XXIV Simposio de Revisiones en Cáncer

"Tratamiento médico del cáncer en el año 2022"

Avances terapéuticos para trombosis asociada a cáncer

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TROMBOSIS ASOCIADA A CÁNCER (TAC)

- Incidencia TEV: 1 por 1000
- Riesgo de TEV en cáncer: 4-7 veces mayor
- El cáncer está presente en el 20% de los pacientes con TEV
- Empeoramiento clínico:
  - TEV recurrente X3
  - Sangrado X2
  - Muerte X4

Blom JW. Et al. JAMA 2005; Heit JA et al. Arch Intern Med 2002;162:1245-48; Timp JF. Et al. Blood 2013;122:1712-23; Monreal M et al. *J Thromb Haemost.* 2006;4:1950-56.

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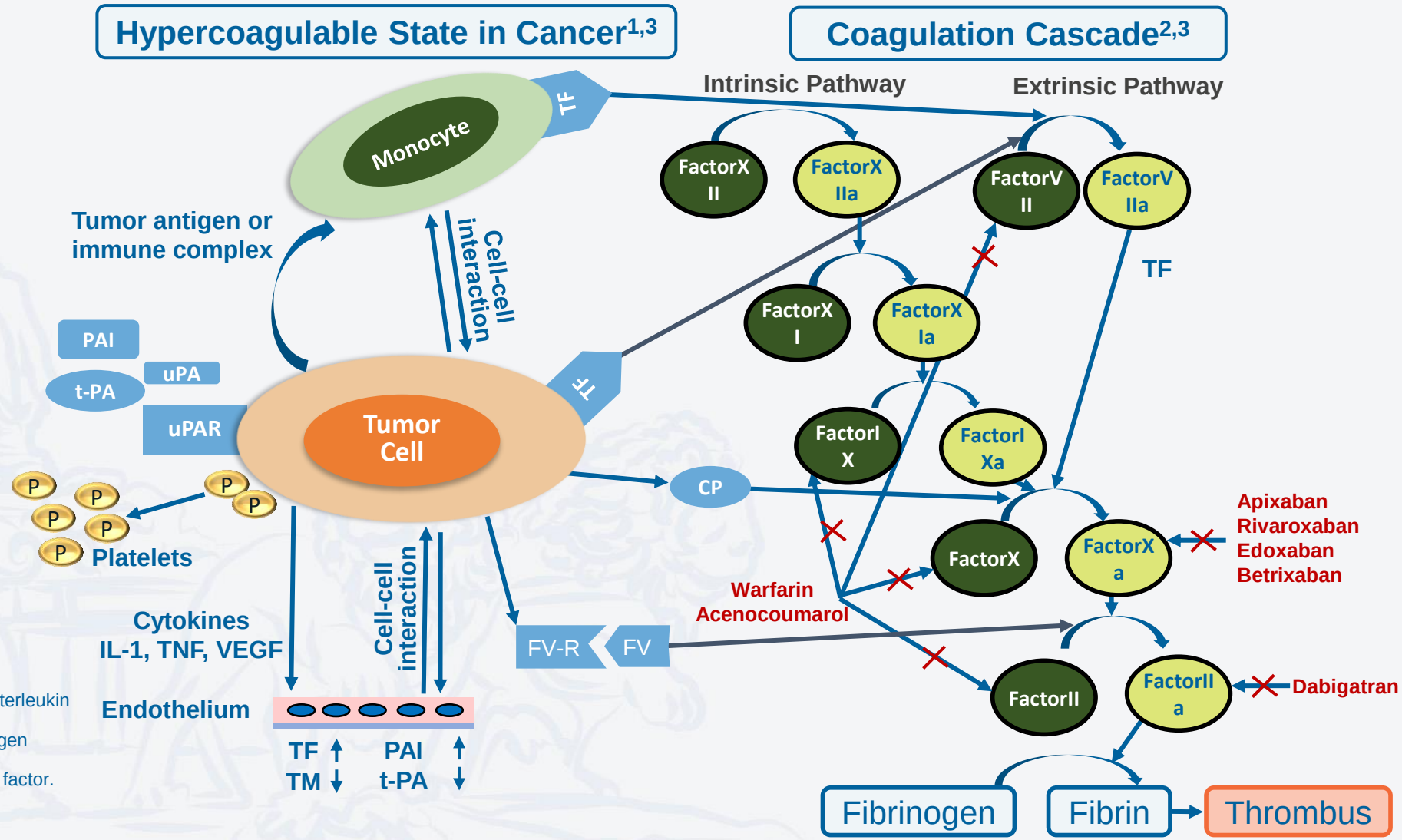
PATOGÉNESIS DEL ESTADO HIPERCOAGULABLE EN EL CÁNCER

- Tumor cells express CP factor and TF, the latter initiates the coagulation cascade.
- The tumor cells promote a hypercoagulable state, activating the hemostatic system, utilizing cell surface proteins such as TF, CP, t-PA, uPA, as well as PAI 1 and 2.
- Interaction with monocytes, platelets, and endothelial cells occurs directly by cell-cell interaction; or indirectly by cytokine release promoting prothrombotic endothelial changes.



CP, cancer procoagulant; F, factor; FV-R, factor V receptor; IL-1, interleukin 1; PAI, plasminogen activator inhibitor; TF, tissue factor; TM, thrombomodulin; TNF, tumor necrosis factor; t-PA, tissue plasminogen activator; uPA, urokinase plasminogen activator; uPAR, urokinase plasminogen activator receptor; VEGF, vascular endothelial growth factor.

1. Adapted from Kuderer NM et al. *J Clin Oncol*. 2009;27:4902-4911.
2. Tsoumani ME et al. *Curr Pharm Des*. 2017;23:1279-1293.

ETV recurrente y complicaciones hemorrágicas durante el tratamiento anticoagulante en pacientes con ETV con y sin cáncer

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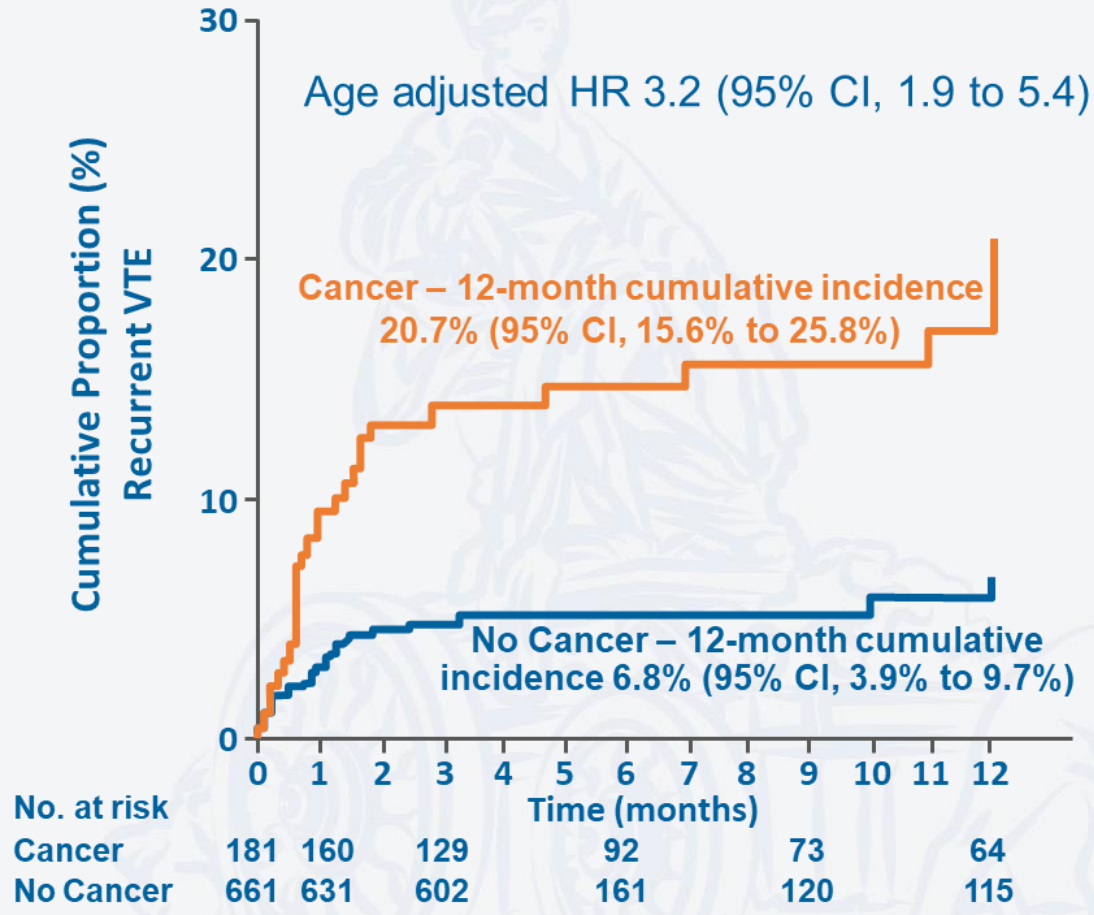
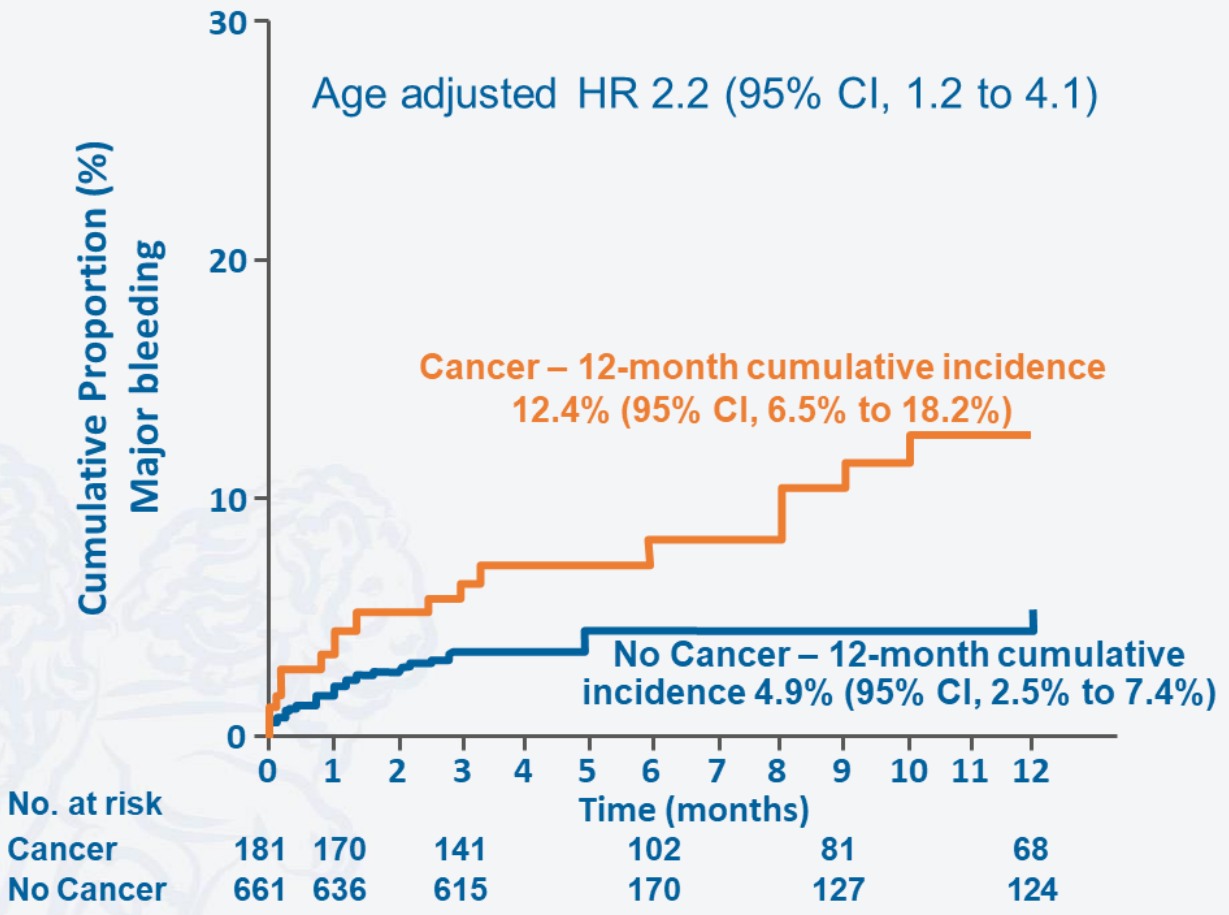
12-Month Cumulative Incidence of Recurrent VTE During Anticoagulation Therapy in DVT Patients With and Without Cancer



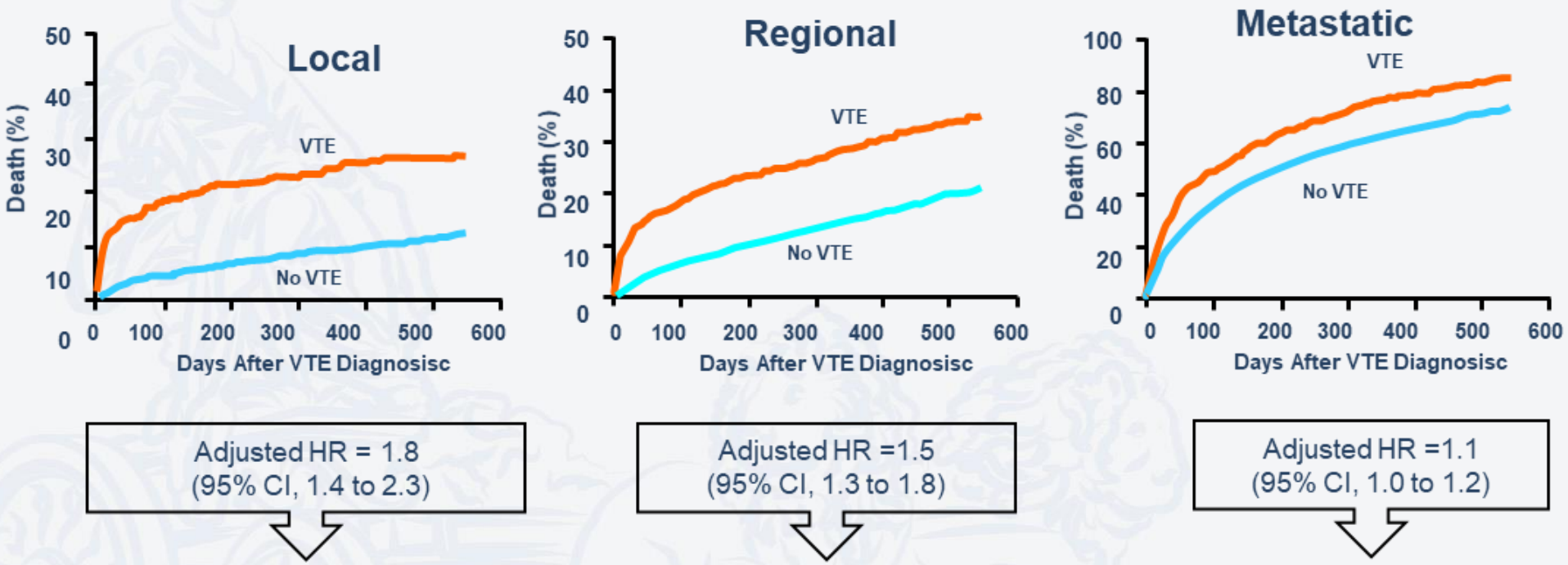
12-Month Cumulative Incidence of Major Bleeding During Anticoagulation Therapy in DVT Patients With and Without Cancer



Prandoni P et al. Blood. 2002;100:3484-3488.

