Cáncer y trombosis

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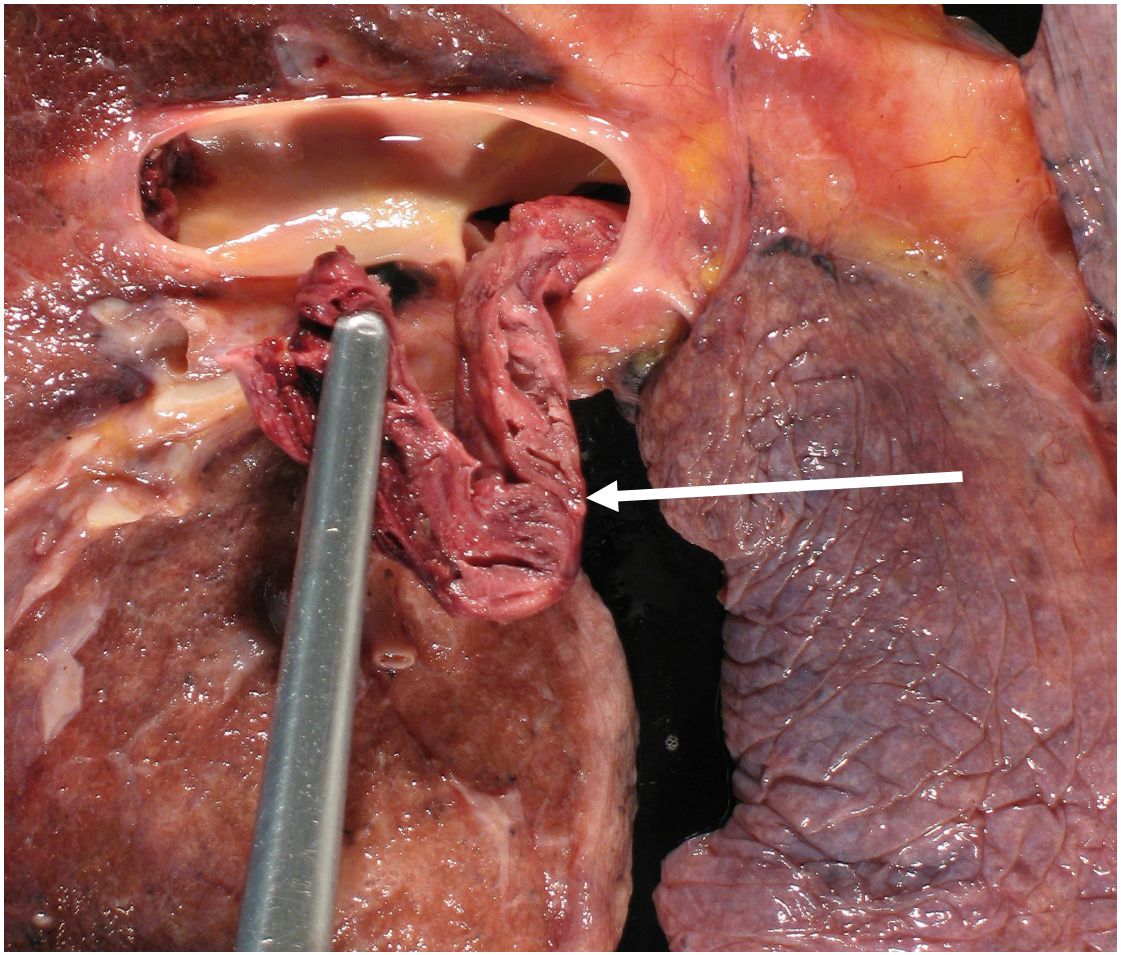
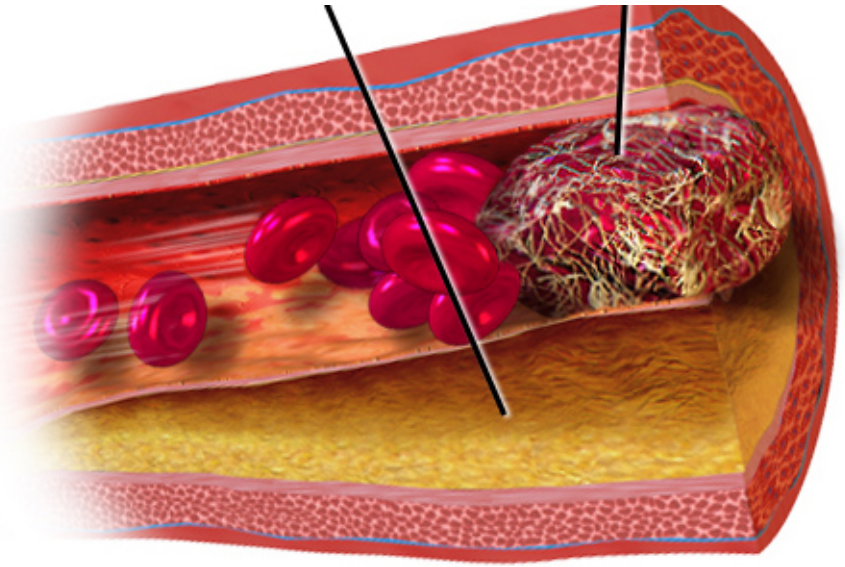
Hospital General Universitario Gregorio Marañón

¿Qué es un trombo?



Trombo = coágulo



Historical Perspective

Trousseau's syndrome (1865)[1]

The hypercoagulable state associated with cancer

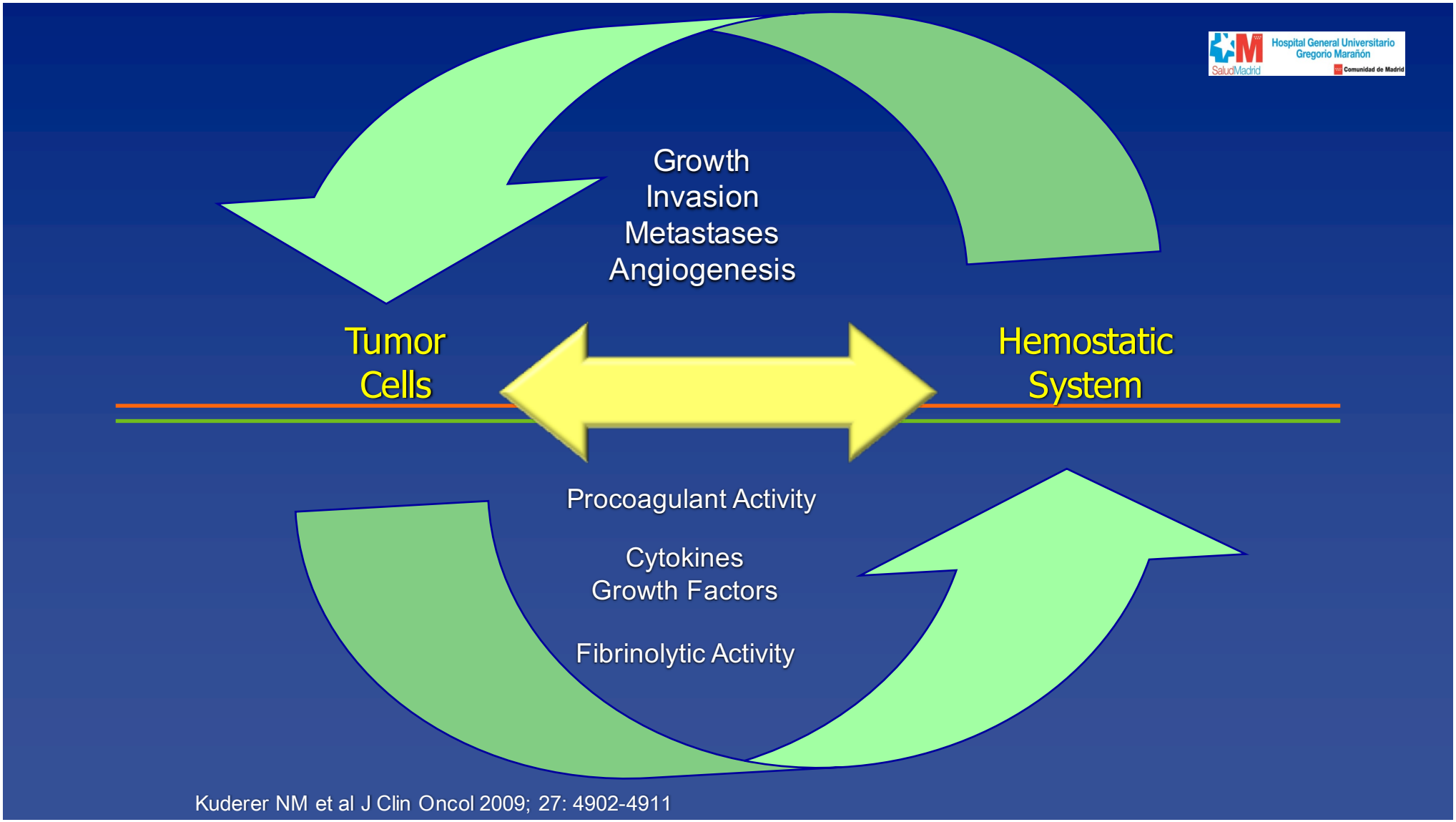
" I have always been struck with the frequency with which cancerous patients are affected with painful oedema of the superior or inferior extremities…." *New Syndenham Society – 1865*

"In other cases, in which the absence of appreciable tumour made me hesitate as to the nature of the disease of the stomach, my doubts were removed, and I knew the disease to be cancerous when phlegmasia alba dolens appeared in one of the limbs."

Lectures in Clinical Medicine, 1865

Armand Trousseau
1801-1867

1. Trousseau A. Clinique médicale de l'hôtel Dieu de Paris, 2nd ed. Paris:JB Ballere et Fils 1865



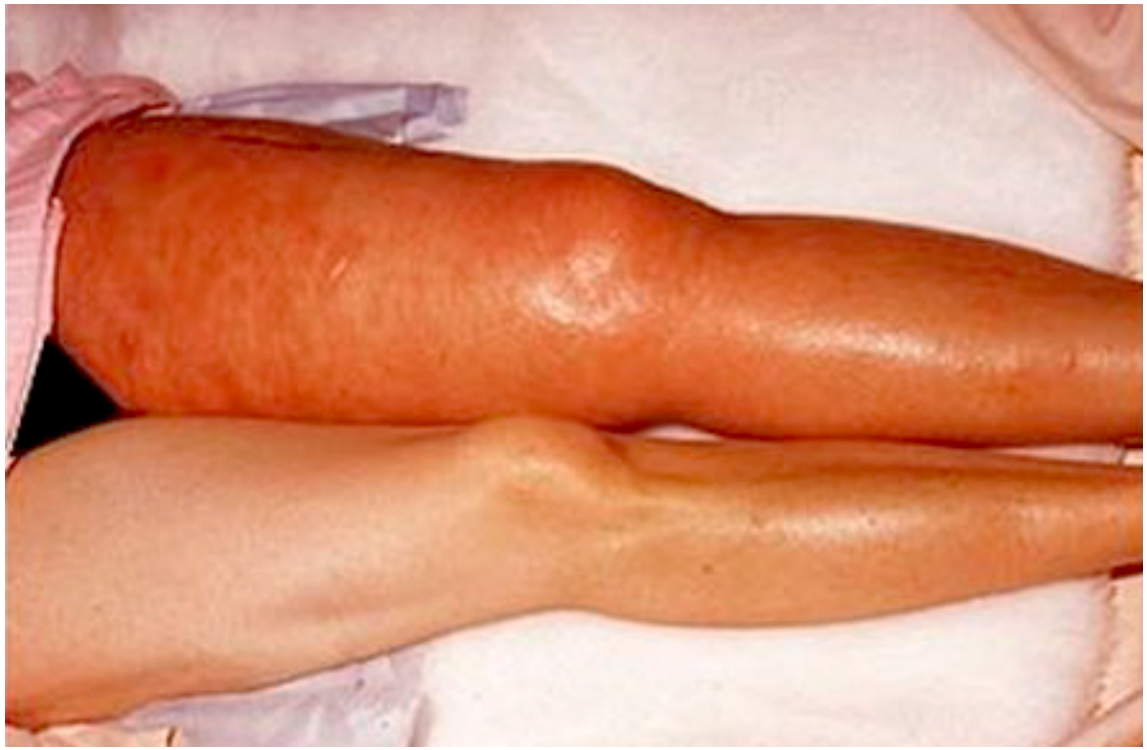
Kuderer NM et al J Clin Oncol 2009; 27: 4902-4911

Trombosis arteraial y venosa

- Trombo en una arteria: trombosis arterial, ejemplos
  - Infarto agudo de miocardio (arterias coronarias)
  - Ictus (arterias cerebrales)
  - Otros

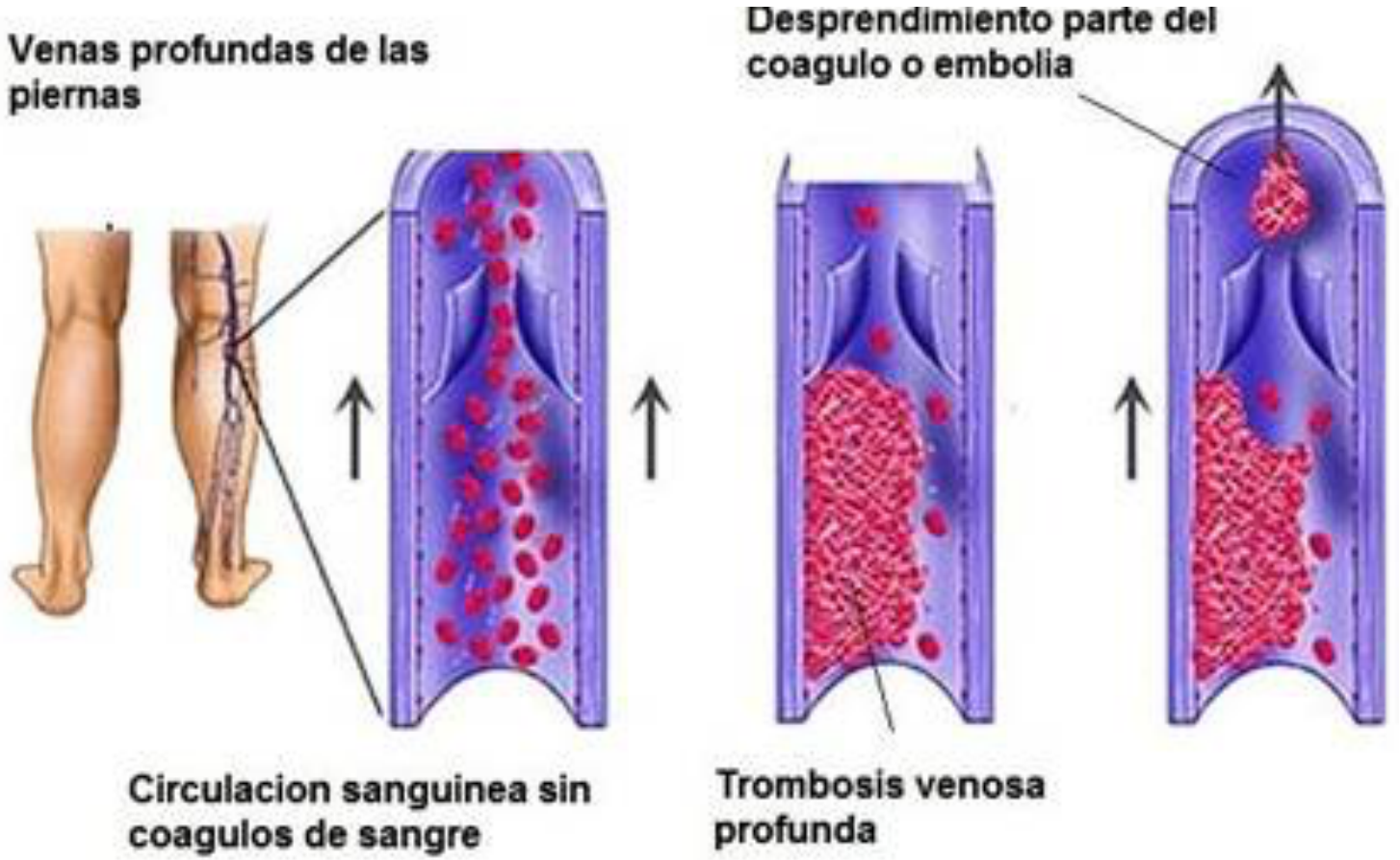
- Trombo en una vena: trombosis venosa
  - Trombosis venosa profunda (trombosis en venas de las piernas)
  - Embolia de pulmón (trombo en las venas pulmonares)
  - Trombosis asociadas a los catéteres (port-a-cath)
  - Trombosis en venas abdominales (trombosis viscerales esplácnicas)

