at least 6 months of anticoagulant therapy
- **Randomization:** ratio 1:1 to receive
 - **Reduced dose apixaban 2.5 mg** twice daily (n= 866 patients)
 - **Full dose apixaban 5.0 mg** twice daily (n= 900)
- **Follow up** : 12 months
- **Primary outcome** : centrally adjudicated fatal or nonfatal recurrent venous thromboembolism, assessed in a noninferiority analysis
- **Secondary outcome** : clinically relevant bleeding, assessed in a superiority analysis



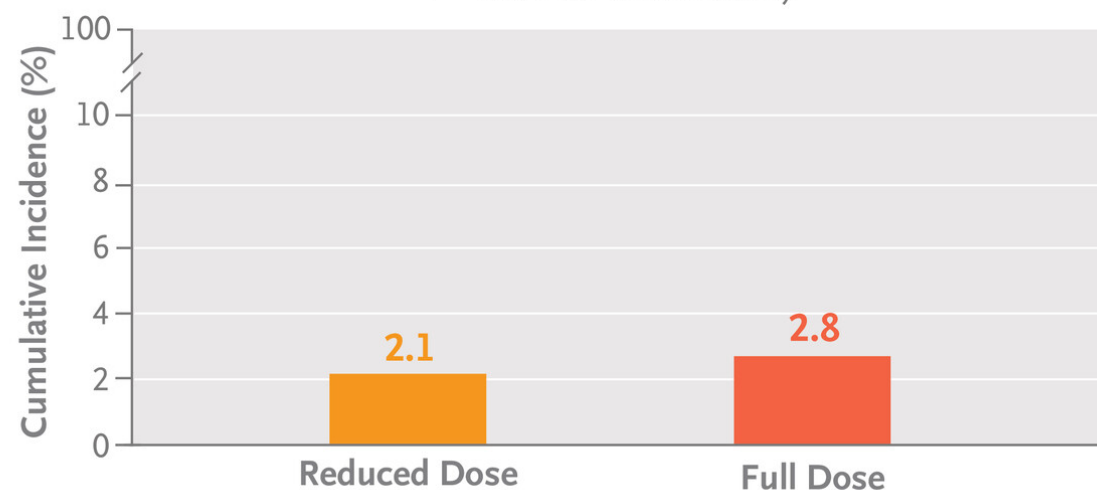
API-CAT trial: Extended Reduced-Dose Apixaban for CAT

Results

Fatal or Nonfatal Recurrent VTE

Adjusted subhazard ratio, 0.76 (95% CI, 0.41–1.41)

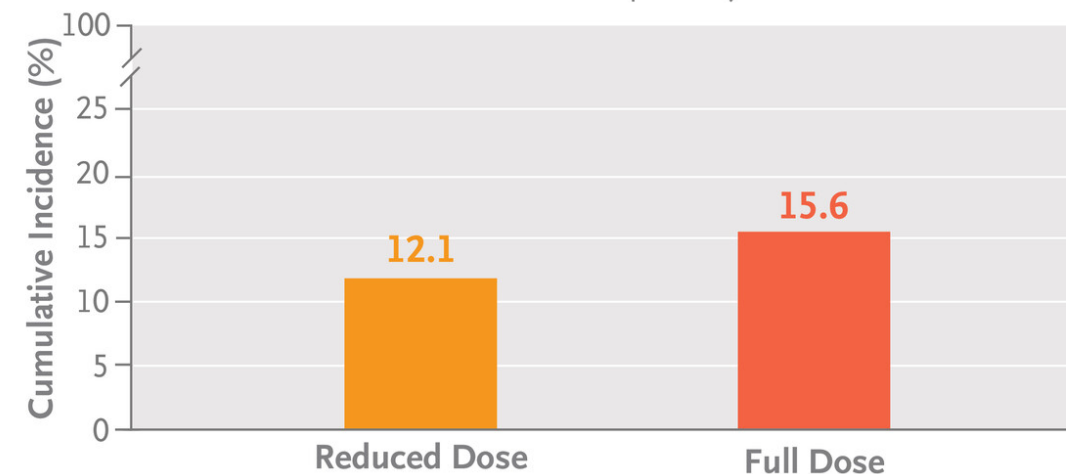
P=0.001 for noninferiority



Clinically Relevant Bleeding

Adjusted subhazard ratio, 0.75 (95% CI, 0.58–0.97)