Impacto de la ETV en la supervivencia según el estadío del cáncer

La aparición de un TEV tiene un efecto más perjudicial en cáncer localizado o regional



En modelos ajustados al riesgo

La ETEV es un predictor significativo de muerte dentro de 1 año del diagnóstico de cáncer entre pacientes con enfermedad en estadio local o regional, pero no entre pacientes con enfermedad metastásica

Alcalay A et al. J Clin Oncol. 2006; 24:1112-1118.

El riesgo del ETV varía a lo largo de la historia natural del cáncer

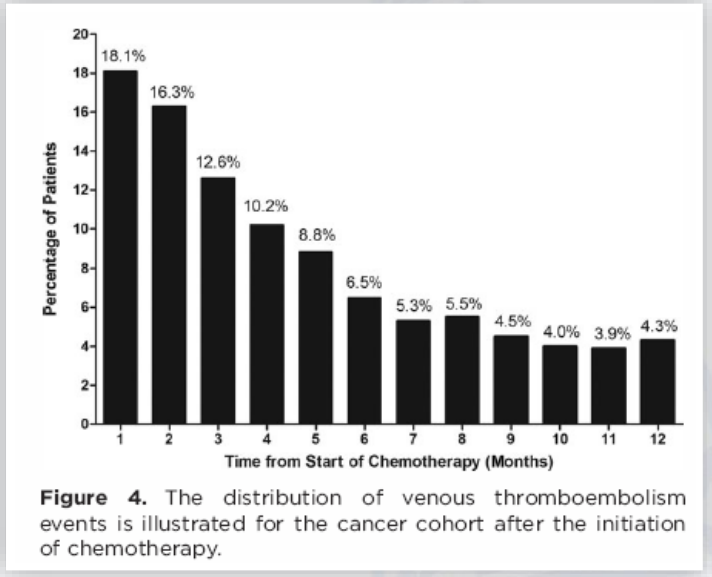
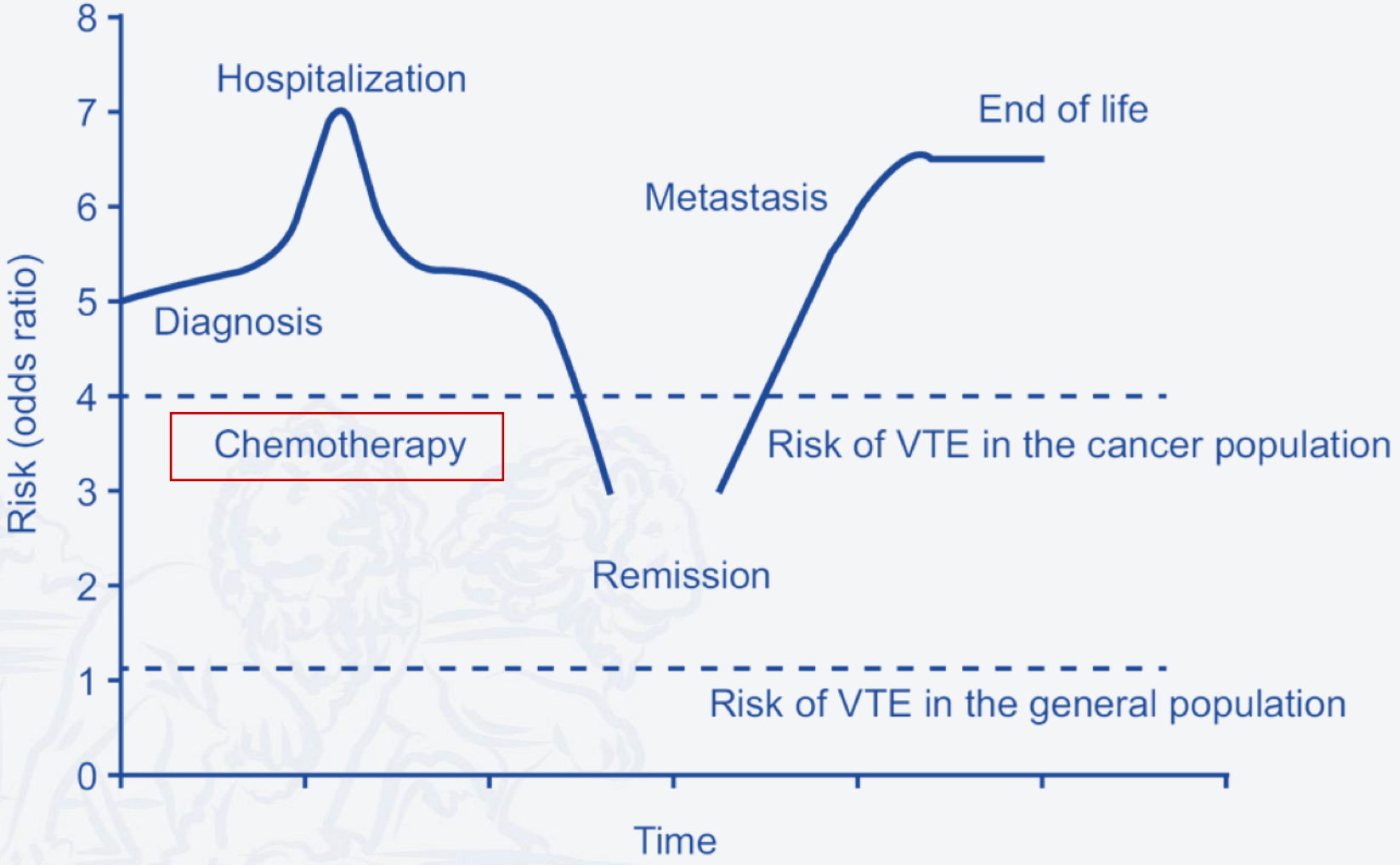


Figure 4. The distribution of venous thromboembolism events is illustrated for the cancer cohort after the initiation of chemotherapy.

Mayor incidencia en los 3-6 primeros meses tras el diagnóstico

Khorana et al. Incidence and predictors of venous thromboembolism (VTE) among ambulatory high-risk cancer patients undergoing chemotherapy in the United States Cancer 2013 Feb 1;119(3):648-55.



Rao MV, Francis CW, Khorana AA. In: Cancer-Associated Thrombosis: New Findings in Translational Science, Prevention, and Treatment. Khorana AA, Francis CW, eds. 2007.27

Consecuencias del ETV en pacientes con cáncer

- **Mayor morbilidad** (hospitalizaciones, complicaciones, riesgo sangrado por tto, etc)
- **Mayor mortalidad** (empeoramiento del pronóstico)
- **Retraso o discontinuación** del tratamiento oncológico
- Incremento de los **costes sanitarios**

Lyman G. Cancer. 2011 Apr 1;117(7):1334-49.

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FACTORES DE RIESGO DE ETV EN CÁNCER

- In patients with cancer, VTE is a major complication, occurring in 4% to 20% of patients, and is a leading cause of death.[1,2]

Patient-Related

- Older age[2]
- Race (African Americans, Asian Pacific Islanders)[2]
- Prior VTE[2]
- Elevated pre-chemotherapy platelet count[2]
- Prothrombotic mutations (factor V Leiden and prothrombin 20210A)[2,3]
- Comorbid conditions (obesity, infection, renal disease, pulmonary disease, arterial thromboembolism)[2]

Cancer-Related

- Primary site (eg, GI, brain, lung, gynecologic, renal, hematologic)[2,3]
- Grade (higher with higher grade cancer)[6]
- Time interval since diagnosis (highest risk in the first few months)[2,3]
- Stage[5]

Treatment-Related

- Surgery[2-4]
- Chemotherapy[2-4]
- Radiotherapy[3,6]
- Hormonal therapy[2]
- Antiangiogenic agents[2]
- Erythropoiesis-stimulating agents[2]
- Hospitalization[2]
- Central venous catheters[2,4]

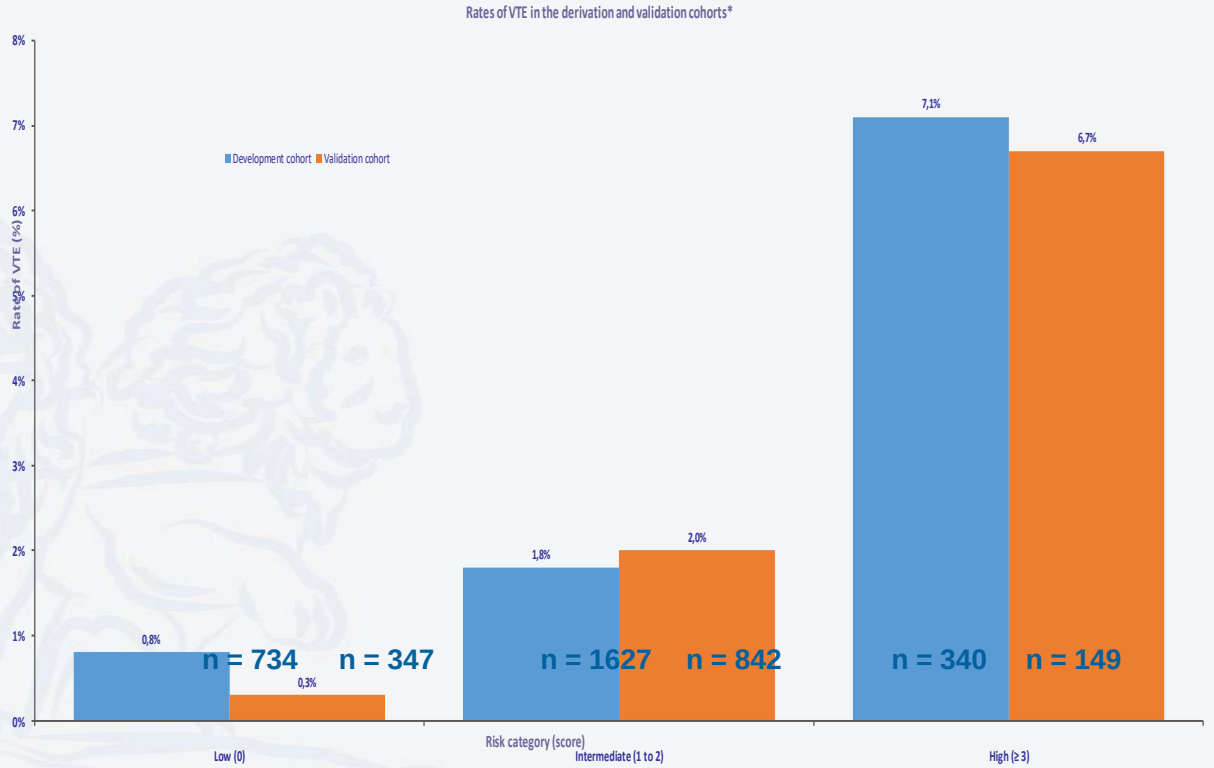
GI, gastrointestinal; VTE, venous thromboembolism.

1. Khorana AA et al. *J Thromb Haemost.* 2007;5:632-634.
2. Lyman GH. *J Clin Oncol.* 2007;25:5490-5505.
4. Blom JW et al. *JAMA*. 2005;293:715-722.
5. Heit JA. *Arch Intern Med.* 2000;160:809-815.
5. Lee AYY et al. *Circulation.* 2003;107:I–17-I-21.
6. Ahlbrecht J et al. *J Clin Oncol.* 2012;30:3870-3875.

MODELOS PREDICTIVOS ETV EN CÁNCER

- Khorana et al. developed a simple risk model for predicting chemotherapy-associated VTE using baseline clinical and laboratory variables in a derivation cohort of 2701 cancer outpatients from a prospective observational study.
- A risk model was derived and validated in an independent cohort of 1365 patients from the same study.
- Five predictive variables were identified.

Patient Characteristic	Risk Score
Site of cancer	
Very high risk (stomach, pancreas)	2
High risk (lung, lymphoma, gynecologic, bladder, testicular)	1
Prechemotherapy platelet count ≥ 350 x 10^9/L	1
Hemoglobin level < 100 g/L or use of red cell growth factors	1
Prechemotherapy leukocyte count > 11 x 10^9/L	1
BMI ≥ 35 kg/m^2	1



*Rate over a median of 2.5 months.

BMI, body mass index; VTE, venous thromboembolism.

Khorana AA et al. *Blood.* 2008;111:4902-4907.

Qué dicen las guías al respecto…

IONES EN CÁNCER
cáncer en el año 2020"

Second Update of the CHEST Guideline and Expert Panel Report

Published:August 02, 2021•DOI:https://doi.org/10.1016/j.chest.2021.07.055

16. In patients with **acute VTE** in the setting of cancer (cancer-associated thrombosis) we **recommend an oral Xa inhibitor** (apixaban, edoxaban, rivaroxaban) **over low molecular weight heparin** (LMWH) for the initiation and treatment phases of therapy (strong recommendation, moderate-certainty evidence).

Remark: Edoxaban and rivaroxaban appear to be associated with a **higher risk of GI major bleeding** than LMWH in patients with cancer-associated thrombosis (CAT) and a luminal GI malignancy, while **apixaban does not. Apixaban or LMWH may be the preferred option** in patients with luminal GI malignancies.

blood advances

CLINICAL GUIDELINES| February 11, 2021

American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer

Blood Adv (2021) 5 (4): 927–974.
https://doi.org/10.1182/bloodadvances.2020003442

Initial treatment (first week) for patients with active cancer and VTE.

Recommendation 20.

For patients with cancer and VTE, the ASH guideline panel suggests **DOAC (apixaban or rivaroxaban) or LMWH** be used for initial treatment of VTE for patients with cancer (conditional recommendation, very low certainty in the evidence of effects ⨁◯◯◯).

Recommendation 21.

For patients with cancer and VTE, we recommend **LMWH over UFH** for initial treatment of VTE for patients with cancer (strong recommendation, moderate certainty in the evidence of effects ⨁⨁⨁◯).

Recommendation 22.

For patients with cancer and VTE, the ASH guideline panel suggests **LMWH over fondaparinux** for initial treatment of VTE for patients with cancer (conditional recommendation, very low certainty in the evidence of effects ⨁◯◯◯).