Trombosis venosa profunda

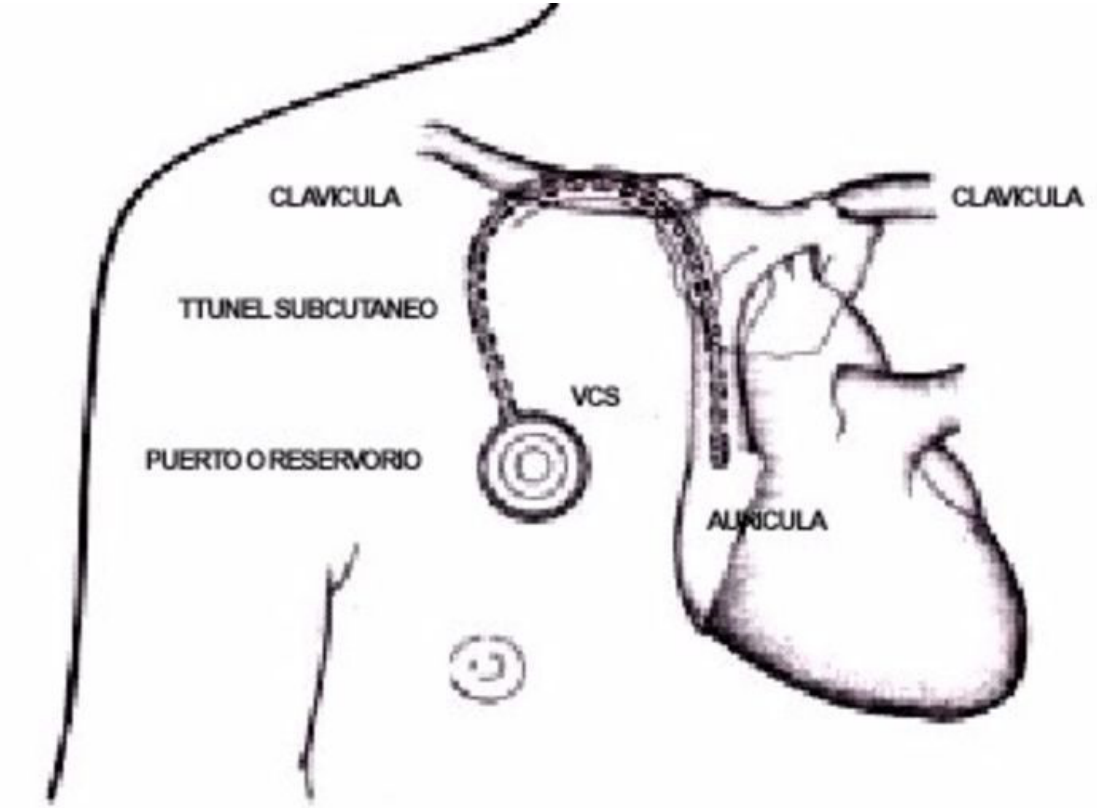


Edema + dolor + eritema

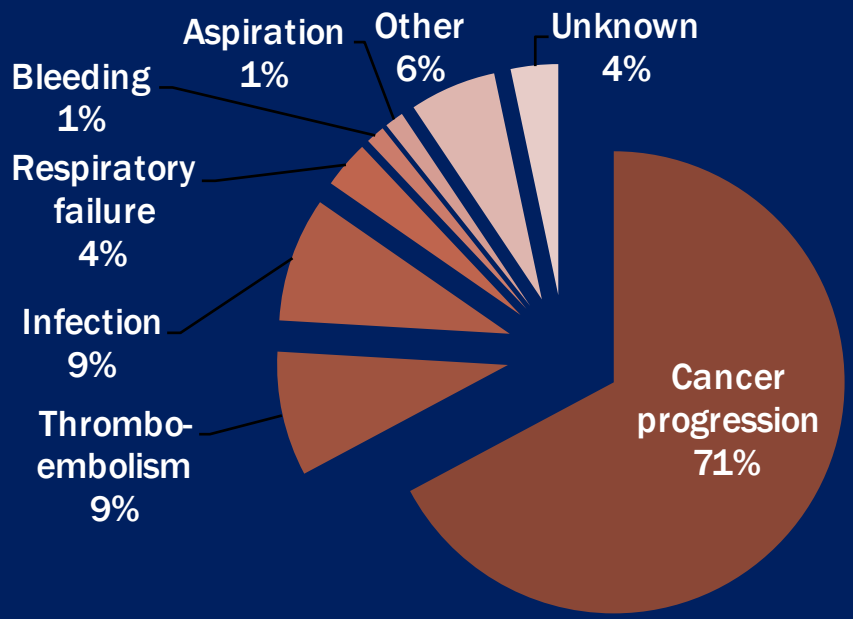
Embolia de pulmón



Trombosis asociada a catéter port-a-cath



WHY YOU SHOULD CARE: VTE AND MORTALITY



2nd leading cause of death in cancer patients

- Accounts for 9% of deaths [1]
- Associated with early mortality during chemotherapy (HR=6.98)[2]
- 47-fold increased risk of mortality from VTE[1]

1. Khorana AA et al. *J Thromb Haemost* 2007
2. Kuderer NM et al *ASCO* 2008 #9521

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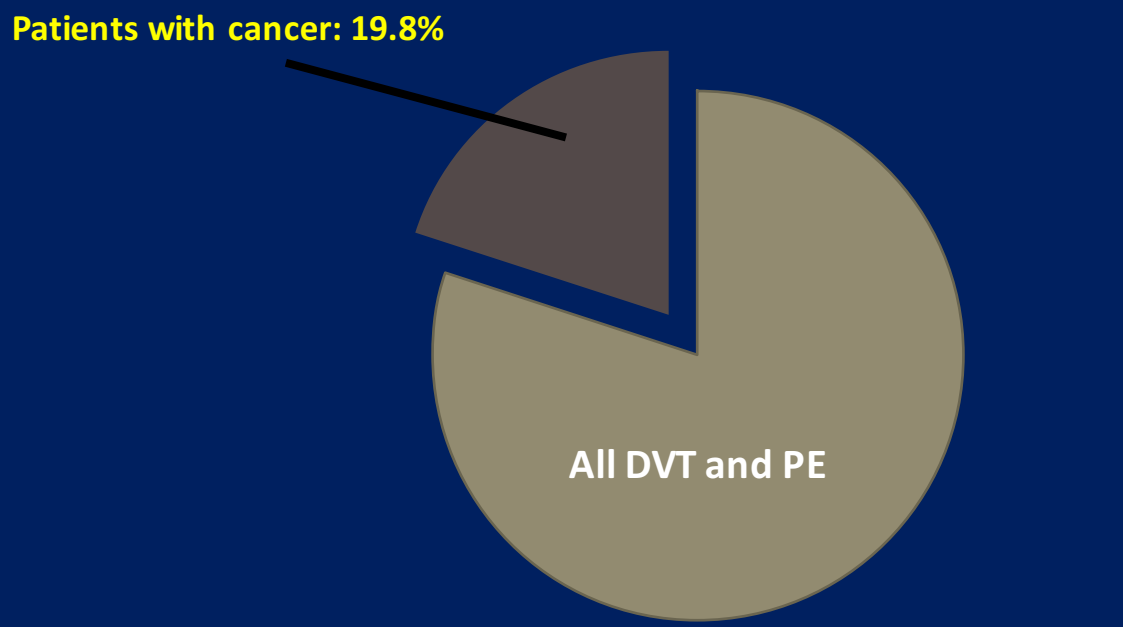
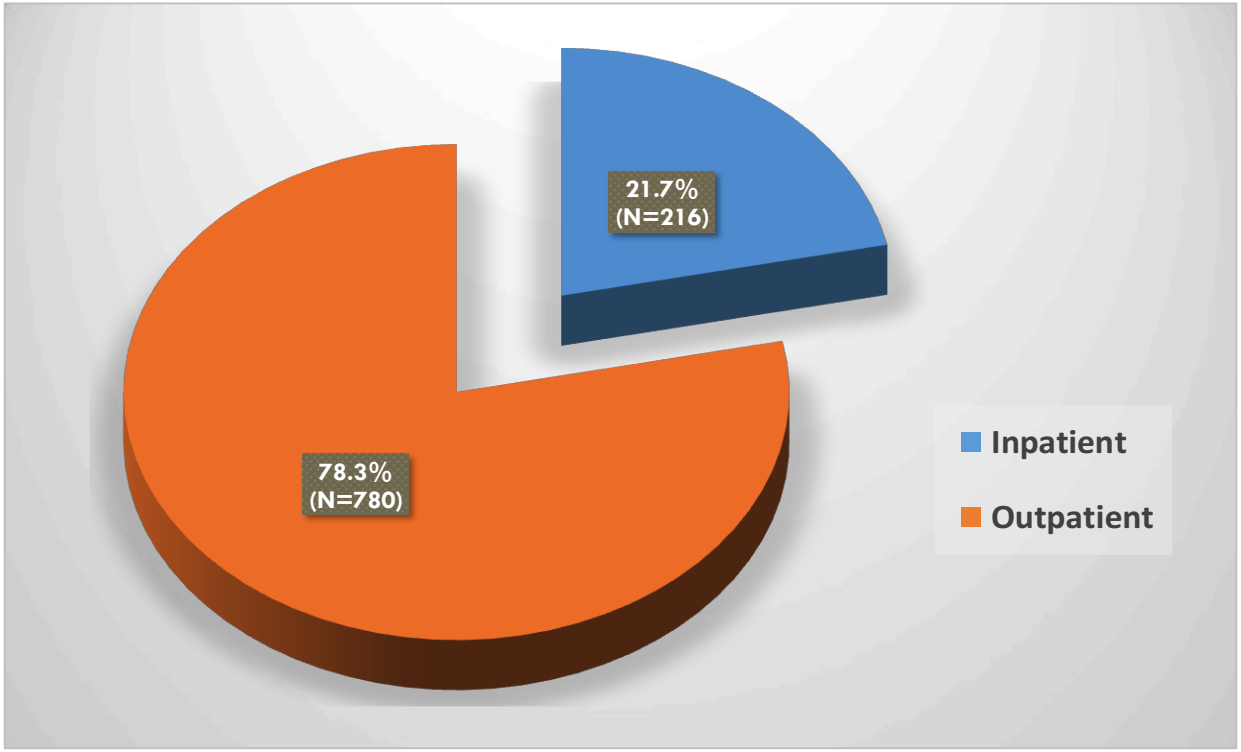
EL 20% DE LAS TROMBOSIS VENOSAS ESTÁN RELACIONADAS CON EL CÁNCER



One-fifth of all VTE occurs in patients with cancer

Heit JA. et al. *Arch Intern Med.* 2002;162:1245-1248.

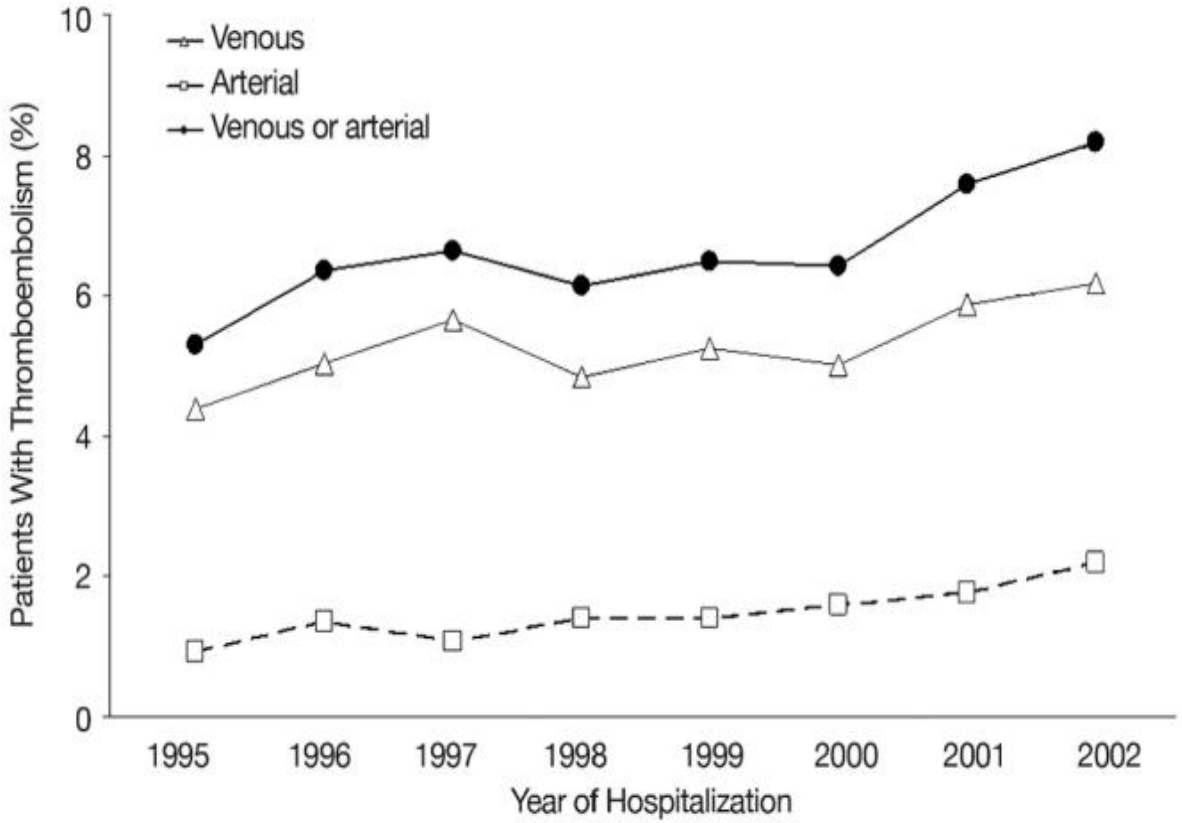
Es una enfermedad fundamentalmente extrahospitalaria (80% de los casos)



Why you should care…
Increasing numbers of patients with VTE

Retrospective cohort study (1995-2002) using the discharge database of the University Health System Consortium.

N= 66,106 adult neutropenic cancer patients with 88,074 hospitalizations at 115 medical centers in the US.



Khorana *et al.* J Clin Oncol. 2006;24(3):484-90.

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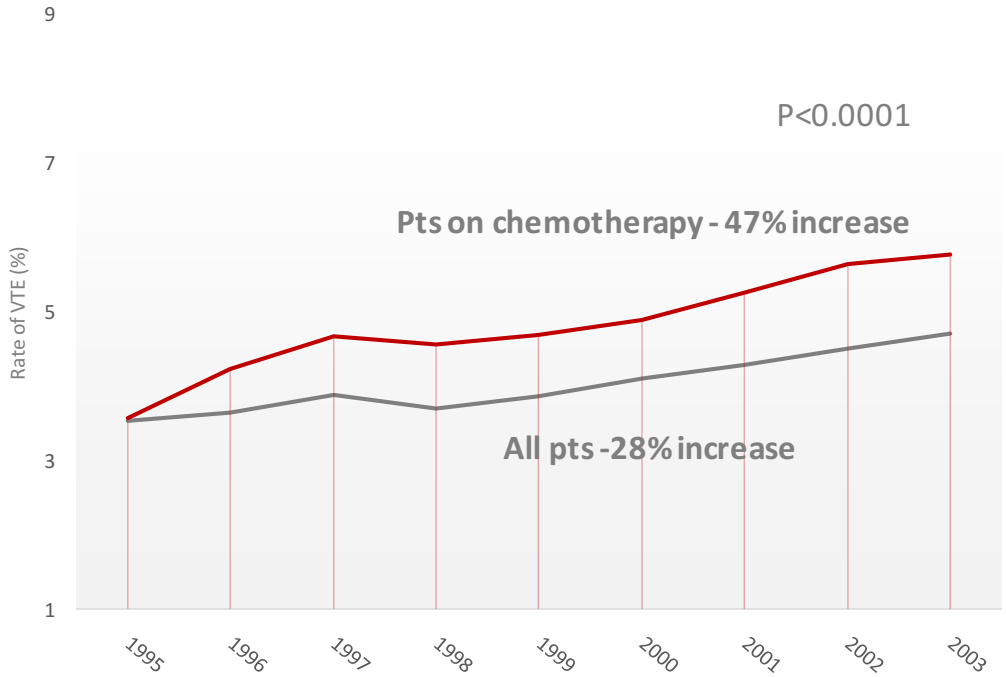
Why you should care…
Outpatients & chemotherapy



Khorana AA et al. *Cancer* 2007

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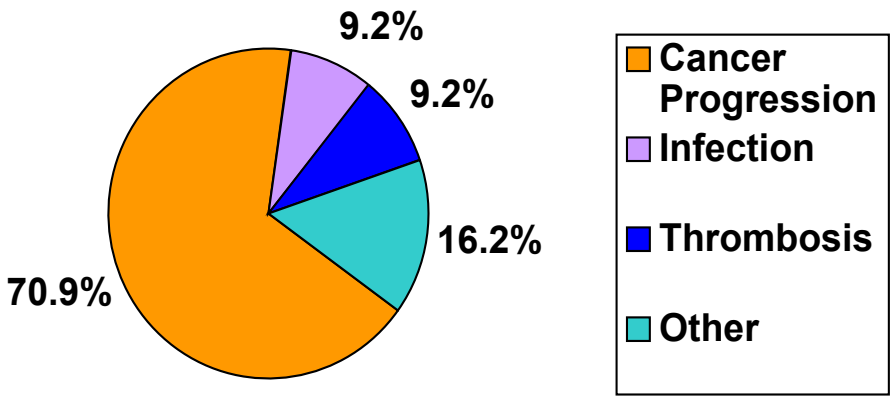
Thrombosis is a Leading Cause of (Preventable) Death in Outpatients Receiving Chemotherapy

- **Prospective observational study of 117 US centers**
- **4,466 consecutively enrolled cancer patients initiating a new chemotherapy regimen**
- **Annualized death rate for VTE in the ambulatory setting was 448 per 100 000 patients, which represented a 47-fold elevation (95% CI 6–89, P = 0.03) over the general population.**



Other: Respiratory failure, bleeding, aspiration pneumonitis, other, unknown

Causes of death exceed total number of deaths because 6 patients had more than 1 cause of death identified

Khorana A et al. *J Thromb Haemost.* 2007;5 632–634.

