

Dr. Vladimir Rosa Salazar.
Unidad de Enfermedad Tromboembólica Venosa
Unidad de Corta Estancia.
Servicio de Medicina Interna.
Hospital Universitario Virgen de la Arrixaca.
Murcia.



Arrixaca
Hospital Universitario
"Virgen de la Arrixaca"

26-28
Octubre
2011

Costa Meloneras

Palacio de Congresos Expomeloneras
Maspalomas, San Bartolomé de Tirajana
Gran Canaria, Las Palmas



JUEVES, 27 DE OCTUBRE

12:45-13:45 h

SALA C

CONTROVERSIA 3

NOVEDADES EN ANTICOAGULACIÓN

¿NOS OLVIDAMOS YA DE LA HEPARINA Y LAS ANTIVITAMINAS K?

Moderadora:

Dra. M^a Reina Valle Bernad

Servicio de Medicina Interna

Hospital Sierrallana. Torrelavega, Cantabria

SI

Dra. Ángeles Blanco Molina

Servicio de Medicina Interna

Hospital Universitario Reina Sofía. Córdoba

NO

Dr. Vladimir Rosa Salazar

Servicio de Medicina Interna

Hospital Universitario Virgen de la Arrixaca. Murcia

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- [Fever and deep venous thrombosis. Findings from the RIETE registry.](#)
 1. Barba R, Di Micco P, **Blanco-Molina A**, Delgado C, Cisneros E, Villalta J, Morales MV, Bura-Riviere A, Debourdeau P, Monreal M. *J Thromb Thrombolysis*. 2011 Oct;32(3):288-92. PMID: 21701950 [PubMed - in process] [Related citations](#)
- [Venous thromboembolism in women taking hormonal contraceptives.](#)
 2. **Blanco-Molina A**, Monreal M. *Expert Rev Cardiovasc Ther*. 2010 Feb;8(2):211-5. Review. PMID: 20136607 [PubMed - indexed for MEDLINE] [Related citations](#)
- [Venous thromboembolism during pregnancy, postpartum or during contraceptive use.](#)
 3. **Blanco-Molina A**, Rota LL, Di Micco P, Brenner B, Trujillo-Santos J, Ruiz-Gamietea A, Monreal M; RIETE Investigators. *Thromb Haemost*. 2010 Feb;103(2):306-11. Epub 2009 Nov 13. PMID: 20126835 [PubMed - indexed for MEDLINE] [Related citations](#)
- [Venous thromboembolism in women using hormonal contraceptives. Findings from the RIETE Registry.](#)
 4. **Blanco-Molina A**, Trujillo-Santos J, Tirado R, Cañas I, Riera A, Valdés M, Monreal M; RIETE Investigators. *Thromb Haemost*. 2009 Mar;101(3):478-82. PMID: 19277408 [PubMed - indexed for MEDLINE] [Related citations](#)
- [\[Anticoagulation treatment withdrawal in primary antiphospholipid syndrome when anticardiolipin antibodies become negative\].](#)
 5. Criado-García J, Fernández-Puebla RA, Jiménez LL, Velasco F, Santamaría M, **Blanco-Molina A**. *Rev Clin Esp*. 2008 Mar;208(3):135-7. Spanish. PMID: 18275767 [PubMed - indexed for MEDLINE] [Related citations](#)
- [The -675 4G/5G polymorphism at the Plasminogen Activator Inhibitor 1 \(PAI-1\) gene modulates plasma Plasminogen Activator Inhibitor 1 concentrations in response to dietary fat consumption.](#)
 6. Pérez-Martínez P, Adarraga-Cansino MD, Fernández de la Puebla RA, **Blanco-Molina A**, Delgado-Lista J, Marín C, Ordovás JM, López-Miranda J, Pérez-Jiménez F. *Br J Nutr*. 2008 Apr;99(4):699-702. Epub 2007 Oct 1. PMID: 17903340 [PubMed - indexed for MEDLINE] [Related citations](#)
- [Venous thromboembolism during pregnancy or postpartum: findings from the RIETE Registry.](#)
 7. **Blanco-Molina A**, Trujillo-Santos J, Criado J, Lopez L, Lecumberri R, Gutierrez R, Monreal M; RIETE Investigators. *Thromb Haemost*. 2007 Feb;97(2):186-90. PMID: 17264945 [PubMed - indexed for MEDLINE] [Related citations](#)
- [\[Cutaneous vasculitis due to hypersensitivity probably caused by ketorolac trometamol\].](#)
 8. Barroso Casamitjana E, Isla Tejera B, Ruano Ruiz J, **Blanco-Molina A**. *Farm Hosp*. 2006 Jan-Feb;30(1):60-2. Spanish. No abstract available. PMID: 16569187 [PubMed - indexed for MEDLINE] **Free Article** [Related citations](#)
- [An aqueous stem bark extract of *Mangifera indica* \(Vimang\) inhibits T cell proliferation and TNF-induced activation of nuclear transcription factor NF-kappaB.](#)
 9. Garrido G, **Blanco-Molina M**, Sancho R, Macho A, Delgado R, Muñoz E. *Phytother Res*. 2005 Mar;19(3):211-5. PMID: 15934029 [PubMed - indexed for MEDLINE] [Related citations](#)
- [\[Venous thromboembolism in patients with neurosurgical process or stroke. A prospective analysis from the RIETE registry\].](#)
 10. **Blanco-Molina A**, Palma I, Rubio C, Suárez C, Barba R, Gutiérrez MR; Grupo RIETE. *Med Clin (Barc)*. 2004 Oct 2;123(11):416-8. Spanish. PMID: 15482715 [PubMed - indexed for MEDLINE] [Related citations](#)
- [Calcium ionophoretic and apoptotic effects of ferutinin in the human Jurkat T-cell line.](#)
 11. Macho A, **Blanco-Molina M**, Spaqliardi P, Apendino G, Bremner P, Heinrich M, Fiebig BL, Muñoz E.

14. Pérez-Jiménez F, López-Miranda J, Pinillos MD, Gómez P, Paz-Rojas E, Montilla P, Marín C, Velasco MJ, **Blanco-Molina A**, Jiménez Perepérez JA, Ordovás JM. Diabetologia. 2001 Nov;44(11):2038-43.
PMID: 11719836 [PubMed - indexed for MEDLINE]
[Related citations](#)
- [Ingenol esters induce apoptosis in Jurkat cells through an AP-1 and NF-kappaB independent pathway.](#)
15. **Blanco-Molina M**, Tron GC, Macho A, Lucena C, Calzado MA, Muñoz E, Appendino G. Chem Biol. 2001 Aug;8(8):767-78.
PMID: 11514226 [PubMed - indexed for MEDLINE]
[Related citations](#)
- [New glycosides from Capsicum annum L. var. acuminatum. Isolation, structure determination, and biological activity.](#)
16. Iorizzi M, Lanzotti V, De Marino S, Zollo F, **Blanco-Molina M**, Macho A, Muñoz E. J Agric Food Chem. 2001 Apr;49(4):2022-9.
PMID: 11308362 [PubMed - indexed for MEDLINE]
[Related citations](#)
- [\[Hepatic inflammatory pseudotumor: apropos a case with a response to steroid treatment\].](#)
17. Fernández de la Puebla Giménez RA, García Alegría J, Lechuga Varona MT, **Blanco Molina MA**. Gastroenterol Hepatol. 1999 Jan;22(1):14-7. Review. Spanish.
PMID: 10089706 [PubMed - indexed for MEDLINE]
[Related citations](#)
- [\[Influence of genetic variation at apoprotein A-1 gene promoter region on plasma lipid levels in heart transplantation patients\].](#)
18. González Amieva A, Zambrana JL, López-Granados A, Concha M, López Miranda J, **Blanco Molina A**, Jiménez Perepérez JA, Pérez Jiménez F. Med Clin (Barc). 1998 Sep 26;111(9):321-4. Spanish.
PMID: 9810532 [PubMed - indexed for MEDLINE]
[Related citations](#)
- [Effects of different dietary cholesterol concentrations on lipoprotein plasma concentrations and on cholesterol efflux from Fu5AH cells.](#)
19. **Blanco-Molina A**, Castro G, Martín-Escalante D, Bravo D, López-Miranda J, Castro P, López-Segura F, Fruchart JC, Ordovás JM, Pérez-Jiménez F. Am J Clin Nutr. 1998 Nov;68(5):1028-33.
PMID: 9808218 [PubMed - indexed for MEDLINE] **Free Article**
[Related citations](#)
- [Dietary fat clearance in normal subjects is modulated by genetic variation at the apolipoprotein B gene locus.](#)
20. Lopez-Miranda J, Ordovas JM, Ostos MA, Marin C, Jansen S, Salas J, **Blanco-Molina A**, Jimenez-Pereperez JA, Lopez-Segura F, Perez-Jimenez F. Arterioscler Thromb Vasc Biol. 1997 Sep;17(9):1765-73.
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MARÍA ÁNGELES BLANCO MOLINA

"El flamenco es una terapia de bienestar"

Orgullosa de que el flamenco sea ya Patrimonio Cultural Inmaterial de la Humanidad por la Unesco, esta profesional del Hospital Reina Sofía lo considera una vía de escape.