Short-term treatment for patients with active cancer (initial 3-6 months).

Recommendation 23.

For the short-term treatment of VTE (3-6 months) for patients with active cancer, the ASH guideline panel suggests **DOAC (apixaban, edoxaban, or rivaroxaban) over LMWH** (conditional recommendation, low certainty in the evidence of effects ⊕⊕◯◯).

Recommendation 30.

For patients with cancer and recurrent VTE despite receiving therapeutic LMWH, the ASH guideline panel suggests **increasing the LMWH dose to a supratherapeutic level or continuing with a therapeutic dose** (conditional recommendation, very low certainty in the evidence of effects ⊕◯◯◯).

Long-term treatment (>6 months) for patients with active cancer and VTE.

Recommendation 34.

For patients with active cancer and VTE requiring long-term anticoagulation (>6 months), the ASH guideline panel suggests using **DOACs or LMWH** (conditional recommendation, very low certainty in the evidence of effects ⊕◯◯◯).

Guía clínica e-Update SEOM de tromboembolismo venoso (TEV) y cáncer (Nov2020)

Tratamiento inicial de TEV en pacientes con cáncer (5-10 días) - Recomendaciones

La **HBPM** a dosis ajustada al peso corporal y los **ACOD (apixaban y rivaroxaban)** son los fármacos de elección para el tratamiento inicial de la TAC (Nivel de evidencia: 1A). Rivaroxaban debe considerarse solo en pacientes con hemorragia de bajo riesgo. Debe usarse con precaución debido a un mayor riesgo de hemorragia principalmente en el tracto GI y GU. Se debe realizar una evaluación específica de interacción fármaco-fármaco antes de usar ACOD.

La **HNF y el fondaparinux** pueden considerarse **agentes alternativos** a la HBPM o a ACOD (Nivel de evidencia: 1B)

Tratamiento a largo plazo de la TEV en pacientes con cáncer: recomendaciones

La **HBPM** a una dosis ajustada al peso corporal y la **ACOD** durante 6 meses son los fármacos de elección para el tratamiento a largo plazo de la TEV en pacientes con cáncer (Nivel de evidencia: 1A). **Apixaban es el único ACOD** con un **perfil de seguridad similar** en comparación con la **HBPM**. **Edoxaban y rivaroxaban aumentan el riesgo de hemorragia GI y probablemente GU**. Se debe realizar una evaluación específica de interacción fármaco-fármaco antes de usar ACOD. Se debe considerar una duración prolongada de la terapia de anticoagulación después de 6 meses para pacientes de alto riesgo, como aquellos con cáncer activo y aquellos que reciben terapia sistémica. Después de los 6 meses, los pacientes deben ser reevaluados con frecuencia para evaluar la relación riesgo-beneficio de continuar el tratamiento anticoagulante (Nivel de evidencia: 2C).

Guía Trombosis SEOM: Guía https://link-springer-com.eu1.proxy.openathens.net/article/10.1007/s12094-019-02263-z
E Update de la guía: https://seom.org/images/e_UPDATE_SEOM_GUIDELINES_2020_161020.pdf

NACOs

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CONSIDERACIONES MANEJO ACOD: FARMACOCINÉTICA

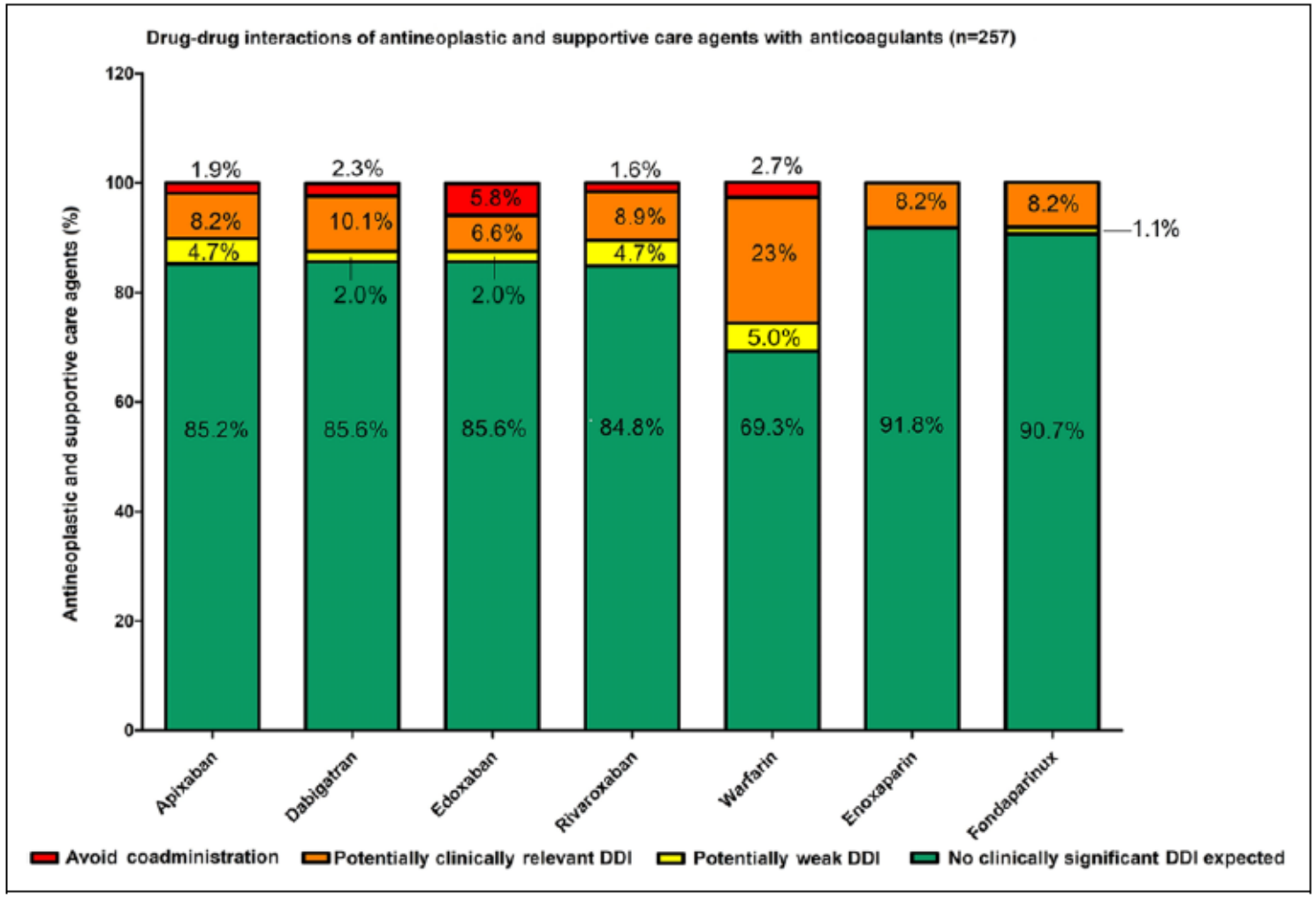
	Warfarin[1,6]	Dabigatran[2]	Rivaroxaban[3]	Apixaban[4]	Edoxaban[5]
Mechanism of action	Inhibitor of vitamin K-dependent factors	Direct thrombin inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor
Oral bioavailability	>95%	~6.5%	80-100%	~50%	~62%
Pro-drug	No	Yes	No	No	No
Food effect	Yes (foods high in vitamin K)	No	Yes (20 mg and 15 mg doses need to be taken with food)	No	No
Renal clearance	Metabolized in liver, and excreted in urine mainly as metabolites	85%	~33%*	~27%	50%
Mean half-life ($t_{1/2}$)	40 h	14-18 h†	5-9 h (young) 11-13 h (elderly)	12 h	10-14 h
T_{max}	72-96 h	0.5-2 h	2-4 h	3-4 h	1-2 h

No head-to-head comparisons between dabigatran, rivaroxaban, apixaban, and edoxaban have been performed in a randomized clinical trial setting. Please refer to the Product Labels for further information.

*direct renal excretion as unchanged active substance
†prolonged in patients with impaired renal function, licensed for patients up to moderate renal impairment
H, hours; OACs, oral anticoagulants; PI, prescribing information; T_{max}, time to reach peak plasma concentration

1. Ansell J et al. *Haematology Am Soc Hematol Educ Program.* 2010:221–228; 2. Dabigatran PI available at www.ema.europa.eu & www.accessdata.fda.gov/scripts/cder/daf/ both accessed November 2017; 3. Rivaroxaban PI available at www.ema.europa.eu & www.accessdata.fda.gov/scripts/cder/daf/ both accessed November 2017; 4. Apixaban PI available at www.ema.europa.eu & www.accessdata.fda.gov/scripts/cder/daf/ both accessed November 2017; 5. Edoxaban PI available at www.ema.europa.eu & www.accessdata.fda.gov/scripts/cder/daf/ both accessed November 2017; 6. Marevan PI available at www.ema.europa.eu & www.accessdata.fda.gov/scripts/cder/daf/ both accessed November 2017

INTERACCIONES ANTINEOPLÁSICOS Y ANTICOAGULANTES



App – SEC Interacciones

InterApp
https://secardiologia.es/publicaciones/apps/11508-interaapp

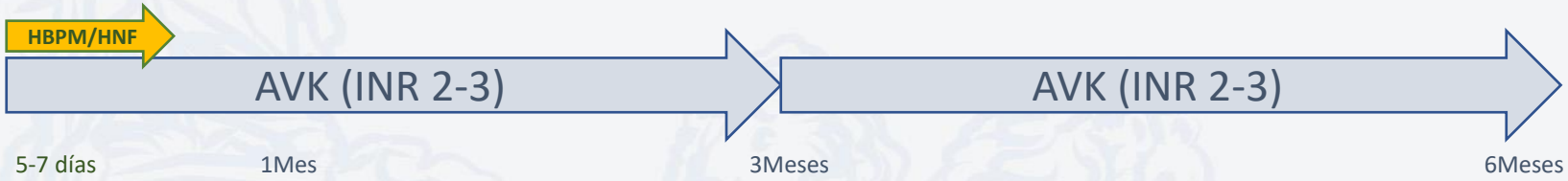
Drug–Drug Interactions of 257 Antineoplastic and Supportive Care Agents With 7 Anticoagulants: A Comprehensive Review of Interactions and Mechanisms. Clin Appl Thromb Hemost. 2020 Jan-Dec;26:1076029620936325.

Tratamiento ETV y Cáncer: estudios previos con anticoagulantes

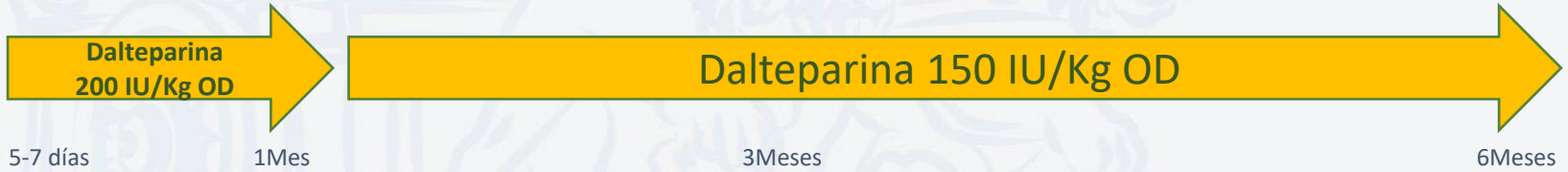
Table 1. Cancer-associated venous thromboembolism: Low-molecular-weight heparin trials

	Trial				
Variable	**CLOT [4]**	**Meyer et al. [8]**	**ONCENOX [7]**	**LITE [5]**	**CATCH [6]**
LMWH	Dalteparin (200 IU/kg per day × 30 days, then 150 IU/kg per day)	Enoxaparin (1.5 mg/kg once daily)	Enoxaparin 1.0 mg/kg b.i.d. × 5 days, then 1.0 mg/kg per day (group 1a) Enoxaparin 1.5 mg/kg daily (group 1b)	Tinzaparin 175 IU/kg daily Treatment duration 3 months	Tinzaparin 175 IU/kg daily
Comparator	Warfarin	Warfarin	Warfarin	Warfarin	Warfarin
n	672	146	102	200	900
Follow-up (months)	6	3	6	3, 12	6

Todos los diseños incluyeron grupo control comparador con AVK



El estudio CLOT* se utilizó de referencia para el diseño de los estudios ACOD en este perfil de paciente



Las HBPM han sido el *gold standard* de tratamiento desde la publicación del estudio CLOT en 2003

O'Connell et al., 2020. Treatment of Cancer-Associated VTE. The Oncologist 2020;25:1–9 .
*Lee AY, et al. Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. N Engl J Med. 2003 Jul 10;349(2):146-53. DOI: 10.1056/NEJMoa025313

EECC de ACODs vs Dalteparina en el tratamiento agudo de TAC

Hokusai-VTE

- **Edoxaban**
- 1046 pacientes
- Objetivo primario : recurrencia TEV + SM

ADAM

- **Apixaban**
- 300 pacientes
- Objetivo primario: Sangrado Mayor (ISTH)

SELECT-D

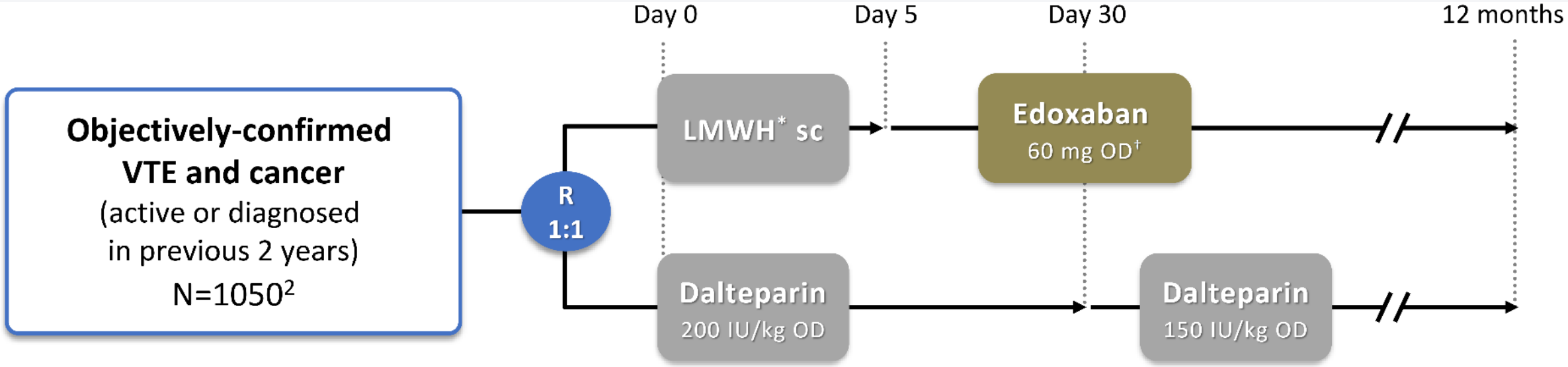
- **Rivaroxaban**
- 406 pacientes
- Objetivo primario: recurrencia TEV

CARAVAGGIO

- **Apixaban**
- 1170 pacientes
- Objetivo primario: recurrencia VTE

Raskob GE et al. N Engl J Med 378;7; 2018; Young AM et al. J Clin Oncol 2018; 36:2017-23;
McBane RD II et al. J Thromb Haemost. 2020;18:411-421; Agnelli G et al. N Engl J Med. 2020;382:1599-1607 .