Original Article

Incidence and Predictors of Venous Thromboembolism (VTE) Among Ambulatory High-Risk Cancer Patients Undergoing Chemotherapy in the United States

Alok A. Khorana, MD[1]; Mehul Dalal, PhD[2]; Jay Lin, PhD[3]; and Gregory C. Connolly, MD[1]

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

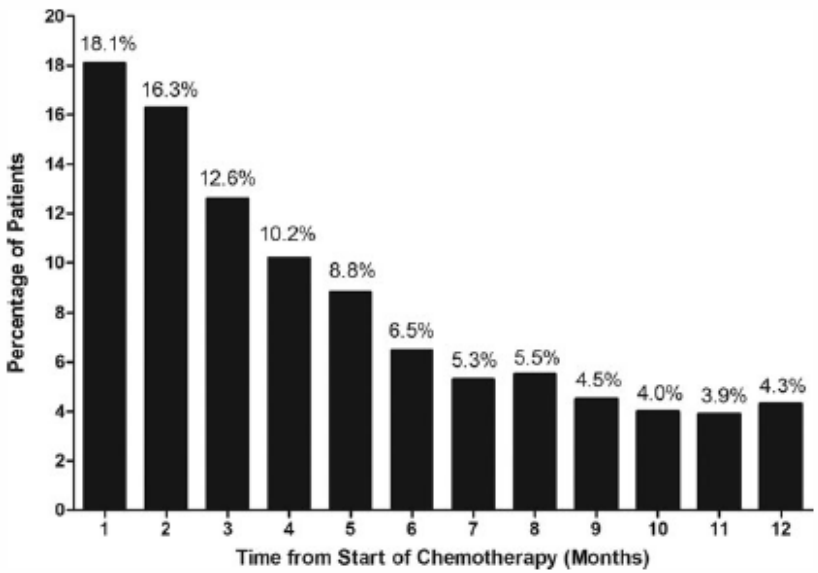

Figure 4. The distribution of venous thromboembolism events is illustrated for the cancer cohort after the initiation of chemotherapy.

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Khorana et al. Cancer 2012

Factores de riesgo de trombosis en pacientes oncológicos

- **Factores realcionados con el paciente**
  - Edad
  - Género: mayor riesgo en mujeres
  - Raza
    - Mayor en afroamericanos
    - Menor en asiáticos
  - Comorbilidades (otras enfermedades asociadas): enfermedades renales, pulmonares, etc.
  - Historia previa de ETV
  - Historia familiar de ETV

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Rao MV et al. In Khorana and Francis, eds. Cancer-associated thrombosis;2007

Factores de riesgo de trombosis en pacientes oncológicos

- **Factores realcionados con el tumor**
  - Tipo de tumor
  - Estadio
  - Adenocarcinoma > epidermoide
  - Células en anillo de sello
  - Alteraciones moleculares:
    - Traslocación ALK – cáncer de pulmón
    - Mutación k-ras – cáncer de colon
    - Mutación IDH

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Rao MV et al. In Khorana and Francis, eds. Cancer-associated thrombosis;2007

Factores de riesgo de trombosis en pacientes oncológicos

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- **Factores realcionados con el tratamiento**
  - Cirugía
  - Hospitalización
  - Catéteres venosos centrales (port-a-cath)
  - Terapia hormnal
  - Fármacos antiangiogénicos (talidomida, lenalidomida, etc.)
  - Agentes estimulantes de la eritropoyesis
  - Trasfusiones

Rao MV et al. In Khorana and Francis, eds. Cancer-associated thrombosis;2007

VTE associated with poor outcome Stage&Different Cancers

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Table 1. Effect of VTE on Mortality Risk Within 1 Year of Diagnosis in Patients With Different Cancer Types Stratified by Cancer Stage

	HR by Stage		
	Local	Regional	Remote
Prostate	5.6[a]	4.7[a]	2.8[b]
Breast	6.6[a]	2.4[b]	1.8[c]
Lung	3.1[a]	2.9[a]	2.5[a]
Colorectal	3.2[a]	2.2[a]	2.0[a]
Melanoma	14.4[a]	NA	2.8[b]
Non-Hodgkin lymphoma	3.2[a]	2.0[b]	2.3[a]
Uterus	7.0[a]	9.1[a]	1.7[c]
Bladder	3.2[a]	3.3[a]	3.3[a]
Pancreas	2.3[c]	3.8[a]	2.3[a]
Stomach	2.4[c]	1.5[c]	1.8[a]
Ovary	11.3[b]	4.8[c]	2.3[a]
Kidney	3.2[c]	1.4	1.3

VTE indicates venous thromboembolism; HR, hazard ratio; NA, not applicable.
[a] $P < .001$.
[b] $P < .01$.
[c] $P < .05$.

Lyman, Cancer 2011

Tumores y riesgo de ETV

- Tumores de bajo riesgo:
  - Cáncer de mama
  - Cáncer de próstata
  - Sarcomas

- Tumores de alto riesgo:
  - Cáncer de pulmón
  - Cán de páncreas
  - Cáncer de estómago
  - Tumores cererbrales (gliomas, etc.)

Cellular Proteolysis and Oncology

Symptomatic and incidental thromboembolism are both associated with mortality in pancreatic cancer

Laurel A. Menapace[1]; Derick R. Peterson[1,2]; Andrea Berry[1,2]; Tarek Sousou[1]; Alok A. Khorana[1]

[1]James P. Wilmot Cancer Center, and the Department of Medicine, University of Rochester, Rochester, New York, USA; [2]Department of Biostatistics, University of Rochester, Rochester, New York, USA

135 patients 34.8% experienced VTE.

Menapace et al. Thromb Haemost. 2011;106(2):371-8

ANTICANCER RESEARCH *30*: 4261-4264 (2010)

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Assessing Risk and Mortality of Venous Thromboembolism in Pancreatic Cancer Patients

WALID SHAIB[1], YANHONG DENG[1], DANIEL ZILTERMAN[2], BRUCE LUNDBERG[1] and MUHAMMAD WASIF SAIF[3]

Stage IV PDAC 39% experienced VTE

Shaib et al. Anticancer Res. 2010

Original Article

Analysis of Incidence and Clinical Outcomes in Patients With Thromboembolic Events and Invasive Exocrine Pancreatic Cancer

Andrew S. Epstein, MD[1]; Gerald A. Soff, MD[2]; Marinela Capanu, PhD[3]; Christopher Crosbie, MS[4]; Manish A. Shah, MD[1]; David P. Kelsen, MD[1]; Brian Denton, MS[3]; Stuart Gardos, BA[4]; and Eileen M. O'Reilly, MD[1]

1915 patients 36% experienced VTE

Epstein et al. Cancer. 2012;118(12):3053-61

Clin Transl Oncol (2014) 16:927–930
DOI 10.1007/s12094-014-1165-y

BRIEF RESEARCH ARTICLE

Incidence of venous thromboembolism (VTE) in ambulatory pancreatic cancer patients receiving chemotherapy and analysis of Khorana's predictive model

A. J. Muñoz Martín · P. García Alfonso · A. B. Rupérez Blanco · S. Pérez Ramírez · M. Blanco Codesido · M. Martín Jiménez

HGUGM PDAC 35.7% experienced VTE

Muñoz et al. Clin Tranls Oncol. 2014

Original Article

Incidence and Predictors of Venous Thromboembolism (VTE) Among Ambulatory High-Risk Cancer Patients Undergoing Chemotherapy in the United States

Alok A. Khorana, MD[1]; Mehul Dalal, PhD[2]; Jay Lin, PhD[3]; and Gregory C. Connolly, MD[1]

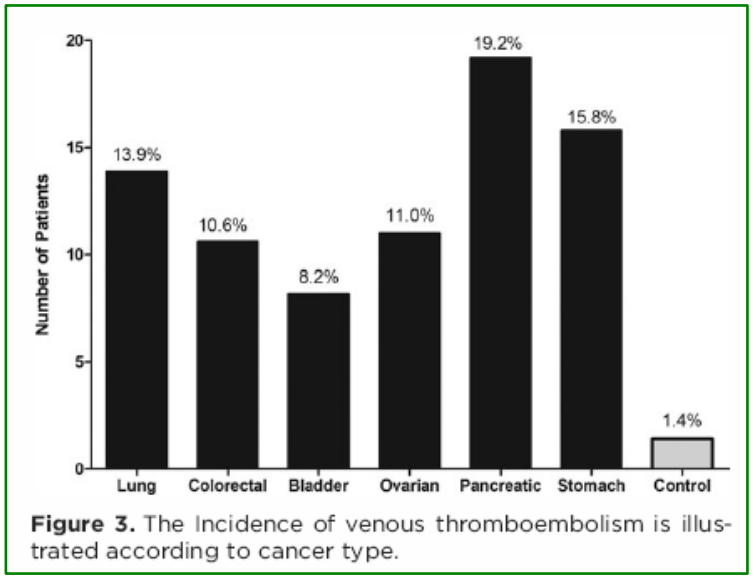

Figure 3. The Incidence of venous thromboembolism is illustrated according to cancer type.

12 months
PE+DVT

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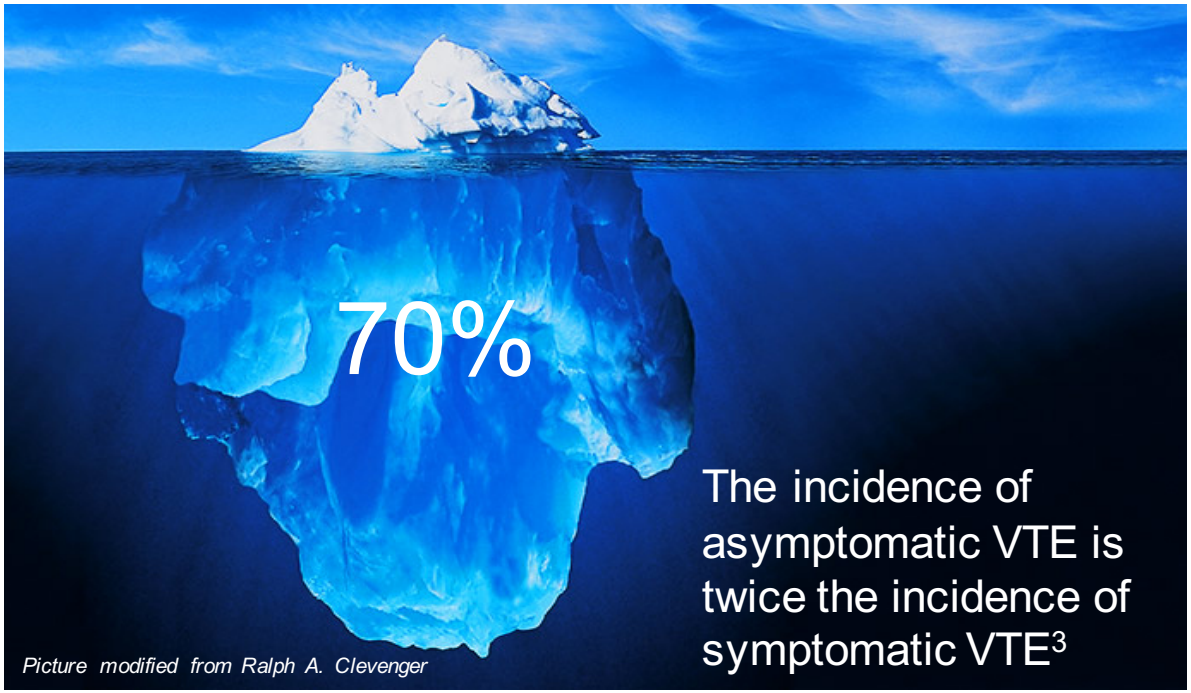
Khorana et al. Cancer 2012

What is the true burden of VTE in cancer patients?

- 60–70% of fatal PEs detected post-mortem are not suspected or diagnosed[1,2]



Incidental PE ≈ 9–21%[1,2]

1. Stein PD *et al. CHEST* 1995; **110**:978–981; 2. Sandler DA, *et al. J R Soc Med.* 1989; **82**:203–205; 3. Kakkar VV *et al. Lancet* 1969; **2**:230–233.

Citostáticos clásicos

Fármaco con más riesgo de ETV: CISPLATINO

932 patients, 169 (18.1%) experienced TEE during treatment or within 4 weeks of the last dose

Arterial thromboembolism 11.3%

VTE: PE 39%, DVT 66.3%

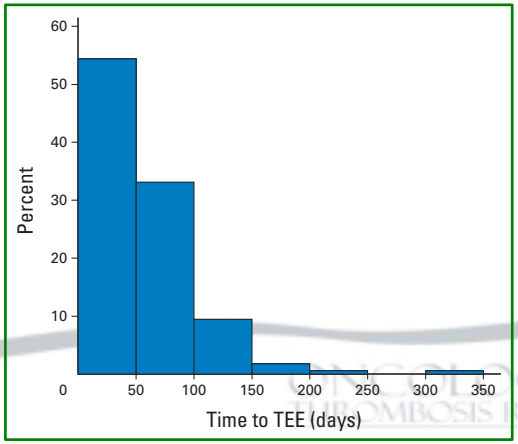
88% occurred within 100 days of initiation of treatment

VOLUME 29 · NUMBER 25 · SEPTEMBER 1 2011

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

High Incidence of Thromboembolic Events in Patients Treated With Cisplatin-Based Chemotherapy: A Large Retrospective Analysis

Russell A. Moore, Nelly Adel, Elyn Riedel, Manisha Bhutani, Darren R. Feldman, Nour Elise Tabbara, Gerald Soff, Rekha Parameswaran, and Hani Hassoun



Citostáticos clásicos sin claro incremento el riesgo de trombosis

Pemetrexed

Raltitrexed

Bleomicina

Temozolamida

Alcaloides de la vinca

Citostáticos clásicos asociados a eventos trombóticos

Ciclofosfamida

Taxanos (docetaxel)

Mitomicina-C

Methotrexate

AEE y trombosis

Tabla 3. Resumen de los principales metaanálisis sobre seguridad de los agentes estimulantes de la eritropoyesis.

Autor	Año	Estudios incluidos	Mortalidad global	Mortalidad estudios con quimioterapia	Riesgo de trombosis
Bohlius *et al.*[15]	2006	Pacientes oncológicos que reciben AEE, tanto **con anemia como sin ella, con y sin quimioterapia**	HR: 1,08; IC95%: 0,99-1,18; 42 estudios, 8.167 pacientes	RR: 1,02; IC95%: 0,90-1,15; 30 estudios, 6.282 pacientes	RR: 1,67; IC95%: 1,35-2,06; 35 estudios, 6.769 pacientes
Bennett *et al*[18]	2008	Pacientes oncológicos en tratamiento **con quimioterapia** y *darbepoetina alfa*	HR: 1,10; IC95%: 1,01-1,2; 51 estudios, 13.611 pacientes	⇧50% Riesgo	RR: 1,57; IC95%: 1,31- 1,87; 31 estudios, 8.172 pacientes
Ludwig *et al.*[19]	2009	Pacientes oncológicos con **anemia inducida por quimioterapia** tratados con *darbepoetina alfa*	HR: 0,97; IC95%: 0,85- 1,1; 6 estudios, 2.122 pacientes		HR: 1,57; IC95%: 1,10-2,26; 6 estudios, 2.122 pacientes
Glaspy *et al.*[20]	2010	Pacientes oncológicos que reciben AEE tanto **con anemia como sin ella, con y sin quimioterapia**	OR: 1,06; IC95%: 0,97-1,15; 60 estudios, 15.323 pacientes	OR: 1,03; IC95%: 0,93-1,13; 47 estudios, 12.108 pacientes	OR: 1,48; IC95%: 1,28-1,72; 44 estudios, 13.196 pacientes
Tonia *et al.*[12]	2012	Pacientes oncológicos que reciben AEE tanto **con anemia como sin ella, con y sin quimioterapia**	HR: 1,17; IC95%: 1,06-1,29; 70 estudios, 15.935 pacientes		RR: 1,52; IC95%: 1,34-1,74; 57 estudios, 15.498 pacientes

Tratamiento de soporte

Factores estimulantes de colonias de granulocitos

G-CSF ETV HR 1.69(1.09-2.64); p=0.02

Glucocorticoides

Se han asociado a un incremento significativo del riesgo de ETV

El riesgo aumenta con la duración del tratamiento y con las dosis elevadas

Mayor riesgo en los 3-6 primeros meses

Tabla 6. Riesgo de tromboembolia venosa y esteroides.