P=0.03 for superiority

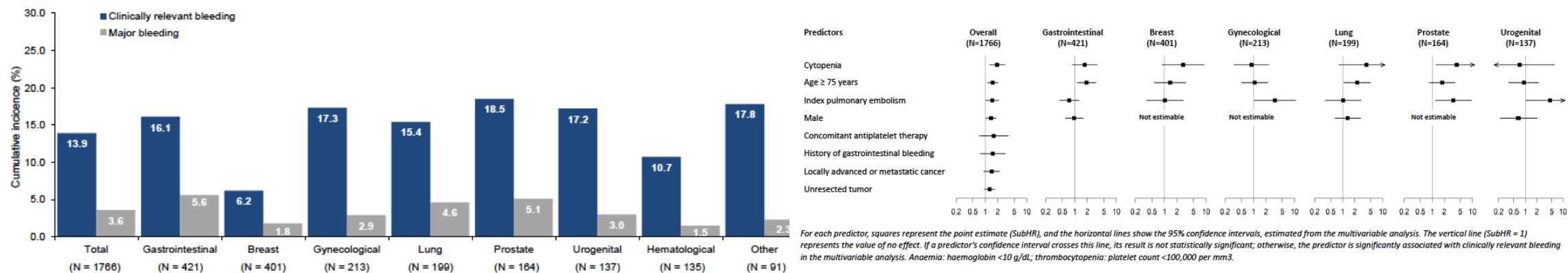


Predictors of clinically relevant bleeding during extended anticoagulation for cancer-associated venous thromboembolism (API-CAT): a post-hoc analysis of a randomised, non-inferiority trial

Prof Isabelle Mahé, MD PhD ^{a,b,c,d} ✉ · Céline Chapelle ^{e,f} · Philippe Girard, MD ^{g,h} · Marc Carrier, MD ^h · Luis Jara Palomares, MD PhD ^{i,j} ·

Prof Charles-Marc Samama, MD PhD ^k · Hélène Helfer, PhD ^a · Prof Grigoris Gerotziakas, MD PhD ^{l,m} · Prof Silvy Laporte, PhD ^{d,e,f} ·

Prof Eric Vicaut, MD ^{n,t} · Prof Patrick Mismetti, MD PhD ^{d,f,o,p,t} for the API-CAT Study Group [†] and API-CAT Investigators [‡] [Show less](#)



Bleeding risk during extended anticoagulation

Four predictors of clinically relevant bleeding (overall population)

The “4 predictors”



**Anaemia and/or
thrombocytopenia**

Blood counts



Age ≥ 75 years

Age



**Pulmonary
embolism
as index event**

Index event



Male sex

Sex

What this means

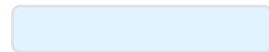
- ✓ Predictors were also associated with major bleeding and across cancer sites (effect sizes vary).
- ✓ Bleeding risk increases as risk factors accumulate → supports risk-stratified decisions.
- ✓ No evidence of interaction with dosing regimen.

Clinical use: Helps balance benefit vs bleeding risk when considering extended anticoagulation (not designed to decide discontinuation).