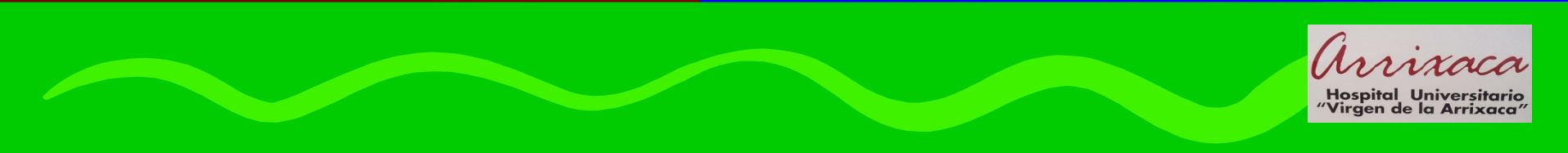
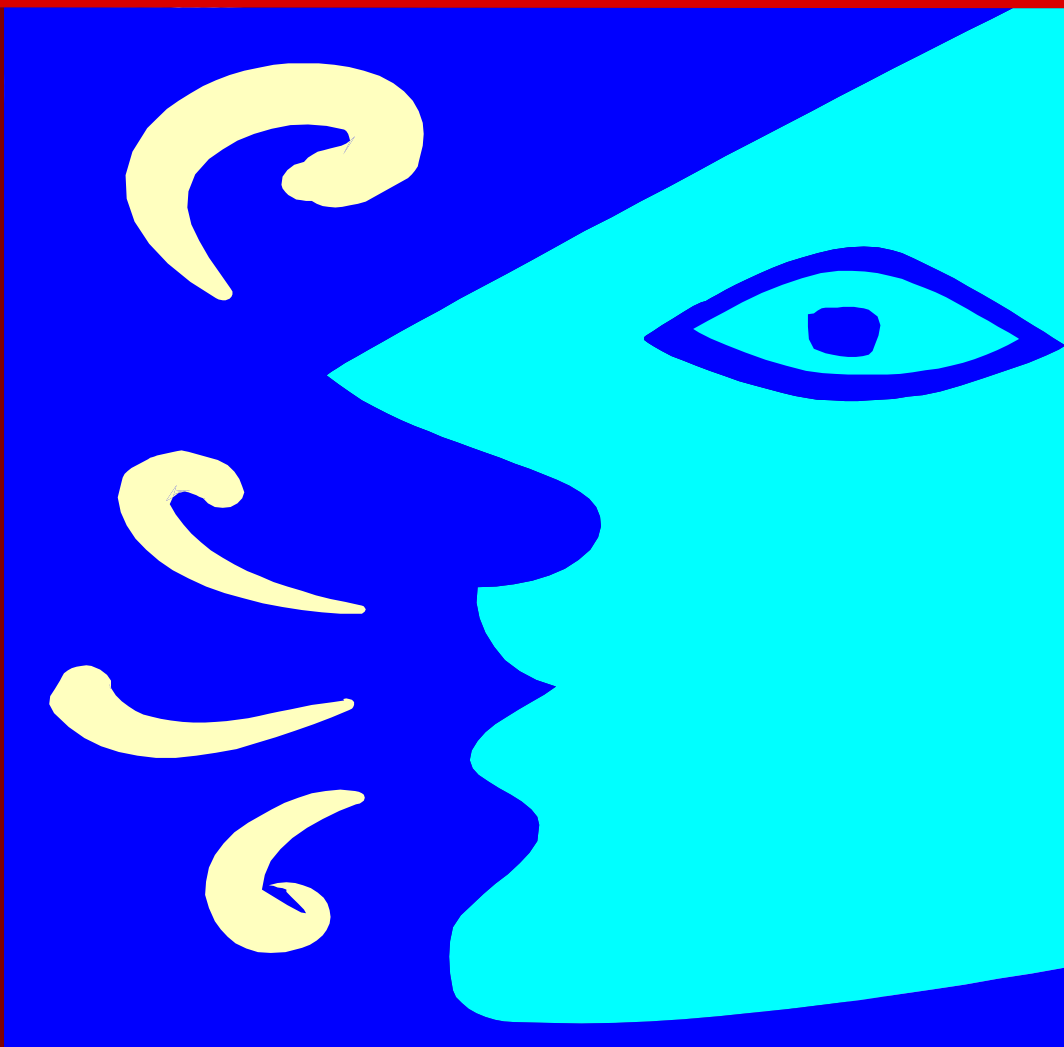
Juana Jiménez. Córdoba | 21/02/2011 00:00

☆☆☆☆☆ |vota! | 0 comentarios

compartir (¿qué es esto?)



María Ángeles Blanco Molina (a la derecha), con una compañera de clase, Pilar Sánchez de Puerta, enfermera supervisora del Servicio de Urología del Hospital Reina Sofía. (DM)





**“AVK y HBPM:
una prejubilación injustificada”**

“En la vida todo está continuamente en evolución”

Ludwig von Mises



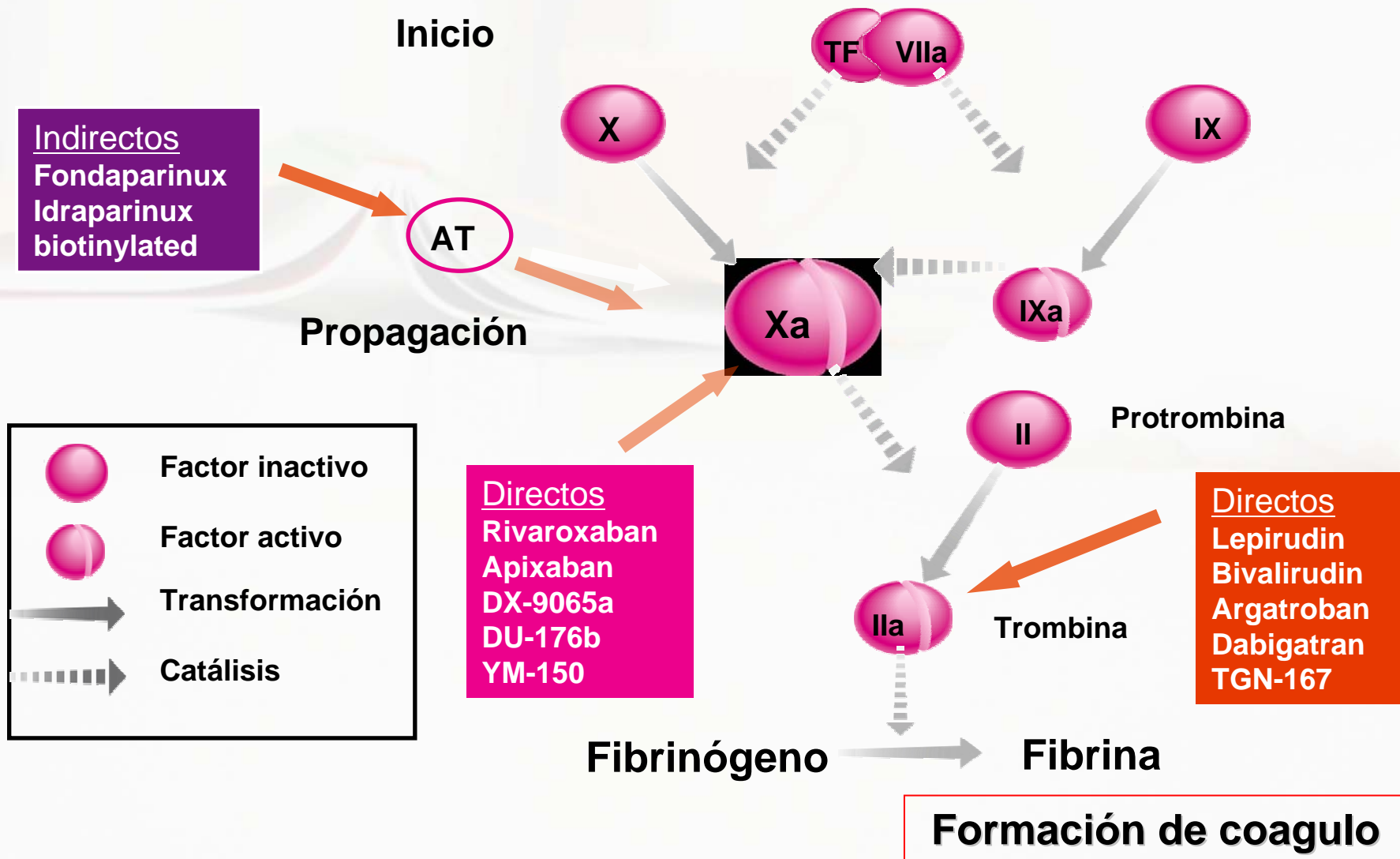
Arrixaca
Hospital Universitario
“Virgen de la Arrixaca”