CC	Número (%)			OR (IC 95%)		
	TVP (n = 3.544)	EP (n = 3.006)	Controles (n = 10.000)	TVP	EP	TVP/EP
Nunca	2.915 (82,2)	2.387 (79,4)	9151 (91,5)	1 (referencia)	1 (referencia)	1 (referencia)
Uso actual	260 (7,3)	304 (10,1)	175 (1,7)	2,48 (1,9-3,1)	3,81 (3,0-4,7)	3,05 (2,5-3,7)
0-30 días	61 (1,7)	92 (3,0)	36 (0,4)	3,39 (2,1-5,3)	6,24 (4,1-9,5)	4,68 (3,2-6,9)
31-365 días	120 (3,4)	134 (4,5)	59 (0,6)	2,71 (1,9-3,9)	4,37 (3,3-6,4)	3,44 (2,5-4,7)
>1 año	79 (2,23)	78 (2,59)	80 (0,80)	1,89 (1,3-2,7)	2,13 (1,5-3,0)	2,00 (1,5-2,7)
Uso previo	359 (10,4)	315 (10,48)	674 (6,74)	1,14 (0,9-1,3)	1,27 (1,1-1,5)	1,18 (1,1-1,3)

Tratamiento de soporte

AINES

No estudios específicos de pacientes oncológicos (estudios población general)

AINES y COXIBs se han relacionado con un amento de fenómenos tromboembólicos arteriales y venosos

Todos los AINES se asocian con aumento del riesgo cardiovascular

Relación riesgo dosis y duración

Metaanálisis Ungprasert et al. Rheumatology

RR VTE AINES 1,80, IC95% 1,28-2,52

The Breast 22 (2013) 121–129

Contents lists available at SciVerse ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Review

Meta-analysis of breast cancer outcome and toxicity in adjuvant trials of aromatase inhibitors in postmenopausal women

Adnan Aydiner*

Thromboembolic events					
Monotherapy	ATAC[18]	Anastrozole 5 yrs	Tamoxifen 5 yrs	0.61 (0.47–0.80) $p < 0.0001$	**0.61 (0.50–0.75)**
	BIG 1–98[19,20]	Letrozole 5 yrs	Tamoxifen 5 yrs	0.62 (0.45–0.85) $p < 0.0001$	**$p < 0.001$**
Sequenced therapy	TEAM (713532)[16]	Tamoxifen 2–3 yrs/Exemestane 2–3 yrs	Tamoxifen 5 yrs	1.87 (1.19–2.93) $p = 0.006$	**1.89 (1.21–2.94)**
	NSAS BC03[17]	Tamoxifen 2 yrs/Anastrozole 3 yrs	Tamoxifen 5 yrs	3.03 (0.12–74.54) $p = 0.498$	**$p = 0.005$**
Cardiovascular events					
Monotherapy	ATAC[18]	Anastrozole 5 yrs	Tamoxifen 5 yrs	1.23 (0.95–1.60) $p = 0.122$	**1.20 (1.02–1.42)**
	BIG 1–98[19,20]	Letrozole 5 yrs	Tamoxifen 5 yrs	1.18 (0.95–1.47) $p = 0.126$	**$p = 0.030$**
Sequenced therapy	ARNO-95[13,21]	Tamoxifen 2 yrs/Anastrozole 3 yrs	Tamoxifen 5 yrs	2.48 (0.87–7.09) $p = 0.091$	**1.15 (1.05–1.25)**
	IE study[12]	Tamoxifen 2–3 yrs/Exemestane 2–3 yrs	Tamoxifen 5 yrs	1.13 (0.98–1.31) $p = 0.094$	**$p = 0.003$**
	ITA[14]	Tamoxifen 2–3 yrs/Anastrozole 2–3 yrs	Tamoxifen 5 yrs	1.24 (0.60–2.59) $p = 0.560$	
	TEAM (713532)[16]	Tamoxifen 2–3 yrs/Exemestane 2–3 yrs	Tamoxifen 5 yrs	1.15 (1.02–1.29) $p = 0.020$	
	NSAS BC03[17]	Tamoxifen 2 yrs/Anastrozole 3 yrs	Tamoxifen 5 yrs	0.67 (0.11–4.03) $p = 0.660$	
Extended therapy	ABCSG 6a[25]	Anastrozole following 5 yrs of tamoxifen	No treatment	4.89 (0.54–43.9) $p = 0.157$	**1.06 (0.84–1.34)**
	MA.17[22,23]	Letrozole following 5 yrs of tamoxifen	Placebo	1.04 (0.82–1.32) $p = 0.751$	**$p = 0.640$**

VTE AI vs Tamoxifen OR=0.61; p<0.001

Cardiovascular events AI vs Tamoxifen OR=1.20; p=0,03

Hormonoterapia y ETE

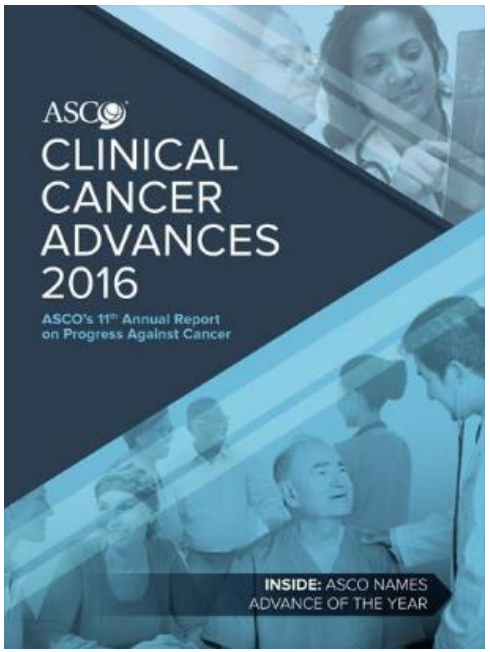
Acetato de megestrol

- Asociado a QT (carbo-taxol, ca de endometrio) dosis 160 mg/día: incidencia ETV 14,2%
- Cáncer de mama monoterapia dosis 160 mg/día: incidencia ETV 10%

Bevis et al. J Reprod Med 2014
[2]Bines et al. Ann Oncol 2014

Immunotherapy

A promising new strategy to treat cancer

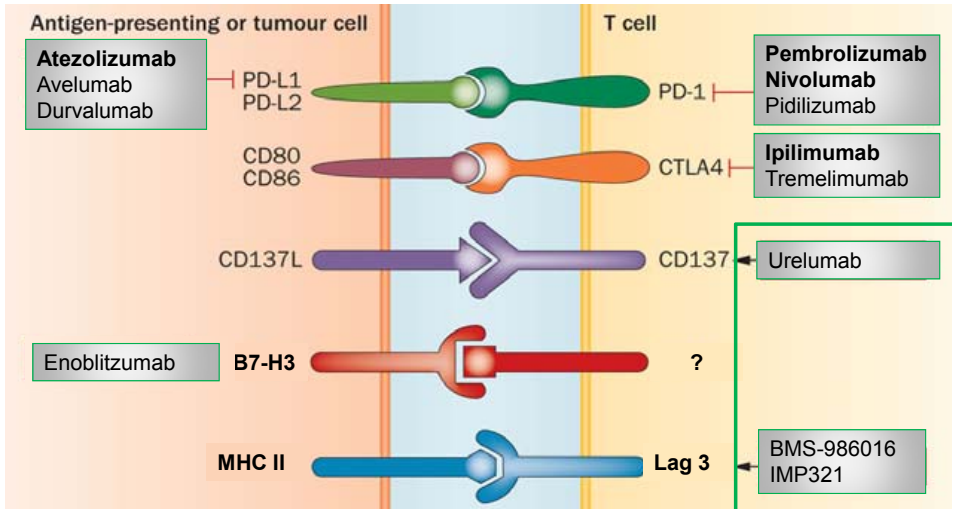


The 2016 & 2017 Clinical Cancer Advance of the Year

Immunotherapy
New Cancer Treatment Modality

- FDA approved drugs:
  - Ipilimumab and tremelimumab (anti-CTLA4)
  - Nivolumab and pembrolizumab (anti-PD1)
  - Atezolizumab and avelumab (anti-PD-L1)

- Indications:
  - Advanced stage melanoma
  - Non small cell lung cancer
  - Renal cell carcinoma
  - Head and neck cancer
  - Hodgkin lymphoma
  - Urothelial carcinoma
  - Gastric cancer (September 2017)



- Many trials underway with theses and related agents, alone or in combination

Adapted from Gangadhar TC. & Vonderheide RH. Nat Rev Clin Oncol. 2014;11(2):91-9

Clinical Case 2
Immunotherapy

- Immune related adverse events (IRAES): New toxicity, a new field
  Autoimmune complications

IRAE	Clinical Characteristics
Colitis	Diarrhea, perforation, death (rare)
Rash	Vitiligo, neutrophilic dermatoses, SJS
Thyroiditis	Hypo/hyper
Pneumonitis	Dyspnea, cough, respiratory failure
Hypophysitis	All hormonal axes or can be selective
Myocarditis	Can lead to heart failure, death
Hepatitis	Transaminitis, with or without elevated bilirubin
Central nervous system	Encephalopathy, aseptic meningitis, transverse myelitis
Peripheral nervous system	Peripheral neuropathy, Guillain-Barré syndrome

- No increase in VTE (despite toxicity inflammatory disease) or arterial thromboembolism!

Adapted from Gangadhar TC. & Vonderheide RH. Nat Rev Clin Oncol. 2014;11(2):91-9

Arterial Thromboembolism (ATE) & Cancer

isth 2017 CONGRESS BERLIN GERMANY

TABLE 1 ATE rate in different tumor types

Primary Organ	No. of Patients (%)	No. of Patients with ATE (%)
Lung	233 (16.8)	12 (5.2)
Breast	228 (16.4)	0 (0.0)
Brain	193 (13.9)	4 (2.1)
Haematologic Malignancies	175 (12.6)	2 (1.1)
Gastric & Pancreatic	155 (11.2)	3 (1.9)
Colorectal	153 (11.0)	2 (1.1)
Kidney	37 (2.7)	3 (8.1)
Others	213 (15.4)	8 (3.8)

ATE increased risk of mortality from any cause
HR=2.6, 95%CI: 1.6-4.3, p< 0.001
Same tumors

Grilz et al. ISTH 2017 (Berlin)

MADRID 2017 ESMO congress

- Spanish observational study, Rogado et al. ESMO 2017 (Madrid)
- The incidence of cancer among stroke survivors was almost twice (7.6% - 18 months) the rate that would be expected in the general population and was associated with increased serum fibrinogen levels

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Risk of Arterial Thromboembolism in Patients With Cancer

Babak B. Navi, MD, MS,[a,b] Anne S. Reiner, MPH,[c] Hooman Kamel, MD,[a] Costantino Iadecola, MD,[a] Peter M. Okin, MD,[d] Mitchell S.V. Elkind, MD, MS,[e,f] Katherine S. Panageas, DrPH,[c] Lisa M. DeAngelis, MD[a,b]

- The 6-month cumulative incidence ATE: 4.7% (95%CI: 4.6%-4.8%) in patients with cancer compared with 2.2% (95%CI: 2.1%-2.2%) in control patients (HR: 2.2; 95%CI: 2.1 to 2.3)
- The 6-month cumulative incidence of myocardial infarction was 2.0% (vs. 0.7%)
- The 6-month cumulative incidence of ischemic stroke was 3.0% (vs 1.6%)
- Excess risk varied by cancer type (greatest for lung), correlated with cancer stage, and generally had resolved by 1 year.

Navi et al. J Am Coll Cardiol. 2017

Khorana Predictive Model

Table 2. Predictors of venous thromboembolism in the derivation cohort by multivariate logistic regression analysis

Patient characteristic	β	Odds ratio* (95% CI)
Site of cancer		
Very high risk (stomach, pancreas)	1.46	4.3 (1.2-15.6)
High risk (lung, lymphoma, gynecologic, genitourinary excluding prostate)	0.43	1.5 (0.9-2.7)
Low risk (breast, colorectal, head and neck)	0.0	1.0 (reference)
Prechemotherapy platelet count 350 × 10^9/L or more	0.60	1.8 (1.1-3.2)
Hemoglobin level less than 100 g/L or use of red cell growth factors	0.89	2.4 (1.4-4.2)
Prechemotherapy leukocyte count more than 11 × 10^9/L	0.77	2.2 (1.2-4)
BMI 35 kg/m^2 or more	0.90	2.5 (1.3-4.7)

*Odds ratios are adjusted for stage.

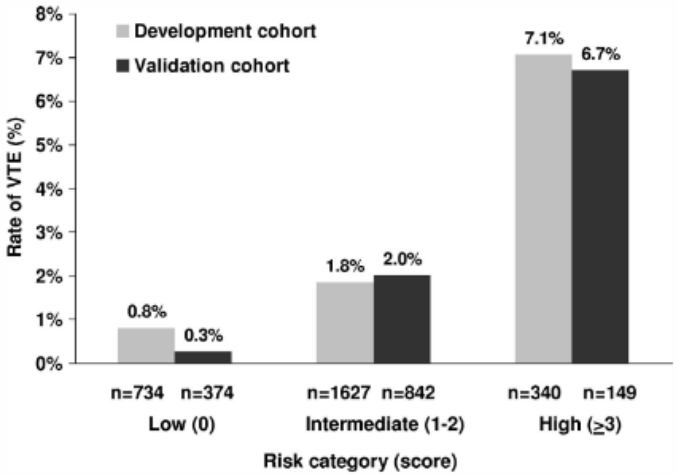


Figure 1. Rates of VTE according to scores from the risk model in the derivation and validation cohorts.

Table 3. Predictive model for chemotherapy-associated VTE

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 × 10^9/L or more	1
Hemoglobin level less than 100 g/L or use of red cell growth factors	1
Prechemotherapy leukocyte count more than 11 × 10^9/L	1
BMI 35 kg/m^2 or more	1

The association of VTE with multiple variables was characterized 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.

Khorana *et al*. Blood. 2008;111(10):4902-7.

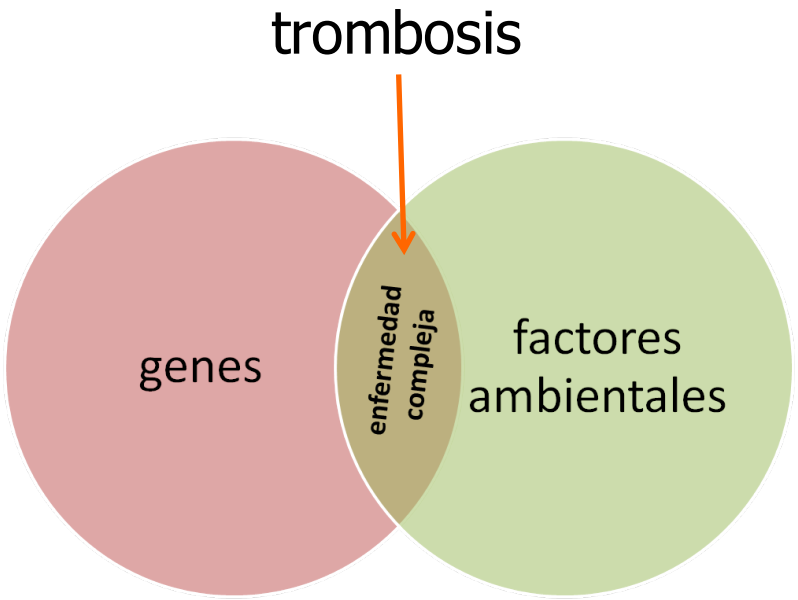
TABLE Risk prediction scores

Item	Khorana score (points)	Vienna CATS score (points)	PROTECHT score (points)	CONKO score (points)
Very high risk tumor / high risk tumor	+2 / +1	+2 / +1	+2 / +1	+2 / +1
Hemoglobin <10 g/dL or ESA use	+1	+1	+1	+1
White blood cell count >11 x 10^9/L	+1	+1	+1	+1
Platelet count ≥350 x 10^9/L	+1	+1	+1	+1
Body mass index >35 kg/m2	+1	+1	+1	+1
D-dimer >1.44 g/L	-	+1	-	-
Soluble P-selectin >53.1 g/L	-	+1	-	-
Gemcitabine / platinum-based chemotherapy	-	-	+1 / +1	-
WHO performance status ≥2	-	-	-	+1

OC 21.2 | Comparison of Risk Prediction Scores for Cancer-Associated Venous Thromboembolism: A Prospective Cohort Study

N. van Es[1], M. Di Nisio[2], G. Cesarman[3], A. Kleinjan[1], H.-M. Otten[4], I. Mahé[5], I.T. Wilts[6], D.C. Twint[7], E. Porreca[8], O. Arrieta[3], A. Stépanian[9], K. Smit[7], M. De Tursi[8], S.M. Bleker[10], R. Nieuwland[1], P.W. Kamphuisen[6,11], P.M. Bossuyt[1], H.R. Büller[1]