Hokusai VTE Cancer: Edoxaban vs LMWH[1]



Primary endpoint: Composite of recurrent VTE or major bleeding

Key secondary endpoints: Recurrent VTE, major bleeding

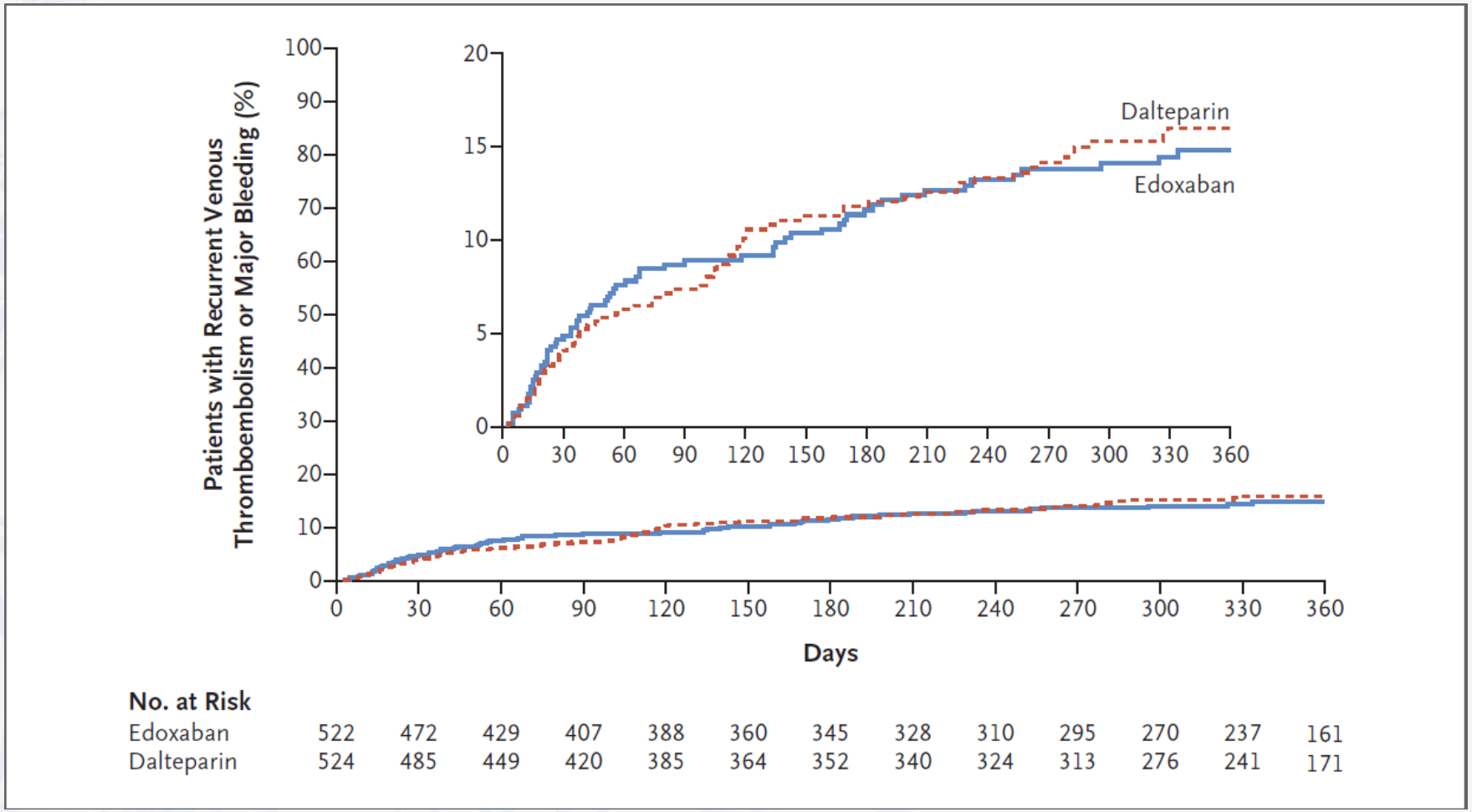
*≥5 days of LMWH. Choice of LMWH type and lead-in duration were left to treating physician

†Edoxaban 30 mg OD for patients requiring dose adjustment for CrCl 30–50 mL/min, body weight ≤60 kg and/or concomitant P–gp inhibitor use

CrCl: creatinine clearance; LMWH: low-molecular-weight heparin; OD: once daily; P-gp: P-glycoprotein; PROBE: Prospective Randomised Open Blinded End-Point; sc: subcutaneous; VTE: venous thromboembolism

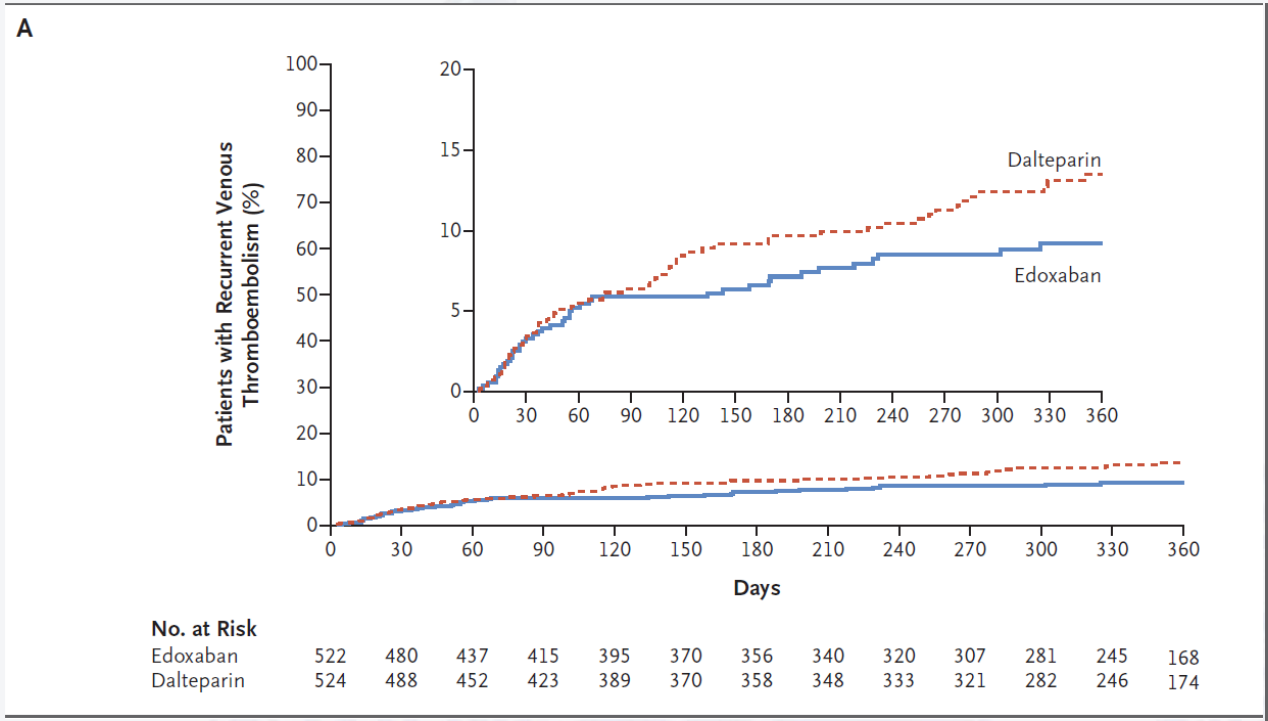
1. Van Es N et al. Thromb Haemost 2015;114:1268–76;
2. Raskob GE et al. N Engl J Med 2018;378:615–24

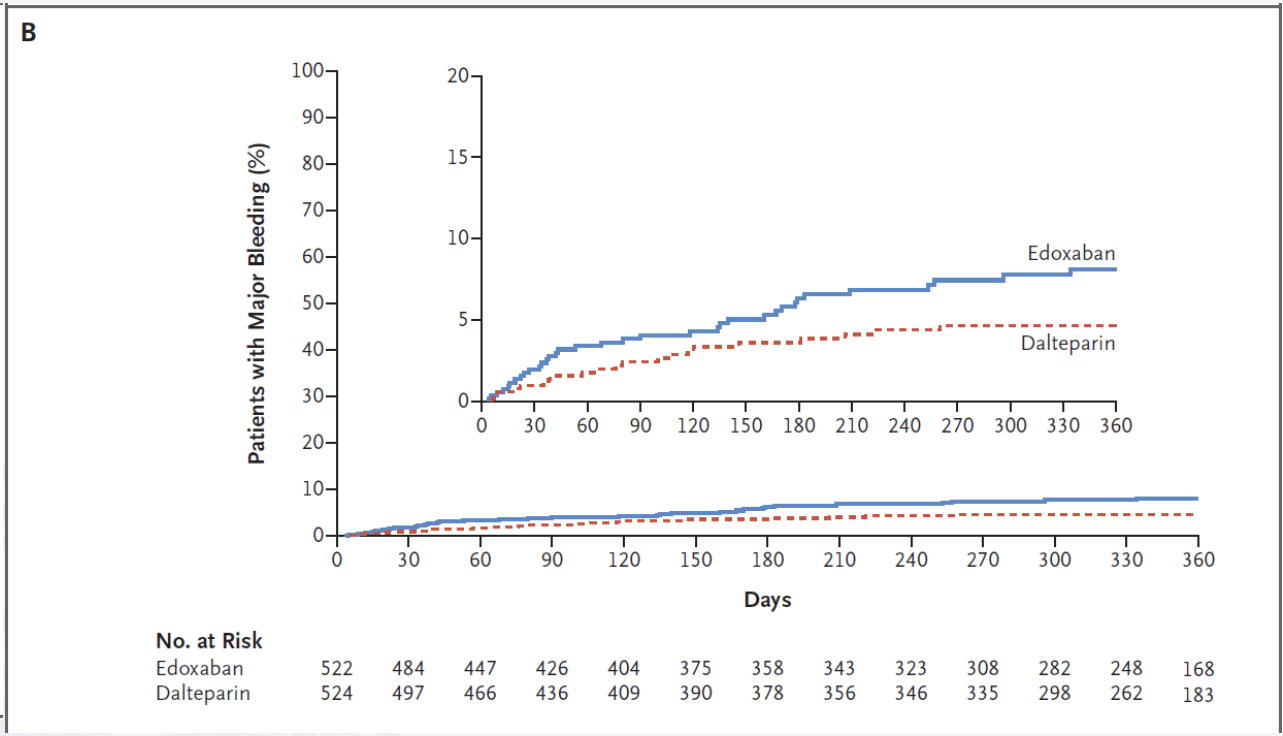
Resultados HOKUSAI VTE – Cancer: Objetivo principal (recurrencia TEV o sangrado mayor)



Raskob GE et al. N Engl J Med 378;7; 2018

Resultados HOKUSAI VTE – Cancer: Objetivos secundarios (recurrencia TEV y sangrado mayor)



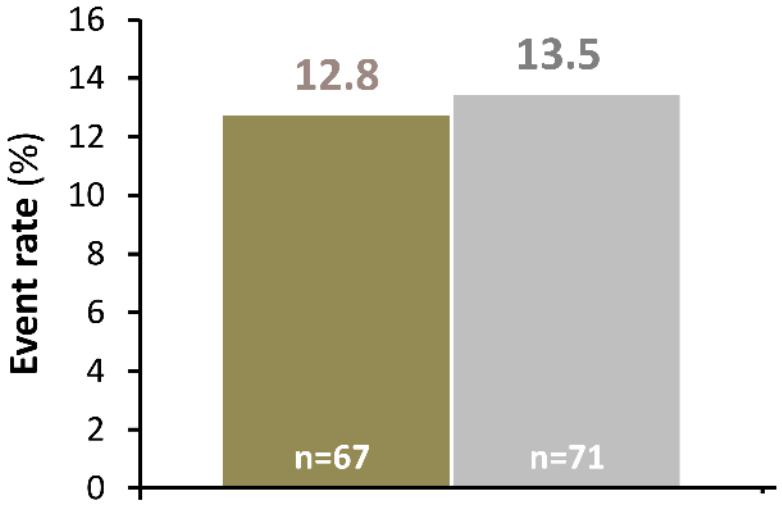


Raskob GE et al. N Engl J Med 378;7; 2018

Hokusai VTE Cancer: Safety and efficacy outcomes[1]

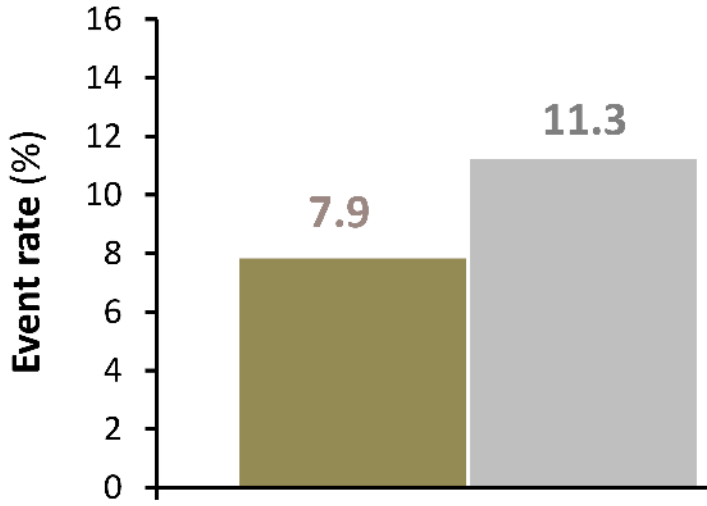
Primary outcome
(Recurrent VTE or major bleeding)

