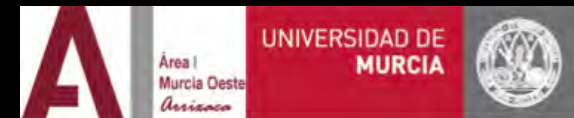


ESTRENOS

ANTICOAGULACIÓN ORAL

2015

Dr. Vladimir Rosa Salazar
Unidad de Corta Estancia/Trombosis.
Servicio de Medicina Interna.
Hospital Clínico Universitario Virgen de la Arrixaca.
Profesor Asociado Universidad de Murcia.



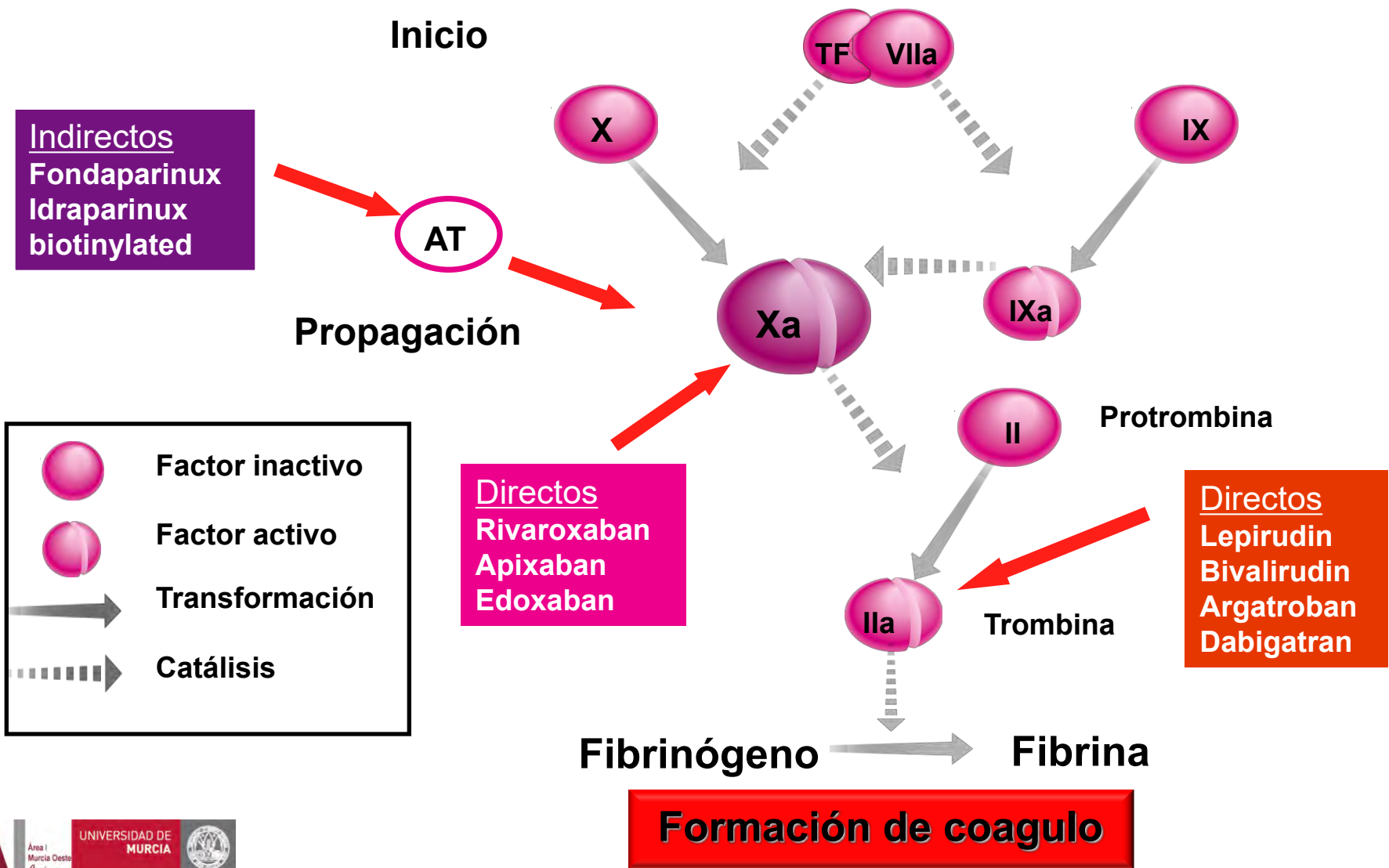
CONFLICTO DE INTERESES







Coagulación



Anticoagulante ideal



- **Eficaz.**
- **Seguro.**
- **Cómodo.**
- **Barato.**



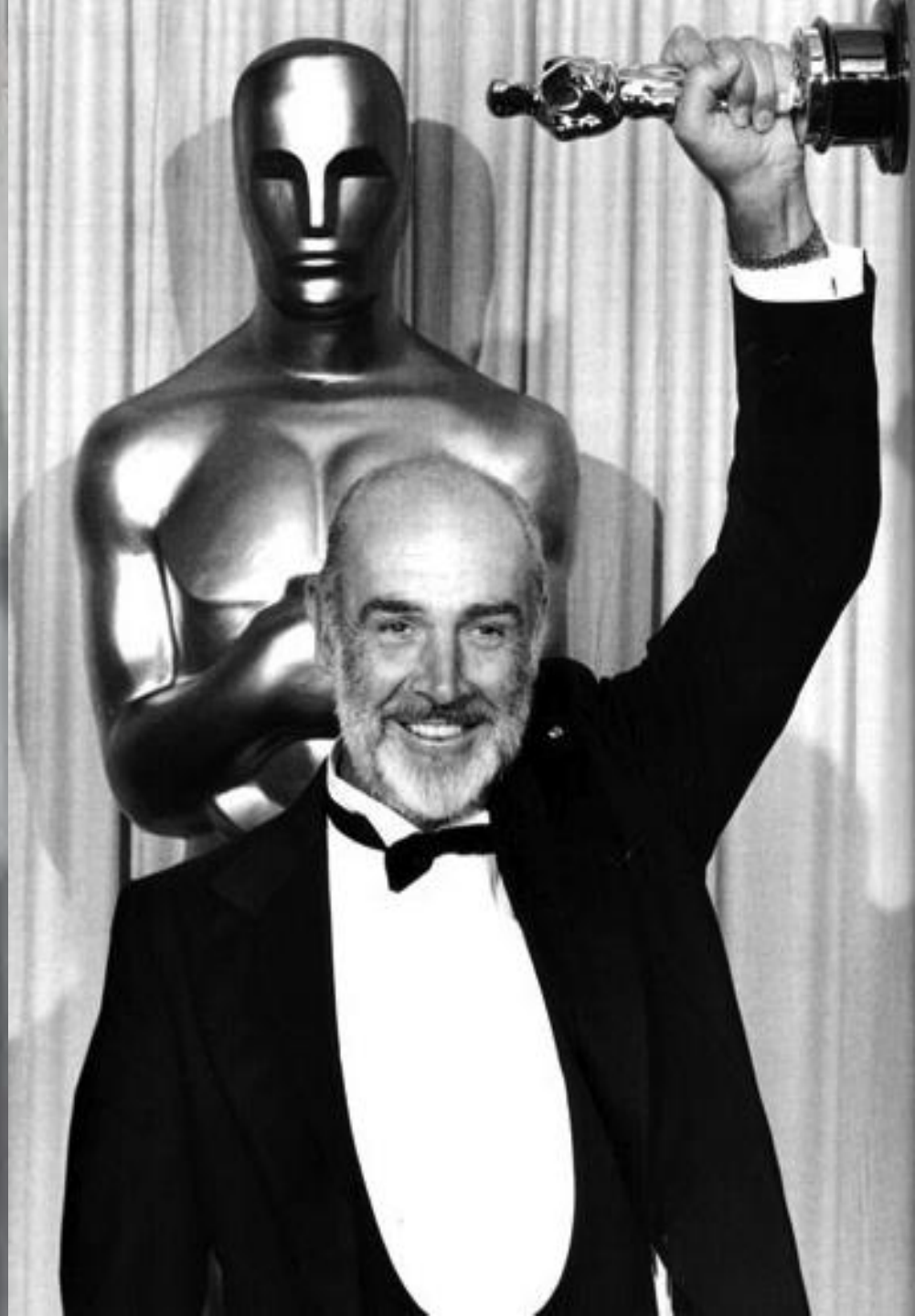
Heparinas



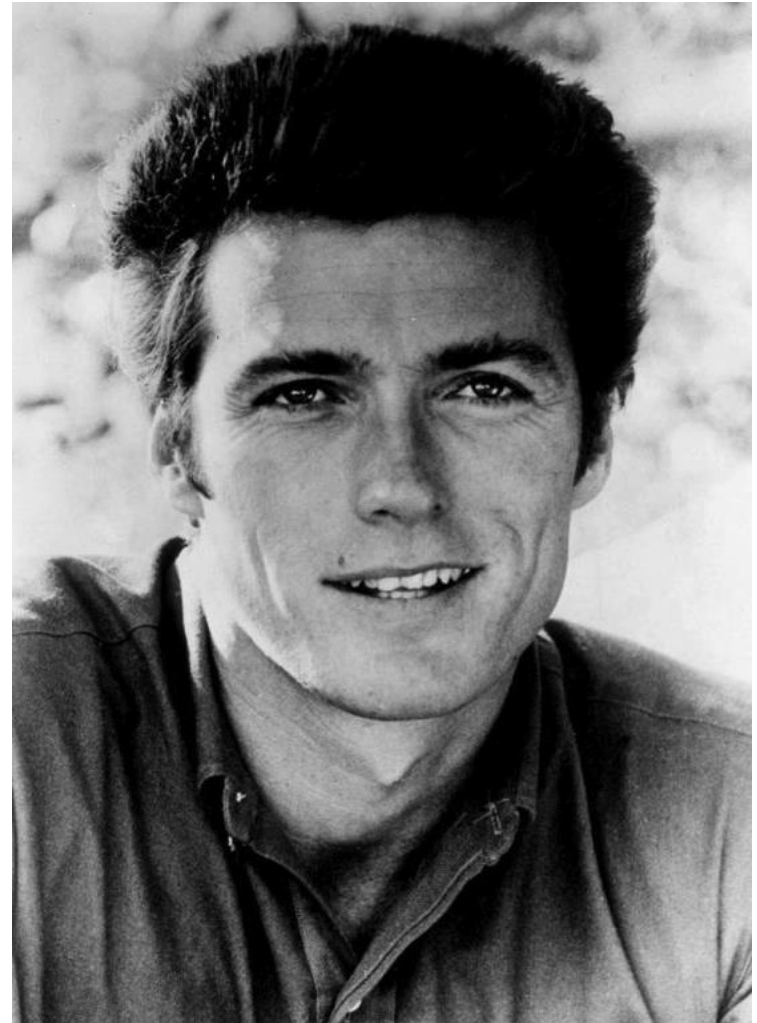
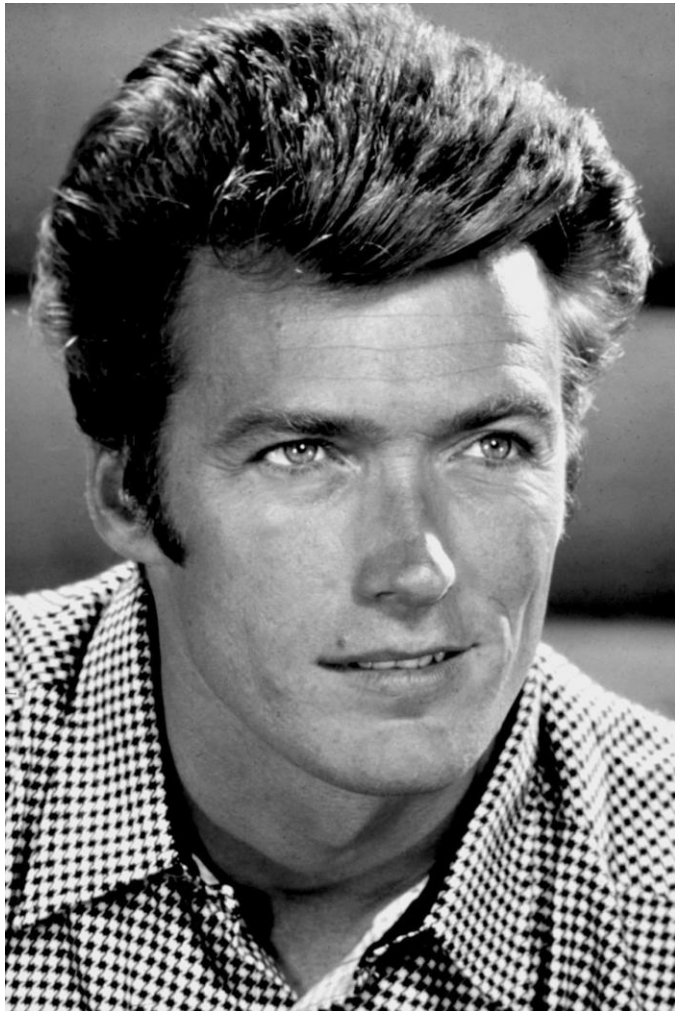
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HBPM