Modelización del riesgo de ETV

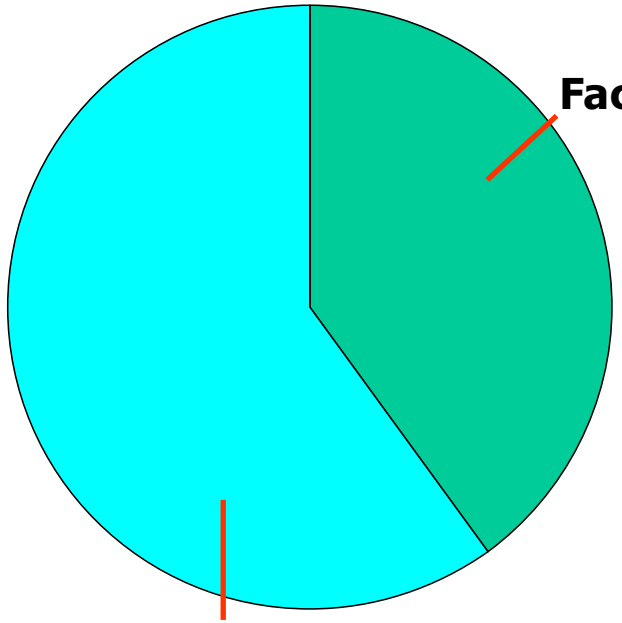


Cualquier trombosis es el resultado de la combinación de factores genéticos y ambientales

La trombosis es una enfermedad multifactorial y compleja donde la suma de ***múltiples genes, cada uno de ellos con un efecto variable, interaccionando con el ambiente***, determinaran en cada individuo el grado de susceptibilidad a la trombosis (Soria JM and Fontcuberta J, 2005)

Modelización del riesgo de ETV

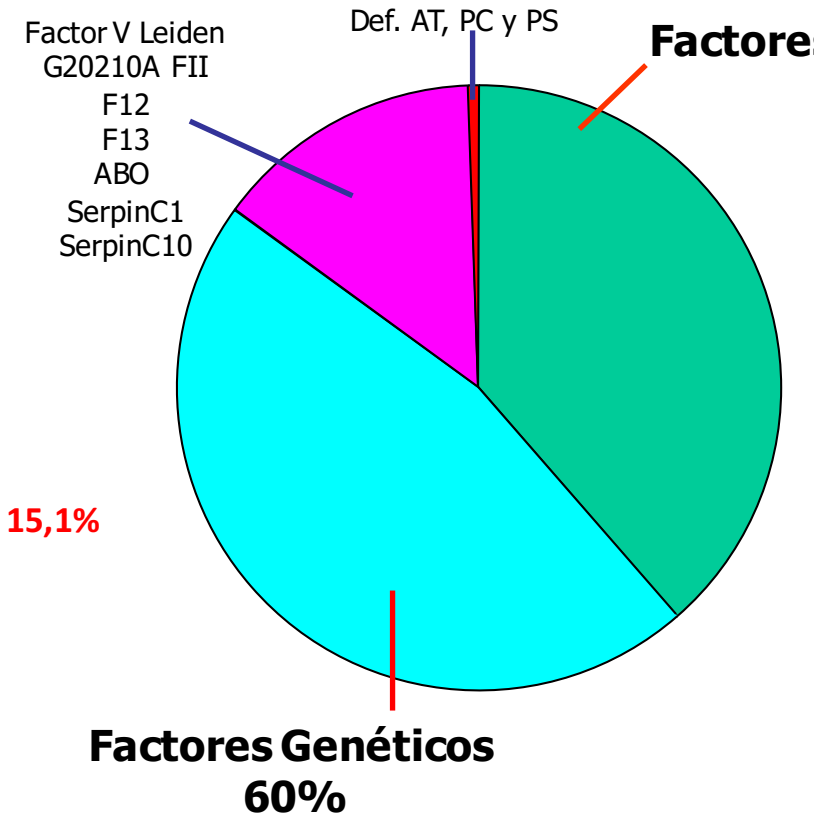
De forma sistemática todos los scores han ignorado la base genética de la ETV en la predicción del riesgo (base genética de la trombosis 60%)



- Edad
- Obesidad
- Tabaquismo
- HTA
- Diabetes mellitus
- Varices
- ICC
- IRC
- Cáncer
- Enfermedad autoinmune
- Infecciones
- Ingreso hospitalario
- Fármacos antipsicóticos
- AINEs
- Tamoxifeno
- Anticonceptivos orales
- THS
- Embarazo y puerperio
- Traumatismo grave
- Cirugía general
- Cirugía ortopédica
- Imovilización en cama
- Escayolamiento
- Viaje > 5 horas

Souto JC et al. Am J Human Genet. 2000;67:1452-59

Modelización del riesgo de ETV



Factores Ambientales
40%

- **Edad**
- **Obesidad**
- **Tabaquismo**
- **HTA**
- **Diabetes mellitus**
- **Varices**
- **ICC**
- **IRC**
- **Cáncer**
- **Enfermedad autoinmune**
- **Infecciones**
- **Ingreso hospitalario**
- **Fármacos antipsicóticos**
- **AINEs**
- **Tamoxifeno**
- **Anticonceptivos orales**
- **THS**
- **Embarazo y puerperio**
- **Traumatismo grave**
- **Cirugía general**
- **Cirugía ortopédica**
- **Imovilización en cama**
- **Escayolamiento**
- **Viaje > 5 horas**

ANÁLISIS DEL SCORE DE KHORANA Y PREDICTORES GENÓMICOS DE RIESGO DE ENFERMEDAD TROMBOEMBÓLICA VENOSA EN PACIENTES TRATADOS CON QUIMIOTERAPIA EN UN MEDIO EXTRAHOSPITALARIO

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SaludMadrid

Comunidad de Madrid

Madrid, 13 de enero 2016

A new clinico-genetic risk score (TiC score)
GRS (12 SNPS/7 genes)

SNPs	Gene	Prevalence in DVT patients	Relative risk
46C>T	FXII	6%	5
rs8176719	ABO Group (A1 carriers)	nd	2-4 (+ FV Leiden: 4-23)
rs7853989			
rs8176743			
rs8176750			
Arg67Stop	Serpin A10 (Pr Z)	4,4 %	3,3
Ala384Ser (Cambridge II)	Serpin C1 (Antitrombina)	1,7 %	10
Arg506Gln (FV Leiden)	Factor V (FV)	15-25%	5
Arg306Thr (FV Cambridge)		nd	nd
Arg306Gly (FV Hong Kong)		nd	nd
Val34Leu	Factor XIII (FXIII)	2%	Protective factor
G20210A	Prothrombin Factor II (FII)	6-16%	2-3

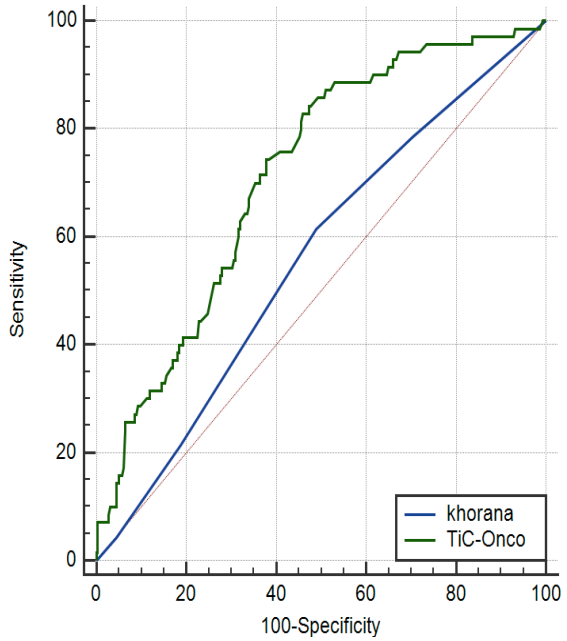
Muñoz AJ et al, OC32, Berlin ISTH 2017

A new clinico-genetic risk score (TiC score)

	TiC Onco	Khorana score	p value TiC-onco vs Khorana
AUC	0.719	0.569	<0.001
AUC (95% CI)	(0.656-0.781)	(0.502-0.63)	

70% of VTE events were detected by TiC onco score vs 21% by Khorana score

Three out of four VTE events (79% of the total events) that were not detected by the Khorana score as high risk were detected as high risk with TiC onco



Variable	P value
GRS	0.0022
BMI>25	0.0422
Primary tumor site	
HR VHR	0.5175 0.0018
Tumor stage	0.0002
VTE family history	0.1098

Treatment group	NNT (all VTE)
All cancer patient	11.8
Khorana ≥3	10.2
TiC cut-off	7.7

Muñoz AJ et al, OC32, Berlin ISTH 2017

Profilaxis Quirúrgica

¿Deben recibir los pacientes con cáncer sometidos a cirugía anticoagulación profiláctica para la ETV?

- ***El riesgo de ETV en el postoperatorio es un hecho bien reconocido***

- ***Sin profilaxis, el riesgo de ETV tras cirugía oncológica es aprox. el doble en comparación cirugía no oncológica***

- ***Múltiples ensayos clínicos randomizados han demostrado beneficio de anticoagular profilacticamente en pacientes quirúrgicos***

Profilaxis Quirúrgica: HBPM

ASCO	NCCN	AIOM ESMO	FNCLCC	SEOM'11
✓	✓	✓	NA	✓
HBPM/HNF Métodos mecánicos en alto riesgo	HBPM/HNF FONDAPARINUX ±Métodos mecánicos	HBPM/HNF (4 semanas)		HBPM/HNF FONDAPARINUX ±Métodos mecánicos

ENOXAPARINA 40mg/d – DALTEPARINA 5.000 U/d - BEMIPARINA 3.500 U/d
FONDAPARINUX 2,5 mg/d

RECOMENDACCIÓN ACCP'2012: GRADO 1A

– HBPM similar eficacia y seguridad (riesgo de sangrado) que HNF

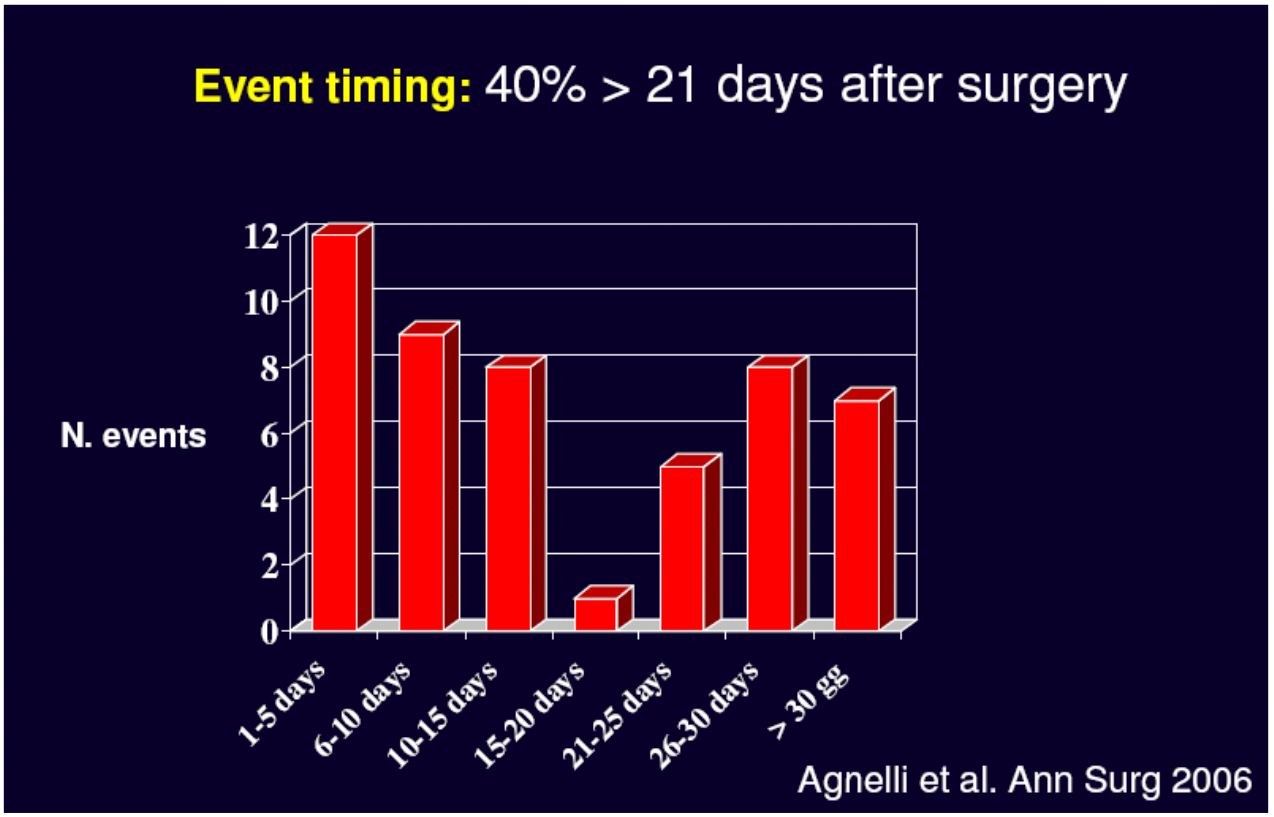
– HBPM mayor comodidad que HNF (24h vs 8h) y menor trombopenia asociada a heparina

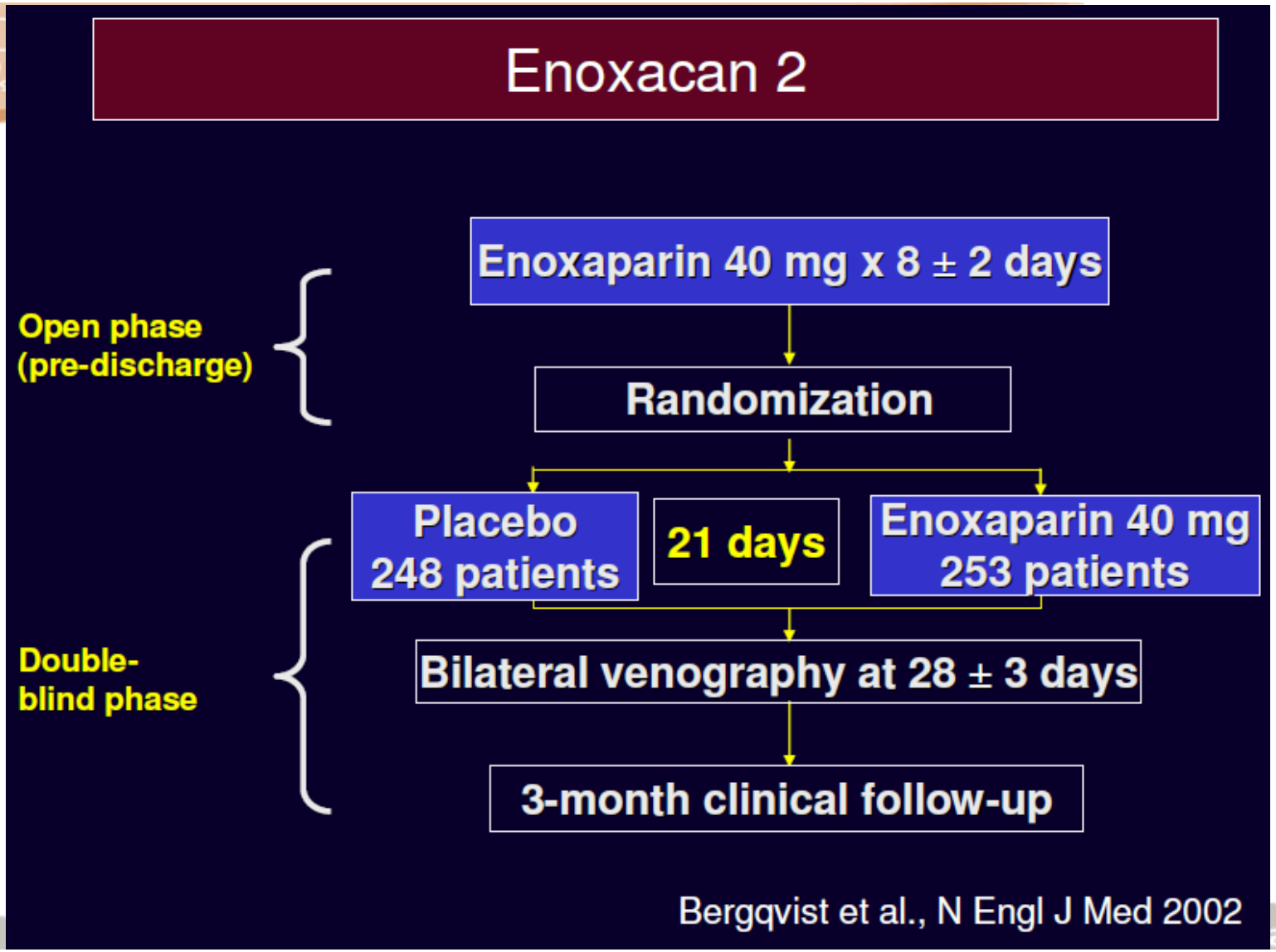
– HBPM fármaco de elección en práctica clínica