HR: 0.97 (95% CI 0.70–1.36)
p=0.006 for non-inferiority
p=0.87 for superiority



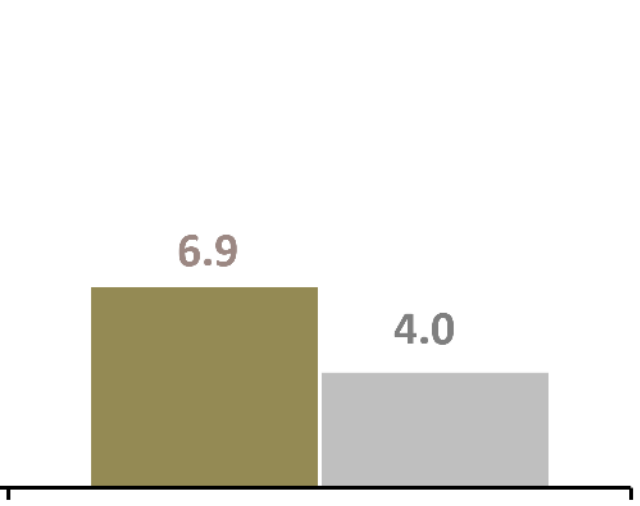
Recurrent VTE*

HR: 0.71
(95% CI 0.48–1.06)
p=0.09



Major bleeding*

HR: 1.77
(95% CI 1.03–3.04)
p=0.04



- No significant interactions between subgroups and treatment, with the exception of GI cancer at randomisation

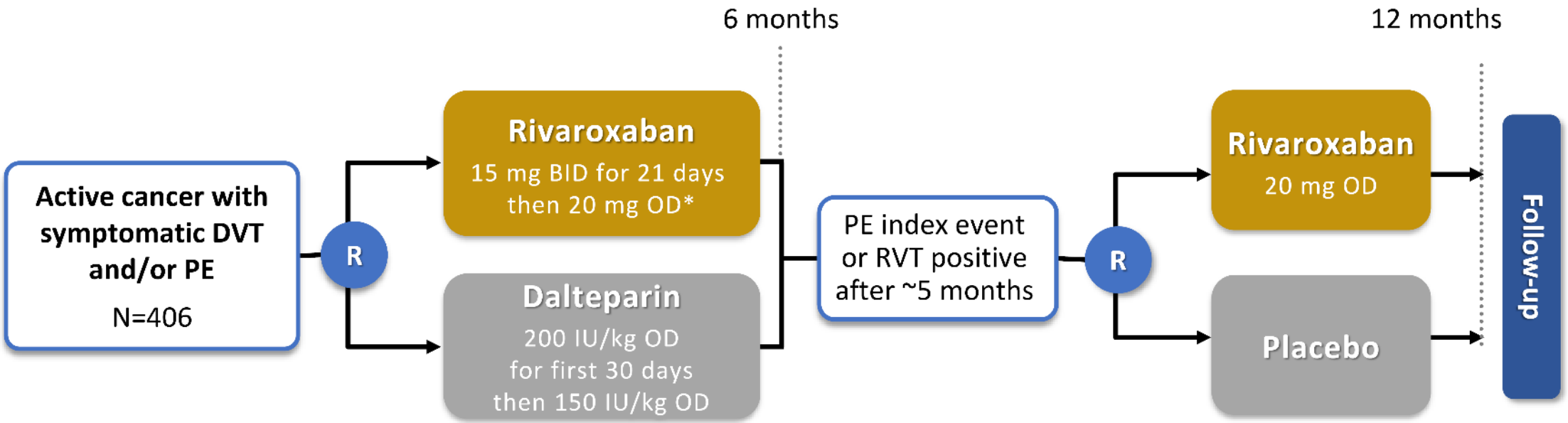
Edoxaban (n=522)
Dalteparin (n=524)

*Secondary outcomes
CI: confidence interval; GI: gastrointestinal; HR: hazard ratio

1. Raskob GE et al. N Engl J Med 2018;378:615–24

SELECT-D: Rivaroxaban vs LMWH[1]

Prospective, randomised, open-label, multicentre pilot phase III study



Efficacy (primary): Rate of VTE recurrence (symptomatic and incidental PE)
Secondary: Rate of major bleeding and CRNM bleeding (also assess survival, health economics)

*Dose reduction or discontinuation specified for different levels of renal impairment. If a patient's platelet counts falls to <50,000/mm^3, rivaroxaban should be discontinued until the platelet count recovers to above 50,000/mm^3

BID: twice daily; CRNM: clinically-relevant nonmajor; PE: pulmonary embolism; RVT: residual vein thrombosis

1. Young AM et al. J Clin Oncol 2018;36:2017–23

Resultados SELECT-D: Objetivo principal (recurrencia TEV) y secundario (sangrado mayor)

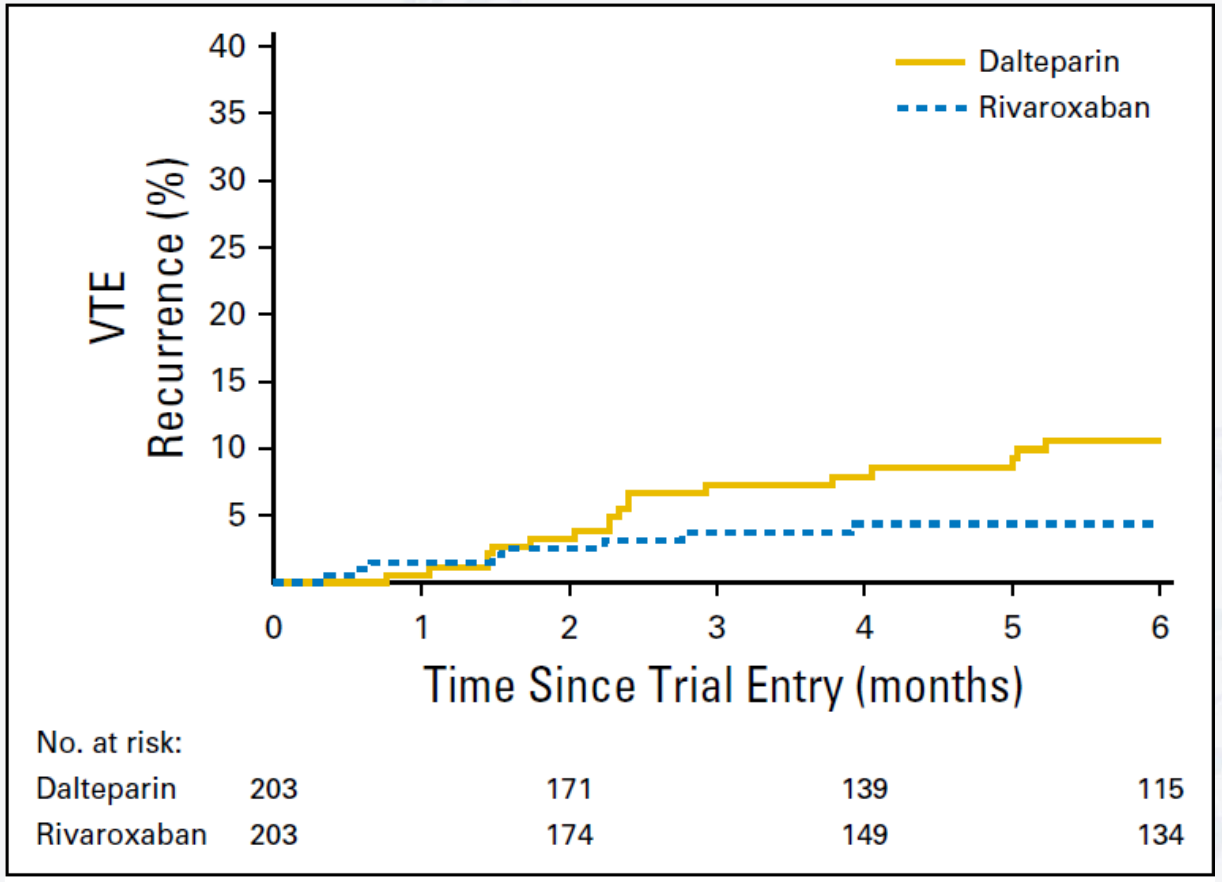


Fig 2. Time to venous thromboembolism (VTE) recurrence within 6 months.

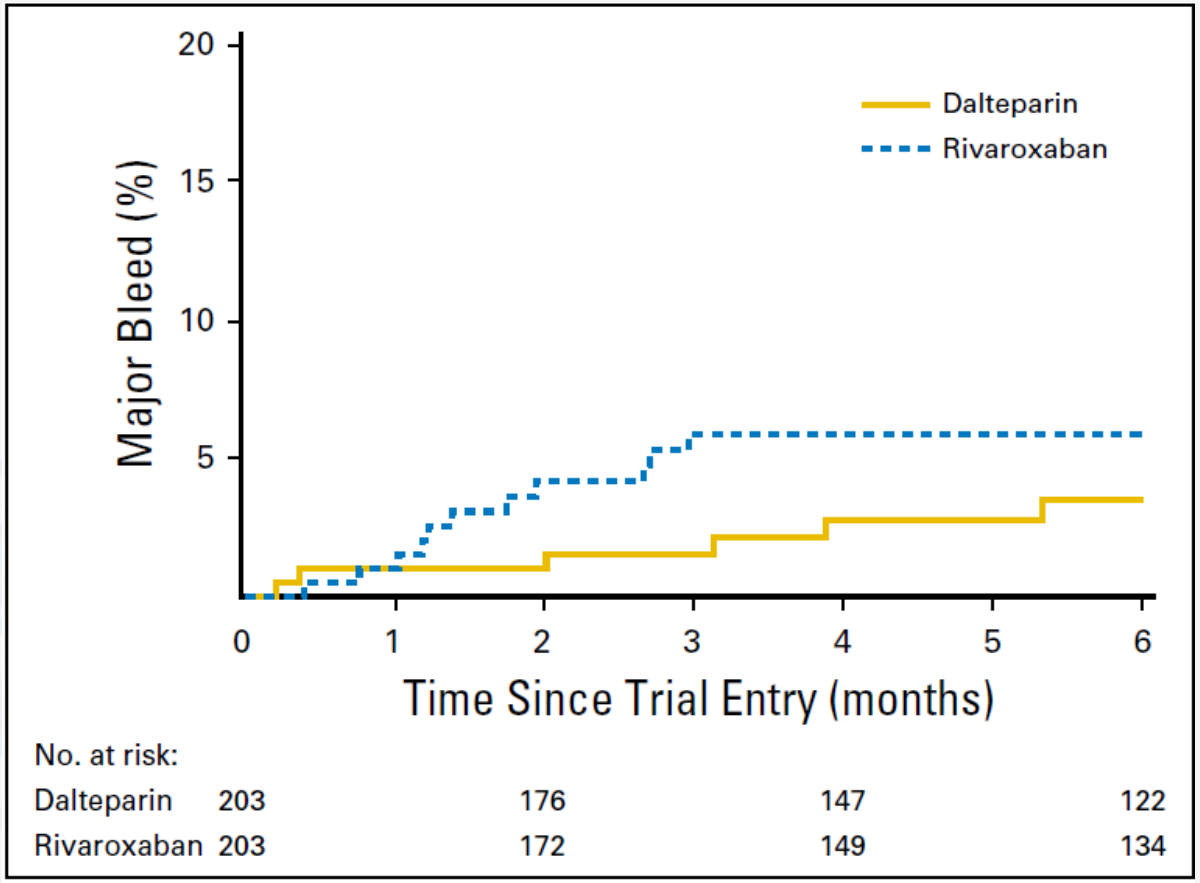


Fig 3. Time to major bleed within 6 months.

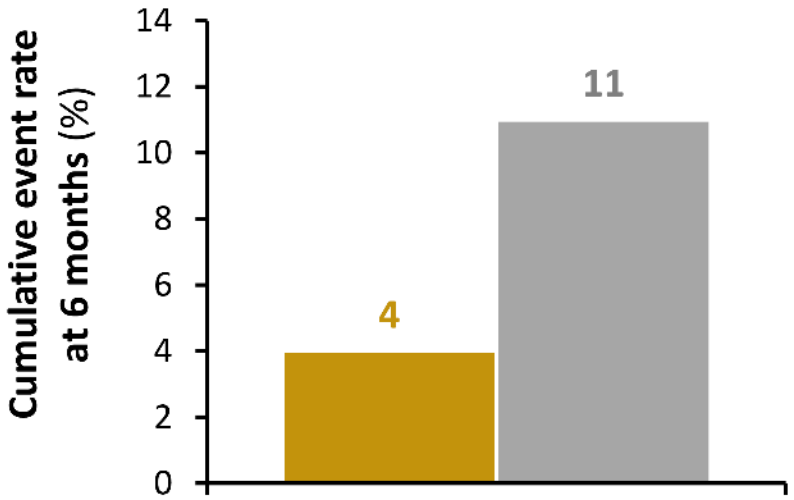
Young AM et al. J Clin Oncol 2018; 36:2017-23

SELECT-D: Safety and efficacy outcomes[1]

Recurrent VTE

HR: 0.43

(95% CI 0.19–0.99)



Major bleeding

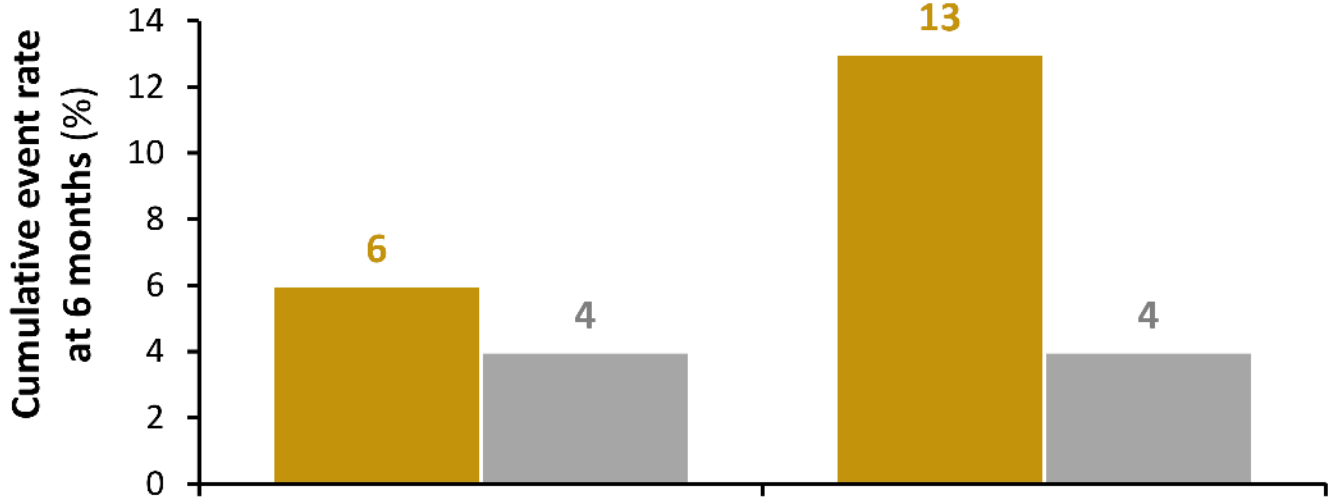
HR: 1.83

(95% CI 0.68–4.96)

CRNM bleeding

HR: 3.76

(95% CI 1.63–8.69)



- 54% of patients completed 6 months of trial treatment
- Most major bleeding events were GI bleeds
- Patients with oesophageal or gastro-oesophageal cancer tended to experience more major bleeds with rivaroxaban than with dalteparin (4 of 11 [36%] vs 1 of 19 [11%])

1. Young AM et al. J Clin Oncol 2018;36:2017–23

Received: 2 August 2019 | Accepted: 14 October 2019
DOI: 10.1111/jth.14662

ORIGINAL ARTICLE

jth

Apixaban and dalteparin in active malignancy-associated venous thromboembolism: The ADAM VTE trial

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Apixaban is not approved for the treatment or prevention of venous thromboembolism in patients with active cancer.