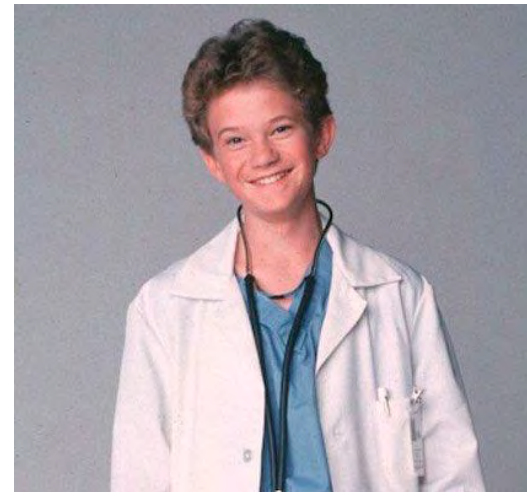


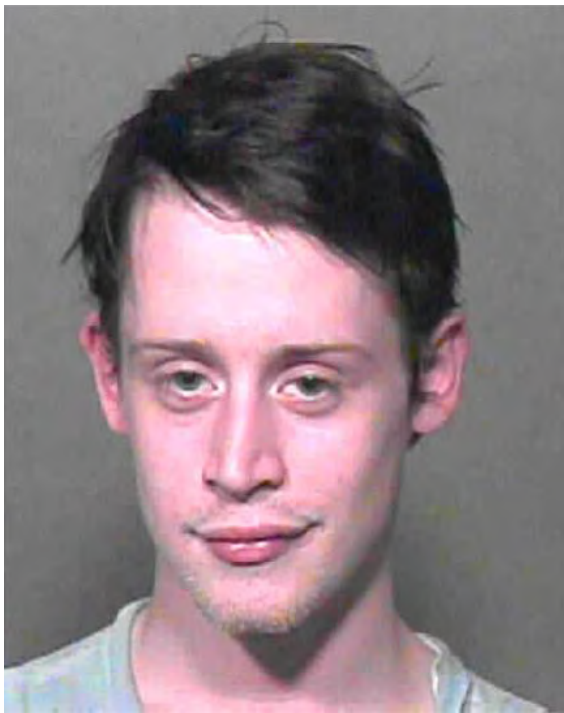
Los antivitaminas K





Gatranes & Xabanes







ORIGINAL ARTICLE

Dabigatran versus Warfarin in Patients with Atrial Fibrillation

Stuart J. Connolly, M.D., Michael D. Ezekowitz, M.B., Ch.B., D.Phil., Malcolm Yusuf, F.R.C.P.C., D.Phil., John Eikelboom, M.D., Jonas Oldgren, M.D., Ph.D., Amit Parekh, M.D., Janice Pogue, M.Sc., Paul A. Reilly, Ph.D., Ellison Themeles, B.A., Jeanne Varrone, M.D., Susan Wang, Ph.D., Marco Alings, M.D., Ph.D., Denis Xavier, M.D., Jun Zhu, M.D., Rafael Diaz, M.D., Basil S. Lewis, M.D., Harald Darius, M.D., Hans-Christoph Diener, M.D., Ph.D., Campbell D. Joyner, M.D., Lars Wallentin, M.D., Ph.D., and the RE-LY Steering Committee and Investigators

N Engl J Med 2009; 361:1139-1151 | September 17, 2009 | DOI: 10.1056/NEJMoa0905561

ORIGINAL ARTICLE

Oral Rivaroxaban for Symptomatic Venous Thromboembolism

The EINSTEIN Investigators

N Engl J Med 2010; 363:2499-2510 | December 23, 2010 | DOI: 10.1056/NEJMoa1007903

ORIGINAL ARTICLE

Oral Apixaban for the Treatment of Acute Venous Thromboembolism

Giancarlo Agnelli, M.D., Harry R. Buller, M.D., Ph.D., Alexander Cohen, M.D., Madelyn Curto, D.V.M., Alexander S. Gallus, M.D., Margot Johnson, M.D., Urszula Masiukiewicz, M.D., Raphael Pak, Ph.D., John Thompson, Ph.D., Gary E. Raskob, Ph.D., and Jeffrey I. Weitz, M.D. for the AMPLIFY Investigators

N Engl J Med 2013; 369:799-808 | August 29, 2013 | DOI: 10.1056/NEJMoa1302507

ORIGINAL ARTICLE

Edoxaban versus Warfarin for the Treatment of Symptomatic Venous Thromboembolism

The Hokusai-VTE Investigators

N Engl J Med 2013; 369:1406-1415 | October 10, 2013 | DOI: 10.1056/NEJMoa1306638

2009

2013



ÚLTIMOS ESTRENOS



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Cirulis MM, Ryan JJ.

J Thorac Dis. 2016 May;8(5):E298-304. doi: 10.21037/jtd.2016.03.67.

PMID: 27162687

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2. [PO-11 - Thrombin and cancer stem-like cells: in vitro support for breast cancer anticoagulation.](#)

Castle J, Farnie G, Kirwan CC.

Thromb Res. 2016 Apr;140 Suppl 1:S180. doi: 10.1016/S0049-3848(16)30144-X. Epub 2016 Apr 8.

PMID: 27161699

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J Trauma Nurs. 2016 May-Jun;23(3):E1-E2. No abstract available.
PMID: 27163227
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- [Developing, Implementing, and Evaluating a Nurse-Driven Rapid Reversal Protocol for Patients With Traumatic Intracerebral Hemorrhage in the Presence of Preinjury Warfarin.](#)
Blackmore AR, Caputo LM, Bourg PW, Mains CW.

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i Filters activated: Publication date from 2015/01/01 to 2016/12/31. [Clear all](#) to show 1292 items.

[The discovery of dabigatran etexilate for the treatment of venous thrombosis.](#)

1. Feuring M, van Ryn J.
Expert Opin Drug Discov. 2016 May 9. [Epub ahead of print]
PMID: 27159158
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[Evaluation of the chromogenic anti-factor IIa assay to assess dabigatran exposure in geriatric patients with atrial fibrillation in an outpatient setting.](#)

2. Brunetti L, Sanchez-Catanese B, Kagan L, Wen X, Liu M, Buckley B, Luyendyk JP, Aleksunes LM.
Thromb J. 2016 May 6;14:10. doi: 10.1186/s12959-016-0084-2. eCollection 2016.
PMID: 27158246
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DABIGATRAN

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[Rivaroxaban-Induced Drug Reaction With Eosinophilia and Systemic Symptoms.](#)

1. Radu C, Barnig C, de Blay F.
 J Investig Allergol Clin Immunol. 2016 Apr;26(2):124-126. doi: 10.18176/jiaci.0027. No abstract available.
 PMID: 27164633
[Similar articles](#)

[PO-41 - Rivaroxaban is effective therapy for high risk cancer patients with venous thromboembolic disease.](#)

2. Wells PS, Theberge IA, Bowdridge JC, Forgie MA, Carrier M.
 Thromb Res. 2016 Apr;140 Suppl 1:S191-2. doi: 10.1016/S0049-3848(16)30174-8. Epub 2016 Apr 8.

RIVAROXABAN

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- [\[Repeated Cerebellar Hemorrhage Related to Rivaroxaban and Apixaban: A Case Report\].](#)
1. Yokoi M, Toyama Y, Tsurusaki Y, Nakamura A, Mima Y, Kuwashiro T, Wakugawa Y, Yasaka M, Okada Y.
Brain Nerve. 2016 May;68(5):573-7. doi: 10.11477/mf.1416200440. Japanese.
PMID: 27156511
[Similar articles](#)
- [Fatal consequences of climbing a ladder under apixaban and drunken.](#)
2. Stöllberger C, Finsterer J.
Neurol Neurochir Pol. 2016;50(3):200-2. doi: 10.1016/j.pjnns.2016.01.012. Epub 2016 Feb 5.

APIXABAN

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[Extended duration of anticoagulation with edoxaban in patients with venous thromboembolism: a post-hoc analysis of the Hokusai-VTE study.](#)

Raskob G, Ageno W, Cohen AT, Brekelmans MP, Grosso MA, Segers A, Meyer G, Verhamme P, Wells PS, Lin M, Winters SM, Weitz JI, Büller HR.

Lancet Haematol. 2016 May;3(5):e228-36. doi: 10.1016/S2352-3026(16)00023-5. Epub 2016 Mar 22.

PMID: 27132697

[Similar articles](#)

[Edoxaban in the secondary prevention of VTE.](#)

2. Levy JH, Hunt BJ.

Lancet Haematol. 2016 May;3(5):e208-9. doi: 10.1016/S2352-3026(16)00037-5. Epub 2016 Mar 22. No abstract available.

PMID: 27132692

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EDOxaban

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LEONARDO DICAPRIO TOM HARDY



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DABIGAT'RAN



> 2.000.000 pacientes

> 200.000 pacientes naïve

> 100 países

> 6 años

UNA PELÍCULA DE ALEJANDRO G. INÁRRITU
LEONARDO DICAPRIO TOM HARDY



SANGRE PÉRDIDA. VIDA ENCONTRADA.
EL RENACIDO

(THE REVENANT)

INSPIRADA EN HECHOS REALES

PRODUCCIÓN MICHAEL PUNKE DIRECTOR DE FOTOGRAFÍA MARK L. SMITH Y ALEJANDRO G. INÁRRITU

DIRIGIDA POR ALEJANDRO G. INÁRRITU PRÓXIMAMENTE

Medicare

 >134.000 pacientes

USA Health Insurance

 >38.000 pacientes

Departamento de defensa USA

 >25.000 pacientes

Registro danés

 >20.000 pacientes

Graham DJ et al. *Circulation* 2015; 131:157-164.

Seeger JD et al. Presented at AHA 2014.

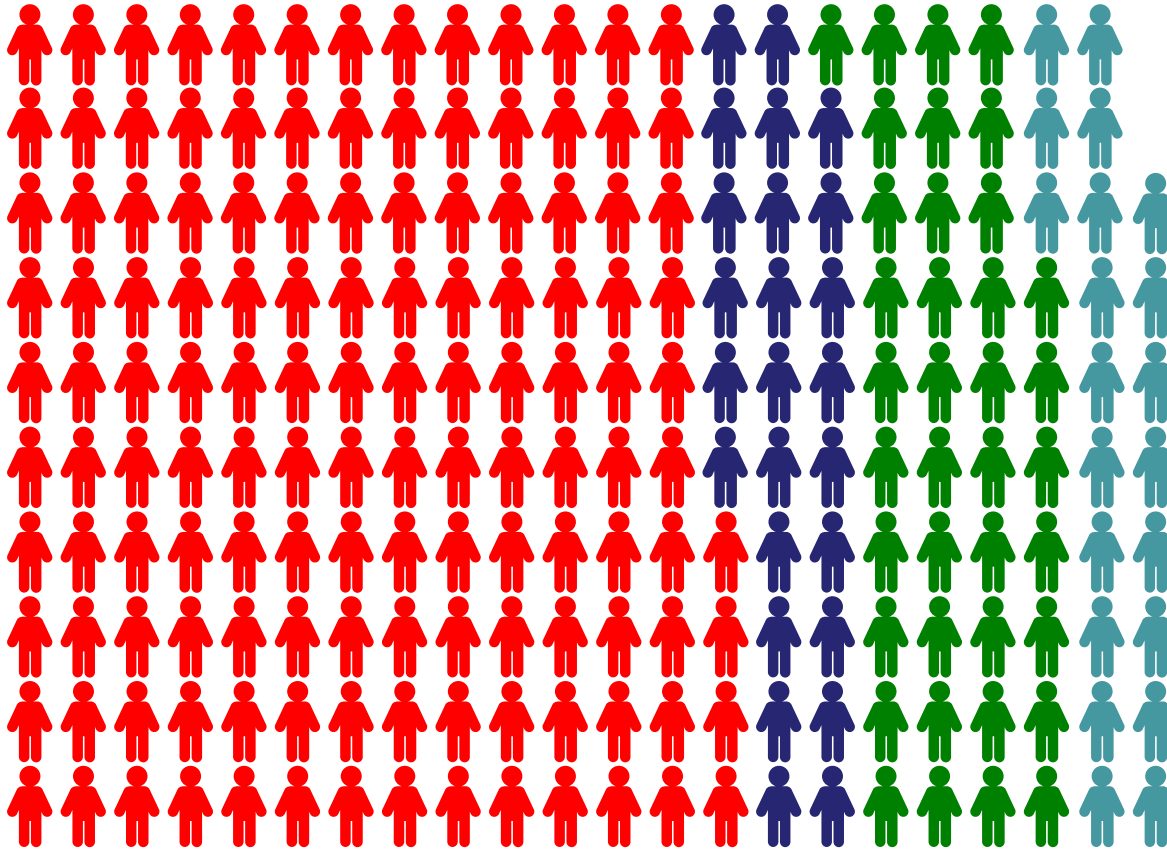
Villines TC et al. Presented at AHA 2014.





Larsen TB et al. *Am J Med* 2014;127:650-656.

Larsen TB et al. *Am J Med* 2014;127:329-336.

Proporción

RE-LY
(n>18 000)



-  FDA Medicare
(n>134 000)
-  Departamento
Defensa USA
(n>25 000)
-  USA Health
insurance
(n>38 000)
-  Registro danés
(n>21 000)

Graham DJ et al. *Circulation* 2015;131:157-164.

Seeger JD et al. Presented at AHA 2014.

Villines TC et al. Presented at AHA 2014.

Larsen TB et al. *Am J Med* 2014;127:650-656.

Larsen TB et al. *Am J Med* 2014;127:329-336.

UNA PELÍCULA DE ALEJANDRO G. INÁRRITU
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Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



Cardiovascular, Bleeding, and Mortality Risks in Elderly Medicare Patients Treated with Dabigatran or Warfarin for Non-Valvular Atrial Fibrillation

David J. Graham, Marsha E. Reichman, Michael Wernecke, Rongmei Zhang, Mary Ross Southworth, Mark Levenson, Ting-Chang Sheu, Katrina Mott, Margie R. Goulding, Monika Houstoun, Thomas E. MaCurdy, Chris Worrall and Jeffrey A. Kelman

Circulation. published online October 30, 2014;

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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INSPIRADA EN HECHOS REALES

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CON LEONARDO DICAPRIO Y TOM HARDY
ALEJANDRO G. INÁRRITU PRÓXIMAMENTE



Graham DJ et al.
Circulation 2015;131:157-164.

Diseño del estudio

- 134.414 pacientes.
 - Diagnosticados reciente de FANV.
 - Edad \geq 65 años.
 - Naïve.
- Dabigatran 67.207 pacientes.
 - ★ 56.576 pacientes: 150 mg c/12h.
 - ★ 10.522 pacientes (16%): 75 mg c/12h.
- Warfarina 67.207 pacientes.