“Todos los cambios, aun los más ansiados, llevan consigo cierta melancolía”

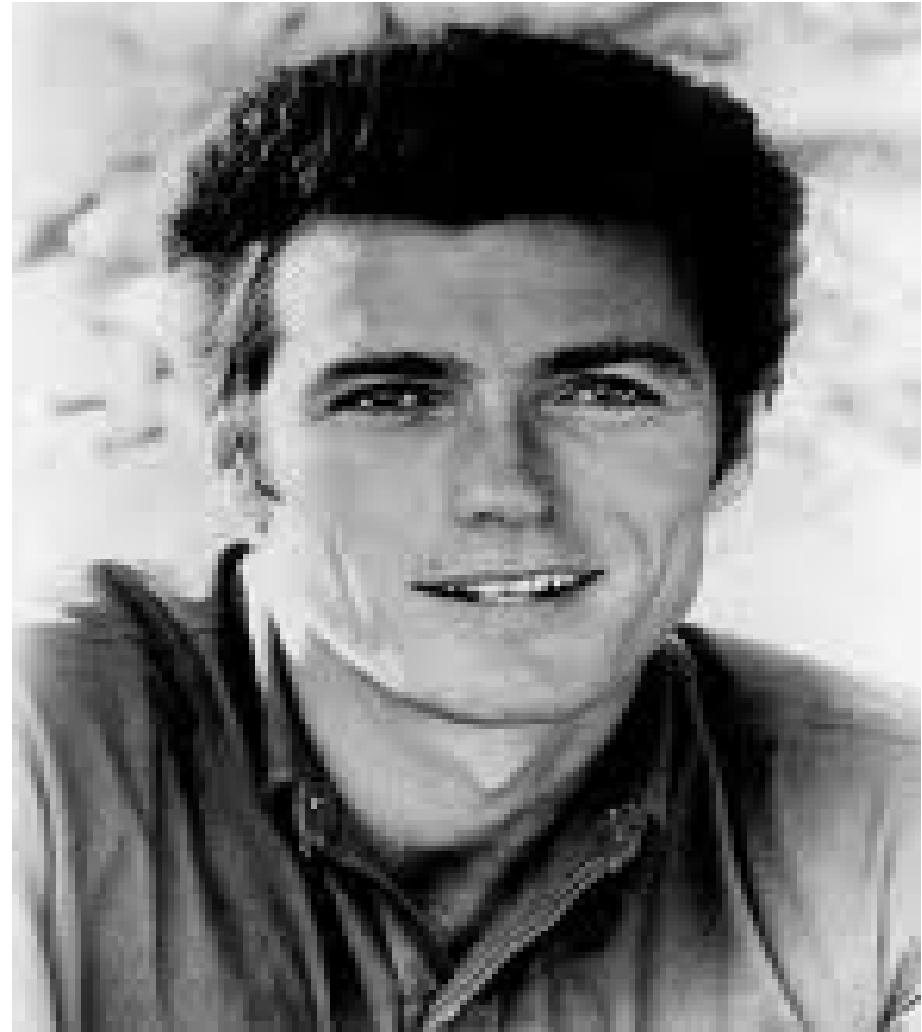


Anticoagulación





Antivitaminas K





Cronología ACO



- 1921: Epidemia en el ganado de EEUU y Canada. Trebol mohoso dulce.
- 1941: patente del Dicumarol.
- 1948: Warfarina (Wisconsin Alumni Research Foundation). Raticida.
- 1951: intento de suicidio de un soldado EEUU con Warfarina.
- 1954: se aprueba su uso en humanos.
- 1978: se descubre que interfiere con la vitamina K.