Profilaxis Quirúrgica

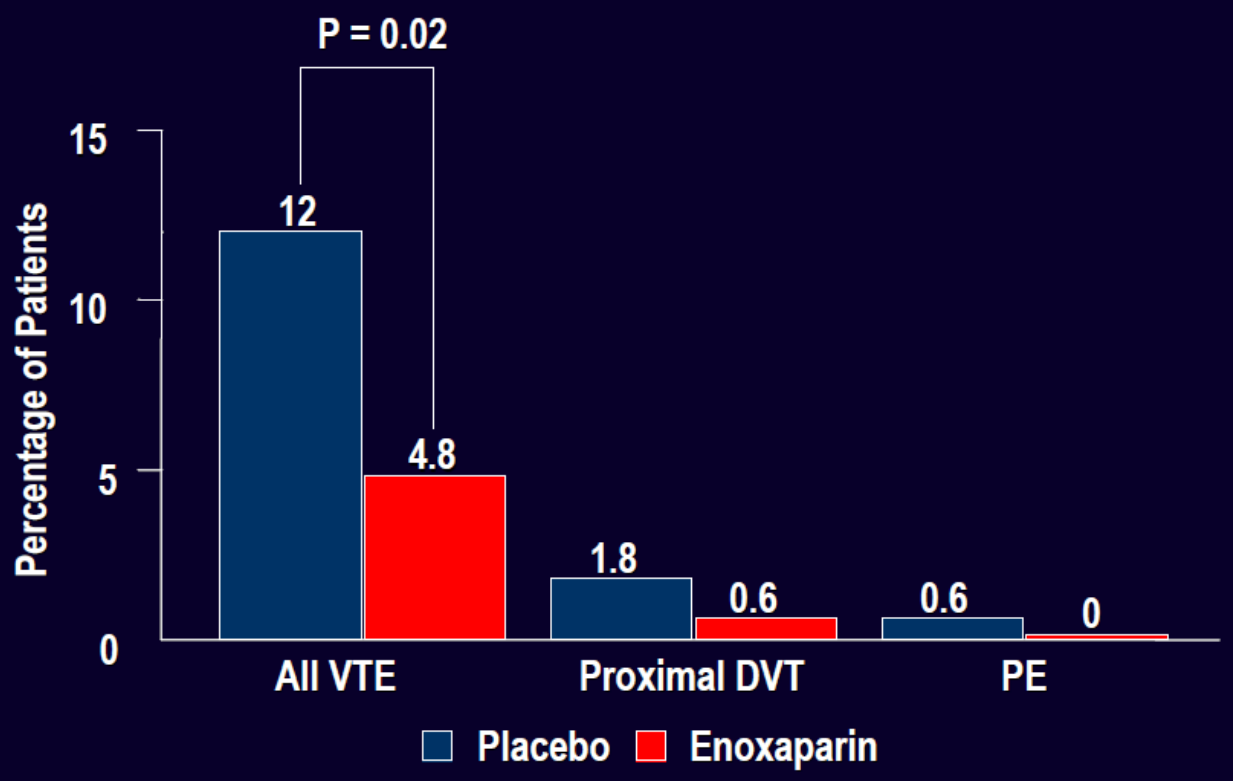
Hospital General Universitario Gregorio Marañón
SaludMadrid
Comunidad de Madrid

VTE timing




Enoxacan 2
Enoxaparin 40 mg x 8 ± 2 days
Open phase
(pre-discharge)
Randomization
Placebo
248 patients
21 days
Enoxaparin 40 mg
253 patients
Double-
blind phase
Bilateral venography at 28 ± 3 days
3-month clinical follow-up
Bergqvist et al., N Engl J Med 2002

Enoxacan 2



Bergqvist et al., N Engl J Med 2002

Profilaxis Quirúrgica-Duración

Hospital General Universitario Gregorio Marañón
SaludMadrid
Comunidad de Madrid

Risk factors

Obese patients

Residual malignant disease after operation

Previous history of VTE

Age ≥60 years

Operative time >2 hours

Advanced cancer

More than 3 days of bed rest

Duration

Low risk	*7-10 days*
High risk[1,2]	*4 weeks*

[1]Bergqvist NEJM 2002, [2]Rasmussen JThromb Haemost 2006

Profilaxis Pacientes Médicos Hospitalizados

¿Deben recibir los pacientes con cáncer hospitalizados anticoagulación profiláctica para la ETV?

- *Ausencia de estudios específicos en pacientes con cáncer (difícil realización, no grupo control sin tratamiento profiláctico)*

- *3 estudios (% pacientes con cáncer)*
  - *MEDENOX-Enoxaparina: 14% (n=1102)*
  - *PREVENT-Dalteparina: 5% (n=3706)*
  - *ARTEMIS-Fondaparinux: 15,4% (n=849)*

- *El riesgo varía significativamente entre los diferentes tipos de tumores y características clínicas*
  - *Mama 2,3% vs Páncreas 8,1% - Renal 7,6%*
  - Ingresos cortos (<3 días) vs largos
  - Grado de movilización

Profilaxis Pacientes Médicos Hospitalizados

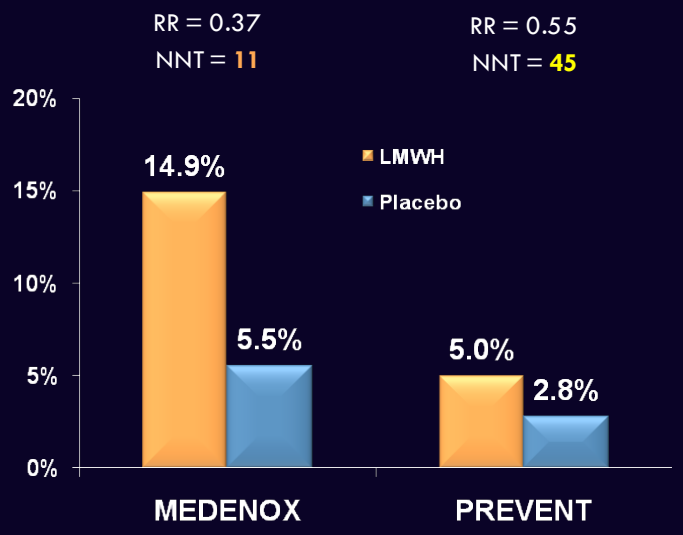
ASCO	NCCN	AIOM/ESMO	FNCLCC	SEOM
✓	✓	✓	NA	✓
All hospitalized cancer patients in the absence of contraindications	All hospitalized cancer patients in the absence of contraindications	In immobilized hospitalized cancer patients with acute medical illness		All hospitalized cancer patients in the absence of contraindications or bleeding

HBPM-FONDAPARINUX-HNF a bajas dosis

- HBPM similar eficacia y seguridad (riesgo de sangrado) que HNF
  - *Metaanálisis, Laporte S et al. J Thromb Hemost 2010 : Enoxa vs UFH*
    - *Reducción significativa VTE + similar riesgo de sangrado*
    - *Tendencia a mayor supervivencia*
- **Sólo una minoría de pacientes con cáncer reciben profilaxis adecuada (Francis, JCO 2009)**

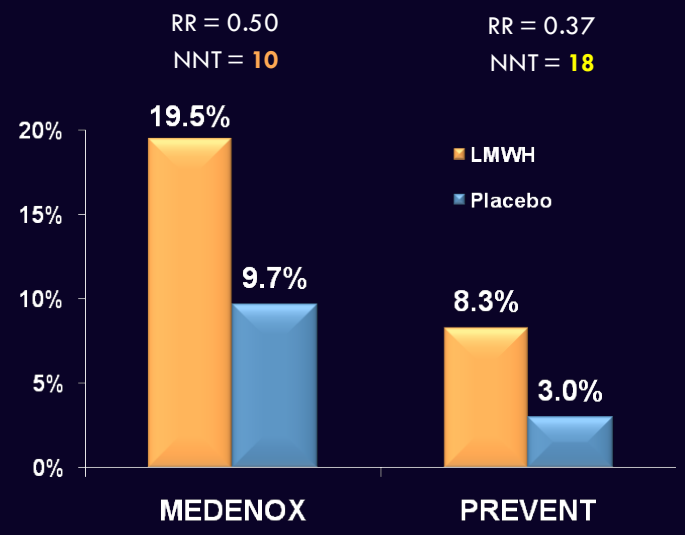
Rationale for prophylaxis with LMWH in Medical Cancer Patients

Overall population



Samama MM et al. N Engl J Med 1999;341:793-800.
Leizorovicz A et al. Circulation. 2004;110:874-879.

Cancer subgroup



Alikhan R al. Blood Coagul Fibrinolysis 14:341–346.
Cohen AT et al. Vasc Med. 2007 May;12(2):123-7.

ETV-Oncología
Profilaxis CVC

¿Deben recibir todos los pacientes portadores de CVC anticoagulación profiláctica para la ETV?

CVC-associated VTE affects approximately 4% of patients with cancer

ASCO	NCCN	AIOM/ESMO	FNCLCC	SEOM
NA	X	X	X	X

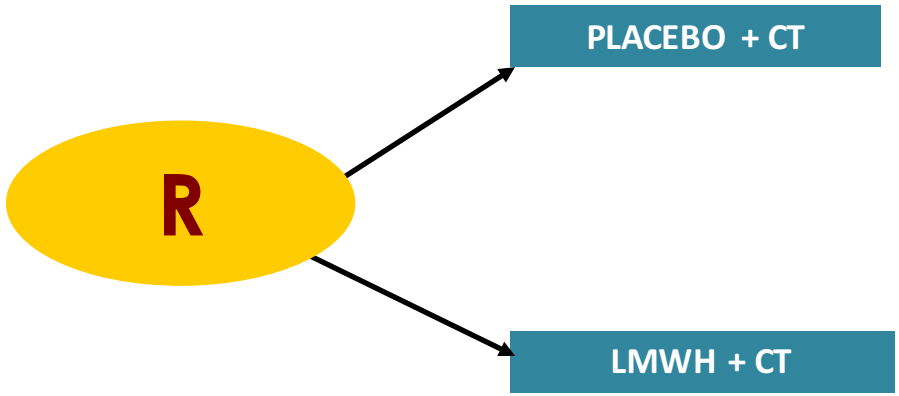
FNCLCC: CVC en VCS-AD

ACCP (2004&2012): NO RECOMENDACIÓN
España: Estudio BECAT (HBPM profilaxis primaria trombosis asociada a catéter)
Elevado número de pacientes para encontrar diferencias significativas

Study Designs
VTE in cancer is primarily an outpatient illness

MULTI-TUMOR
PROTECHT
SAVE ONCO

PANCREAS
FRAGEM UK
CONKO 004



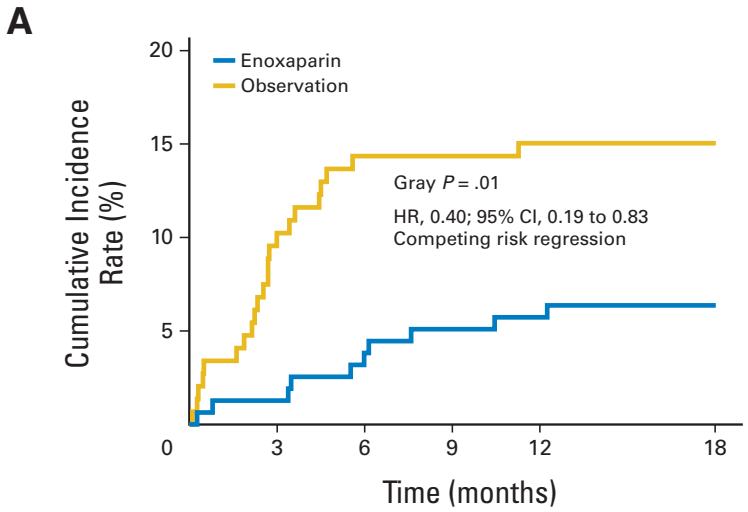
Outpatients with solid tumors receiving chemotherapy

Adapted from Akl *et al*. N Engl J Med. 2012;366(7):661-2

Patients with histologically proven APC were randomly assigned to ambulant first-line chemotherapy and prophylactic use of enoxaparin or chemotherapy alone to investigate the probable reduction in symptomatic VTEs and the impact on survival.

CONKO-004

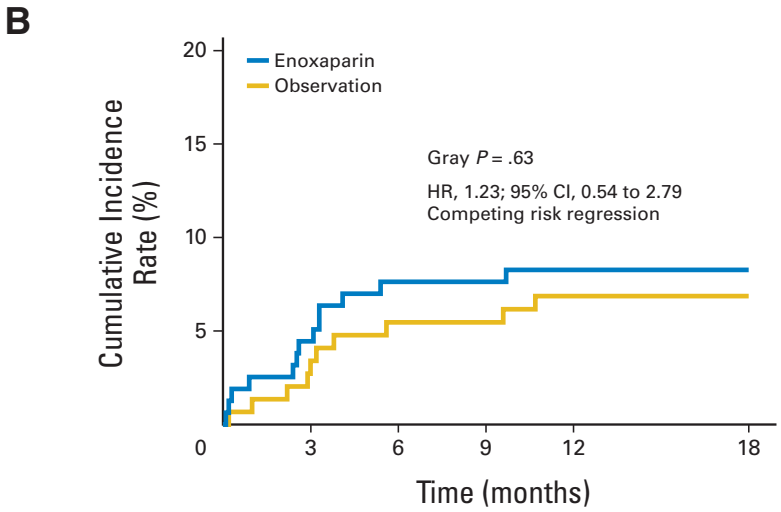
Symptomatic VTE events



No. at risk						
Enoxaparin	160	102	55	26	12	4
Observation	152	87	47	27	14	5

Incidence rate, %						
Enoxaparin	0	1.3	3.8	5.1	5.7	6.4
Observation	0	10.2	14.4	14.4	15.1	15.1

Bleeding events



No. at risk						
Enoxaparin	160	99	52	26	14	5
Observation	152	94	52	26	13	4

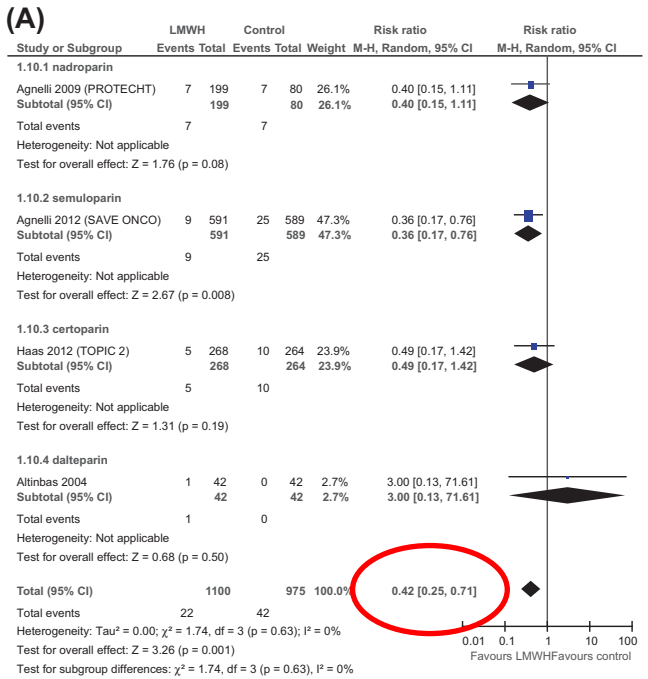
Incidence rate, %						
Enoxaparin	0	4.5	7.6	7.6	8.3	8.3
Observation	0	3.4	5.5	5.5	6.9	6.9

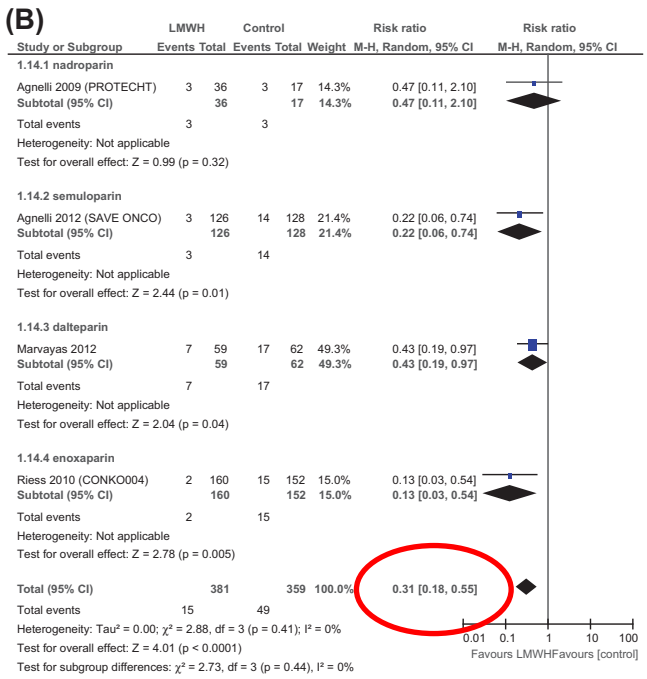
PFS: HR 1.06; 95% CI, 0.84 to 1.32; p=0.64
OS: HR 1.01; 95% CI, 0.87 to 1.38; p=0.44

CI = confidence interval; HR = hazard ratio;
PFS = progression-free survival; OS = overall survival.