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Características pacientes

Características, %	Medicare		RE-LY®	
	Dabigatrán* (n = 67.207)	Warfarina (n = 67.207)	Dabigatrán 150 mg (n = 6.076)	Warfarina (n = 6.022)
Edad 75-84 años	43	43	36	
Edad ≥ 85 años	16	16	4	
Género masculino	49	48	63	63
Puntuación CHADS ₂ ≥ 3	31	32	33	32
Hipertensión	87	87	79	79
Antecedentes de IAM	2	2	17	16
Diabetes	33	34	23	23
Insuficiencia cardiaca	18	18	32	32
Antecedentes de ictus	3	4		
Antecedentes de AIT	7	7	20	20

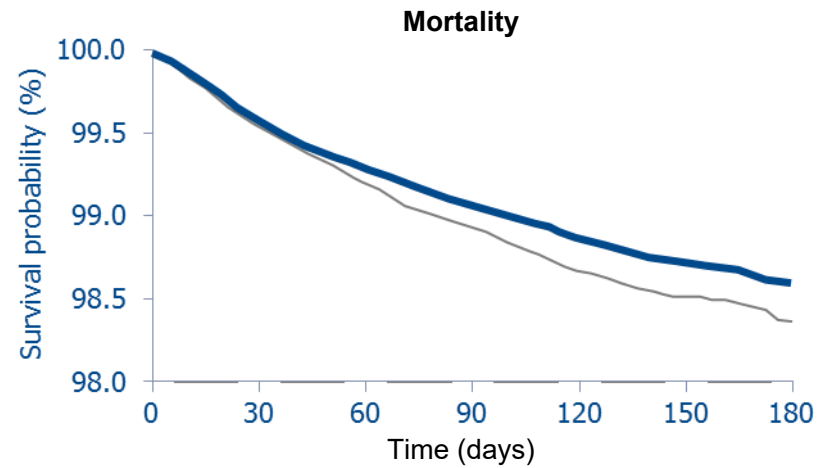
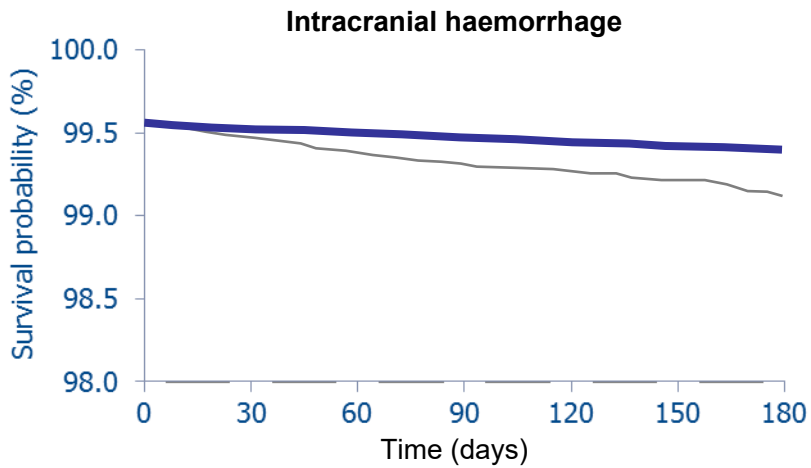
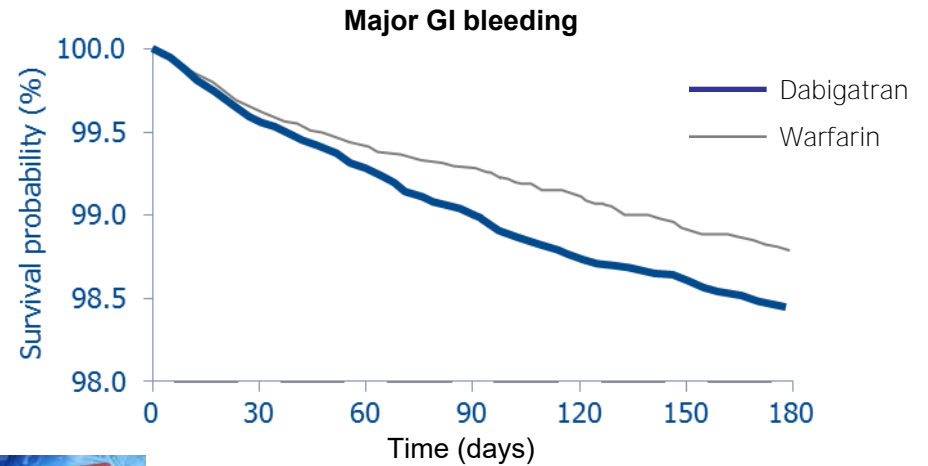
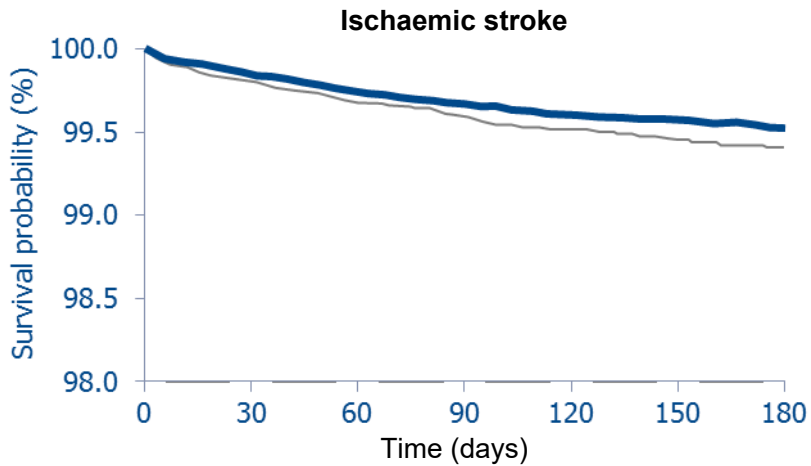


Resultados

	Tasa de incidencia por 1.000 personas-años		HR ajustada (IC del 95%)
	Dabigatrán	Warfarina	
Ictus isquémico	11,3	13,9	0,80 (0,67-0,96)
Hemorragia intracraneal	3,3	9,6	0,34 (0,26-0,46)
Hemorragia intracerebral	2,4	7,3	0,33 (0,24-0,47)
Mortalidad	32,6	37,8	0,86 (0,77-0,96)
Hemorragia grave	42,7	43,9	0,97 (0,88-1,07)
Total de hemorragias hospitalizadas	59,3	58,8	1,00 (0,92-1,09)
Hemorragia gastrointestinal grave	34,2	26,5	1,28 (1,14-1,44)
IAM	15,7	16,9	0,92 (0,78-1,08)



Resultados a lo largo del tiempo



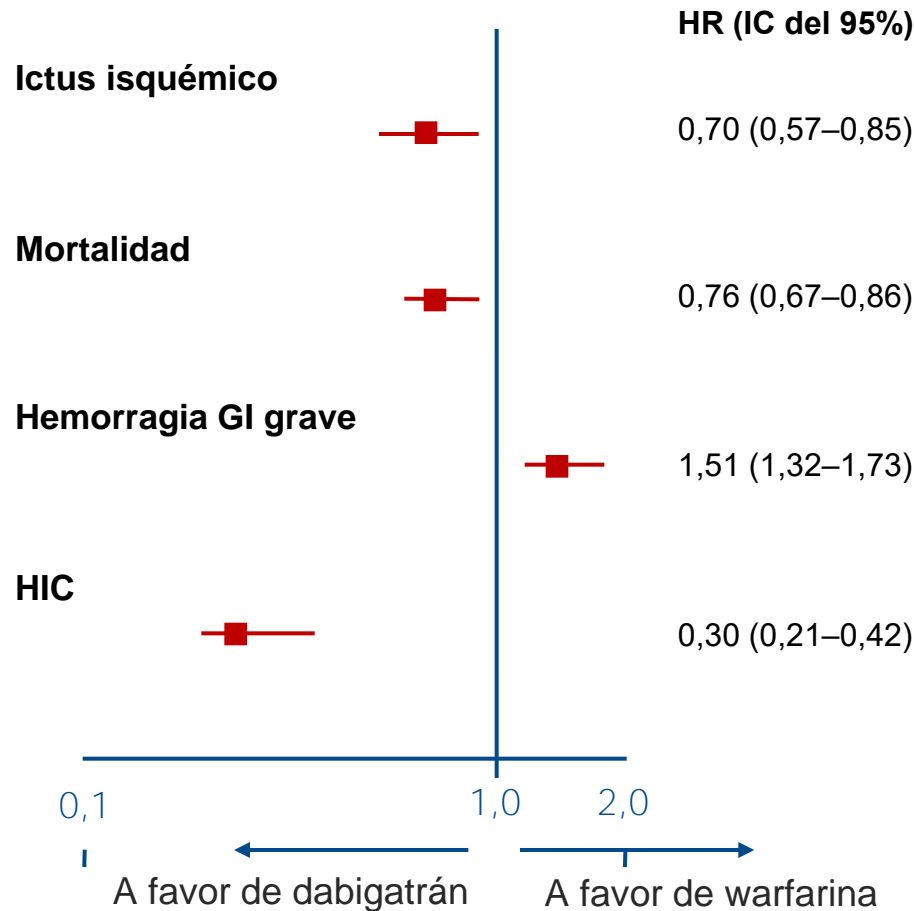
Resultados dabigatran 150 mg

Dabigatran vs warfarina

RR 30%

RR 24%

RR 70%



—■— Dabigatrán 150 mg BID (n = 56.576)

La hemorragia GI grave con dabigatrán **solo fue superior** en los grupos de:

- Mujeres de 75 años o más
- Hombres de 85 años o más

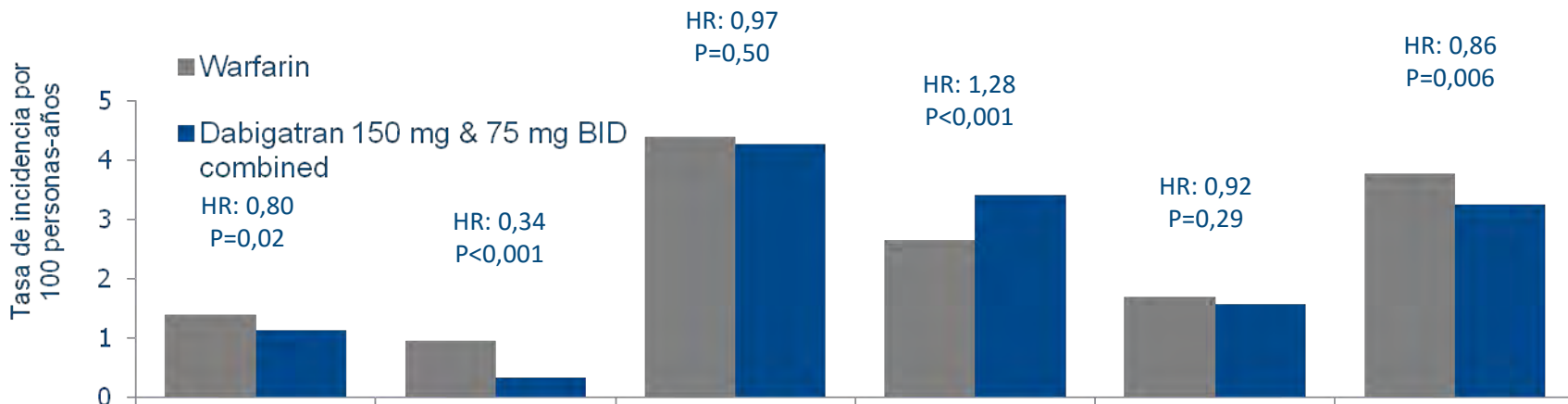
En las edades inferiores, no hubo diferencias significativas vs. warfarina



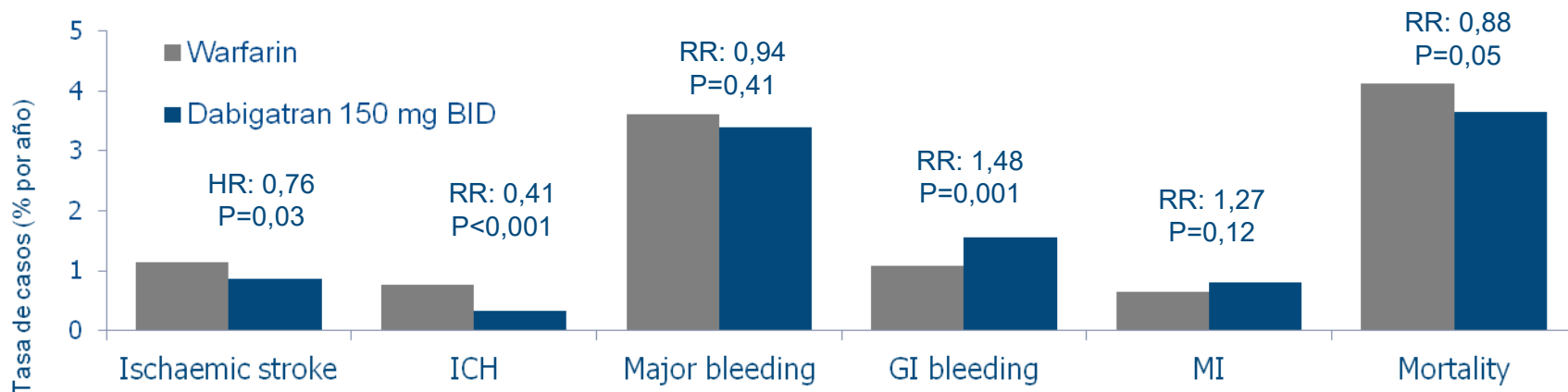
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Medicare vs RE-LY

Medicare



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DABIGAT'RAN



Antídotos



RE-VERSE AD™

Study of reversal effects of idarucizumab
in patients on active dabigatran

Praxbind®
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ORIGINAL ARTICLE

Idarucizumab for Dabigatran Reversal

BACKGROUND

Specific reversal agents for non-vitamin K antagonist oral anticoagulants are lacking. Idarucizumab, an antibody fragment, was developed to reverse the anticoagulant effects of dabigatran.

METHODS

We undertook this prospective cohort study to determine the safety of 5 g of intravenous idarucizumab and its capacity to reverse the anticoagulant effects of dabigatran in patients who had serious bleeding (group A) or required an urgent procedure (group B). The primary end point was the maximum percentage reversal of the anticoagulant effect of dabigatran within 4 hours after the administration of idarucizumab, on the basis of the determination at a central laboratory of the dilute thrombin time or ecarin clotting time. A key secondary end point was the restoration of hemostasis.