Heparinas



HNF



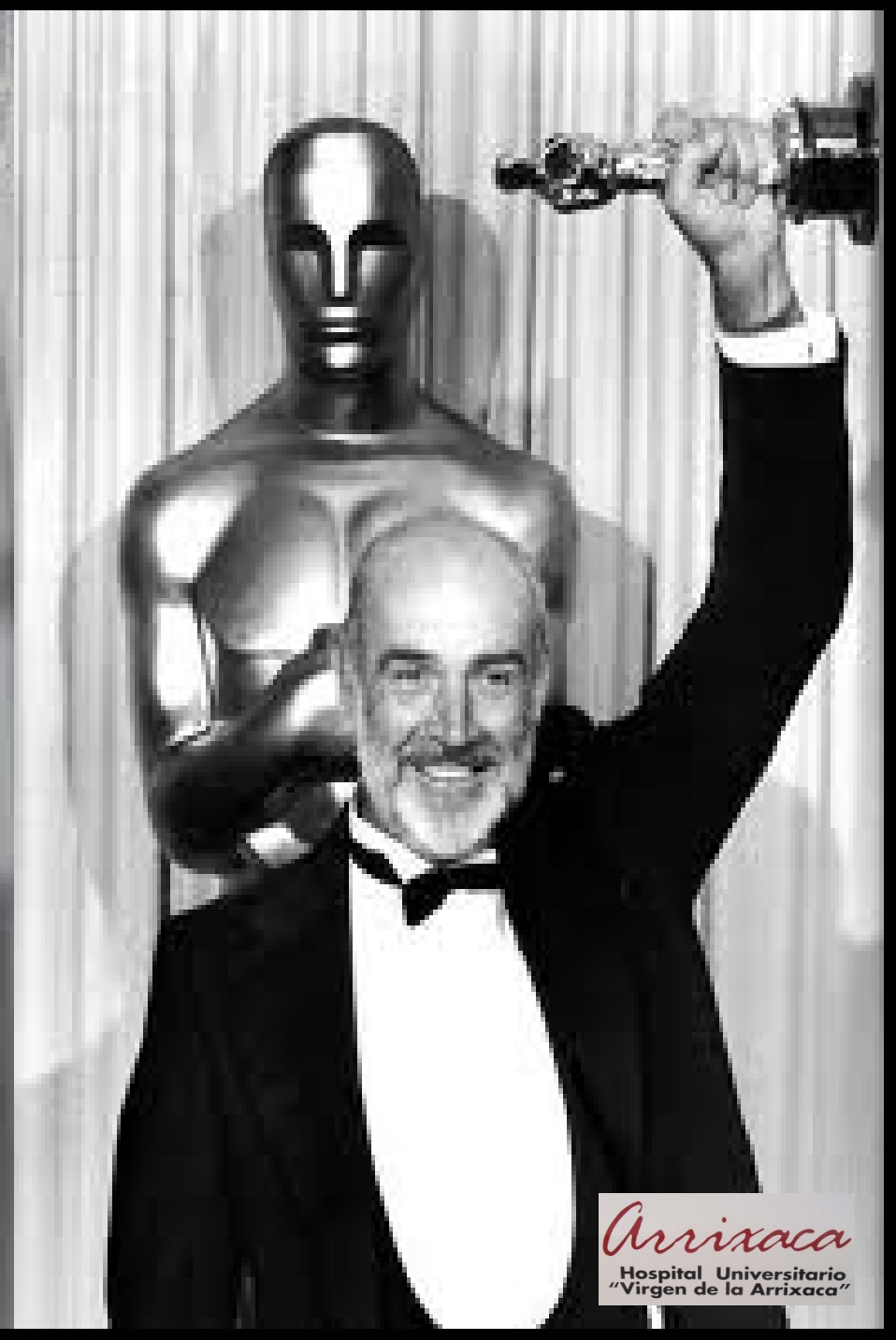
HBPM



Cronología Heparina



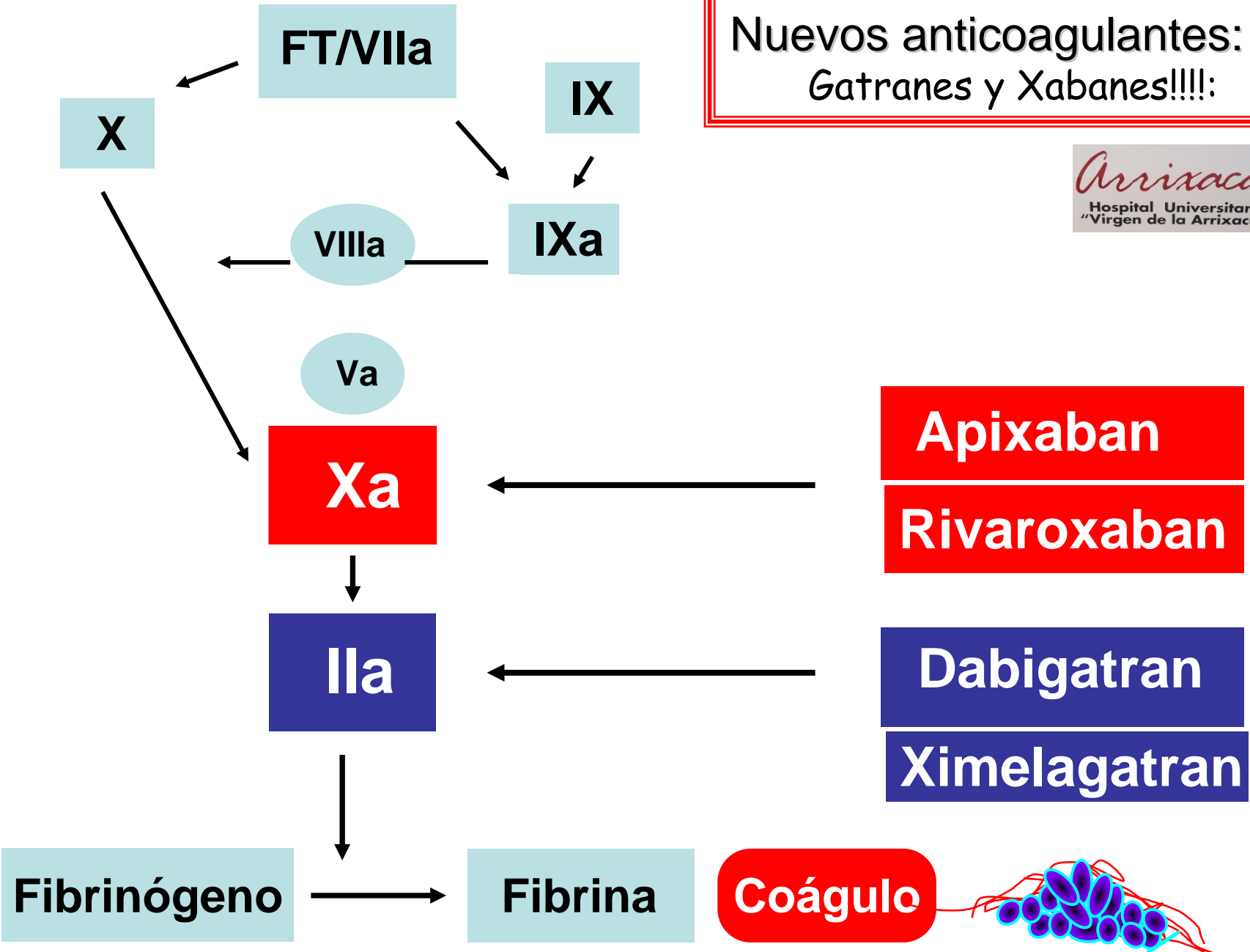
- 1922: William Howell aisló la heparina procedente del hígado (Universidad Johns Hopkins)
- 1933-37: preparados de heparina con la suficiente pureza (pulmón bovino).
- 1937: comienzan a inyectarse preparados de heparina para evitar trombosis postoperatorias.
- 1960: se descubre que solo una parte es necesaria para inhibir el factor Xa.
- 1980: síntesis y comercialización de HBPM.



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**Nuevos anticoagulantes:
Gatranes y Xabanes!!!!**




Gatranes y Xabanes



¿futuro?







Indicaciones de anticoagulación

Indicaciones de anticoagulación



- ⊙ Profilaxis embolia arterial en ACxFA.
- ⊙ Profilaxis embolia arterial en prótesis valvulares.
- ⊙ Profilaxis ETEV.
- ⊙ Tratamiento fase aguda ETEV.
- ⊙ Tratamiento fase crónica ETEV.
- ⊙ Tratamiento SCA.



Anticoagulante ideal



■ Eficaz.

- ✓ Beneficio igual o mayor que warfarina.

■ Seguro.

- ✓ Menor o igual número de hemorragias.
- ✓ No toxicidad.
- ✓ Antídoto eficaz.

■ Cómodo.

- ✓ Buena biodisponibilidad vía oral.
- ✓ Dosis fijas sin monitorización.
- ✓ Rápido inicio de acción.
- ✓ Respuesta terapéutica predecible.
- ✓ No interacciones farmacológicas ni alimentarias.

■ Barato.



■ Eficaz:

✓ Beneficio igual o mayor que warfarina.



■ Seguro:

* ≤ número de hemorragias.

* No toxicidad.

* Antídoto eficaz.



Seguridad



Eficacia

Dabigatran REVOLUTION

Programa de desarrollo clínico Fase III

El programa de ensayos clínicos en enfermedad tromboembólica más amplio realizado (>34.000 pacientes)

Prevención Primaria de TVP (Cir. Ortop)

11 centros en España



Prótesis Cadera (EU) Prótesis Rodilla (EU)

Prótesis Rodilla (US)

Tratamiento TVP

8 centros en España



Prevención sec. TVP



SPAF



SCA



Rivaroxaban: Indicación aprobada y futuras indicaciones

Estudios de fase III

Indicaciones agudas

Prevencción de ETV en cirugía electiva de reemplazo de cadera o rodilla

RECORD^{1,2,3,4}

Prevencción ETV en pacientes médicos hospitalizados

MAGELLAN^{*}

Indicaciones crónicas

Tratamiento ETV y prevencción secundaria

eINSTEIN^{OUT IN OUT}

Prevencción Ictus en Fibrilación Auricular (FA)

ROCKET AF^{AF}

Prevencción secundaria en Síndrome Coronario Agudo (SCA)

ATLAS^{ACS TIME 51}



Estudio Finalizado

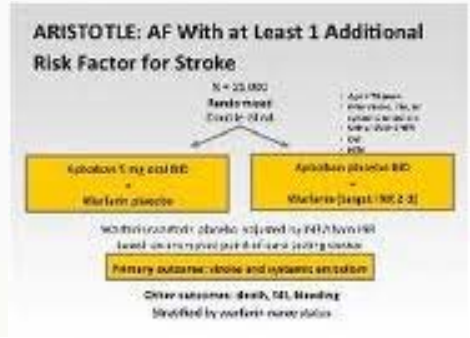


Estudio con resultados. Indicación no aprobada



Estudio en curso

Apixaban

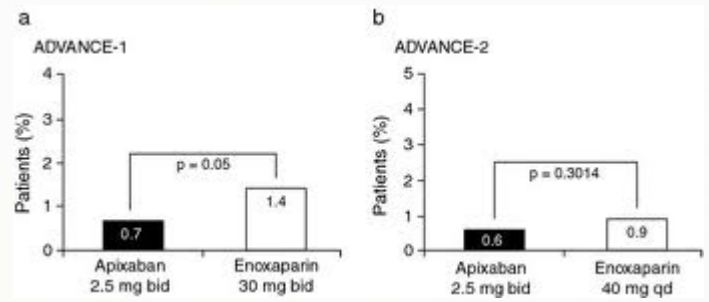
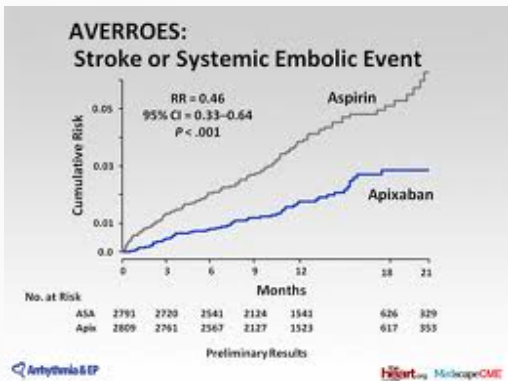
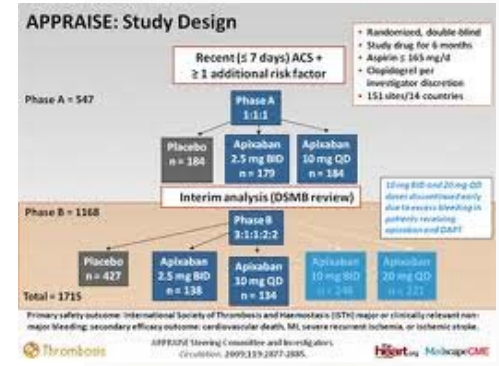


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Apixaban versus Warfarin in Patients with Atrial Fibrillation