McBane RD II et al. *J Thromb Haemost*. 2020;18:411-421.

Patient Population

- Aged ≥ 18 years.
- Acute VTE[a].
- Confirmed active cancer[b].
- Life expectancy > 60 days.
- ECOG performance status 0, 1, or 2.
- Platelet count ≥ 50 000/µL, INR ≤ 1.6, ALT/AST ≤ 3 x ULN, CrCl ≥ 30 mL/min.

Investigator-initiated[c], multicenter, randomized, open-label, superiority study

300 patients randomized

28 US sites

R

n = 150 → **Apixaban 10 mg BID for 7 days followed by 5 mg BID**

n = 150 → **Dalteparin 200 IU/kg/day for 30 days followed by 150 IU/kg/day**

Treatment duration: 6 months[d]

Apixaban is not approved for the treatment or prevention of venous thromboembolism in patients with active cancer.

ALT/AST, alanine aminotransferase/aspartate aminotransferase; BID, twice daily; CrCl, creatinine clearance; CRNM, clinically relevant non-major; DVT, deep vein thrombosis; ECOG, Eastern Cooperative Oncology Group; INR, international normalized ratio; ISTH, international society on thrombosis and haemostasis; MI, myocardial infarction; PE, pulmonary embolism; TIA, transient ischemic attack; ULN, upper limit of normal; VTE, venous thromboembolism.

McBane RD II et al. *J Thromb Haemost*. 2020;18:411-421.

OBJETIVOS

Primary Safety Outcome
- Major bleeding including fatal bleeding (ISTH definition).

Secondary Safety Outcome
- Composite of ISTH major bleeding and CRNM bleeding.

Secondary Efficacy Outcome
- VTE recurrence including recurrent DVT, PE, fatal PE or arterial thromboembolism (MI, stroke, TIA or peripheral arterial embolism).

[a]The qualifying thrombus could be an acute lower/upper extremity (jugular, innominate, subclavian, axillary, brachial) DVT, PE, splanchnic (hepatic, portal, splenic, mesenteric, renal, gonadal), or cerebral vein thrombosis confirmed by appropriate cross-section imaging.

[b]Any evidence of cancer on cross-sectional or positron emission tomography imaging, metastatic disease, and/or cancer-related surgery, chemotherapy or radiation therapy within the prior 6 months.

[c]The primary investigator, in collaboration with the Academic and Community Cancer Research United (ACCRU) research consortium, was responsible for the trial design, protocol development, data collection, statistical analysis, data interpretation, manuscript preparation, and trial oversight. Institutional review boards at each participating center approved the protocol.

[d]At monthly intervals: patient interview (outcome events, ECOG status, adverse event recording, medication reconciliation, study drug compliance); laboratory testing (complete blood count, liver and renal function testing); anticoagulation satisfaction and bruise surveys.

Apixaban is not approved for the treatment or prevention of venous thromboembolism in patients with active cancer.

ALT/AST, alanine aminotransferase/aspartate aminotransferase; BID, twice daily; CrCl, creatinine clearance; CRNM, clinically relevant non-major; DVT, deep vein thrombosis; ECOG, Eastern Cooperative Oncology Group; INR, international normalized ratio; ISTH, international society on thrombosis and haemostasis; MI, myocardial infarction; PE, pulmonary embolism; TIA, transient ischemic attack; ULN, upper limit of normal; VTE, venous thromboembolism.

McBane RD II et al. *J Thromb Haemost*. 2020;18:411-421.

RESULTADOS: CARACTERÍSTICAS BASALES DE LOS PACIENTES

	Apixaban (n = 150)	Dalteparin (n = 150)	*P* Value
Age (years)	64.4 (11.3)	64.0 (10.8)	0.4857
Female gender, n (%)	78 (52.0%)	77 (51.3%)	0.9080
Creatinine clearance 30 to 50 mL/min, n (%)	14 (9.3%)	14 (9.3%)	1.0000
Platelet count 50 to 100 000/mm^3, n (%)	10 (6.7%)	13 (8.7%)	0.5150
Body weight, mean (SD)	84.8 (23.2)	86.8 (20.5)	0.1712
< 60 kg, n (%)	19 (12.9%)	13 (8.8%)	0.2528
> 120 kg, n (%)	10 (6.8%)	8 (5.4%)	0.6161
Qualifying Thrombus, n (%)			
Any PE	81 (55.1%)	75 (50.7%)	0.4463
Any DVT	71 (48.3%)	70 (47.3%)	0.8632
PE only	64 (43.5%)	57 (38.5%)	0.3804
PE with DVT	17 (11.6%)	18 (12.2%)	0.8739
DVT only	54 (36.7%)	52 (35.1%)	0.7747
Lower extremity DVT	46 (31.3%)	50 (33.8%)	0.6479
Upper extremity DVT	25 (17.0%)	21 (14.2%)	0.5048
Cerebral VT	2 (1.4%)	0 (0.0%)	0.1545
Splanchnic VT	12 (8.2%)	27 (18.2%)	0.0106
Missing	3 (2.0%)	2 (1.4%)	

Apixaban is not approved for the treatment or prevention of venous thromboembolism in patients with active cancer.

DVT, deep vein thrombosis; PE, pulmonary embolism; SD, standard deviation; VT, venous thrombosis.

McBane RD II et al. *J Thromb Haemost*. 2020;18:411-421.

Resultados: Eventos clínicos durante el periodo de tratamiento

	Apixaban (n = 145)	Dalteparin (n = 142)	Hazard Ratio (95% CI)	*P* Value
Primary safety endpoint			NE	0.138
Major bleeding, n (%)	0 (0.0%)	2 (1.4%)		
Secondary safety endpoint				
CRNM bleeding, n (%)	9 (6.2%)	7 (4.2%)		
Major plus CRNM bleeding, n (%)	9 (6.2%)	9 (6.3%)	0.931 (0.43 to 2.02)	0.8816
Secondary efficacy endpoint*			0.099 (0.013 to 0.780)	0.0281
Venous thromboembolism, n (%)	1 (0.7%)	9 (6.3%)		
Pulmonary embolism	0 (0.0%)	1 (0.7%)		
Lower extremity DVT	0 (0.0%)	4 (2.8%)		
Upper extremity DVT	0 (0.0%)	2 (1.4%)		
Splanchic VT	0 (0.0%)	2 (1.4%)		
Cerebral VT	1 (0.7%)	0 (0.0%)		
Arterial thrombosis, n (%)	1 (0.7%)	1 (0.7%)		
Mortality, n (%)	23 (16%)	15 (11%)	1.40 (0.82 to 2.43)	0.3078

*Six of the VTE events occurred on treatment. The remaining four occurred within three days of going off treatment. Of the recurrent VTE events, five were symptomatic. There was one arterial thrombosis in each treatment group. These events occurred in patients who also suffered concurrent venous thrombi and were thus already accounted for.

Apixaban is not approved for the treatment or prevention of venous thromboembolism in patients with active cancer.

CI, confidence interval; CRNM, clinical relevant non-major; DVT, deep vein thrombosis; NE, not estimable; VT, venous thrombosis; VTE, venous thromboembolism.

McBane RD II et al. *J Thromb Haemost*. 2020;18:411-421.

Resultados: Cuestionarios de calidad de vida

Cycle*	Fear of Bleeding Limited Participation in Vigorous Activities	Fear of Bleeding Limited Participation in Activities of Daily Life	Concern for Excessive Bruising	Limited My Diet	Added Stress to My Life	Was Difficult to Carry Out	Caused Me a Great Deal of Worry	Caused Me a Great Deal of Irritation	Caused Me a Great Deal of Frustration	Was a Burden to Me	Negatively Impacted My Quality of Life	Confidence That the Drug Protected Me From Clots	I am Satisfied With My Blood Thinner
0	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
1	Neutral	Neutral	Favors apixaban	Neutral	Favors apixaban	Favors apixaban	Favors apixaban	Favors apixaban	Favors apixaban	Favors apixaban	Favors apixaban	Favors dalteparin	Favors apixaban
2	Neutral	Neutral	Neutral	Neutral	Favors apixaban	Favors apixaban	Favors apixaban	Favors apixaban	Favors apixaban	Favors apixaban	Neutral	Neutral	Favors apixaban
3	Neutral	Neutral	Neutral	Neutral	Favors apixaban	Neutral	Favors apixaban	Favors apixaban	Neutral	Favors apixaban	Neutral	Neutral	Favors apixaban
4	Neutral	Neutral	Favors apixaban	Neutral	Neutral	Favors apixaban	Neutral	Favors apixaban	Neutral	Favors apixaban	Neutral	Neutral	Favors apixaban
5	Neutral	Neutral	Favors apixaban	Neutral	Favors apixaban	Favors apixaban	Neutral	Favors apixaban	Neutral	Favors apixaban	Neutral	Neutral	Neutral
6	Neutral	Neutral	Favors apixaban	Neutral	Neutral	Favors apixaban	Neutral	Favors apixaban	Neutral	Favors apixaban	Neutral	Neutral	Neutral

*The designation of "Favors" was applied when differences reached a *P* value < 0.05.
Yellow highlighted boxes pictorially denotes "Favors Apixaban".
Blue highlighted boxes denotes "Favors Dalteparin".
White boxes denotes those questions where there were no significant differences between arms.

Apixaban is not approved for the treatment or prevention of venous thromboembolism in patients with active cancer.

McBane RD II et al. *J Thromb Haemost*. 2020;18:411-421.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

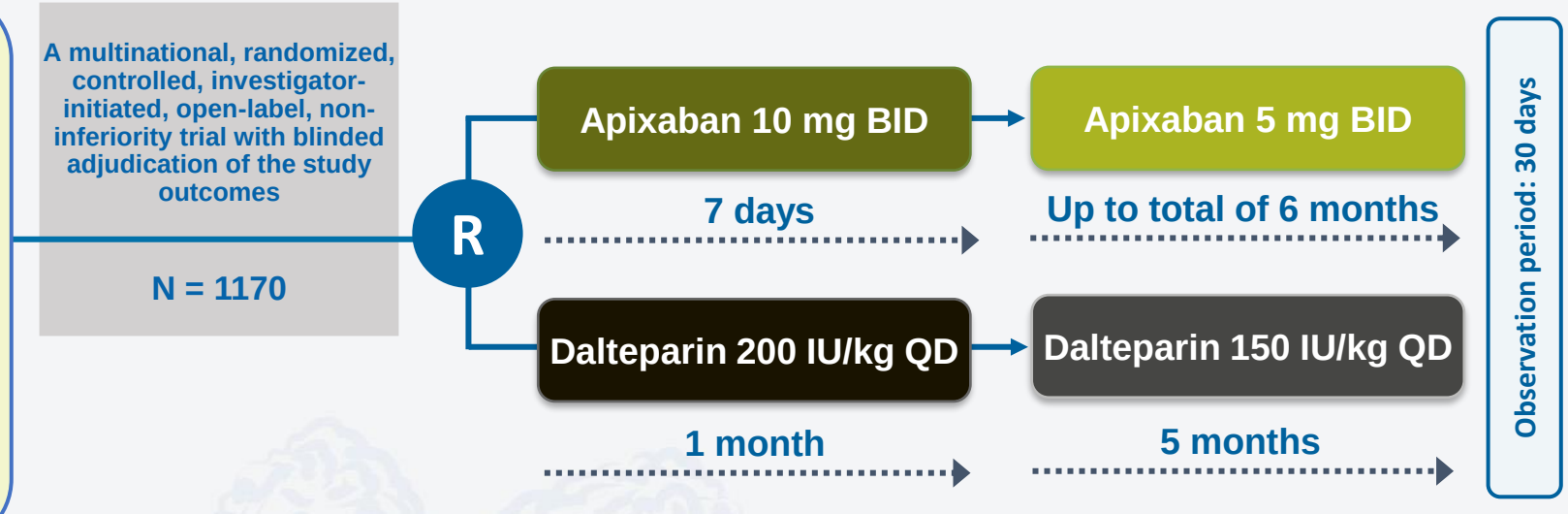
Apixaban for the Treatment of Venous Thromboembolism Associated with Cancer

Giancarlo Agnelli, M.D., Cecilia Becattini, M.D., Guy Meyer, M.D., Andres Muñoz, M.D., Menno V. Huisman, M.D., Jean M. Connors, M.D., Alexander Cohen, M.D., Rupert Bauersachs, M.D., Benjamin Brenner, M.D., Adam Torbicki, M.D., Maria R. Sueiro, M.D., Catherine Lambert, M.D., Gualberto Gussoni, M.D., Mauro Campanini, M.D., Andrea Fontanella, M.D., Giorgio Vescovo, M.D., and Melina Verso, M.D., for the Caravaggio Investigators*

Agnelli G et al. *N Engl J Med*. 2020;382:1599-1607

Poblacion de pacientes

- Edad ≥ 18 años.
- Pacientes consecutivos con una TVP de extremidad inferior proximal sintomática o incidental recién diagnosticada (ubicada en la vena poplítea o más proximal) o EP (que involucra una arteria pulmonar segmentaria o más proximal).
- Cualquier tipo de cáncer (excepto el carcinoma de piel de células basales o de células escamosas, tumor cerebral primario o metástasis intracerebral conocida y leucemia aguda).



Efficacy and safety of apixaban in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt) in patients with active cancer have not been established.[2]

La dosis diaria máxima permitida de dalteparina fue de 18 000 UI. Durante el ensayo, el protocolo se modificó para permitir ajustes de dosis de dalteparina en función del recuento de plaquetas de acuerdo con el etiquetado específico del país del medicamento.
Los fármacos del ensayo se podrían suspender temporalmente en caso de un recuento de plaquetas inferior a 50 000 / mm3 o cualquier afección asociada con un mayor riesgo de hemorragia, incluida la cirugía, los procedimientos invasivos o el deterioro de la función renal.

ACTS, Anti-Clot Treatment Scale; BID, twice daily; CRNM, clinically relevant non-major; DVT, deep vein thrombosis; ISTH; International Society on Thrombosis and Haemostasis; MACE; major cardiovascular event; PE, pulmonary embolism; QD, once daily; QoL, quality of life; SmPC, summary of product characteristics; VTE, venous thromboembolism; VTEt, venous thromboembolism treatment.

1. Agnelli G et al. *N Engl J Med*. 2020;382:1599-1607 and supplementary appendix available online; 2. Apixaban SmPC available at https://www.ema.europa.eu/en/medicines/human/EPAR/eliquis#product-information-section accessed April 2020.