Pelzer U, *et al. J Clin Oncol* 2015; 33:2028–2034.

Ben-Aharon Meta-analysis
Lung & Pancreas Cancer



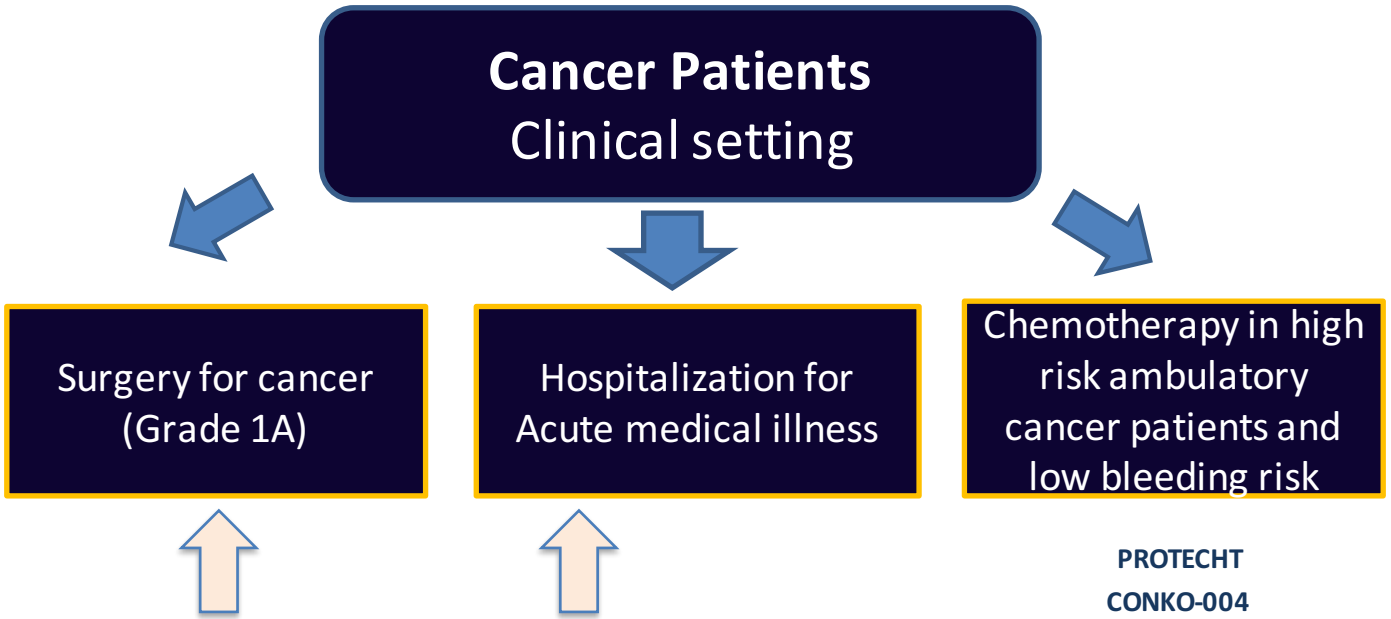


LUNG CANCER
RR 0.42

PANCREATIC CANCER
RR 0.31

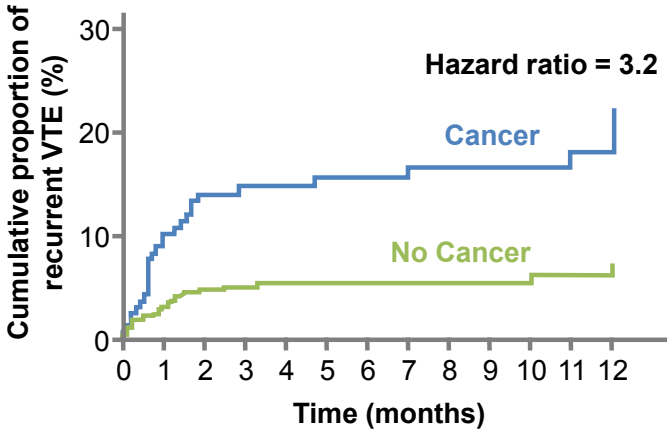
Ben-Aharon et al. Acta Oncol. 2014;53(9):1230-7.

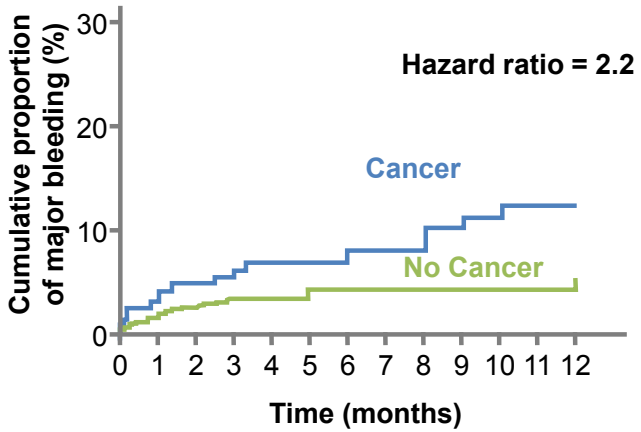
Cancer Patients-Thromboprophylaxis 2017 Recommendations?



VTE recurrence: The risk of clinically important bleeding in cancer patients during anticoagulant therapy

Prospective follow-up study. Of the 842 included patients, 181 had known cancer at entry.





Time (months)	0	1	3	6	9	12
Cancer	181	160	129	92	73	64
No Cancer	661	631	602	161	120	115

Time (months)	0	1	3	6	9	12
Cancer	181	170	141	102	81	68
No Cancer	661	636	615	170	127	124

VTE = venous thromboembolism.

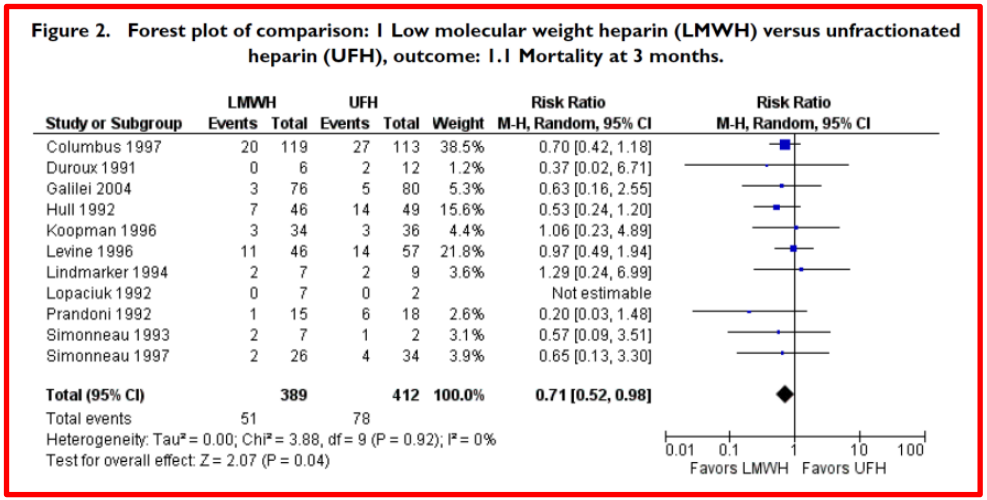
Prandoni P, *et al. Blood* 2002; **100**:3484–3488.

Initial treatment of VTE

- Data on the relative efficacy and safety of LMWH and UFH for initial treatment in patients with cancer come from post hoc subgroup analysis of large RCTs
- Cochrane review
  - 16 randomized-controlled trials
  - Significant mortality reduction at 3 months in patients treated with LMWH compared with those treated with UFH RR 0.71; 95% CI 0.52-0.98
  - Recurrent VTE did not show a significant advantage of LMWH over UFH

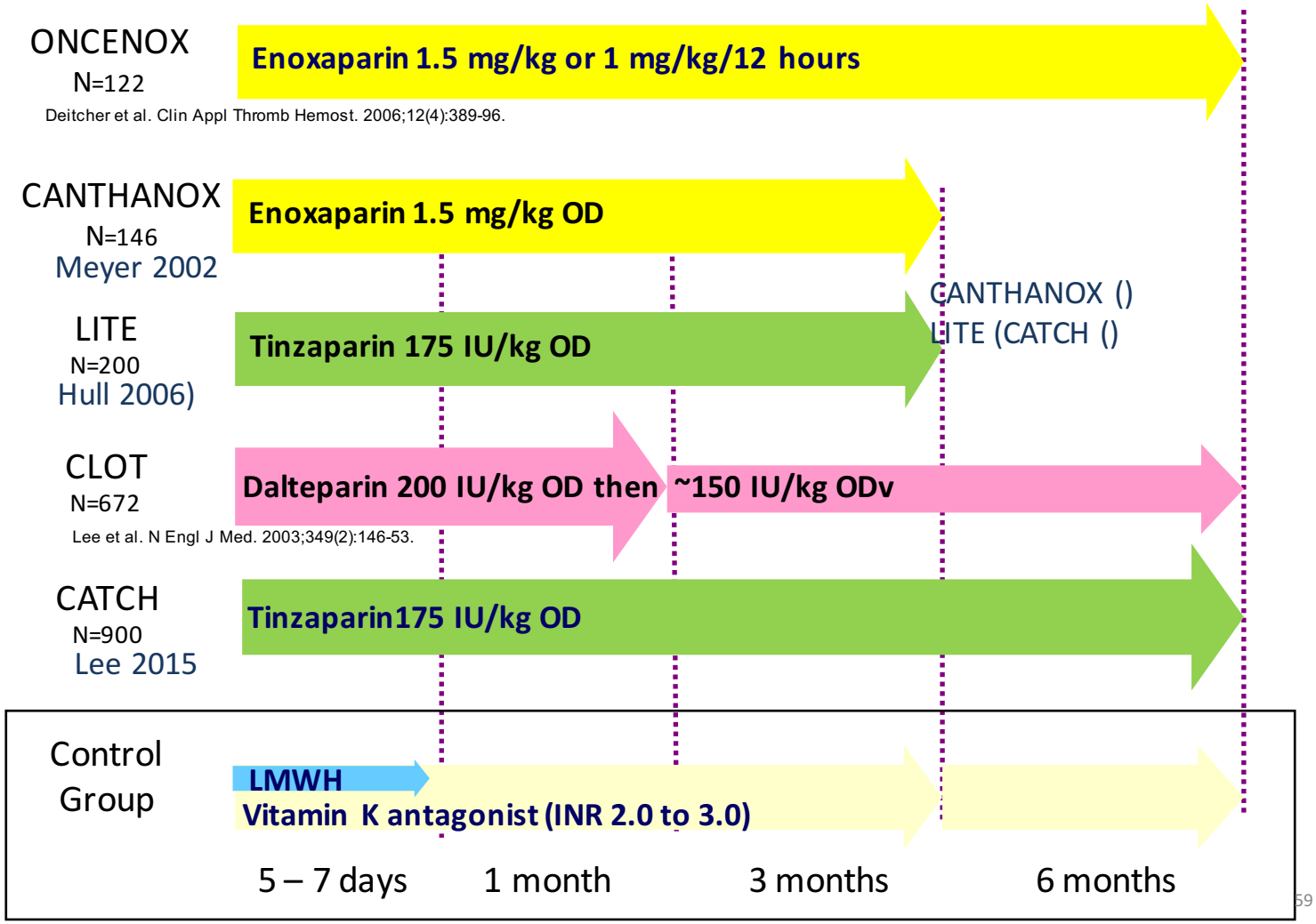
    RR 0.78; 95% CI 0.29-2.08

Figure 2. Forest plot of comparison: 1 Low molecular weight heparin (LMWH) versus unfractionated heparin (UFH), outcome: 1.1 Mortality at 3 months.



Akl *et al.* Cochrane Database Syst Rev. 2014 Jun 19;(6):CD006649

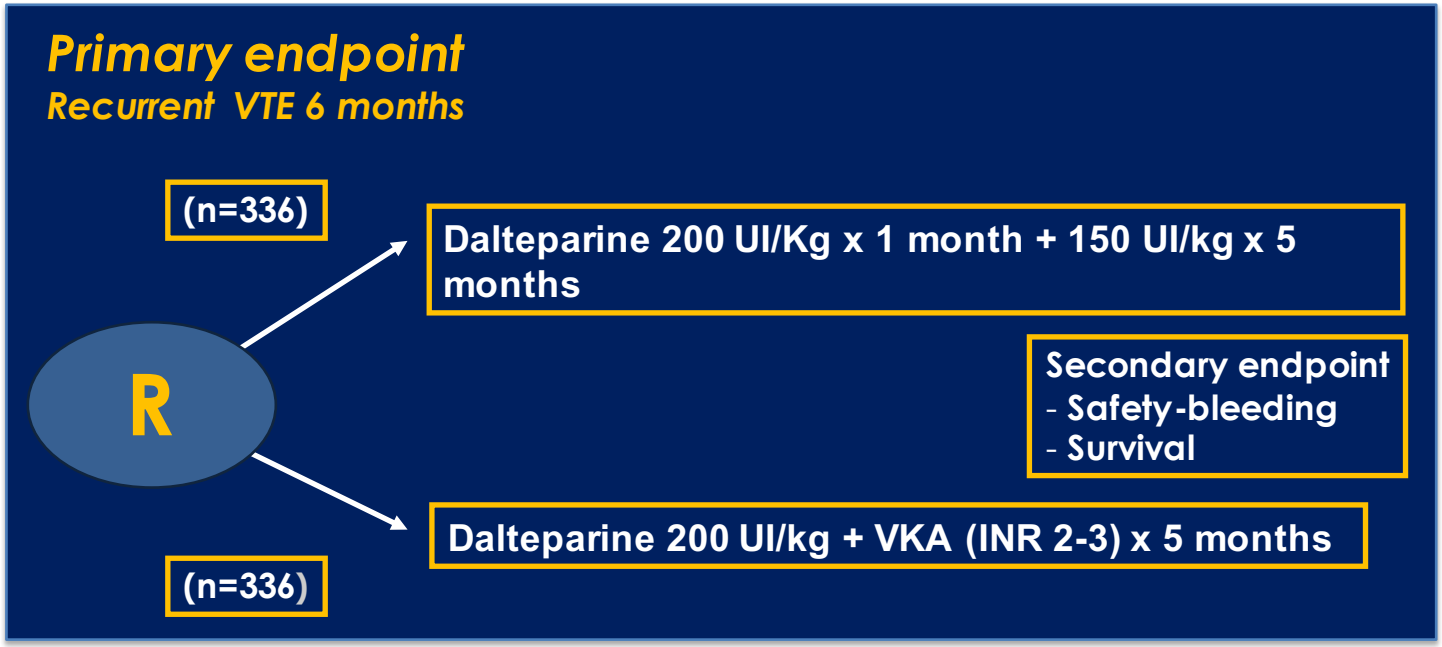
Treatment of VTE in Cancer



CLOT trial

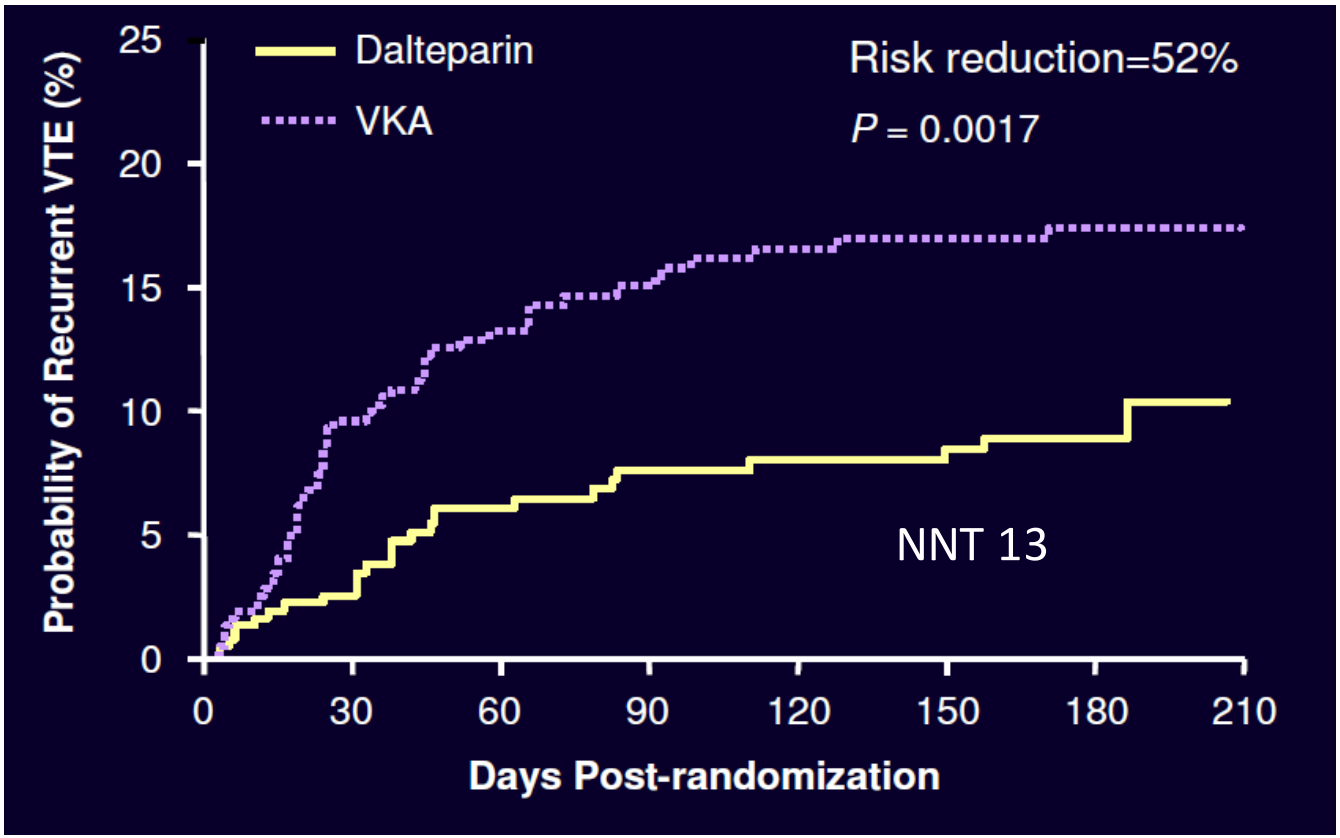
ORIGINAL ARTICLE

Low-Molecular-Weight Heparin versus a Coumarin for the Prevention of Recurrent Venous Thromboembolism in Patients with Cancer



Lee et al. N Engl J Med. 2003;349(2):146-53.