Christopher B. Granger, M.D., John H. Alexander, M.D., M.H.S., John J.V. McMurray, M.D., Renato D. Lopes, M.D., Ph.D., Elaine M. Hylek, M.D., M.P.H., Michael Hanna, M.D., Hussein R. Al-Khalidi, Ph.D., Jack Ansell, M.D., Dan Atar, M.D., Alvaro Avezum, M.D., Ph.D., M. Cecilia Bahit, M.D., Rafael Diaz, M.D., J. Donald Easton, M.D., Justin A. Ezekowitz, M.B., B.Ch., Greg Flaker, M.D., David Garcia, M.D., Margarida Geraldes, Ph.D., Bernard J. Gersh, M.D., Sergey Golitsyn, M.D., Ph.D., Shinya Goto, M.D., Antonio G. Hermosillo, M.D., Stefan H. Hohnloser, M.D., John Horowitz, M.D., Puneet Mohan, M.D., Ph.D., Petr Jansky, M.D., Basil S. Lewis, M.D., Jose Luis Lopez-Sendon, M.D., Prem Pais, M.D., Alexander Parkhomenko, M.D., Freek W.A. Verheugt, M.D., Ph.D., Jun Zhu, M.D., and Lars Wallentin, M.D., Ph.D., for the ARISTOTLE Committees and Investigators*



Comodidad





■ Cómodo:

- * Dosis fija sin monitorización:
- * Buena disponibilidad v.o.:
- * Rápido inicio de acción:
- * Respuesta predecible:
- * No interacciones farmacológicas ni alimentarias



“No es oro todo lo que reluce, ni todo lo que anda errante está perdido”

J. R.

B. Tolkien



Comodidad → Adherencia

Ensayos clínicos



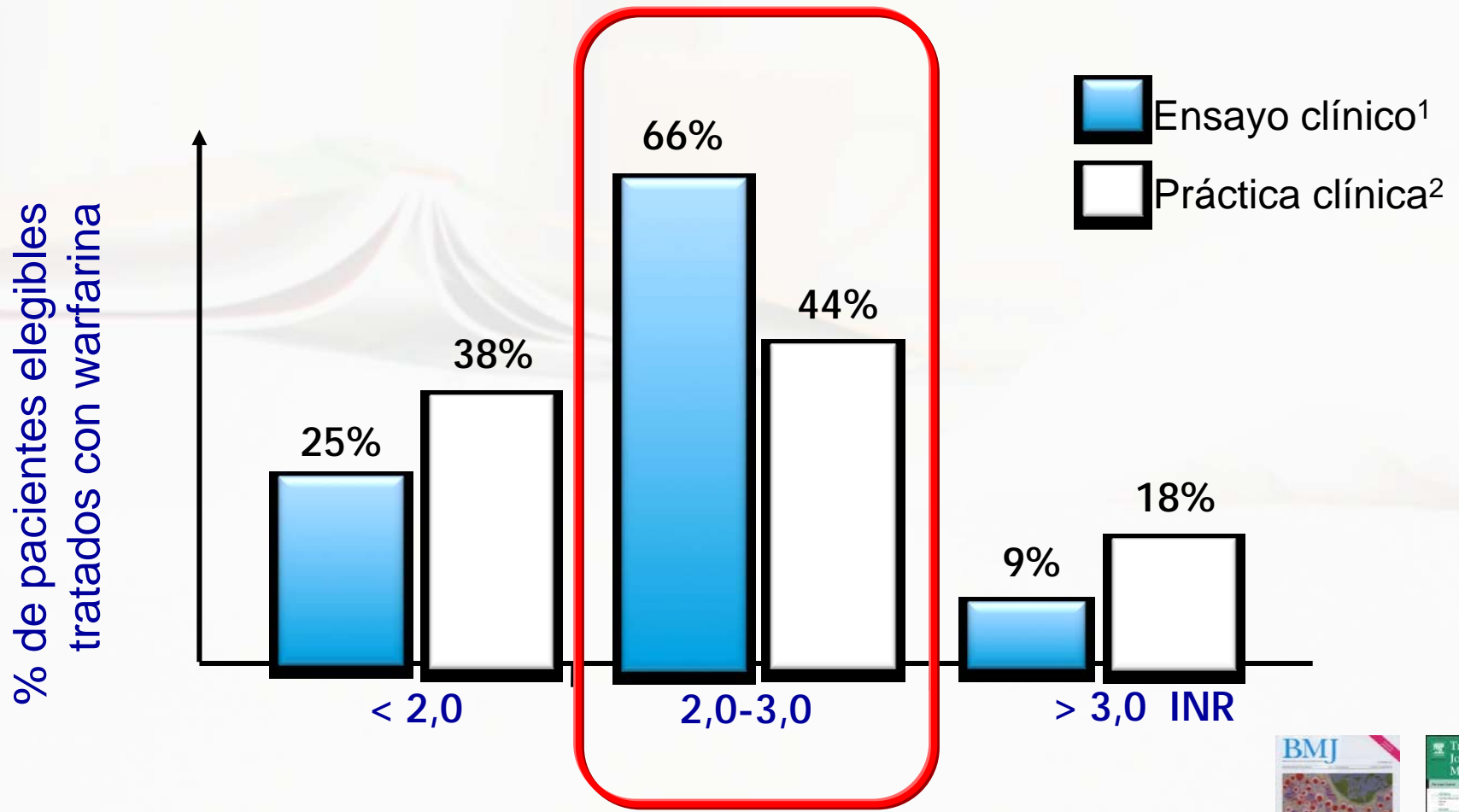
Vida real



TD

Telediario

Control del INR: ensayos clínicos frente a práctica clínica



* TIT = Tiempo en el intervalo terapéutico (INR 2,0-3,0)



Abandono del tratamiento en RE-LY



	Warafarina	Dabigatran 110 mg	Dabigatran 150 mg
Tasa abandono 1 ^{er} año.	10%	15%	16%
Tasa abandono 2 ^o año	17%	21%	21%

RE-COVER (TVP o TEP agudo sintomático)



Eventos adversos	Dabigatran	Warfarina	p
Dispepsia	3,1%	0,7%	<0.001
IAM	0,2%	0,2%	0.69
ALT > 3 veces	3,4%	3,8%	0.68
AST > 3 veces	3,1%	2,1%	0.14
ALT > 3 veces + bilirrubina > 2 veces	0,2%	0,4%	0.69
Abandono del estudio por eventos adversos	9%	6,8%	0.05

Adverse Events and Discontinuation

	Rivaroxaban (N=7111)	Warfarin (N=7125)
Any Adverse Event	82.4	82.2
Any Serious Adverse Event	37.3	38.2
AE leading to study drug discontinuation	15.7	15.2
Study drug discontinuation	23.7	22.2

Values are N (%)





■ Cómodo:

* Dosis fija sin monitorización:



* Buena disponibilidad v.o.:



* Rápido inicio de acción:



* Respuesta predecible:

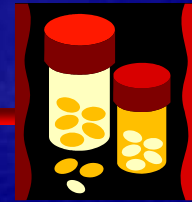


* No interacciones farmacológicas
ni alimentarias





Interacciones AVK



Incremento respuesta INR

Specific Drugs Reported		
acetaminophen	fenofibrate	oxymetholone
alcohol†	fenopropfen	pantoprazole
allopurinol	fluconazole	paroxetine
aminosalicylic acid	fluorouracil	penicillin G, intravenous
amiodarone HCl	fluoxetine	pentoxifylline
argatroban	flutamide	phenylbutazone
aspirin	fluvastatin	phenytoin†
atenolol	fluvoxamine	piperacillin
atorvastatin†	gefitinib	piroxicam
azithromycin	gemfibrozil	pravastatin†
bivalirudin	glucagon	prednisone†
capecitabine	halothane	propafenone
cefamandole	heparin	propoxyphene
cefazolin	ibuprofen	propranolol
cefoperazone	ifosfamide	propylthiouracil†
cefotetan	indomethacin	quinidine
cefoxitin	influenza virus vaccine	quinine
ceftriaxone	itraconazole	rabeprazole
celecoxib	ketoprofen	ranitidine†
cerivastatin	ketorolac	rofecoxib
chenodiol	lansoprazole	sertraline
chloramphenicol	lepirudin	simvastatin
chloral hydrate†	levamisole	stanazolol
chlorpropamide	levofloxacin	streptokinase
cholestyramine†	levothyroxine	sulfamethizole
cimetidine	liothyronine	sulfamethoxazole
ciprofloxacin	lovastatin	sulfapyrazone
cisapride	mefenamic acid	sulfisoxazole
clarithromycin	methimazole†	sulindac
clofibrate	methyl dopa	tamoxifen
COUMADIN overdose	methylphenidate	tetracycline
cyclophosphamide†	methylsalicylate ointment (topical)	thyroid
danazol	metronidazole	ticarcillin
dextran	miconazole (intravaginal, oral, systemic)	ticlopidine
dextrothyroxine	moricyzine hydrochloride†	tissue plasminogen activator (t-PA)
diazoxide	nalidixic acid	tolbutamide
diclofenac	naproxen	tramadol
dicumarol	neomycin	trimethoprim/sulfamethoxazole
diffunisal	norfloxacin	urokinase
disulfiram	ofloxacin	valdecoxib
doxycycline	olsalazine	valproate
erythromycin	omeprazole	vitamin E
esomeprazole	oxandrolone	zafirlukast
ethacrynic acid	oxaprozin	zileuton
ezetimibe		