RESULTS

This interim analysis included 90 patients who received idarucizumab (51 patients in group A and 39 in group B). Among 68 patients with an elevated dilute thrombin time and 81 with an elevated ecarin clotting time at baseline, the median maximum percentage reversal was 100% (95% confidence interval, 100 to 100). Idarucizumab normalized the test results in 88 to 98% of the patients, an effect that was evident within minutes. Concentrations of unbound dabigatran remained below 20 ng per milliliter at 24 hours in 79% of the patients. Among 35 patients in group A who could be assessed, hemostasis, as determined by local investigators, was restored at a median of 11.4 hours. Among 36 patients in group B who underwent a procedure, normal intraoperative hemostasis was reported in 33, and mildly or moderately abnormal hemostasis was reported in 2 patients and 1 patient, respectively. One thrombotic event occurred within 72 hours after idarucizumab administration in a patient in whom anticoagulants had not been reinitiated.

CONCLUSIONS

Idarucizumab completely reversed the anticoagulant effect of dabigatran within minutes. (Funded by Boehringer Ingelheim; RE-VERSE AD ClinicalTrials.gov number, NCT02104947.)

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DABIGAT'RAN



An evidence summary of the management of patients taking direct oral anticoagulants (DOACs) undergoing dental surgery

*International Journal of
Oral &
Maxillofacial
Surgery*

Dabigatran but not rivaroxaban or apixaban treatment decreases fibrinolytic resistance in patients with atrial fibrillation



RESEARCH ARTICLE

Open Access

Cost-effectiveness analysis of dabigatran and anticoagulation monitoring strategies of vitamin K antagonist



Johnston S. et al.

Int J Oral Maxillo Fact Surg 2016;in press.

Semeraro F. Et al.

Thrombosis Research 2016;138;22-29.

Carles M. Et al.

BMC Health Services Research 2015;15:289.

SPOTLIGHT

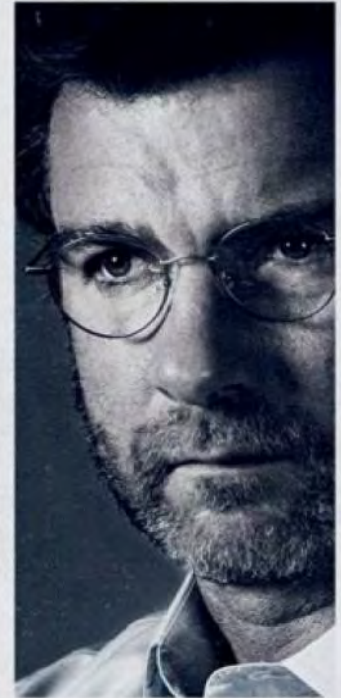
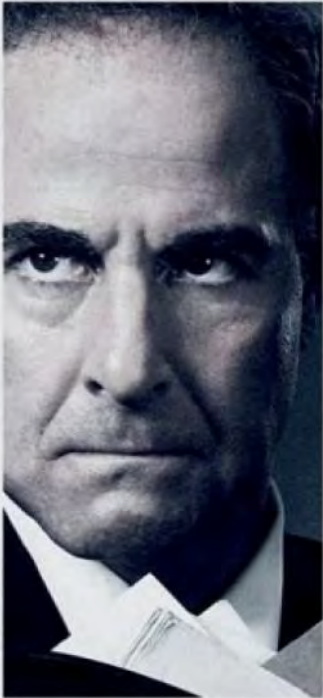
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RIVAROXABAN



SPOTLIGHT

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RUFFALO KEATON MADAMS SCHREIBER TUCCI

XANTUS: a real-world, prospective, observational study of patients treated with rivaroxaban for stroke prevention in atrial fibrillation

- Estudio observacional prospectivo.
- Condiciones de vida real.
- 6784 pacientes.
- 5336 Rivaroxaban 20 mg.
- 96% sin ningún tipo de eventos.

Camm AJ, et al.
XANTUS study.

Eur Heart J. 2015 Sep 1. pii: ehv466. [Epub ahead of print]



SPOTLIGHT

MARK RUFFALO MICHAEL KEATON RACHEL MADAMS LEE STANLEY STANLEY TUCCI

XANTUS: a real-world, prospective, observational study of patients treated with rivaroxaban for stroke prevention in atrial fibrillation



ROCKET AF vs XANTUS: CHADS₂-scores

		ROCKET AF ²⁻⁴	XANTUS ¹
		 14,264	 6,784
C	CHF*	64 [%]	19 [%]
H	Hypertension	91 [%]	75 [%]
A	Age ≥75 years	44 [%]	37 ^{%b}
D	Diabetes mellitus	40 [%]	20 [%]
S₂	Prior stroke or TIA	52 [%]	19 ^{%c}
Renal impairment		21 [%] Moderate ^d	9 ^{%e} Moderate to severe ^f
Mean CHADS₂-score (range):		3.5 (2–6)	2.0 (0–6)^g

Camm AJ, et al.
XANTUS study.

Eur Heart J. 2015 Sep 1. pii: ehv466. [Epub ahead of print]

BASED ON THE PULITZER PRIZE-WINNING INVESTIGATION



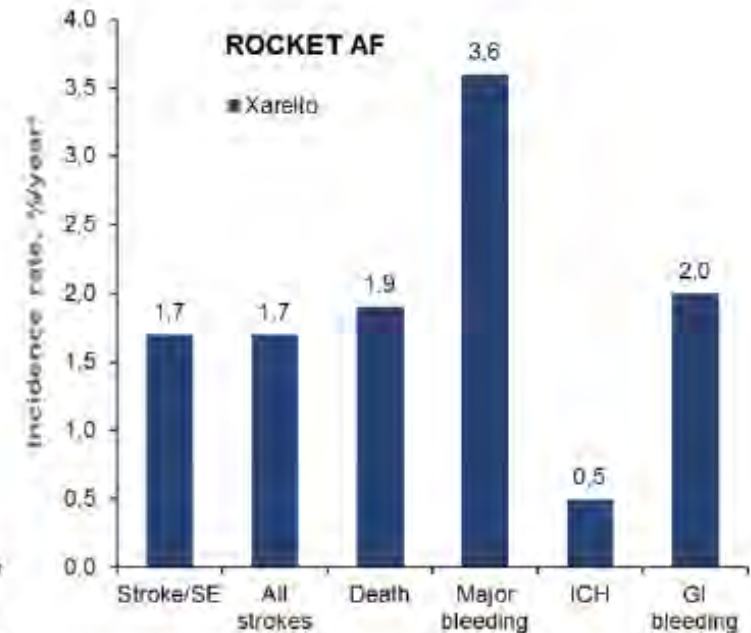
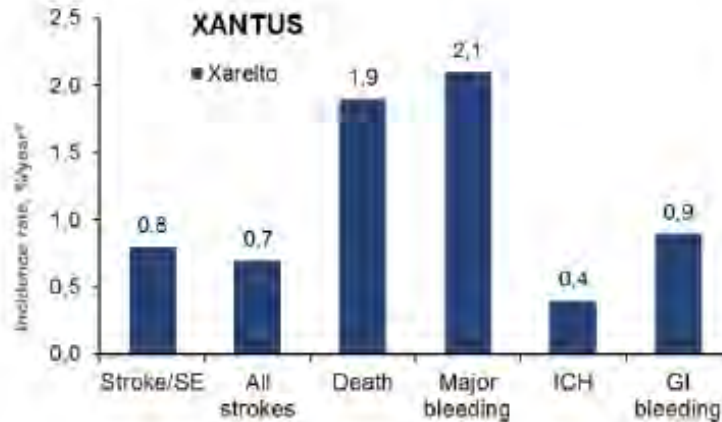
SPOTLIGHT

MARK RUFFALO MICHAEL KEATON RACHEL MADAMS LEE STANLEY TUCCI
 RUFFALO KEATON MADAMS STANLEY TUCCI

XANTUS: a real-world, prospective, observational study of patients treated with rivaroxaban for stroke prevention in atrial fibrillation



	CHADS ₂	ictus previo ³
ROCKET AF ¹	3.5	55%
XANTUS ²	2.0	19%



BASED ON THE PULITZER PRIZE-WINNING INVESTIGATION

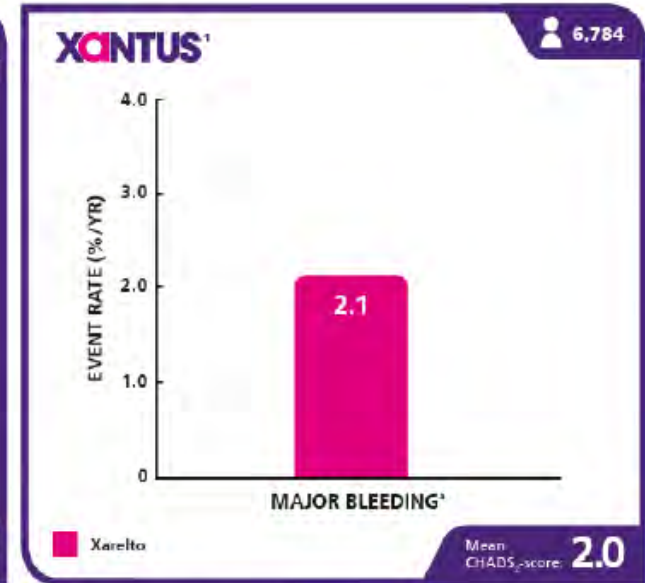
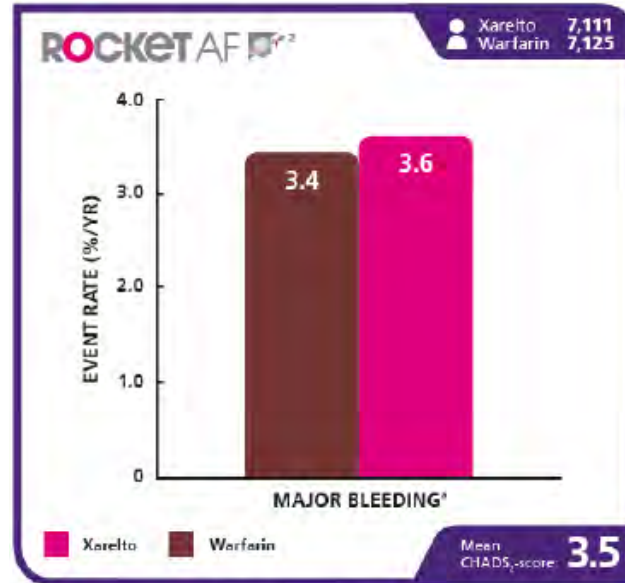


Camm AJ, et al.
XANTUS study.
 Eur Heart J. 2015 Sep 1. pii: ehv466. [Epub ahead of print]

SPOTLIGHT

MARK RUFFALO MICHAEL KEATON RACHEL MADAMS LEE STANLEY STANLEY TUCCI

XANTUS: a real-world, prospective, observational study of patients treated with rivaroxaban for stroke prevention in atrial fibrillation



Safety population during treatment analysis
Results are not intended for direct comparison

Safety population during treatment analysis

	Bleeding endpoint: ^a	Critical organ	ICH	Fatal	Major GI
ROCKET AF ^{c,2,5}	Xarelto %/YR	0.8	0.5	0.2	2.0
	Warfarin %/YR	1.2	0.7	0.5	1.2
XANTUS ^{d,7}	Xarelto %/YR	0.7	0.4	0.2	0.9



BASED ON THE PULITZER PRIZE-WINNING INVESTIGATION



SPOTLIGHT

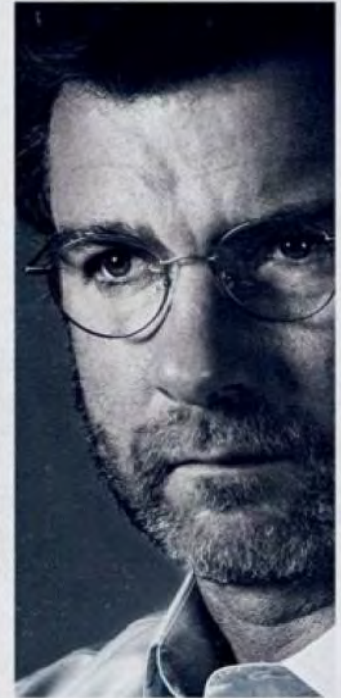
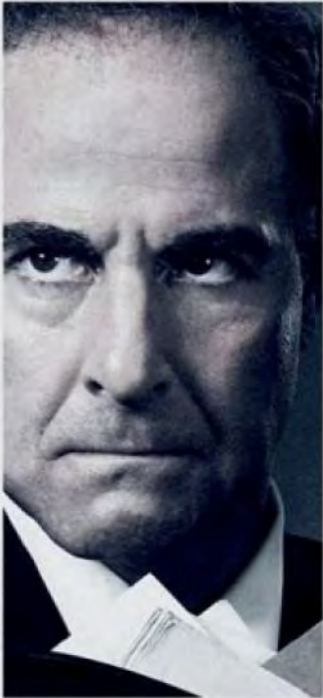
MARK
RUFFALO

MICHAEL
KEATON

RACHEL
McADAMS

LIEV
SCHREIBER

AND
STANLEY
TUCCI



BASED ON THE PULITZER PRIZE-WINNING INVESTIGATION

RIVAROXABAN

SPOTLIGHT

MARK
RUFFALO
MICHAEL
KEATON
RACHEL
WADSWORTH
LEY
SCHREIBER
STANLEY
TUCCI

Articles

Safety and effectiveness of oral rivaroxaban versus standard anticoagulation for the treatment of symptomatic deep-vein thrombosis (XALIA): an international, prospective, non-interventional study

- 2012-2014.
- Multicéntrico.
- 4768 pacientes con TVP.
- 2505 con Rivaroxaban

Agno W et al.

XALIA study Lancet Hematology 2015,
[dx.doi.org/10.1016/S2352-3026\(15\)00257-4](https://doi.org/10.1016/S2352-3026(15)00257-4).