OBJETIVOS

End point primario

- TEV recurrente confirmada objetivamente (TVP proximal de las extremidades inferiores (sintomática o incidental), TVP sintomática de las extremidades superiores y EP (sintomática, incidental o fatal) que ocurrieron durante el período de prueba de 6 meses.

End point del principio de seguridad

- Sangrado mayor (definición de ISTH más sangrado que resulta en una intervención quirúrgica) en el período de prueba hasta 72 horas después de la última dosis.

End point secundarios

- Componentes individuales del resultado primario de eficacia; recurrencia sintomática de TEV; muerte por todas las causas; combinación del resultado primario de eficacia más hemorragia mayor; combinación del resultado primario de eficacia más hemorragia mayor más muerte por cualquier causa; compuesto del resultado primario de eficacia más muerte por cualquier causa; Hemorragia CRNM; hemorragia mayor más CRNM; MAZO; todos los eventos de TEV; QoL según ACTs; interrupción permanente por motivos de seguridad

Efficacy and safety of apixaban in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt) in patients with active cancer have not been established.[2]

ACTS, Anti-Clot Treatment Scale; BID, twice daily; CRNM, clinically relevant non-major; DVT, deep vein thrombosis; ISTH; International Society on Thrombosis and Haemostasis; MACE; major cardiovascular event; PE, pulmonary embolism; QD, once daily; QoL, quality of life; SmPC, summary of product characteristics; VTE, venous thromboembolism; VTEt, venous thromboembolism treatment.

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XXIV Simposio de Revisiones en Cáncer
"Tratamiento médico del cáncer en el año 2022"

RESULTADOS:
Características de los pacientes al inicio del estudio

Characteristic*	Apixaban n = 576	Dalteparin n = 579
Age, years	67.2 ± 11.3	67.2 ± 10.9
Male sex, n (%)	292 (50.7)	276 (47.7)
Weight, kg	75.7 ± 16.1	76.1 ± 16.7
Platelet count < 100 000/mm^3, n (%)	21 (3.6)	22 (3.8)
Creatinine clearance ≤ 50 mL/min, n (%)	51 (8.9)	61 (10.5)
Qualifying diagnosis of venous thromboembolism, n (%)		
Pulmonary embolism with or without deep vein thrombosis	304 (52.8)	334 (57.7)
Deep vein thrombosis only	272 (47.2)	245 (42.3)
Symptomatic deep vein thrombosis or pulmonary embolism	460 (79.9)	465 (80.3)
Incidental deep vein thrombosis or pulmonary embolism†	116 (20.1)	114 (19.7)
History of venous thromboembolism before index event, n (%)	45 (7.8)	61 (10.5)
Type of cancer, n (%)		
Active	559 (97.0)	565 (97.6)
Recurrent locally advanced or metastatic	389 (67.5)	396 (68.4)
Cancer treatment, n (%)‡		
At enrollment	350 (60.8)	367 (63.4)
Within previous 6 months	143 (24.8)	129 (22.3)
During trial period	344 (59.7)	346 (59.8)
ECOG performance-status score, n (%)§		
0	186 (32.3)	170 (29.4)
1	281 (48.8)	277 (47.8)
2	109 (18.9)	132 (22.8)

Efficacy and safety of apixaban in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt) in patients with active cancer have not been established.[2]

*Plus–minus values are means ± standard deviation.
†Incidental venous thromboembolism (deep-vein thrombosis or pulmonary embolism) was defined as thromboembolism detected by imaging tests performed for reasons other than clinical suspicion of venous thromboembolism.
‡Cancer treatments include anticancer drug therapy (cytotoxic, hormonal, targeted, or immunomodulatory), radiotherapy, surgery, or a combination of these therapies.
§Eastern Cooperative Oncology Group performance-status scores range from 0 to 4, with higher values indicating greater disability.

DVT, deep vein thrombosis; ECOG, Eastern Cooperative Oncology Group; PE, pulmonary embolism; SmPC, summary of product characteristics; VTEt, venous thromboembolism treatment.

1. Agnelli G et al. *N Engl J Med*. 2020;382:1599-1607; 2. Apixaban SmPC available at https://www.ema.europa.eu/en/medicines/human/EPAR/eliquis#product-information-section accessed April 2020.

RESULTADOS:
Tipos de cáncer al inicio del estudio

	Apixaban n = 576	Dalteparin n = 579
Solid tumor, n (%)		
Colorectal	121 (21.0%)	113 (19.5%)
Lung	105 (18.2%)	95 (16.4%)
Breast	79 (13.7%)	76 (13.1%)
Genitourinary	66 (11.5%)	73 (12.6%)
Gynecological	60 (10.4%)	59 (10.2%)
Pancreatic or hepatobiliary	44 (7.6%)	43 (7.4%)
Upper gastrointestinal	23 (4.0%)	31 (5.4%)
Head and neck	14 (2.4%)	8 (1.4%)
Bone/soft tissue	11 (1.9%)	7 (1.2%)
Skin - melanoma	4 (0.7%)	7 (1.2%)
Other	16 (2.8%)	15 (2.6%)
Hematological malignancy, n (%)	33 (5.7%)	52 (9.0%)

Efficacy and safety of apixaban in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt) in patients with active cancer have not been established.[2]

DVT, deep vein thrombosis; PE, pulmonary embolism; SmPC, summary of product characteristics; VTEt, venous thromboembolism treatment.

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XXIV Simposio de Revisiones en Cáncer
"Tratamiento médico del cáncer en el año 2022"

RESULTADOS:
Terapias con fármacos contra el cáncer*

Anticancer Drug Therapies Continuing After Randomization†	Apixaban n = 576	Dalteparin n = 579
Antimetabolites, n (%)	109 (18.9%)	120 (20.7%)
Platinum-based chemotherapy, n (%)	85 (14.8%)	85 (14.7%)
Monoclonal antibodies, n (%)	46 (8.0%)	57 (9.8%)
Antiangiogenic monoclonal antibodies, n (%)	15 (2.6%)	21 (3.6%)
Checkpoint inhibitors, n (%)	8 (1.4%)	13 (2.2%)
Non-antiangiogenic monoclonal antibodies, n (%)	24 (4.2%)	23 (4.0%)
Bevacizumab, n (%)	11 (1.9%)	19 (3.3%)
Taxanes, n (%)	39 (6.8%)	36 (6.2%)
Hormonal therapy, n (%)	57 (9.9%)	60 (10.4%)
Topoisomerase inhibitors, n (%)	27 (4.7%)	25 (4.3%)
Alkylating agents, n (%)	19 (3.3%)	15 (2.6%)
Anthracyclines, n (%)	16 (2.8%)	9 (1.6%)
Vinca alkaloids, n (%)	7 (1.2%)	10 (1.7%)
Kinase inhibitors, n (%)	23 (4.0%)	28 (4.8%)
Immunomodulating agents, n (%)	10 (1.7%)	12 (2.1%)
Proteasome inhibitors, n (%)	7 (1.2%)	4 (0.7%)
Antitumor antibiotics, n (%)	2 (0.3%)	1 (0.2%)

Anticancer Drug Therapies Started After Randomization	Apixaban n = 576	Dalteparin n = 579
Antimetabolites, n (%)	64 (11.1%)	60 (10.4%)
Platinum-based chemotherapy, n (%)	49 (8.5%)	46 (7.9%)
Monoclonal antibodies, n (%)	34 (5.9%)	40 (6.9%)
Antiangiogenic monoclonal antibodies, n (%)	13 (2.3%)	10 (1.7%)
Checkpoint inhibitors, n (%)	12 (2.1%)	18 (3.1%)
Non-antiangiogenic monoclonal antibodies, n (%)	9 (1.6%)	13 (2.2%)
Bevacizumab, n (%)	9 (1.6%)	8 (1.4%)
Taxanes, n (%)	38 (6.6%)	38 (6.6%)
Hormonal therapy, n (%)	36 (6.3%)	42 (7.3%)
Topoisomerase inhibitors, n (%)	21 (3.6%)	17 (2.9%)
Alkylating agents, n (%)	15 (2.6%)	12 (2.1%)
Anthracyclines, n (%)	15 (2.6%)	9 (1.6%)
Vinca alkaloids, n (%)	9 (1.6%)	10 (1.7%)
Kinase inhibitors, n (%)	16 (2.8%)	19 (3.3%)
Immunomodulating agents, n (%)	2 (0.3%)	5 (0.9%)
Proteasome inhibitors, n (%)	3 (0.5%)	5 (0.9%)
Antitumor antibiotics, n (%)	3 (0.5%)	0 (0%)

*Patients could receive more than one anticancer drug.
†Treatment does not include anticancer therapy initiated after randomization.

Efficacy and safety of apixaban in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt) in patients with active cancer have not been established.[2]

DVT, deep vein thrombosis; PE, pulmonary embolism; SmPC, summary of product characteristics; VTE, venous thromboembolism; VTEt, venous thromboembolism treatment.

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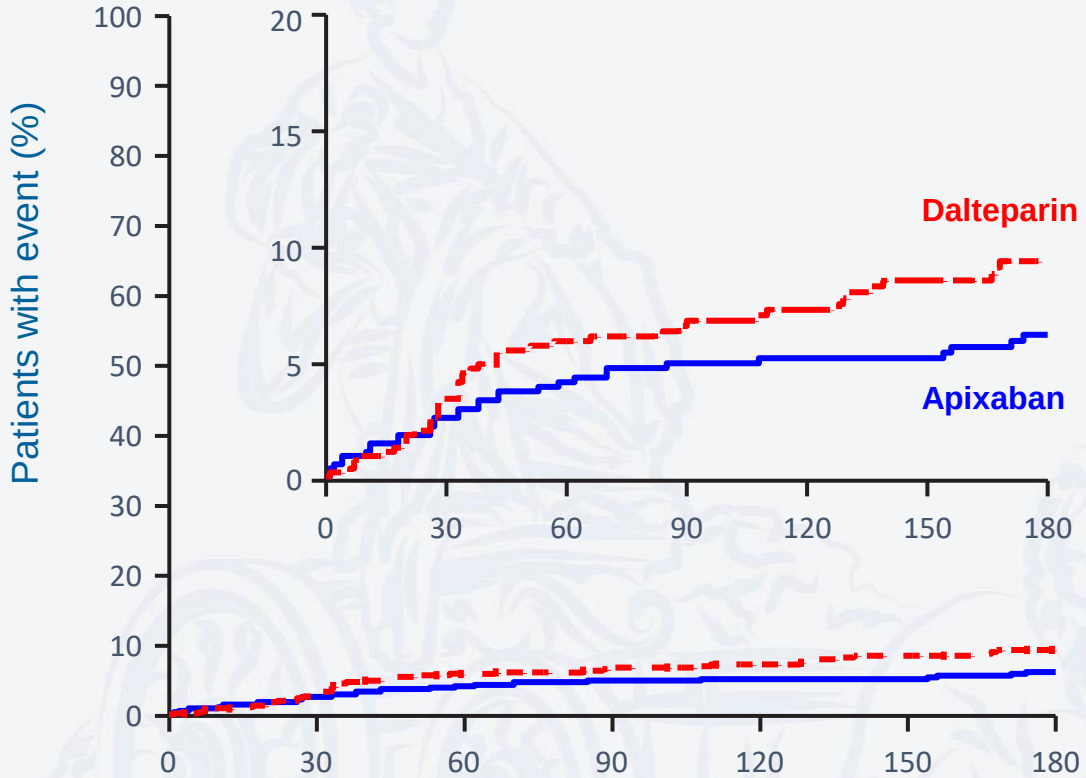
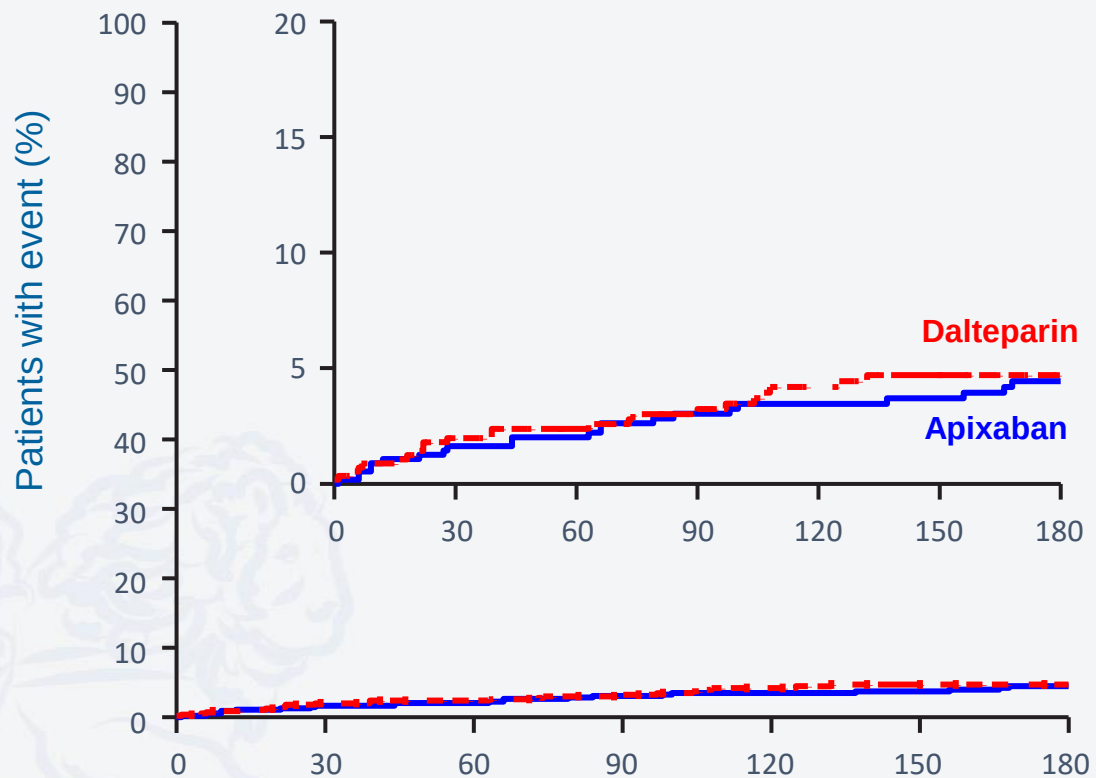
RESULTADOS:
ETV recurrente y hemorragia mayor

Recurrent Venous Thromboembolism



Number at Risk							
Dalteparin	579	507	462	417	383	352	217
Apixaban	575	522	481	453	424	399	241

Major Bleeding



Number at Risk							
Dalteparin	579	510	473	430	387	355	222
Apixaban	575	527	490	458	427	402	238

Efficacy and safety of apixaban in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt) in patients with active cancer have not been established.[2]

DVT, deep vein thrombosis; PE, pulmonary embolism; SmPC, summary of product characteristics; VTEt, venous thromboembolism treatment.