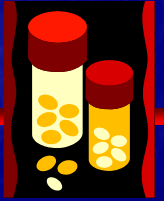
Disminución respuesta INR

Specific Drugs Reported		
alcohol†	COUMADIN underdosage	phenytoin†
aminoglutethimide	cyclophosphamide†	pravastatin†
amobarbital	dicloxacillin	prednisone†
atorvastatin†	ethchlorvynol	primidone
azathioprine	glutethimide	propylthiouracil†
butabarbital	griseofulvin	raloxifene
butalbital	haloperidol	ranitidine†
carbamazepine	meprobamate	rifampin
chloral hydrate†	6-mercaptopurine	secobarbital
chlordiazepoxide	methimazole†	spironolactone
chlorthalidone	moricyzine hydrochloride†	suльфate
cholestyramine†	nafcillin	trazodone
clozapine	paraldehyde	vitamin C (high dose)
corticotropin	pentobarbital	vitamin K
cortisone	phenobarbital	

also: diet high in vitamin K
unreliable PT/INR determinations

Rivaroxaban

Dabigatran



■ Contraindicado con:

- ➔ Antimicóticos azólicos.
- ➔ Antirretrovirales: IP.

■ Asociación con inductores metabólicos del CYP 3A4:

- ➔ Rifampicina ,Fenitoína, Fenobarbital, o Carbamacepina
- ➔ Disminuye el efecto del Rivaroxaban en plasma lo que puede modificar su efecto anticoagulante.

■ Contraindicado con:

- ➔ Ketoconazol, itraconazol.
- ➔ Tacrolimus y Ciclosporina.

■ Reducir dosis con:

- ➔ Verapamilo.

■ Vigilar con:

- ➔ Claritromicina.
- ➔ Rifampicina.
- ➔ Amiodarona.
- ➔ Quinidina.



- **Eficaz.**
 - ✓ Beneficio igual o mayor que warfarina.

- **Seguro.**
 - ✓ ≤ número de hemorragias.
 - ✓ No toxicidad.
 - ✓ Antídoto eficaz.

- **Cómodo.**
 - ✓ Dosis fijas sin monitorización.
 - ✓ Buena biodisponibilidad v.o.
 - ✓ Rápido inicio de acción.
 - ✓ Respuesta predecible.
 - ✓ No interacciones farmacológicas y alimentarias.

- **Barato**



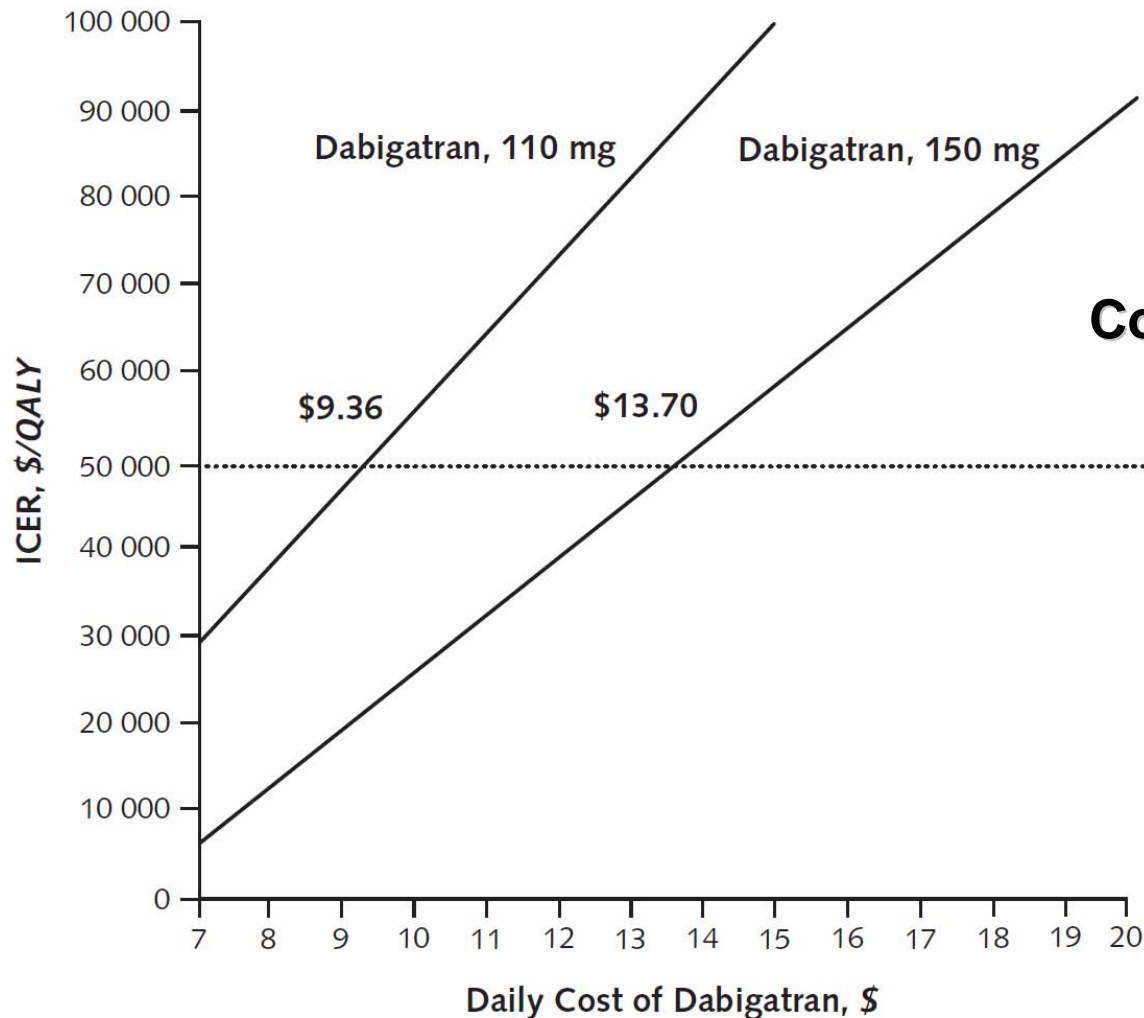
“Poderoso caballero es don dinero”

Quevedo.

Antivitaminas K: 0.12 €/día.



Figure 1. Cost-effectiveness of fixed-dose dabigatran, 110 mg (low dose) and 150 mg (high dose) twice daily, compared with adjusted-dose warfarin anticoagulation at varying daily costs of dabigatran.



**Coste por día: 6.5 \$
(equiv. 4.64 €)**



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- ✓ No interacciones farmacológicas y alimentarias.



■ **Barato**





¡¡ QUE MIEDO
NO TENER MIEDO !!

Experiencia





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1. [No authors listed]
Ann Intern Med. 2011 Sep 20;155(6):JC303. No abstract available.
PMID: 21930840 [PubMed - in process]
- [Enoxaparin once daily vs. twice daily dosing for the treatment of venous thromboembolism in cancer patients: A literature summary.](#)
2. Diaz AH, Rodgers GM, Gilreath JA.
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50 años

10 años



Arrixaca
Hospital Universitario
"Virgen de la Arrixaca"

Poblaciones excluidas



Poblaciones excluidas



- Cáncer.
- Prótesis valvulares.
- Gestantes.
- Niños: <18 años.
- Insuficiencia renal: $\text{CICr} < 15 \text{ ml/min}$.
- Insuficiencia hepática.
- Ictus reciente.