CLOT: Recurrent VTE



Lee et al. N Engl J Med. 2003;349(2):146-53.

CLOT: Bleeding

Outcome	LMWH n=338 (%)	VKA n=335 (%)	p*
Major bleed	19 (5.6)	12 (3.6)	0.27
Any bleed	46 (13.6)	62 (18.5)	0.093

*Fisher's exact test.

Lee et al. N Engl J Med. 2003;349(2):146-53.

LMWH drug of choice for long term treatment of cancer-associated VTE

Journal of Thrombosis and Haemostasis, 11: 56–70 DOI: 10.1111/jth.12070

ORIGINAL ARTICLE

International clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer

D. FARGE,*† P. DEBOURDEAU,‡ M. BECKERS,§ C. BAGLIN,¶ R. M. BAUERSACHS,** B. BRENNER,†† D. BRILHANTE,‡‡ A. FALANGA,§§ G. T. GEROTZIAFAS,¶¶ N. HAIM,*** A. K. KAKKAR,††† A. A. KHORANA,‡‡‡ R. LECUMBERRI,§§§ M. MANDALA,¶¶¶ M. MARTY,**** M. MONREAL,†††† S. A. MOUSA,‡‡‡‡ §§§§ S. NOBLE,¶¶¶¶ I. PABINGER,***** P. PRANDONI,††††† M. H. PRINS,‡‡‡‡‡ M. H. QARI,§§§§§ M. B. STREIFF,¶¶¶¶¶ K. SYRIGOS,****** H. BOUNAMEAUX†††††¹ and H. R. BÜLLER‡‡‡‡‡¹

Clin Transl Oncol (2014) 16:1079–1090
DOI 10.1007/s12094-014-1238-y

CLINICAL GUIDES IN ONCOLOGY

Clinical guide SEOM on venous thromboembolism in cancer patients

A. J. Muñoz Martín · C. Font Puig · L. M. Navarro Martín · P. Borrega García · M. Martín Jiménez

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Venous Thromboembolic Disease

NCCN National Comprehensive Cancer Network®

Version 2.2013

NCCN.org

clinical practice guidelines

Annals of Oncology 22 (Supplement 6): vi85–vi92, 2011
doi:10.1093/annonc/mdr392

Management of venous thromboembolism (VTE) in cancer patients: ESMO Clinical Practice Guidelines

M. Mandalà[1], A. Falanga[2] & F. Roila[3]

On behalf of the ESMO Guidelines Working Group*

[1]*Unit of Medical Oncology;* [2]*Division Immunohaematology and Transfusion Medicine, Haemostasis and Thrombosis Center, Department of Oncology and Haematology, Ospedali Riuniti, Bergamo;* [3]*Department of Medical Oncology, S. Maria Hospital, Terni, Italy*

ASCO Recommendations

Q4. Treatment and Secondary Prophylaxis

4.1 LMWH is preferred over UFH for the initial 5 to 10 days of anticoagulation for the cancer patient with newly diagnosed VTE who does not have severe renal impairment (defined as creatinine clearance < 30 mL/min).

4.2 For long term anticoagulation, LMWH for at least 6 months is preferred due to improved efficacy over Vitamin K antagonists. Vitamin K antagonists are an acceptable alternative for long-term therapy if LMWH is not available.

4.3 Anticoagulation with LMWH or Vitamin K antagonist beyond the initial 6 months may be considered for select patients with active cancer, such as those with metastatic disease or those receiving chemotherapy.

4.4 The insertion of a vena cava filter is only indicated for patients with contraindications to anticoagulant therapy (see Table 4). It may be considered as an adjunct to anticoagulation in patients with progression of thrombosis (recurrent VTE or extension of existing thrombus) despite optimal therapy with LMWH.

www.asco.org/guidelines/VTE last access May 2016

VKA in cancer patients

VKA-time in therapeutic range:

- 41% in CANTHANOX [1]
- 45% in LITE [2]
- 46% in CLOT [3]
- 47% in CATCH [4]

1. Meyer G et al. Arch Intern Med. 2002;162(15):1729-35
2. Hull R et al. Am J Med. 2006;119(12):1062-72
3. Lee AY et al. J Clin Oncol. 2005;23(10):2123-9
4. Lee AY et al. JAMA. 2015;314(7):677-86

Treatment of cancer-associated VTE

INR (range)	Recurrent VTE		Major Bleeding	
	Cancer	No Cancer	Cancer	No Cancer
< 2.0	**54**	**15.9**	30.6	0
2.0–3.0	18.9	7.2	11.2	0.8
> 3.0	18.4	6.4	0	6.3
Overall	27	9	13.3	2.1
Number of events per 100 patients/yrs				

Hutten BA et al. J Clin Oncol. 200;18: 3078-83.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 24, 2012 VOL. 366 NO. 21

Aspirin for Preventing the Recurrence of Venous Thromboembolism

Cecilia Becattini, M.D., Ph.D., Giancarlo Agnelli, M.D., Alessandro Schenone, M.D., Sabine Eichinger, M.D., Eugenio Bucherini, M.D., Mauro Silingardi, M.D., Marina Bianchi, M.D., Marco Moia, M.D., Walter Ageno, M.D., Maria Rita Vandelli, M.D., Elvira Grandone, M.D., and Paolo Prandoni, M.D., Ph.D., for the WARFASA Investigators*

20-30% VTE risk reduction when compared to placebo

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 22, 2012 VOL. 367 NO. 21

Low-Dose Aspirin for Preventing Recurrent Venous Thromboembolism

Timothy A. Brighton, M.B., B.S., John W. Eikelboom, M.B., B.S., Kristy Mann, M.Biostat., Rebecca Mister, M.Sc., Alexander Gallus, M.B., B.S., Paul Ockelford, M.B., Harry Gibbs, M.B., Wendy Hague, Ph.D., Denis Xavier, M.Sc., Rafael Diaz, M.D., Adrienne Kirby, M.Sc., and John Simes, M.D., for the ASPIRE Investigators*

Hospital General Universitario Gregorio Marañón

SaludMadrid

Comunidad de Madrid

Cancer patients

?

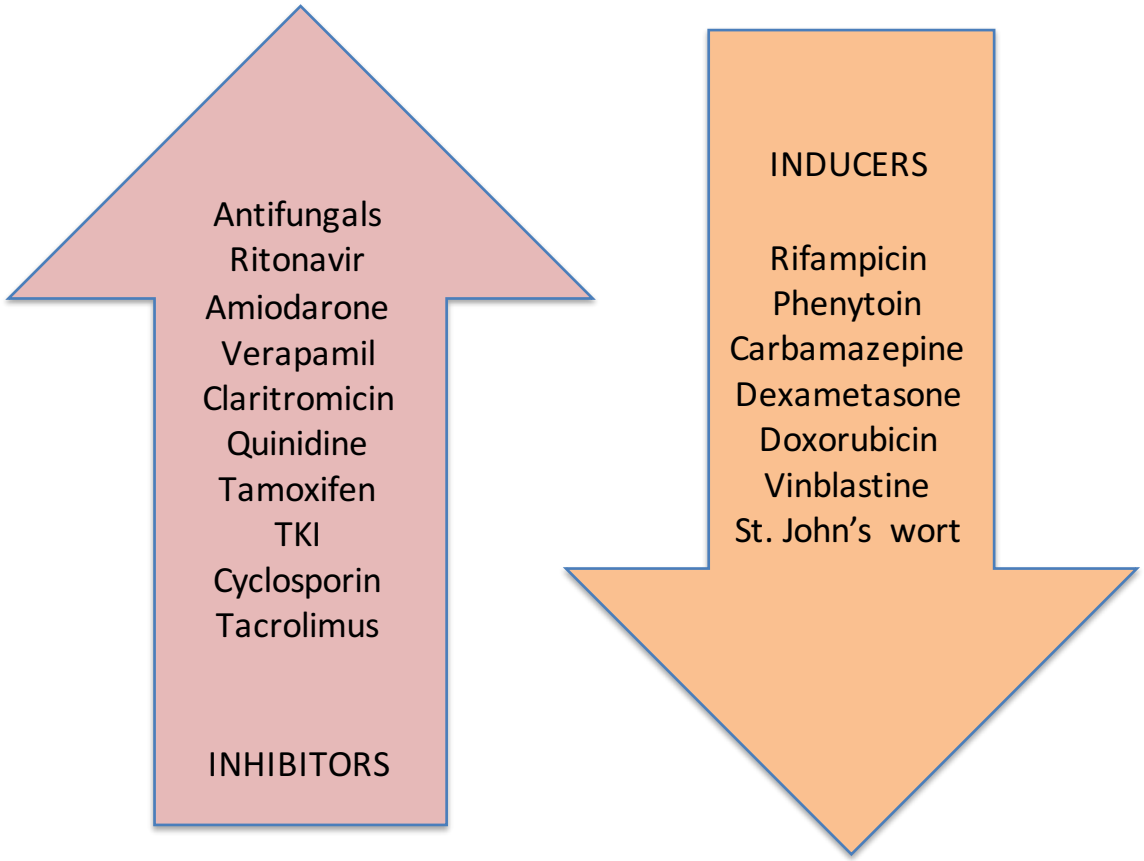
DOACs: Are drug interactions with chemotherapy agents clinically relevant?

Table 2. Interactions between chemotherapeutic agents and immunosuppressants with NOACs based on known metabolic pathway activity

	Dabigatran	Rivaroxaban	Apixaban
Interaction effect*	**P-glycoprotein**	**P-glycoprotein CYP3A4**	**P-glycoprotein CYP3A4**
Increases NOAC plasma levels†	Cyclosporine Tacrolimus Tamoxifen Lapatinib Nilotinib Sunitinib	Cyclosporine Tacrolimus Tamoxifen Lapatinib Nilotinib Sunitinib Imatinib	Cyclosporine Tacrolimus Tamoxifen Lapatinib Nilotinib Sunitinib Imatinib
Reduces NOAC plasma levels‡	Dexamethasone Doxorubicin Vinblastine	Dexamethasone Doxorubicin Vinblastine	Dexamethasone Doxorubicin Vinblastine

Lee *et al* Blood. 2013;122(14):2310 – 2317

DOACS & Interactions



DOACs in Cancer Patients
Current Clinical Trials

Clinical Trial	Indication	Drug	Number of Patients
SELECT-D	Treatment	Rivaroxaban vs dalteparin	N=530
CASTA-DIVA	Treatment	Rivaroxaban vs dalteparin	N=200
CONKO-011 **Primary outcome measures patient-reported treatment satisfaction (convenience)**	Treatment	Rivaroxaban vs LMWH	N=450
HOKUSAI-VTE Cancer	Treatment	Edoxaban vs dalteparin	N=1.000
CARAVAGGIO **EU-USA**	Treatment	Apixaban vs dalteparin	N≈1.200
NCT02585713 **Primary outcome major bleeding including fatal bleeding**	Treatment	Apixaban vs dalteparin	N=315

www.clinicaltrials.gov Last access July 2017

ETV-Oncología
Tratamiento de trombosis asociada a catéter

Table 2. Recommendations for Treatment of VTE in Patients With Cancer by the Guideline Panels

Parameter	ASCO	NCCN	AIOM/ESMO	FNCLCC
Treatment of catheter-related thrombosis	NA	LMWH or VKA for as long as catheter is in place and for at least 3 months after catheter removal	NA	LMWH for up to 6 months; consider VKA after 6 months as long as cancer is active or catheter in place; anticoagulate for up to 6 weeks after catheter removal if cancer is not active

- **Manejo similar a la TVP de MMII.**
- **No indicación de retirada inmediata de catéter**
  - **Refractariedad tratamiento anticoagulante**
  - **Contraindicación tratamiento anticoagulante**
  - **Riesgo vital/pérdida de miembro**
- **Alto riesgo de TEP y de evolución fatal a pesar de tratamiento anticoagulante óptimo**
- **Duración: 6 meses de tratamiento anticoagulante. Tto indefinido si cáncer activo**
- **Anticoagulación mientras permanezca el catéter y al menos 6 sem-3 meses tras retirada del catéter si cáncer no activo**

Journal of Clinical Oncology Vol 27, October 2009

ETV-Oncología
Terapia trombolítica inicial ETV

Thrombolytic therapy in the initial treatment of VTE in patients with cancer	Restricted to patients with life- or limb-threatening thrombotic events	Restricted to appropriate candidates with massive DVT or massive or sub-massive PE with moderate to severe right ventricular dysfunction	NA	Restricted to PE with hemodynamic collapse

- **Terapia trombolítica reduce rápidamente el trombo y el síndrome postrombótico**
- **Aumento del riesgo de sangrados mayores y sangrados fatales**
- **No hay estudios específicos que evalúen su en pacientes con cáncer**
- **Misma indicación que en pacientes no oncológicos**
- **Únicamente recomendado en**
  - **Situaciones de riesgo vital (TEP masivo con inestabilidad hemodinámica, etc.)**
  - **Pérdida de extremidad**

Journal of Clinical Oncology Vol 27, October 2009

ETV-Oncología
Filtro de VCI y ETV

Hospital General Universitario Gregorio Marañón
SaludMadrid
Comunidad de Madrid

Table 2. Recommendations for Treatment of VTE in Patients With Cancer by the Guideline Panels

Parameter	ASCO	NCCN	AIOM/ESMO	FNCLCC
Inferior vena cava filters	Restricted to patients with contraindications to anticoagulation or recurrent VTE despite adequate long-term LMWH	Restricted to patients with contraindications to or failure of anticoagulation, cardiac or pulmonary dysfunction severe enough to make any new PE life-threatening or multiple PE with chronic pulmonary hypertension	Contraindications to anticoagulation or PE despite adequate long-term LMWH	Contraindications to anticoagulation or PE despite adequate long-term LMWH; start anticoagulation as soon as possible

- **No hay estudios específicos que evalúen su eficacia en pacientes con cáncer[1]**
- **Estudio PREPIC (Decousus NEJM 1998):**
  - **Estudio randomizado, 25% pacientes con cáncer**
  - **Protección a corto plazo EP**
  - **Incremento significativo TVP y trombosis de filtro**
- **Indicaciones (recomendación ASCO/SEOM):**
  - **Contraindicación absoluta para anticoagulación o**
  - **TEP/TVP recurrente durante tratamiento anticoagulante óptimo**
- **Si es posible se recomienda anticoagular tras la implantación del filtro de VCI tan pronto como sea posible**

[1]Mismetti Pathol Biol 2008. Khorana et al. JCO 2009

¿Efecto antitumoral de las heparinas?

- No bservado con jel Sitrom
- Algunos estudios lo sugieren: cáncer de pulmón microcítico, tumores con poca carga tumoral, etc.
- Sin embargo múltiples estudios los niegan
- Actualmente: ¿?

TESEO Registry

SEOM
Sociedad Española de Oncología Médica

- VTE & Cancer Registry
- Cancer & Thrombosis Working Group, Spanish Society of Medical Oncology (SEOM)
- Start: January 2018, Spain 20-30 starting centers
- International registry

TESEOm

Muchas gracias por su atención