1. Agnelli G et al. *N Engl J Med*. 2020;382:1599-1607; 2. Apixaban SmPC available at https://www.ema.europa.eu/en/medicines/human/EPAR/eliquis#product-information-section accessed April 2020.

RESULTADOS: eficacia y seguridad durante los 6 meses tras aleatorización*

Outcome	Apixaban n = 576	Dalteparin n = 579	Hazard Ratio 95% CI	*P* Value
Primary efficacy outcome, n (%)†				
Recurrent venous thromboembolism‡	32 (5.6)	46 (7.9)	0.63 (0.37 to 1.07)	< 0.001 for non-inferiority; 0.09 for superiority
Recurrent deep vein thrombosis	13 (2.3)	15 (2.6)	0.87 (0.34 to 2.21)	
Recurrent pulmonary embolism	19 (3.3)	32 (5.5)	0.54 (0.29 to 1.03)	
Fatal pulmonary embolism§	4 (0.7)	3 (0.5)	1.93 (0.40 to 9.41)	
Primary safety outcome, n (%)				
Major bleeding¶	22 (3.8)	23 (4.0)	0.82 (0.40 to 1.69)	0.60
Major gastrointestinal bleeding	11 (1.9)	10 (1.7)	1.05 (0.44 to 2.50)	
Major non-gastrointestinal bleeding	11 (1.9)	13 (2.2)	0.68 (0.21 to 2.20)	
Secondary outcomes, n (%)				
Recurrent venous thromboembolism or major bleeding	51 (8.9)	66 (11.4)	0.70 (0.45 to 1.07)	
Clinically relevant non-major bleeding	52 (9.0)	35 (6.0)	1.42 (0.88 to 2.30)	
Major or clinically relevant non-major bleeding‖	70 (12.2)	56 (9.7)	1.16 (0.77 to 1.75)	
Death from any cause**	135 (23.4)	153 (26.4)	0.82 (0.62 to 1.09)	
Event-free survival††	422 (73.3)	397 (68.6)	1.36 (1.05 to 1.76)	

*The overall trial period for the primary efficacy outcome was the time from randomization through 6 months.
†The primary efficacy outcome (objectively confirmed recurrent venous thromboembolism) during the 6-month trial period was also the primary outcome.
‡Two of the recurrences of venous thromboembolism in the apixaban group were upper-extremity deep vein thrombosis.
§ A total of 3 patients in the apixaban group and 3 patients in the dalteparin group died from unexplained causes for which pulmonary embolism could not be ruled out.
¶One patient in the apixaban group had an event that was categorized as major bleeding since it resulted in a surgical intervention.
‖In patients who had more than one event, only the first event was counted.
**Death was assessed up to 210 days after randomization.
††Event-free survival was defined as the absence of recurrent venous thromboembolism, major bleeding, or death.

Efficacy and safety of apixaban in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt) in patients with active cancer have not been established.[2]

CI, confidence interval; DVT, deep vein thrombosis; PE, pulmonary embolism; SmPC, summary of product characteristics; VTEt, venous thromboembolism treatment.

1. Agnelli G et al. *N Engl J Med*. 2020;382:1599-1607; 2. Apixaban SmPC available at https://www.ema.europa.eu/en/medicines/human/EPAR/eliquis#product-information-section accessed April 2020.

RESULTADOS: Localización del Sangrado mayor

Primary Safety Outcomes (Major Bleeding)	Apixaban n = 576	Dalteparin n = 579
Major bleeding, n (%)	22 (3.8%)	23 (4.0%)
Fatal†	0	2
Abdominal	1	0
Intracranial	0	2
Intraspinal	0	1
Pericardial	1	0
Intra-articular	0	1
Retroperitoneal	0	1
Cutaneous	1	1
Genito-urinary	4	1
Lung	1	1
Muscle	0	2
Upper airways	1	2
Gastrointestinal	11	10
Upper	5	6
Lower	6	4
Undetermined site	2	2

†The site of fatal bleeding was intracranial in 1 patient and retroperitoneal in 1 patient.

Efficacy and safety of apixaban in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt) in patients with active cancer have not been established.[2]

CRNM, clinically relevant non-major; DVT, deep vein thrombosis; PE, pulmonary embolism; SmPC, summary of product characteristics; VTE, venous thromboembolism; VTEt, venous thromboembolism treatment.

1. Agnelli G et al. *N Engl J Med*. 2020;382:1599-1607 supplementary appendix available online; 2. Apixaban SmPC available at https://www.ema.europa.eu/en/medicines/human/EPAR/eliquis#product-information-section accessed April 2020.

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RESULTADOS:
ETV recurrente (análisis por ITT)

Subgroup Type	Apixaban n/N (%)	Dalteparin n/N (%)	Interaction *P* Value	Hazard Ratio (95% CI)
Characteristic presenting diagnosis				
DVT only	18/272 (6.6)	28/245 (11.4)	0.3337	
PE with/without DVT	14/304 (4.6)	18/334 (5.4)		
Characteristic presenting diagnosis				
Symptomatic	29/460 (6.3)	39/465 (8.4)	0.4176	
Unsuspected	3/116 (2.6)	7/114 (6.1)		
Age group				
< 65 years	7/199 (3.5)	27/201 (12.9)	0.0065	
≥ 65 to < 75 years	16/206 (7.8)	14/192 (7.3)		
> 75 years	9/171 (5.3)	5/177 (2.8)		
Gender				
Male	19/292 (6.5)	21/276 (7.6)	0.3064	
Female	13/284 (4.6)	25/303 (8.3)		
Race				
White	24/454 (5.3)	35/473 (7.4)		
Other than White	1/18 (5.6)	1/13 (7.7)		
Not applicable	7/104 (6.7)	10/93 (10.8)		
Weight				
≤ 60 kg	8/148 (5.4)	14/166 (8.4)	0.9713	
> 60 to 90 kg	19/338 (5.6)	22/293 (7.5)		
> 90 kg	5/90 (5.6)	10/120 (8.3)		
Platelet at randomization				
≤ 100 000/mL	2/21 (9.5)	1/22 (4.5)		
> 100 000/mL	30/553 (5.4)	45/550 (8.2)		
Surgery 2 weeks prior to randomization				
Yes	0/13 (0.0)	0/7 (0.0)		
No	32/563 (5.7)	46/572 (8)		
RLA or metastasis at randomization				
Yes	23/385 (6)	34/386 (8.8)	0.9026	
No	9/191 (4.7)	12/193 (6.2)		

Subgroup Type	Apixaban n/N (%)	Dalteparin n/N (%)	Interaction *P* Value	Hazard Ratio (95% CI)
Survival in study				
Died < 3 months	7/72 (9.7)	9/88 (10.2)	0.5877	
Alive plus early discontinuation < 3 months	3/25 (12)	4/31 (12.9)		
Stay in study ≥ 3 months	22/477 (4.6)	33/459 (7.2)		
Active cancer at randomization				
Active	31/559 (5.5)	46/565 (8.1)		
Past	1/17 (5.9)	0/14 (0)		
Type of cancer at randomization				
Solid tumor	30/542 (5.5)	44/526 (8.4)		
Hematological	2/33 (6.1)	2/52 (3.8)		
Receiving cancer treatment at randomization				
No	9/247 (3.6)	14/235 (6)	0.6656	
Yes	23/329 (7)	32/344 (9.3)		
Baseline Eastern Cooperative Oncology Group (ECOG)				
0	9/186 (4.8)	6/170 (3.5)	0.1721	
1	17/281 (6)	33/277 (11.9)		
≥ 2	6/109 (5.5)	7/132 (5.3)		
Body mass index at randomization				
≤ 25 kg/m^2	11/216 (5.1)	22/245 (9)	0.4200	
> 25 to ≤ 30 kg/m^2	16/233 (6.9)	13/194 (6.7)		
> 30 kg/m^2	5/127 (3.9)	11/140 (7.9)		
Creatinine clearance at randomization				
≤ 30 mL/min	0/1 (0.0)	0/1 (0.0)		
> 30 to ≤ 80 mL/min	9/257 (3.5)	19/253 (7.5)		
> 80 mL/min	23/300 (7.7)	26/307 (8.5)		
Any chemotherapy/radiotherapy during the study				
No	6/200 (3)	14/196 (7.1)	0.2094	
Yes	26/376 (6.9)	32/383 (8.4)		

CI, confidence interval; DVT, deep vein thrombosis; PE, pulmonary embolism; SmPC, summary of product characteristics; VTEt, venous thromboembolism treatment.

Efficacy and safety of apixaban in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt) in patients with active cancer have not been established.[2]

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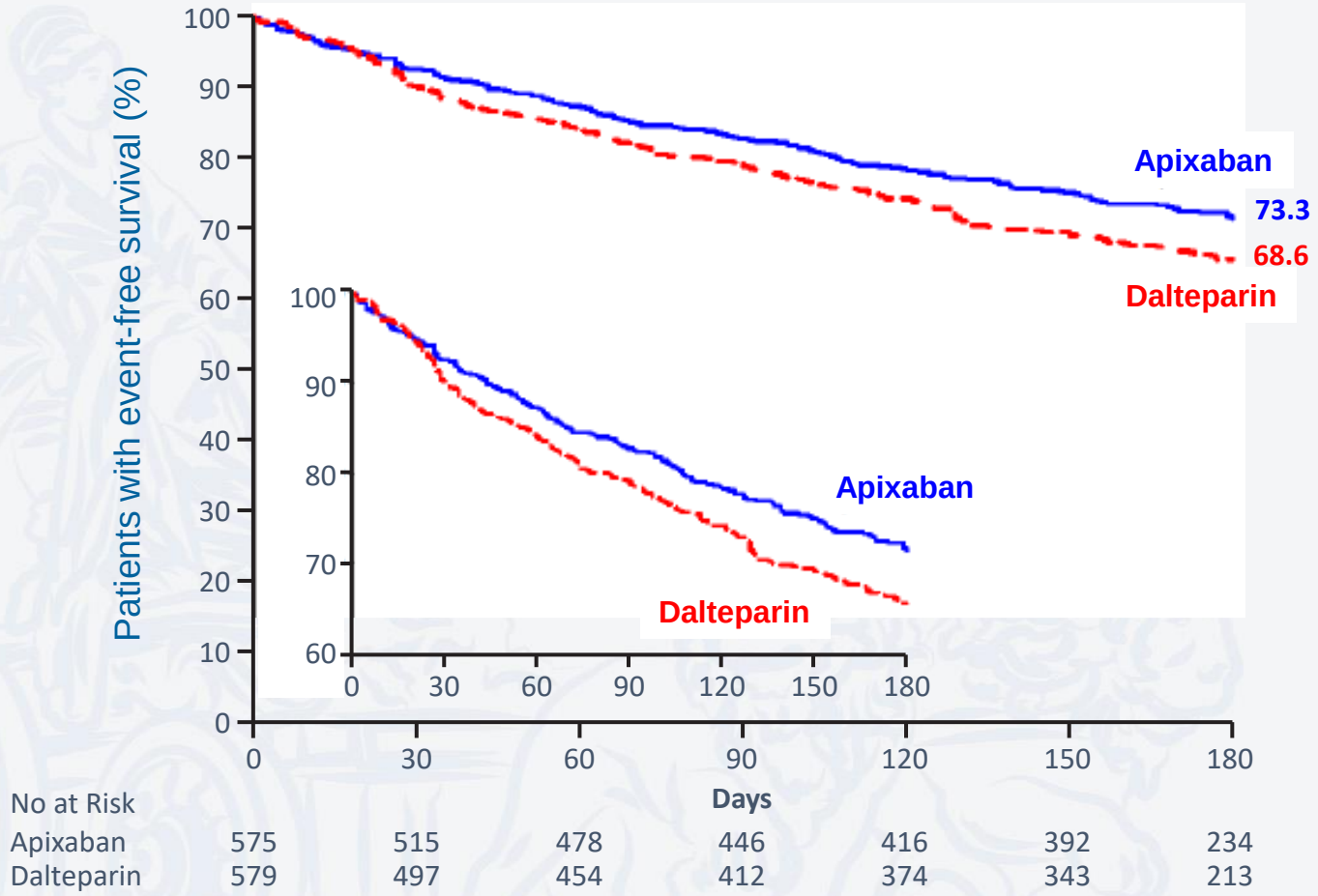
RESULTADOS: Supervivencia libre de eventos



HR=1.36 (1.05 to 1.76)

Event-free survival was defined as the absence of recurrent venous thromboembolism, major bleeding or death.

Efficacy and safety of apixaban in the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE (VTEt) in patients with active cancer have not been established.[2]

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1. Agnelli G et al. *N Engl J Med*. 2020;382:1599-1607 and supplementary appendix available online; 2. Apixaban SmPC available at https://www.ema.europa.eu/en/medicines/human/EPAR/eliquis#product-information-section accessed April 2020.

CONCLUSIONES

Guía clínica e-Update SEOM de tromboembolismo venoso (TEV) y cáncer (Nov2020)

Tratamiento inicial de TEV en pacientes con cáncer (5-10 días) - Recomendaciones

La **HBPM** a dosis ajustada al peso corporal y los **ACOD (apixaban y rivaroxaban)** son los fármacos de elección para el tratamiento inicial de la TAC (Nivel de evidencia: 1A). Rivaroxaban debe considerarse solo en pacientes con hemorragia de bajo riesgo. Debe usarse con precaución debido a un mayor riesgo de hemorragia principalmente en el tracto GI y GU. Se debe realizar una evaluación específica de interacción fármaco-fármaco antes de usar ACOD.

La **HNF y el fondaparinux** pueden considerarse **agentes alternativos** a la HBPM o a ACOD (Nivel de evidencia: 1B)

Tratamiento a largo plazo de la TEV en pacientes con cáncer: recomendaciones

La **HBPM** a una dosis ajustada al peso corporal y la **ACOD** durante 6 meses son los fármacos de elección para el tratamiento a largo plazo de la TEV en pacientes con cáncer (Nivel de evidencia: 1A). **Apixaban es el único ACOD** con un **perfil de seguridad similar** en comparación con la **HBPM**. **Edoxaban y rivaroxaban aumentan el riesgo de hemorragia GI y probablemente GU**. Se debe realizar una evaluación específica de interacción fármaco-fármaco antes de usar ACOD. Se debe considerar una duración prolongada de la terapia de anticoagulación después de 6 meses para pacientes de alto riesgo, como aquellos con cáncer activo y aquellos que reciben terapia sistémica. Después de los 6 meses, los pacientes deben ser reevaluados con frecuencia para evaluar la relación riesgo-beneficio de continuar el tratamiento anticoagulante (Nivel de evidencia: 2C).

Guía Trombosis SEOM: Guía https://link-springer-com.eu1.proxy.openathens.net/article/10.1007/s12094-019-02263-z
E Update de la guía: https://seom.org/images/e_UPDATE_SEOM_GUIDELINES_2020_161020.pdf

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Gracias

ARÁN