Dalteparina vs AVK en pacientes con cáncer y ETV

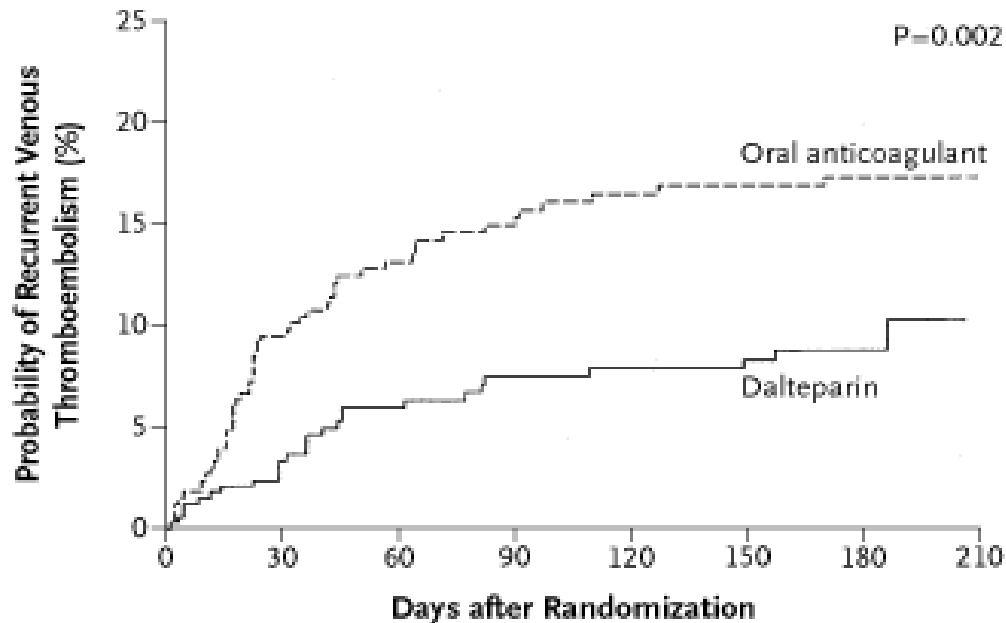


CLOT Study n:676

Dalteparina 200 UI/Kg 1 mes → 150 UI/Kg 5 meses

Tto. agudo 5-7 días

AVK INR 2.0-3.0 6 meses



HR 0.48
(CI 95% 0.30-0.77)

A stack of seven books is placed on a dark red table in a library. The books have various colored spines: green, blue, red, and brown. The text 'Guías Clínicas' is overlaid in the center of the stack. The background shows blurred bookshelves filled with books.

Guías Clínicas

ACCP: Guías basadas en la evidencia en tratamiento antitrombótico y trombolítico



- ➔ Para los pacientes con EP y cáncer, recomendamos HBPM durante los primeros 3-6 meses de terapia anticoagulante a largo plazo (**Grado 1A**).
- ➔ Para estos pacientes, recomendamos terapia anticoagulante posterior con AVK o HBPM a largo plazo o hasta la resolución del cáncer (**Grado 1C**).

1: los expertos tienen la certeza de que los beneficios > riesgos.

2 : los expertos no tienen la certeza de que los beneficios > riesgos.

A: basado en estudios aleatorizados con resultados consistentes.

B: basado en estudios aleatorizados resultados inconsistentes o debilidades metodológicas.

C: basado en estudios observacionales.

Poblaciones excluidas



- Cáncer.
- Prótesis valvulares.
- Gestantes.
- Niños: <18 años.
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- Insuficiencia hepática.
- Ictus reciente.

ACCP: Guías basadas en la evidencia en tratamiento antitrombótico y trombolítico



➔ Para los pacientes con prótesis cardíacas mecánicas, recomendamos terapia con AVK (**Grado 1A**).

- 1: los expertos tienen la certeza de que los beneficios > riesgos.
- 2 : los expertos no tienen la certeza de que los beneficios > riesgos.
- A: basado en estudios aleatorizados con resultados consistentes.
- B: basado en estudios aleatorizados resultados inconsistentes o debilidades metodológicas.
- C: basado en estudios observacionales.

Poblaciones excluidas



- Cáncer.
- Prótesis valvulares.
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- Niños: <18 años.
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- Insuficiencia hepática.
- Ictus reciente.

Dabigatran	Rivaroxaban	Apixaban
Contraindicado en embarazo y lactancia.	Contraindicado en embarazo y lactancia	Contraindicado en embarazo y lactancia
Contraindicado en <18 años.	Contraindicado en <18 años.	Contraindicado en <18 años.
Contraindicado en ClCr < 30 ml/min.	Contraindicado en ClCr < 15 ml/min.	Contraindicado en ClCr < 25 ml/min.
Contraindicado en ALT>x2 LSN	Contraindicado en hepatopatía con coagulopatía	Contraindicado en hepatopatía con coagulopatía

Poblaciones excluidas



- Cáncer.
- Prótesis valvulares.
- Gestantes.
- Niños: <18 años.
- Insuficiencia renal: $\text{ClCr} < 15 \text{ ml/min}$.
- Insuficiencia hepática.
- Ictus reciente.

RE-LY Exclusion Criteria



1. ...

2. Severe, disabling stroke within the previous 6 months, or any stroke within the previous 14 days.

3. Conditions associated with an increased risk of bleeding:

a. ...

c. History of intracranial, intraocular, spinal, retroperitoneal or atraumatic intra-articular bleeding.

d. Gastrointestinal hemorrhage within the past year.

e.

j. ...

4. Contraindication to warfarin treatment

5.