THE LANCET Haematology

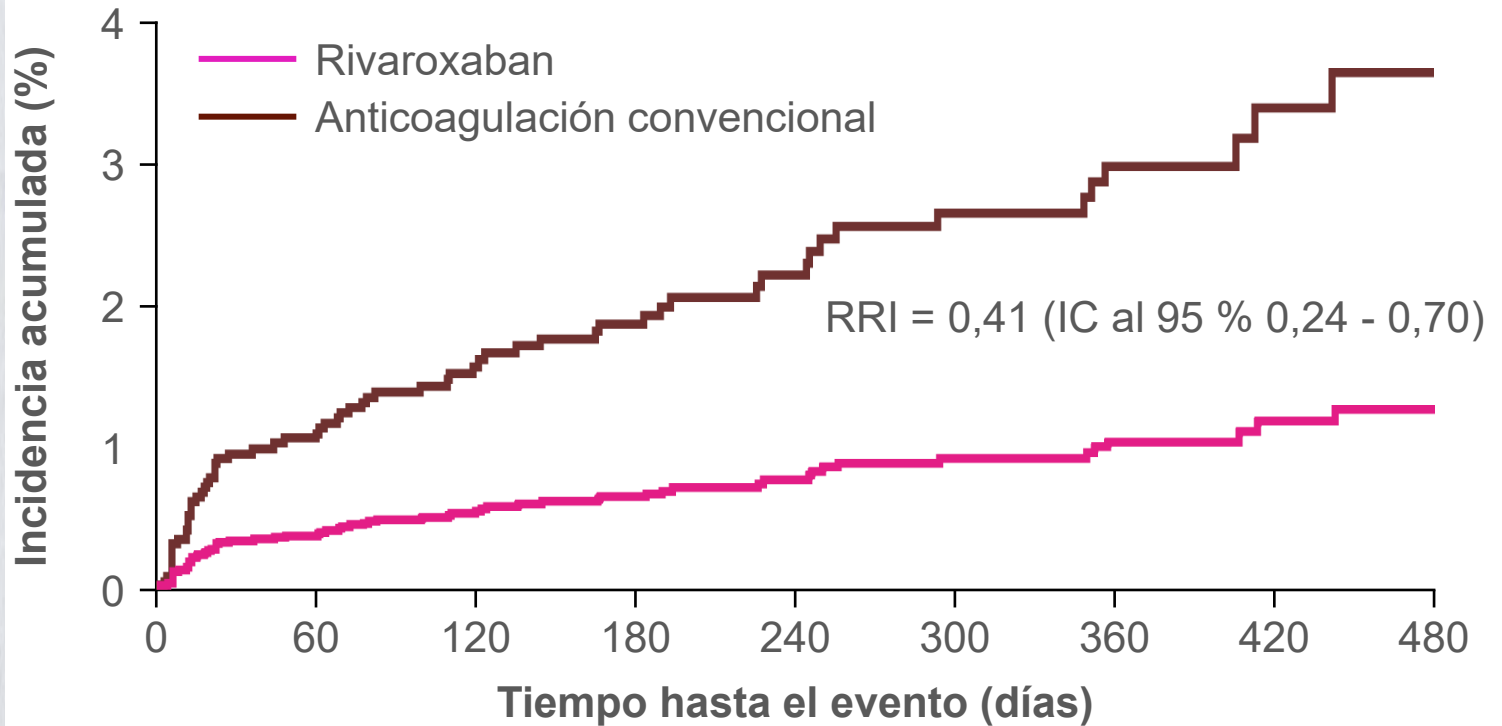
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MARK RUFFALO MICHAEL KEATON RACHEL MADANS LEV SCHREIBER STANLEY TUCCI