Risk accumulation concept



0



1



2



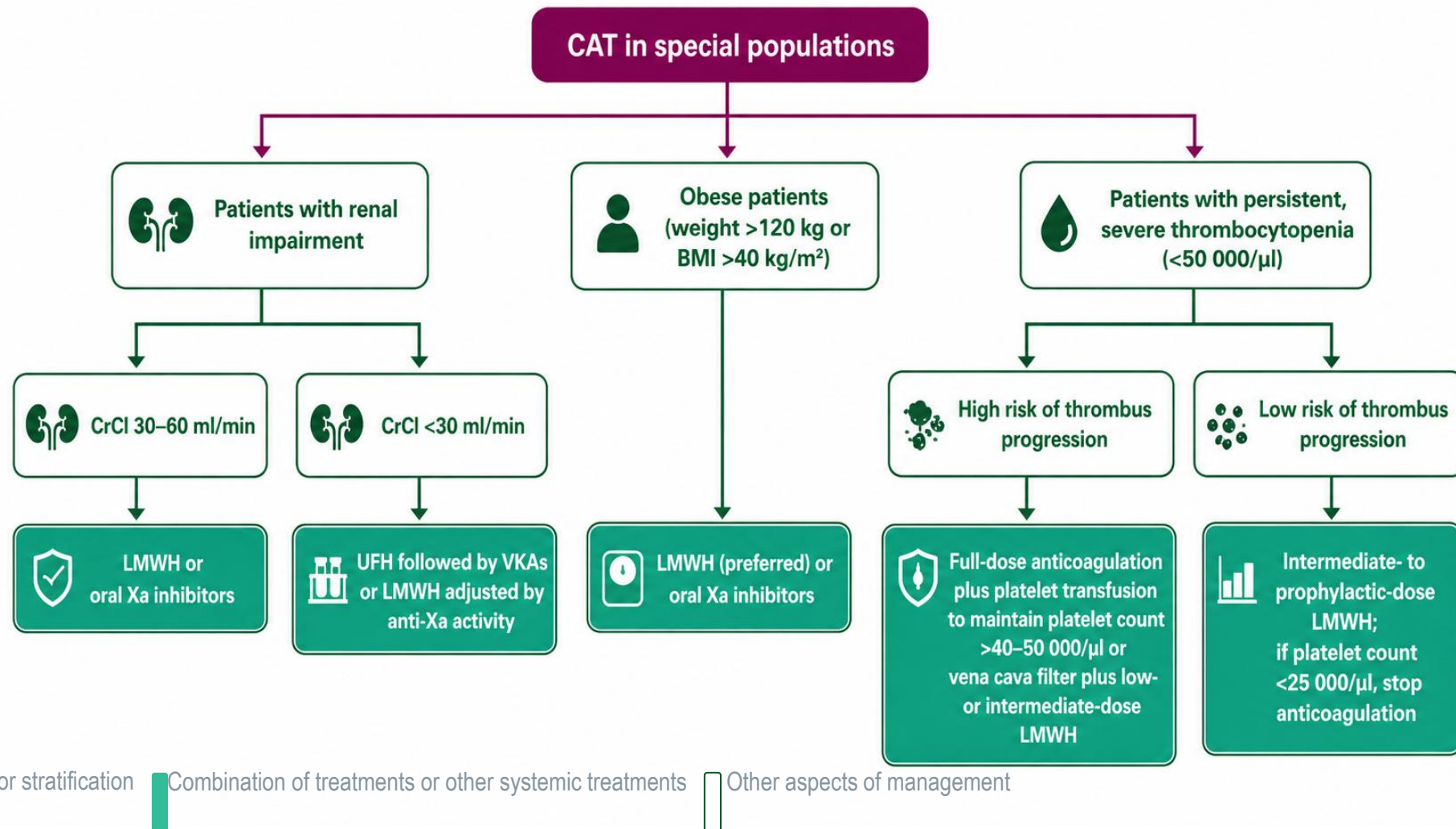
3



4

Number of risk factors → higher bleeding risk

Treatment of CAT in special populations



Take home messages

VTE in patients with multiple myeloma:

common, life-threatening, reduces quality of life, and interrupts treatment.

Key actions for clinicians:

- 🔥 **Educate** patients on VTE risk, symptoms, and prompt care.
- 🔥 Regularly assess **VTE and bleeding risk**.
- 🔥 **Thromboprophylaxis:**
 - ▶ High/intermediate risk → prophylactic doses of LMWH or oral direct FXa inhibitors (apixaban, edoxaban or rivaroxaban)
 - ▶ Low risk → low-dose ASA
 - ▶ All starting IMiD or carfilzomib → LMWH or direct factor Xa inhibitors
 - ▶ Duration: ≥6 months, then individualized
- 🔥 **VTE treatment:**
 - ▶ **Acute phase:** therapeutic doses of LMWH or oral direct FXa inhibitors (apixaban, edoxaban or rivaroxaban)
 - ▶ **≥6 months** if the disease is active: therapeutic dose of LMWH or apixaban 2.5 mg d.o.d.; personalize long-term secondary prevention.
- 🔥 Consider patient preference, quality of life, and drug interactions.
- 🔥 Establish clear pathways for prompt diagnosis and management.