ROCKET-AF Exclusion Criteria



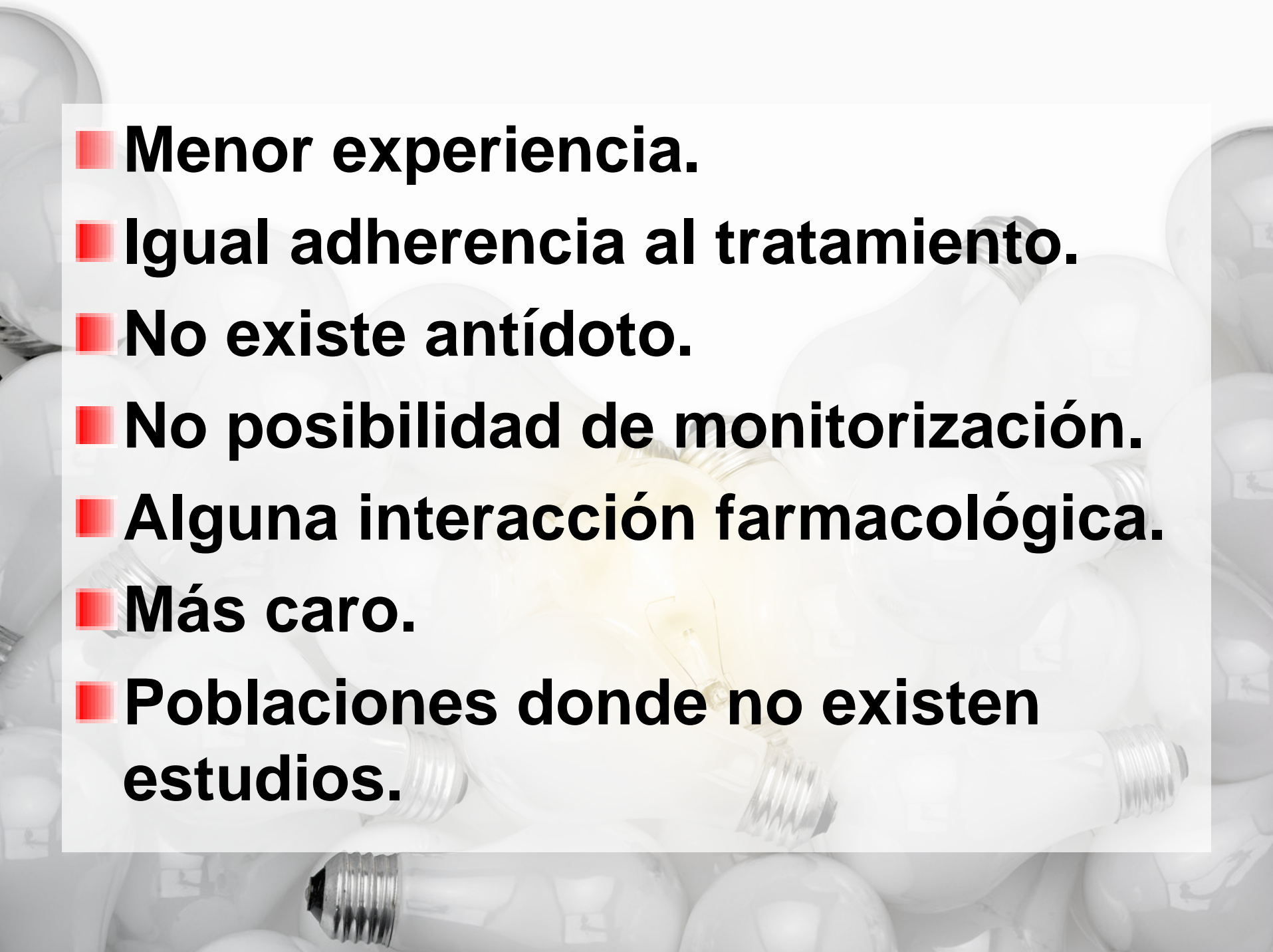
Hemorrhage risk-related criteria

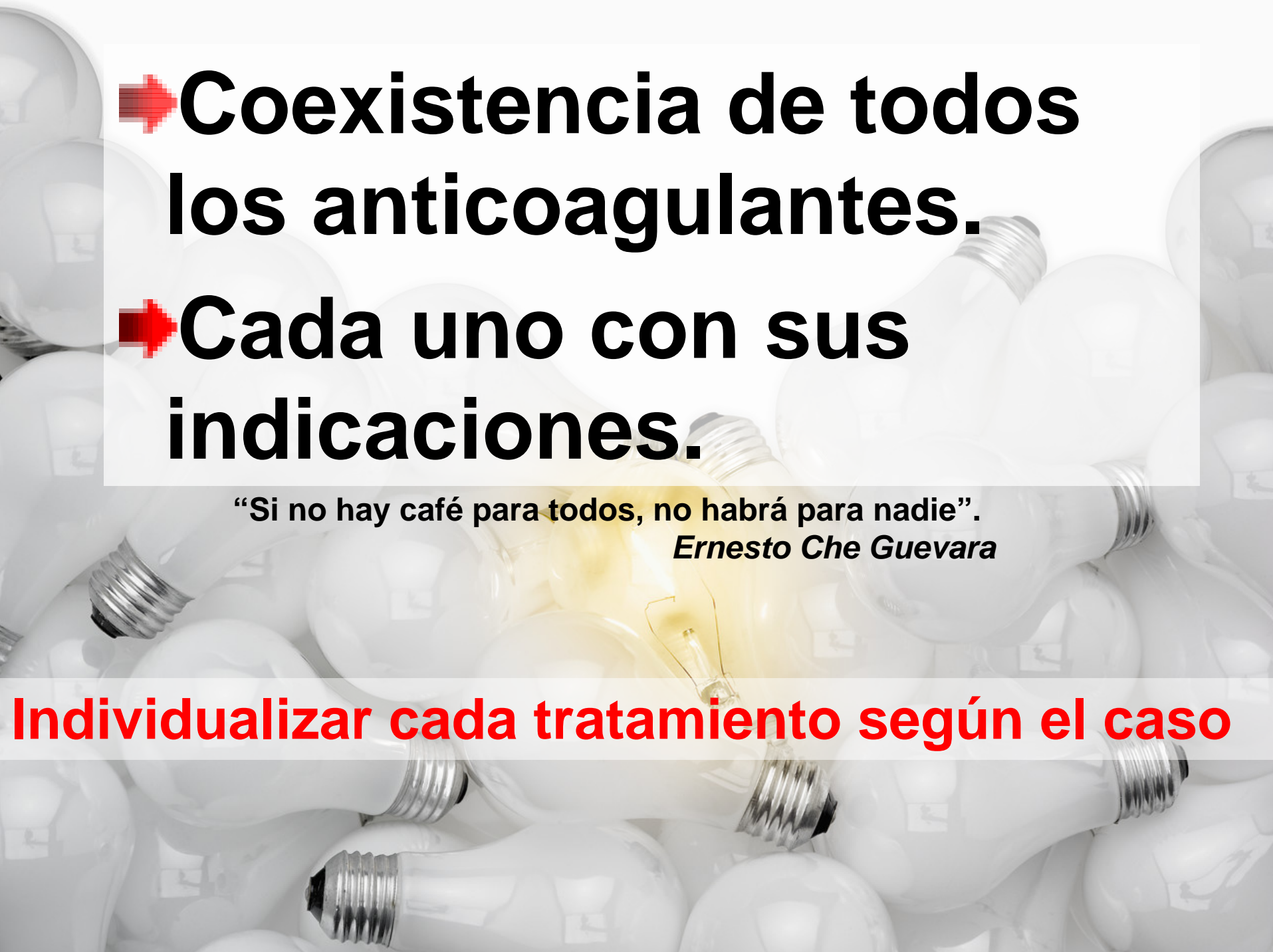
- ...
- History of, or condition associated with, increased bleeding risk, including

- **Severe, disabling stroke (modified Rankin score of 4 to 5, inclusive) within 3 months or any stroke within 14 days before the randomization visit.**
- **Transient ischemic attack within 3 days before the randomization visit....**

Conclusiones



- 
- The background of the slide features a collection of light bulbs. Most are white and unlit, but one bulb in the center is glowing with a warm yellow light, creating a focal point. The bulbs are scattered across the frame, with some in sharp focus and others blurred in the background.
- **Menor experiencia.**
 - **Igual adherencia al tratamiento.**
 - **No existe antídoto.**
 - **No posibilidad de monitorización.**
 - **Alguna interacción farmacológica.**
 - **Más caro.**
 - **Poblaciones donde no existen estudios.**



➡ **Coexistencia de todos los anticoagulantes.**

➡ **Cada uno con sus indicaciones.**

“Si no hay café para todos, no habrá para nadie”.

Ernesto Che Guevara

Individualizar cada tratamiento según el caso

4 GANADORA DE
PREMIOS DE LA ACADEMIA
MEJOR PELÍCULA



DVD ALGULLEN

TOMMY LEE
JONES

JEFFREY
BRIDGES

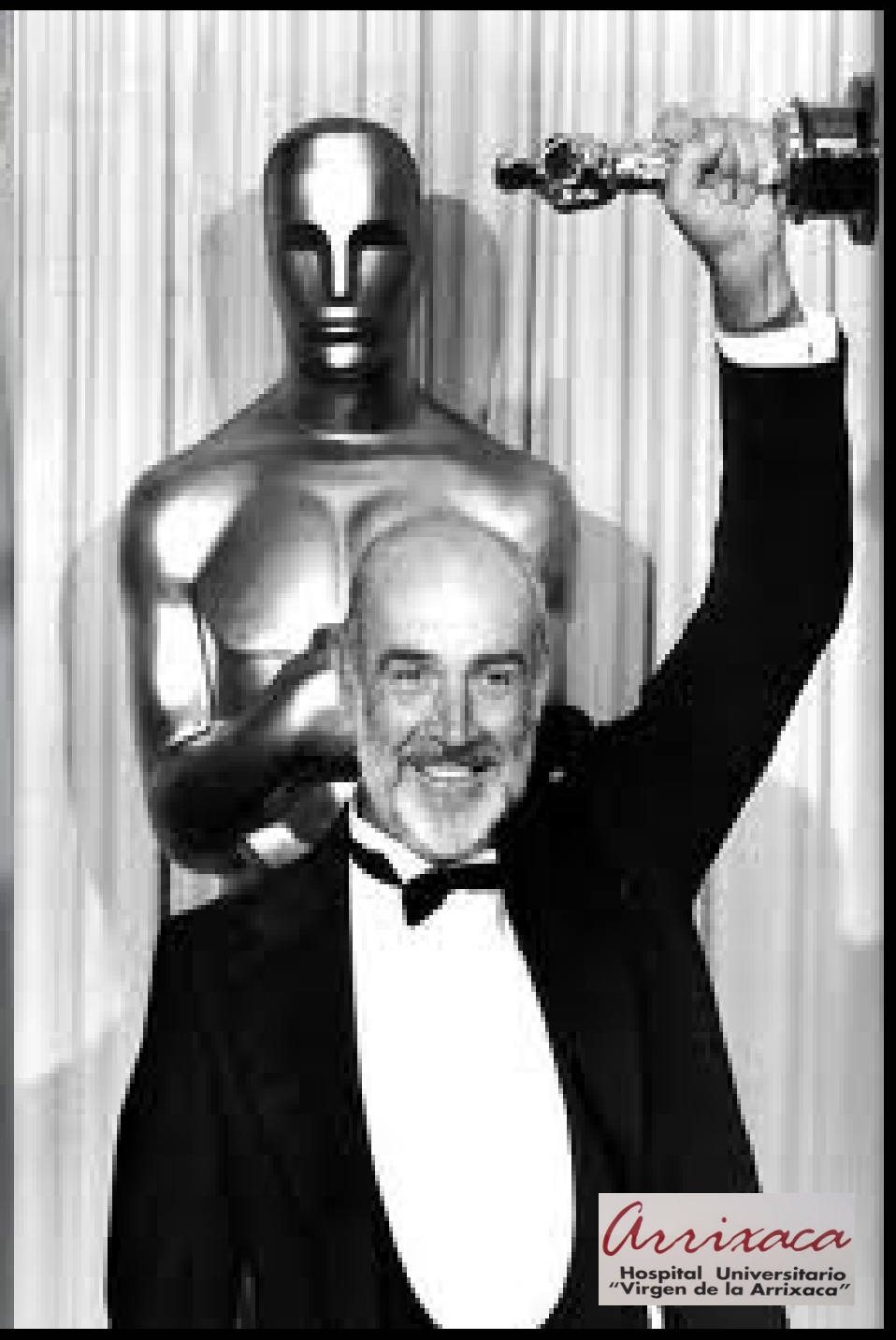
JOHN
CASH

NO ES PAÍS PARA VIEJOS

UNA PELÍCULA DE LOS HERMANOS COEN

NO EXISTE LA VEIDA PERFECTA





Arrixaca
Hospital Universitario
"Virgen de la Arrixaca"

“No todo el monte es orégano”
Refranero español

Muchas gracias