BASED ON THE PULITZER PRIZE-WINNING INVESTIGATION

Incidencia acumulada de hemorragia grave



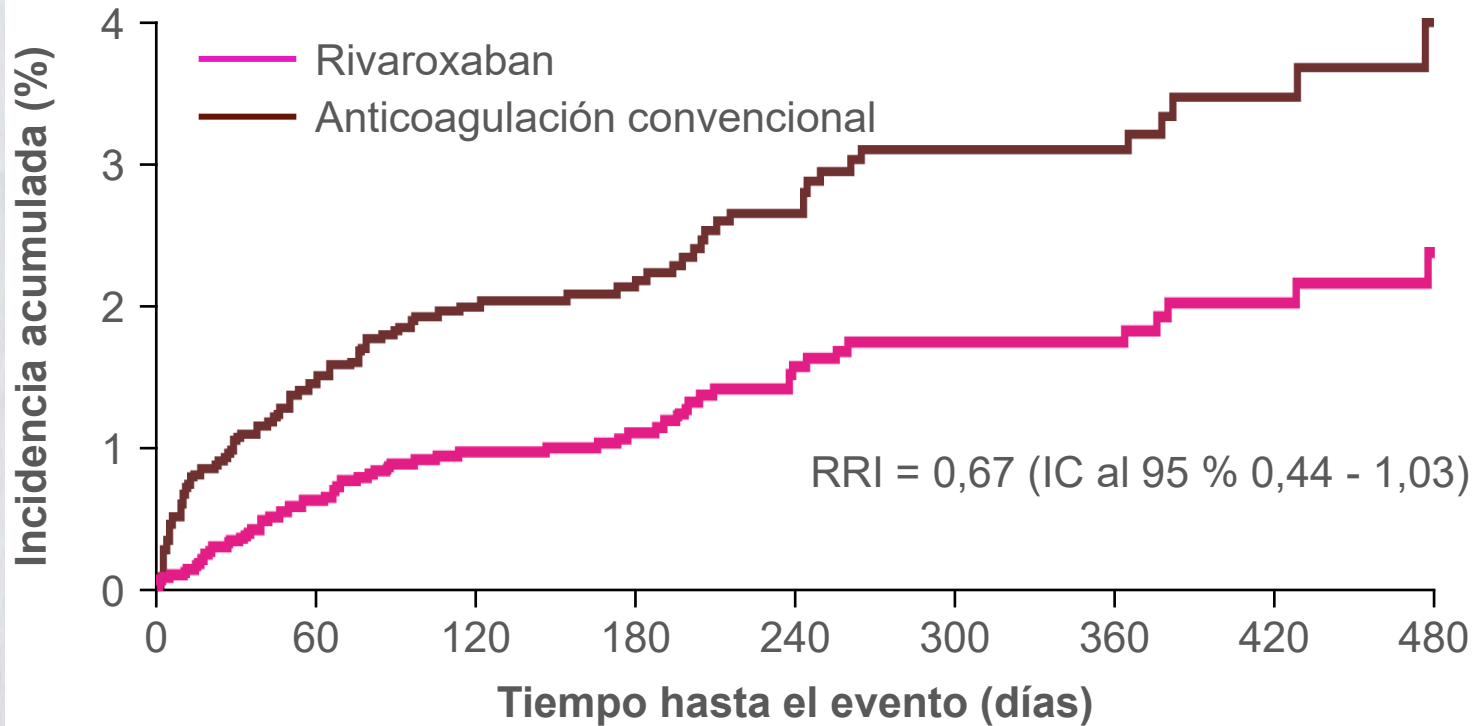
SPOTLIGHT

MARK RUFFALO MICHAEL KEATON RACHEL MADANSKY LEV SCHREIBER STANLEY TUCCI



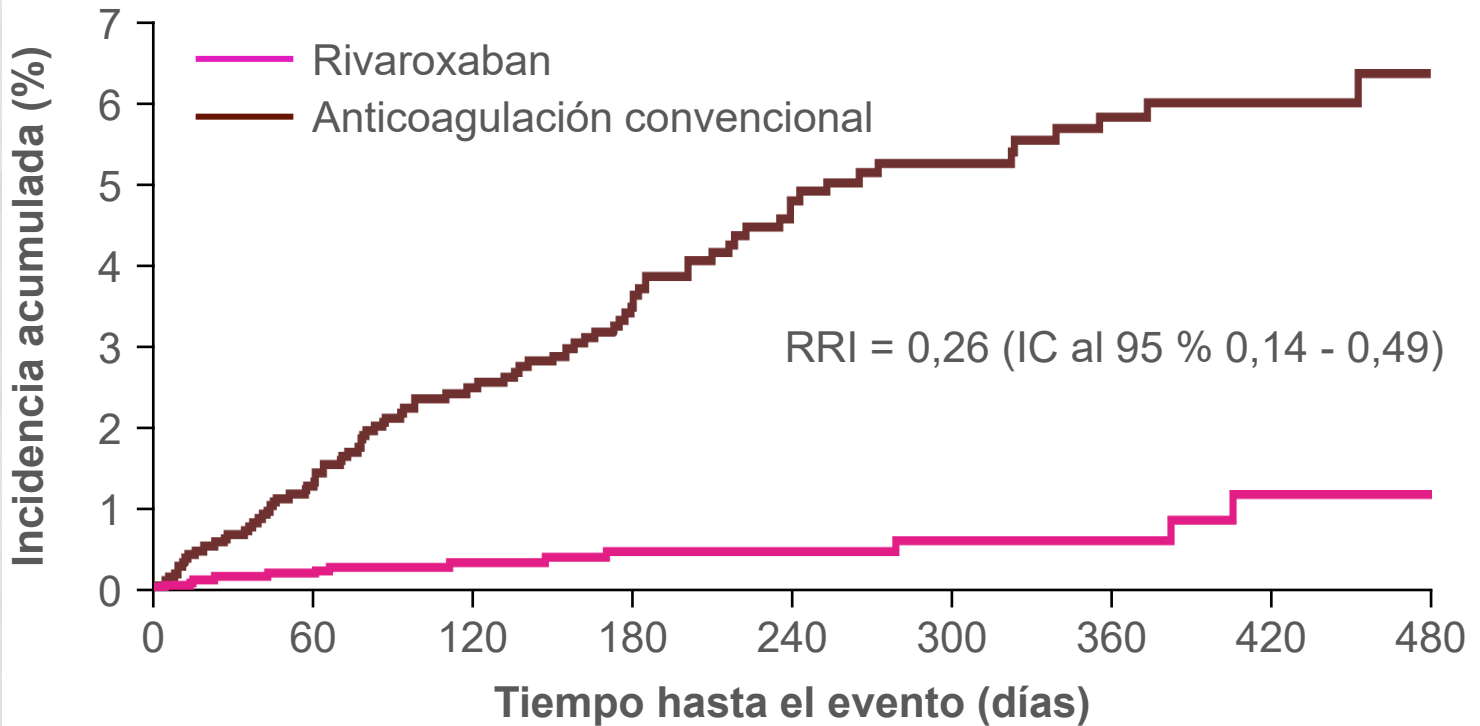
BASED ON THE PULITZER PRIZE-WINNING INVESTIGATION

Incidencia acumulada de recurrencia de ETEV



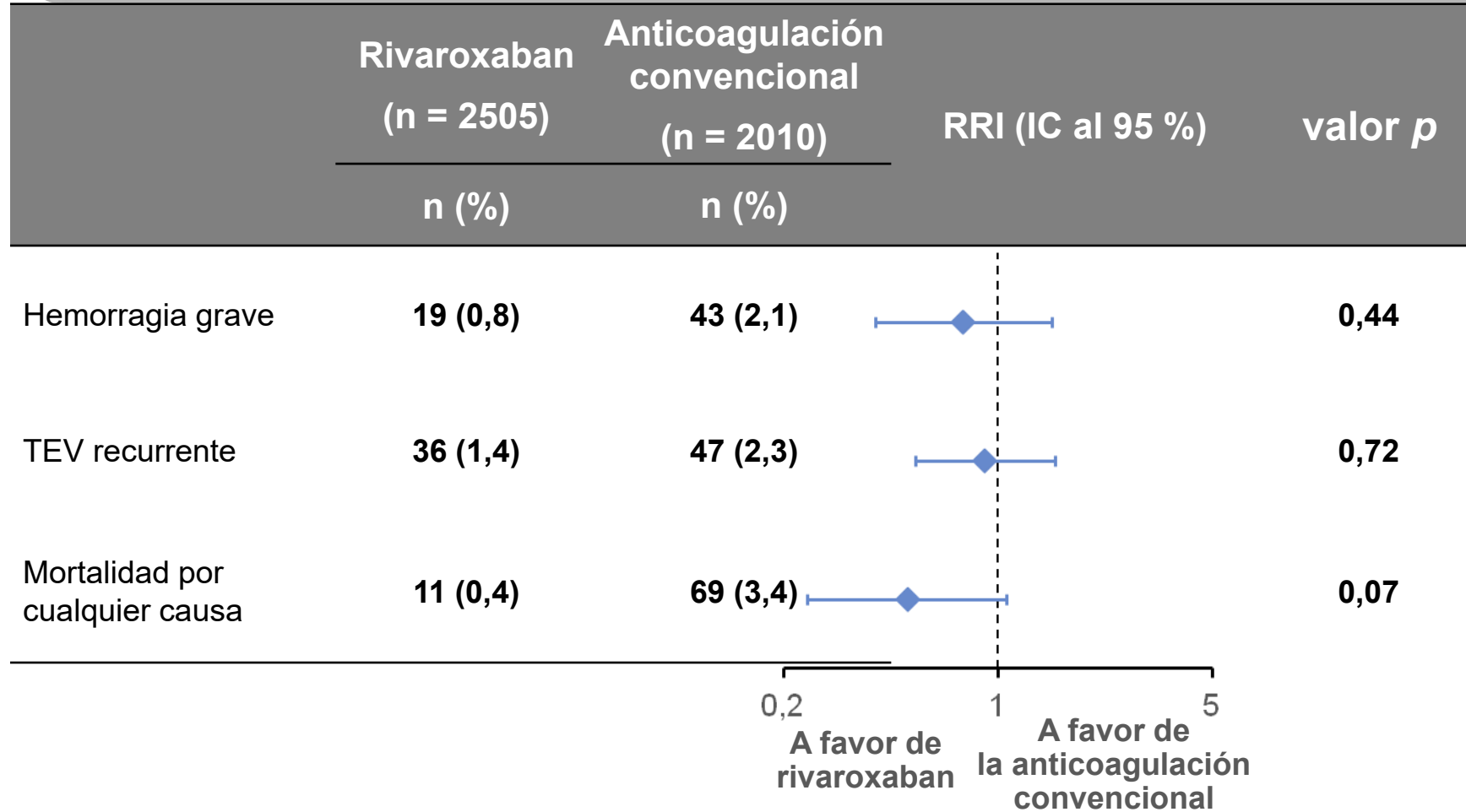
SPOTLIGHT

MARK RUFFALO MICHAEL KEATON RACHEL MADANS LEV SCHREIBER STANLEY TUCCI

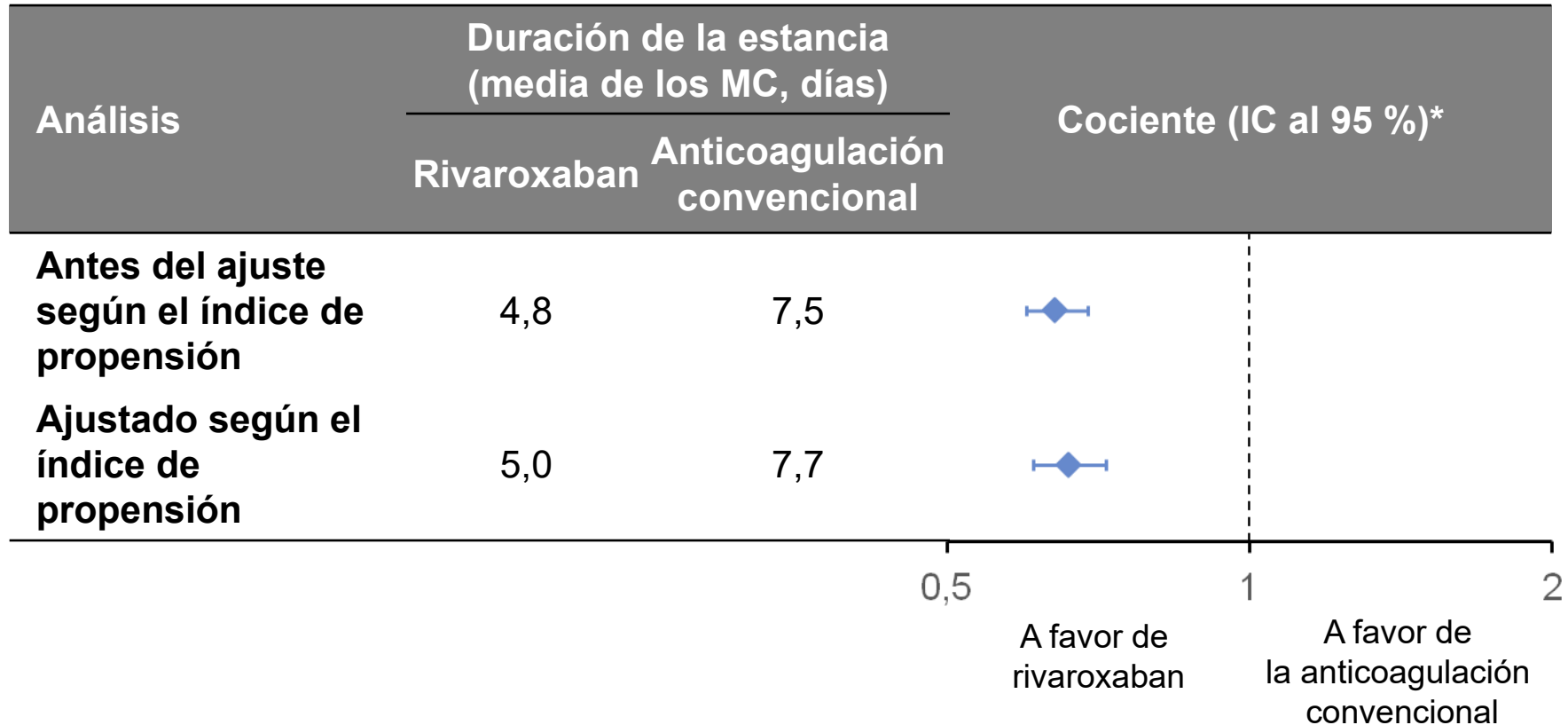


BASED ON THE PULITZER PRIZE-WINNING INVESTIGATION

Resultados ajustados según índice de propensión

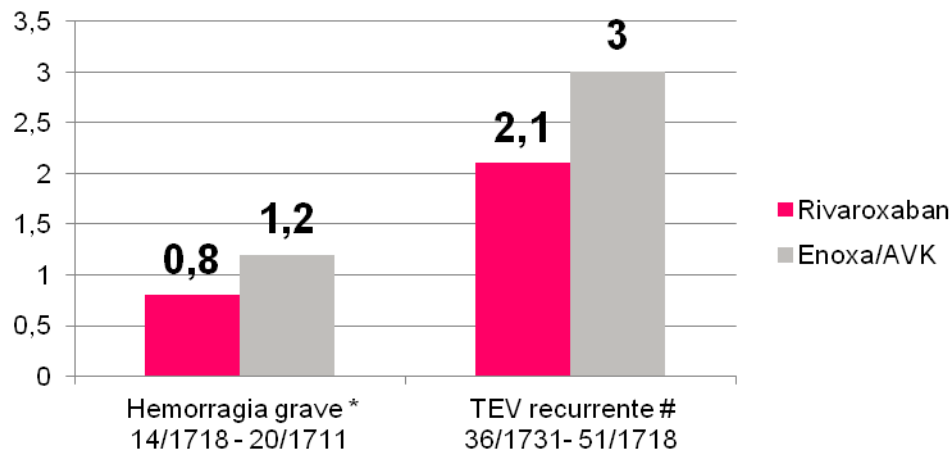


Estancia hospitalaria

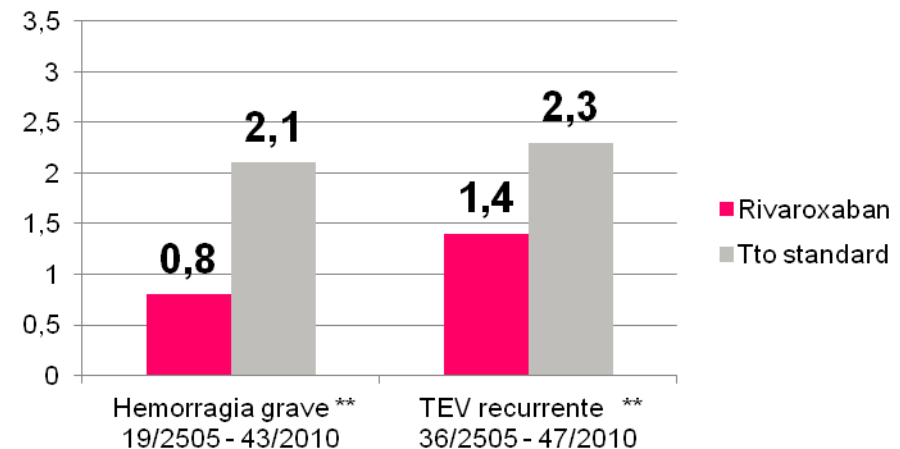


EINSTEIN-DVT vs XALIA

EINSTEIN DVT



XALIA



#Análisis por ITT; *Población de seguridad (pacientes que tomaron ≥ 1 dosis del fármaco del estudio) The EINSTEIN Investigators, *N Engl J Med* 2010;363:2499–2510
EINSTEIN DVT, Hemorrhagia grave HR (IC95%) 0,97 (0,76-1,22) $p=0,77$. TEV recurrente HR (IC95%) 0,68 (0,44-1,04) $p<0,001$ para no inferioridad

**XALIA: población ajustada según el índice de propensión. Hemorrhagia grave HR (IC95%) 0,77 (0,4-1,5) $p=0,44$. TEV recurrente: HR IC95% 0,91 (0,54-1,54) $p=0,72$
Eje ordenadas: incidencia pacientes en %

SPOTLIGHT

MARK RUFFALO MICHAEL KEATON RACHEL MADAMS LEE STANLEY TUCCI
RUFFALO KEATON MADAMS SCHREIBER TUCCI



BASED ON THE PULITZER PRIZE-WINNING INVESTIGATION

i Non-vitamin K antagonist oral anticoagulants and major bleeding-related fatality in patients with atrial fibrillation and venous thromboembolism: a systematic review and meta-analysis

i Adherence to non-vitamin-K-antagonist oral anticoagulant medications based on the Pharmacy Quality Alliance measure

i Doses of apixaban and rivaroxaban prescribed in real-world United States cardiology practices compared to registration trials

i Pharmacy quality alliance measure: adherence to non-warfarin oral anticoagulant medications



TOM HARDY CHARLIZE THERON

MAD

FURIA EN LA CARRETERA

MAX

APIXABAN



An early evaluation of bleeding-related hospital readmissions among hospitalized patients with nonvalvular atrial fibrillation treated with direct oral anticoagulants

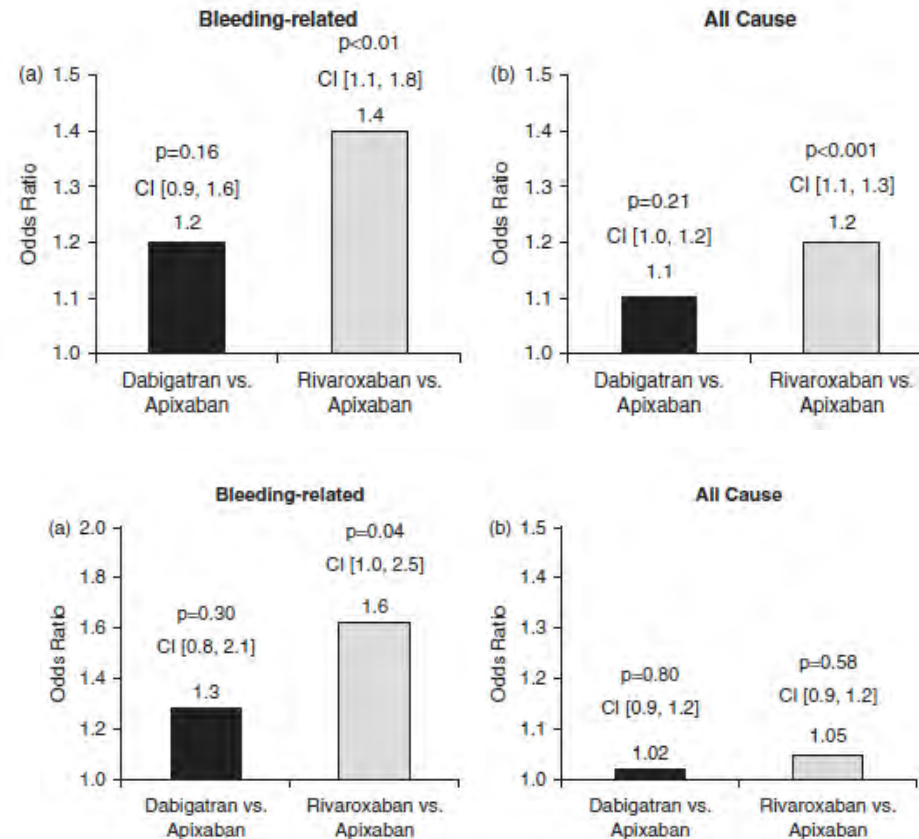
CMRO

Current Medical Research & Opinion Vol. 32, No. 3, 2016, 573-582

- 74.730 pacientes.
- Dabigatran 32.838 pacientes.
- Rivaroxaban 37.754 pacientes.
- Apixaban 4.138 pacientes.
- Reingresos en 30 días.



An early evaluation of bleeding-related hospital readmissions among hospitalized patients with nonvalvular atrial fibrillation treated with direct oral anticoagulants





Comparison of Treatment Persistence in the Real-World Use of Novel Oral Anticoagulants Among Patients With Non-Valvular Atrial Fibrillation

Real-world Bleeding Risk among Non-valvular Atrial Fibrillation Patients Prescribed Apixaban, Dabigatran, Rivaroxaban, and Warfarin: Analysis of Electronic Health Records

Real-world Comparison of Bleeding Risks among Non-Valvular Atrial Fibrillation Patients on Apixaban, Dabigatran, Rivaroxaban: Cohorts Comprising New Initiators and/or Switchers from Warfarin

Major Bleeding, Hospitalization Rates, and Healthcare Costs Among Non-valvular Atrial Fibrillation Patients (NVAF) Who Were Naïve Users of Direct Oral Anticoagulants (DOACs)

Real World Comparison of Major Bleeding Risk Among Non-valvular Atrial Fibrillation Patients Newly Initiated on Apixaban, Warfarin, Dabigatran or Rivaroxaban: A 1:1 Propensity-Score Matched Analysis

Tepper et al.

Poster presentation at ESC Aug/Sept 2015; London, UK Poster/oral poster no.1975.

Lin I et al.

Poster presentation at ESC Aug/Sept 2015; London, UK Poster/oral poster no. P6215

Lefevre et al.

Poster presentation at ACC 2016, Chicago, USA.

Deitelzweig et al.

Poster presentation at ESC Aug/Sept 2015; London, UK Poster/oral poster no.1971).

Lip et al.

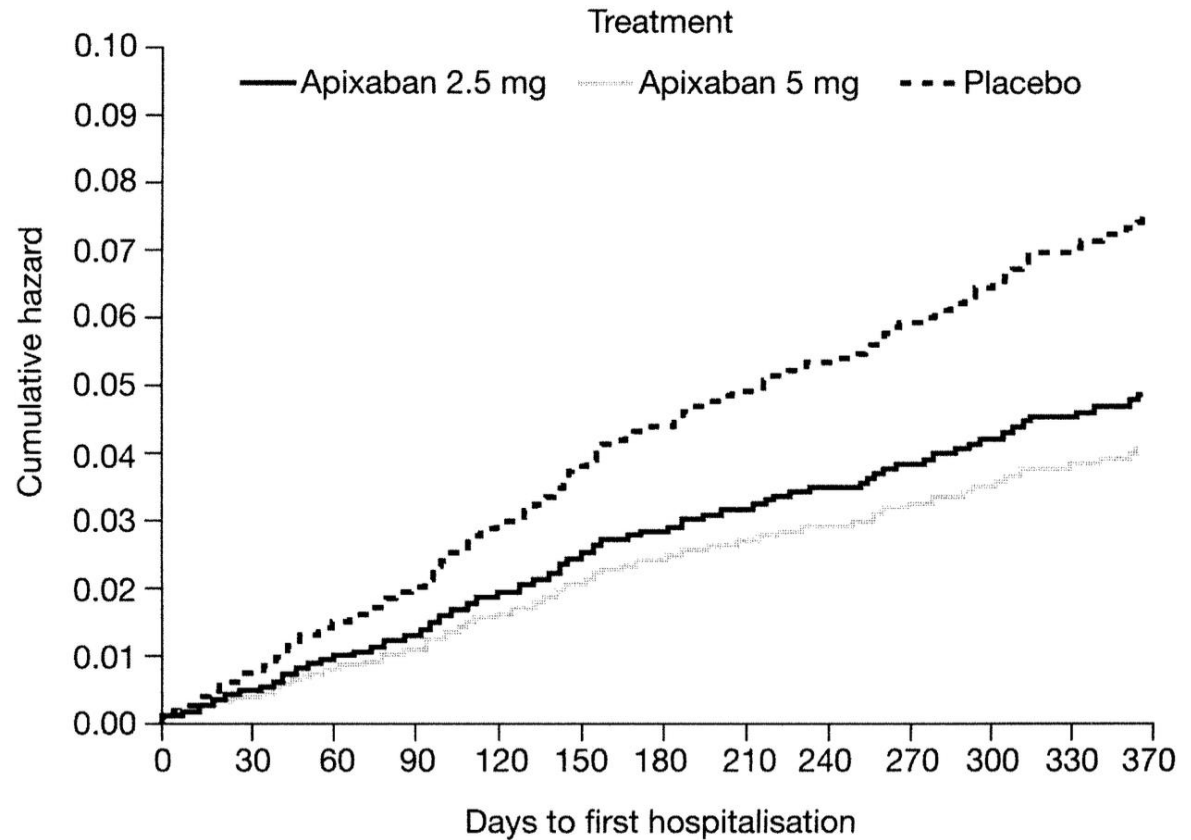
Poster presentation at ACC 2016, Chicago, USA.