Take home messages

Outpatient Consultation specialized on Thrombosis in Oncology

Check profile

Optimise management



Agree multidisciplinary approach


Guarantee the quality of life



Diplôme Universitaire DU T2H

Thrombose, hémostase en hématologie

Thrombosis, Haemostasis, Diagnosis and Therapy



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OBJECTIFS / COMPÉTENCES PUBLIC & PRÉ-REQUIS PROGRAMME MÉTHODES / MOYENS PÉDAGOGIQUES

OBJECTIFS
L'objectif principal de ce diplôme est l'amélioration des compétences des professionnels impliqués dans l'offre des soins chez les patients atteints de pathologies hématologiques et des cancers solides :

1. à évaluer le risque thrombotique ou hémorragique
2. à utiliser de manière optimale et à l'échelle personnalisée les outils diagnostiques et thérapeutiques
3. à traiter les thromboses et les hémorragies de manière conforme aux recommandations des consensus d'experts

L'objectif secondaire de ce diplôme est la transmission des connaissances et de l'expérience sur l'organisation de Réunions de Concertation Pluridisciplinaire Cancer – Thrombose et la mise en place des Consultations Spécialisées en Thrombose et Hémostase en Hématologie.

**RESPONSABLE(S)
PÉDAGOGIQUE**



GRIGORIOS GEROTZIAPAS
Voir le CV



Friday, 10 July 2026
Saint-Antoine Hospital
Kourilsky Building

Conference Room
 34 rue Crozatier, 75012

Format: In-person **Virtual**

Practical Information
In-person Access
 Limited to 60 participants
Interactive Format
 Round-table discussion
Live Zoom Access
 Limited to 150 participants

PROGRAM

15:00	Welcome from the Director of the CRSA <i>Pr Xavier Huard</i>
15:15	Introduction & Objectives. <i>Pr A Falanga</i>
15:30	Patient Pathways in CAT: Barriers & Solutions. <i>Pr I Mahé</i>
15:50	ESMO Recommendations in CAT (Solid Tumors): Barriers & Perspectives. <i>Pr L J Palomares</i>
16:10	EMN Recommendations in Multiple Myeloma: Barriers & Perspectives. <i>Pr G Gerotziakas</i>
16:30	VTE Risk After Cancer Surgery: Role of the Caprini Score. <i>Pr J Caprini</i>
16:50	Cancer-Associated Arterial Thrombosis: Challenges & Perspectives. <i>Pr A Khorana</i>
17:10	International Round-Table Discussion
18:30	Summary & Proposed Actions
18:45	Networking Buffet

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Rudolf Virchow (1821–1902)

Physician, pathologist, and pioneer of social medicine

Rudolf Virchow and the Typhus Epidemic in Upper Silesia, 1848

Excerpts from Virchow's Report and His Social Medicine Perspective

On the epidemic and its investigation

“At the beginning of this year reports on the outbreak of a disastrous disease in Upper Silesia, which up to that time had appeared in the newspapers only sporadically, increased in frequency and urgency. The Prussian Minister for Religious, Educational and Medical Affairs, nevertheless, not only did not receive from the local medical authorities any reports on the nature of the malady but not even notification of its presence. Thus, when the press published increasingly horrible details on this so-called hunger-typhus, when the whole of Germany was resounding with a cry for help for the inhabitants of Upper Silesia.”¹

Regarding the contagiousness of typhus, Virchow argued that the prerequisites for the disease must be local and endemic. An enlargement of the spleen was noted in three patients, but this was attributed to malaria.

Cadaver blood was “well clotted with a buffy coat.”²

Virchow defined typhus as “a general putrid infection known then as ‘septicemic enteritis.’”³

... an acute disease, which generally starts with a considerable upheaval of the nervous system and with severe fever, constant drunkenness, tremulousness, and “Peyer’s gland groups were entirely unchanged.”²



Typhus as a consequence of social evils

“I am firmly convinced that the typhus epidemic of Upper Silesia was the **consequence of social evils, and that these evils could be fought only by ways of deep going social reforms.**”^{3,4}

He also maintained that **“Medicine is a social science, and politics nothing else but medicine on a large scale.”**³



Virchow’s solution: education, liberty, and prosperity

“How to prevent a recurrence of typhus in Upper Silesia? Virchow’s solution is **education, with its daughters, liberty and prosperity.**”⁵ He recognized that

Less easy and simple is the practical answer, the solution of this great social problem. ... Medicine has imperceptibly led us into the social field and placed us in a position of confronting directly the great problems of our time. ... ⁴