APIXABAN

Extended anticoagulation with apixaban reduces hospitalisations in patients with venous thromboembolism

An analysis of the AMPLIFY-EXT trial



No. at risk	0	30	60	90	120	150	180	210	240	270	300	330	370
Apixaban 2.5 mg	840	837	832	827	821	816	813	808	799	796	788	787	782
Apixaban 5 mg	813	805	805	801	793	789	783	780	779	770	766	762	753
Placebo	829	818	808	801	788	780	770	762	760	750	744	738	731

Extended anticoagulation with apixaban reduces hospitalisations in patients with venous thromboembolism

An analysis of the AMPLIFY-EXT trial

Treatment	n	No. of hospitalised patients	Hospitalisations		P-value*
			Event rate % (95 % CI)	HR (95 % CI)	
Placebo	829	62	7.48 (5.69, 9.27)		
Apixaban 2.5 mg BID	840	42	5.00 (3.53, 6.47)	0.64 (0.43, 0.95)	0.026
Apixaban 5 mg BID	813	34	4.18 (2.81, 5.56)	0.54 (0.36, 0.82)	0.004
Apixaban 5 mg vs 2.5 mg BID				0.84 (0.54, 1.32)	0.455

BID, twice daily; CI, confidence interval; HR, hazard ratio. *Based on Cox proportional hazards model.

Treatment	n	No. of hospitalised patients	Days to first hospitalisation		Length of stay during first hospital visit, days
			Mean	Median (25th, 75th)	Median (25th, 75th)
Placebo	829	62	153.7	147.0 (61.0, 253.0)	7.0 (3.0, 12.0)
Apixaban 2.5 mg BID	840	42	196.9	200.5 (102.0, 291.0)	5.0 (3.0, 13.0)
Apixaban 5 mg BID	813	34	202.4	181.5 (100.0, 316.0)	4.5 (3.0, 6.0)

BID, twice daily.

★★★★★

“IT’S MIIKE AT HIS MOST GLEEFULLY LUNATIC”

THE DISSOLVE

★★★★★

“DEMENTED BRILLIANCE”

ROBBIE COLLIN, THE TELEGRAPH



FROM THE DIRECTOR OF 13 ASSASSINS & THE PRODUCERS OF THE RAID

YAKUZA APOCALYPSE

A TAKASHI MIIKE FILM

HAYATO ICHIHARA YAYAN RUHIAN

CAST: YOSHIOKA TAMOGUCHI, KOJI ENDO, NAOKI SATO, KEIZO YURI, OSAMU FUJIOKA, TADAYOSHI KIUCHI, YOSHIKI OKI NO, YOSHIE TANAKA, YOSHISUKE NAGATA, YOSHIMORICHIBA, SHUNICHIRO MASUDA, SHINJIRO NISHIMURA, MISAKO SAKA, TOMOYUKI IMAI, TOMOYO HIKATA, YOSHIKI SUGIYAMA, HAJIME KANDA, YOSHIMI WATABE, JUN NAKABARA, AKIRA SAKAMOTO, KENJI YAMASHITA, YOSHIKI OKIYAMA, TAKASHI MIIKE
CREDITS: SCREENPLAY: YAKUZA APOCALYPSE FILM PARTNERS, DIRECTOR OF PHOTOGRAPHY: OLM, EXECUTIVE PRODUCERS: BANGKO FILM, NIKKATSU, PRODUCED BY: TAKASHI MIIKE

EDOXABAN



Edoxaban vs. warfarin in vitamin K antagonist experienced and naive patients with atrial fibrillation[†]

Michelle L. O'Donoghue^{1*}, Christian T. Ruff¹, Robert P. Giugliano¹, Sabina A. Murphy¹, Laura T. Grip¹, Michele F. Mercuri², Howard Rutman³, Minggao Shi², Grzegorz Kania⁴, Ondrej Cermak⁵, Eugene Braunwald¹, and Elliott M. Antman¹

¹TIMI Study Group, Cardiovascular Division, Brigham and Women's Hospital, 350 Longwood Avenue, 1st Floor, Boston, MA 02115, USA; ²Daiichi Sankyo Pharma Development, Edison, NJ, USA; ³Daiichi Sankyo, Inc., Parsippany, NJ, USA; ⁴Centrum Medyczne 'Ogrodowa', Skierniewice, Poland; and ⁵Slany Municipal Hospital, Slany, Czech Republic



EUROPEAN
SOCIETY OF
CARDIOLOGY

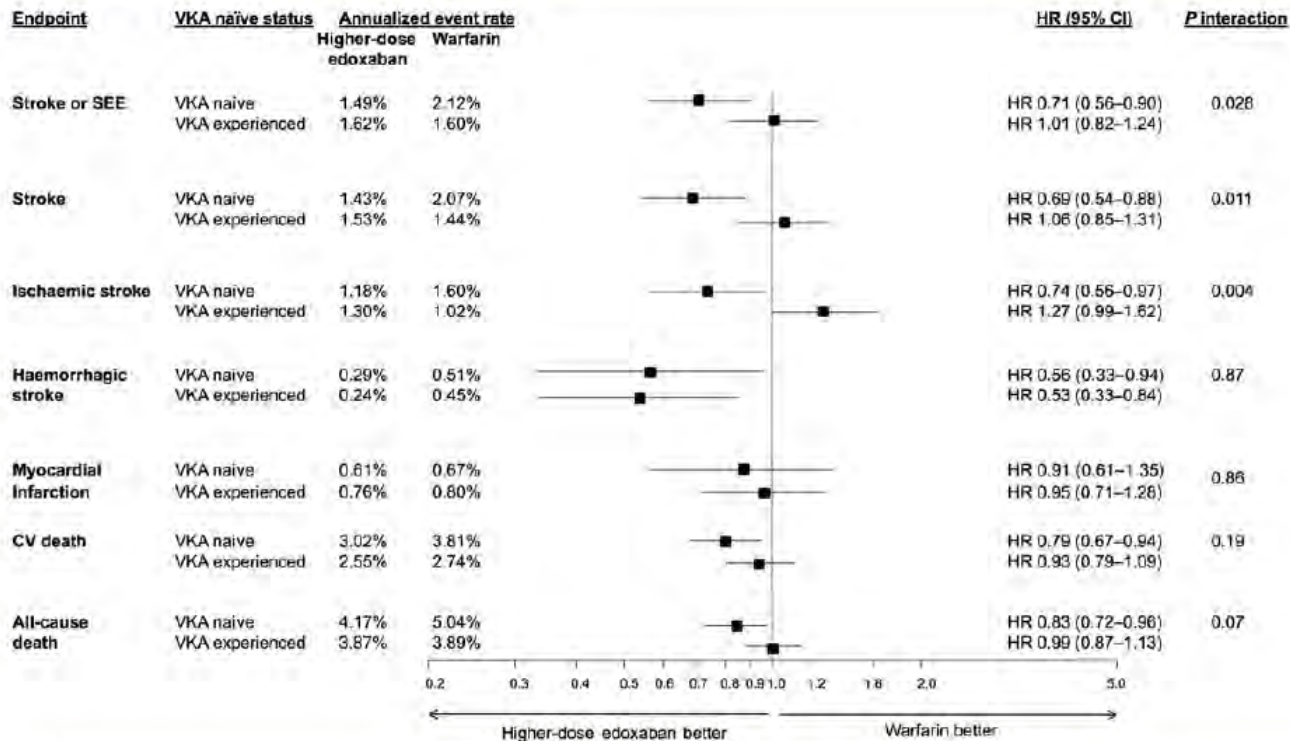


Figure 1 Efficacy of higher-dose edoxaban in the intention-to-treat population stratified by prior vitamin K antagonist exposure (vitamin K antagonist naïve defined as ≤ 60 consecutive days of prior vitamin K antagonist use). *P* interaction reflects the two-way interaction between treatment arm and prior vitamin K antagonist exposure.

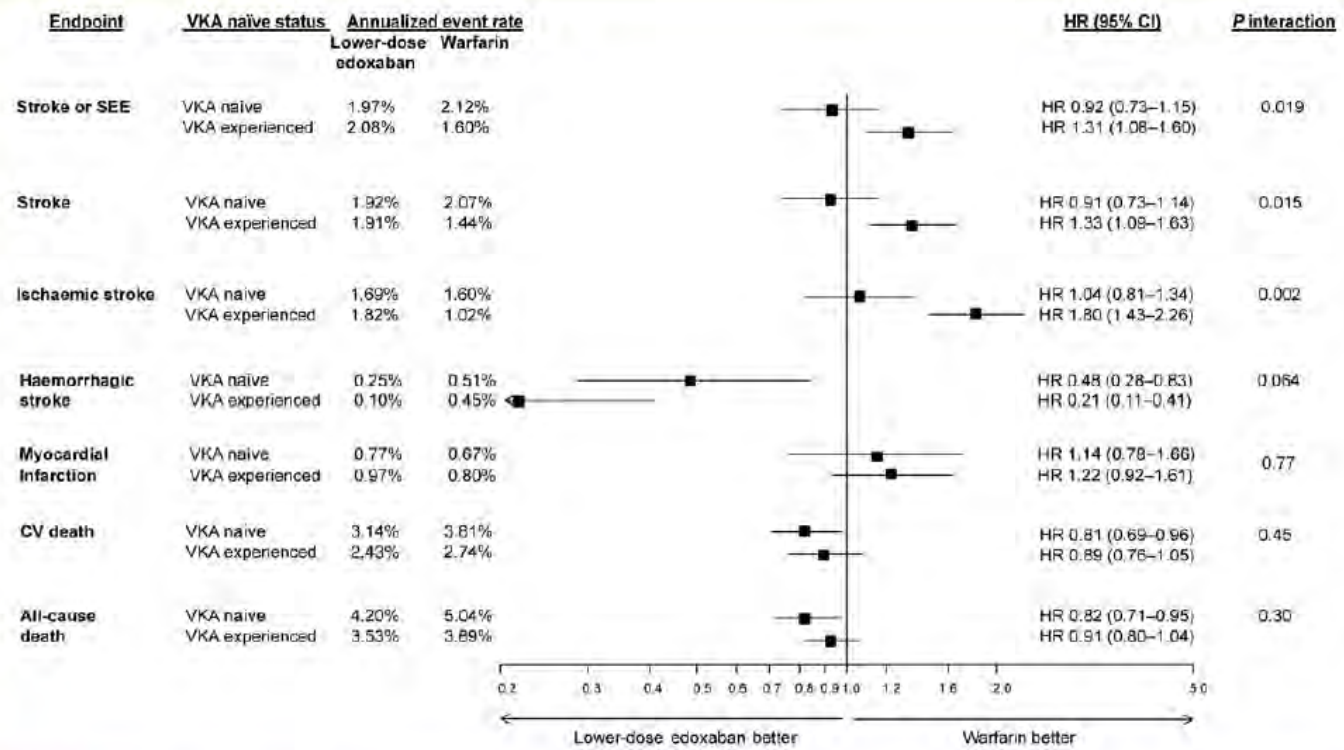


Figure 2 Efficacy of lower-dose edoxaban in the intention-to-treat population stratified by prior vitamin K antagonist exposure (vitamin K antagonist naïve defined as ≤ 60 consecutive days of prior vitamin K antagonist use). P interaction reflects the two-way interaction between treatment arm and prior vitamin K antagonist exposure.

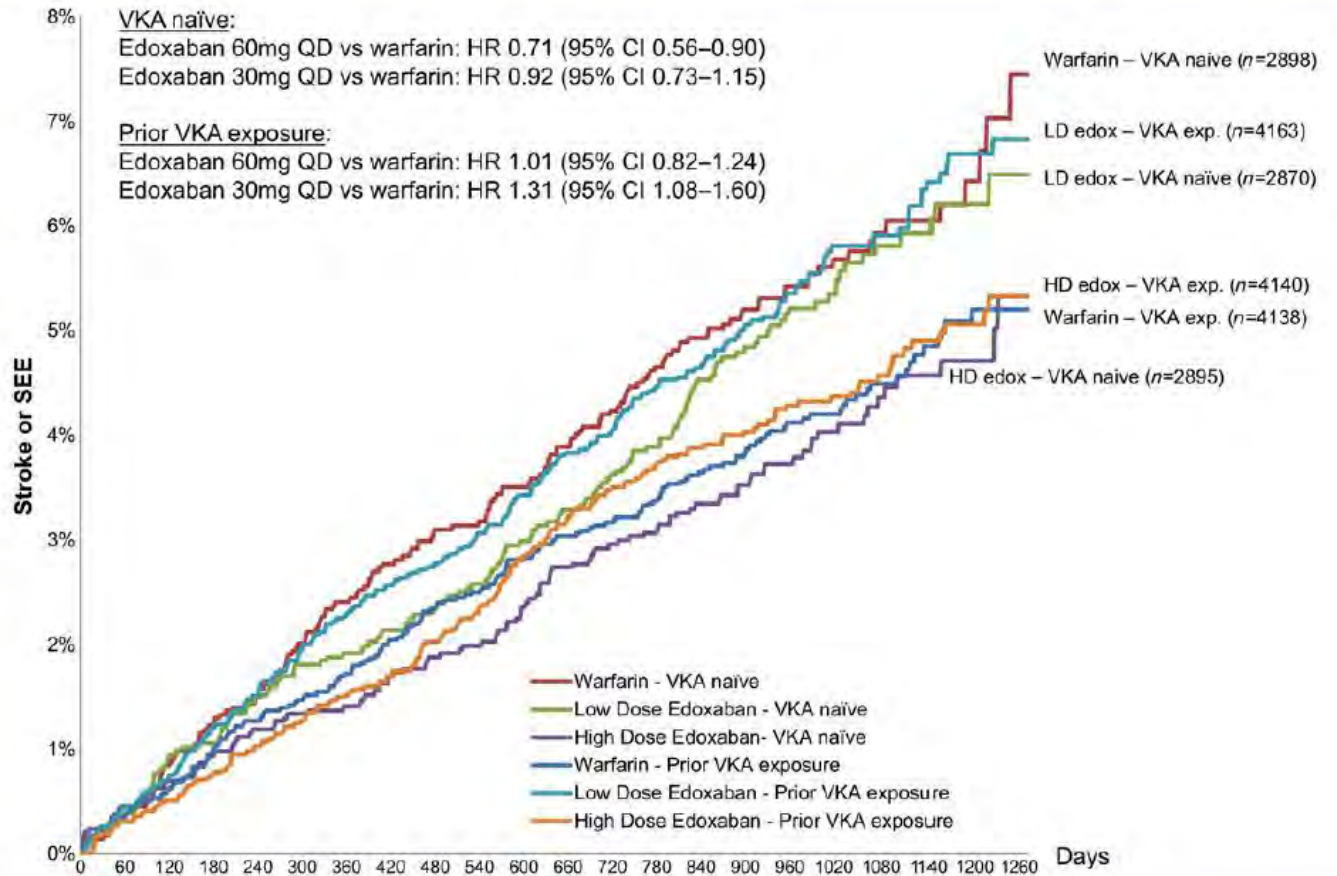


Figure 3 The cumulative incidence of stroke or systemic embolic event by treatment arm for those individuals who were vitamin K antagonist naïve and those who were vitamin K antagonist experienced. A significant treatment interaction for edoxaban was observed based on prior vitamin K antagonist exposure [P for interaction (higher dose) = 0.028; P for interaction (lower dose) = 0.019].

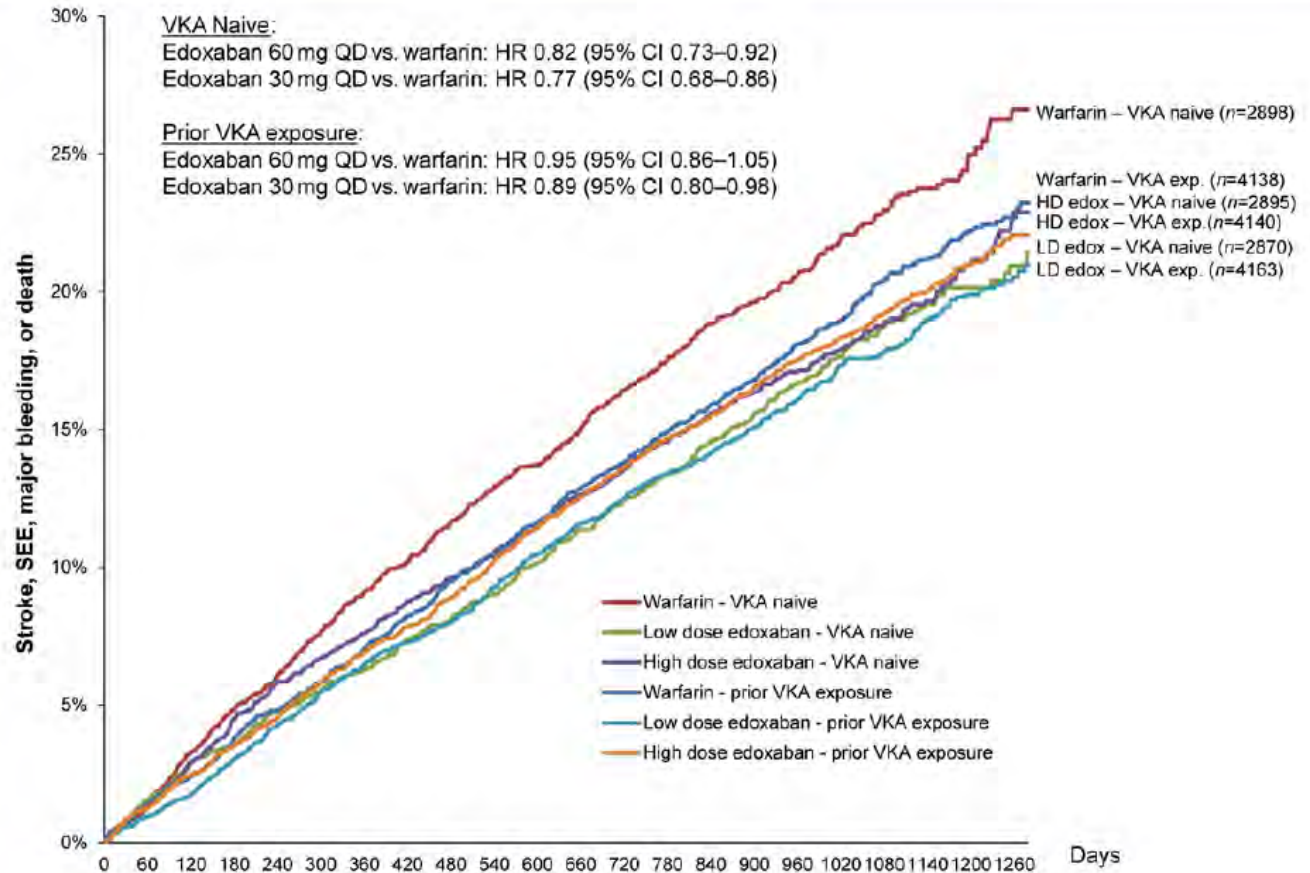


Figure 4 The cumulative incidence of the net clinical outcome of stroke, systemic embolic event, major bleeding, or death by treatment arm for those individuals who were vitamin K antagonist naive and those who were vitamin K antagonist experienced [*P* for interaction (higher dose) = 0.049; *P* for interaction (lower dose) = 0.055].



Association between edoxaban dose, concentration, anti-Factor Xa activity, and outcomes: an analysis of data from the randomised, double-blind ENGAGE AF-TIMI 48 trial

Genetics and the clinical response to warfarin and edoxaban: findings from the randomised, double-blind ENGAGE AF-TIMI 48 trial

Extended duration of anticoagulation with edoxaban in patients with venous thromboembolism: a post-hoc analysis of the Hokusai-VTE study

ADIS DRUG EVALUATION

Edoxaban: A Review in Nonvalvular Atrial Fibrillation



SILENCE

CAN BE

KILLER

HUSH

BY TILT AND INTREPID PICTURES PRESENT AN INTREPID PICTURES AND BLOOMHOUSE PRODUCTION A MIKE FLANAGAN FILM "HUSH" JOHN CALLAGHER JR., MICHAEL TRUCCO AND IN SUPPORTING KATE SIEGEL
CASTING BY ANNE MCCARTHY & KELLY GOY MUSIC BY THE NEWTON BROTHERS COSTUME DESIGNER LYNN PELZMAN EDITOR MIKE FLANAGAN PRODUCTION DESIGNER ELIZABETH BOLLER PRODUCTION OFFICER JAMES KWIEST
EXECUTIVE PRODUCERS MICHAEL J. TOURTOLO SR. KATE LUMPKIN COOPER SAMUELSON JENNIFER BRILL PRODUCED BY TREVOR MACY P.S.A. JASON BLUM WRITTEN BY MIKE FLANAGAN & KATE SIEGEL DIRECTED BY MIKE FLANAGAN

INTREPID PICTURES



COMING SOON



#HUSHMOVIE

ETHAN HAWKE

EMMA WATSON

REGRESIÓN

UNA PELÍCULA DE ALEJANDRO AMENÁBAR

EL MAL
SIEMPRE ENCUENTRA
SU VÍCTIMA



PRÓXIMAMENTE

INTREPID PICTURES AOP BLOOMHOUSE PRODUCTIONS BY TILT CANAL+ 1 DOLBY DIGITAL UNIVERSAL PICTURES

#REGRESION

UNA PELÍCULA DE ALEJANDRO AMENÁBAR

REGRESIÓN

EL MAL
SIEMPRE ENCUENTRA
SU VÍCTIMA

“Mi cine no es un cine de
respuestas,
sino de preguntas”



ETHAN HAWKE EMMA WATSON

REGRESIÓN

UNA PELÍCULA DE ALEJANDRO AMENÁBAR

EL MAL
SIEMPRE ENCUENTRA
SU VÍCTIMA



European Heart Journal (2012) 33, 2719–2747
doi:10.1093/eurheartj/ehs253

ESC GUIDELINES



2012 focused update of the ESC Guidelines for the management of atrial fibrillation

An update of the 2010 ESC Guidelines for the management

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society

Craig T. January, L. Samuel Wann, Joseph S. Alpert, Hugh Calkins, Joseph C. Cleveland, Jr, Joaquin E. Cigarroa, Jamie B. Conti, Patrick T. Ellinor, Michael D. Ezekowitz, Michael E. Field, Katherine T. Murray, Ralph L. Sacco, William G. Stevenson, Patrick J. Tchou, Cynthia M. Tracy and Clyde W. Yancy

Antithrombotic Therapy for VTE Disease CHEST Guideline and Expert Panel Report



Kearon C et al.
Chest 2016;149:31-352.

Fibrilación Auricular



NACOS

TVP + TEP

CONSTITUCION ESPAÑOLA

Aprobada
POR LAS CORTES
EL 31 DE OCTUBRE
DE 1.978

REFERENDUM NACIONAL 6 DE DICIEMBRE.

La nueva Ley del Medicamento

Ley 29/2006, de 26 de julio,
de garantías y uso racional
de los medicamentos
y productos sanitarios

QUINTA EDICIÓN

CON LAS 100 MODIFICACIONES
INTRODUCIDAS POR LA LEY 10/2013,
DE 24 DE JULIO

tecnos

CONSTITUCION ESPAÑOLA

Aprobada
POR LAS CORTES
EL 31 DE OCTUBRE
DE 1978

REFERENDUM NACIONAL 6 DE DICIEMBRE.

Artículo 43.

Ley 14/1986, de 25 Abril, General de Sanidad

- Según la Ley General de Sanidad, los poderes públicos orientarán sus políticas de gasto sanitario en orden a corregir desigualdades sanitarias y garantizar la igualdad de acceso a los servicios sanitarios públicos en todo el territorio español, según lo dispuesto en los artículos 9.2 y 158.1 de la Constitución (art.12).
- Las normas de utilización de los servicios sanitarios serán iguales para todos, independientemente de la condición en la que se acceda a los mismos (art.16).

Ley 29/2006, de 26 Julio, garantías y uso racional de los medicamentos y productos sanitarios

La nueva Ley del Medicamento

Ley 29/2006, de 26 de julio,
de garantías y uso racional
de los medicamentos
y productos sanitarios

QUINTA EDICIÓN

CON LAS 100 MODIFICACIONES
INTRODUCIDAS POR LA LEY 10/2013,
DE 24 DE JULIO



- Se reconoce el derecho de todos los ciudadanos a obtener medicamentos en condiciones de igualdad en todo el Sistema Nacional de Salud.
- Las medidas tendentes a racionalizar la prescripción y utilización de medicamentos y productos sanitarios que pueden adoptar las comunidades autónomas no producirán diferencias en las condiciones de acceso a los medicamentos y productos sanitarios financiados por el Sistema Nacional de Salud, catálogo y precios.

Prescripción de los nuevos anticoagulantes en Atención Primaria



DICIEMBRE 2011



ETEV

FANV



-  El médico de Atención Primaria SI PUEDE iniciar tratamiento
-  El médico de Atención Primaria NO PUEDE iniciar tratamiento



MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD

agencia española de medicamentos y productos sanitarios



CONDICIONES PARA LA PRESCRIPCIÓN	Prescripción por médicos de atención primaria	Prescripción de inicio en casos justificados	Condiciones iguales a las recomendadas por el Ministerio y el CI-SNS (IPT)	Adhesión a las condiciones de financiación para el SNS y recomendaciones del IPT aprobado por el CI-SNS					Otras condiciones /Comentarios
				Definición de mal control anticoagulación con AVK	Pacientes con antecedentes de hemorragia intracraneal	Ictus isquémico con criterios de alto riesgo de HIC	Pacientes en AVK y buen control INR con episodios tromboembólicos arteriales graves		
ÁMBITO									
Andalucía	Si	Si	No	No	Si	Si	Si	Se requiere un periodo de mal control de un año.	
Aragón	Si	Si	Si	Si	Si	Si	Si		
Asturias	No	Si	No	Si	Si	Si	Si	Hasta 2014 se pedía consentimiento informado del paciente	
Baleares	Si	Si	No	No	Si	Si	Si	No incluye la imposibilidad de acceso al control de INR convencional	
Canarias	No	Si	No	Si	Si	Si	Si	El médico debe declarar que el paciente ha sido informado de la falta de disponibilidad de antídoto que permita detener la hemorragia en caso de sangrado o necesidad de cirugía urgente. Esto no se exige para las heparinas de bajo peso u otros anticoagulantes	
Cantabria	No	Si	No	Si	Si	Si	Si		
Castilla León	No	Si	No	Si	Si	Si	Si		
Castilla-La Mancha	No	Si	No	Si	Si	Si	Si		
Cataluña	Si	No	No	No	No	No	No	No incluye la imposibilidad de acceso al control de INR convencional	
C Valenciana	Si		No	Si	Si	No	Si		
Extremadura	No	Si	No	Si	Si	Si	Si	Incluye escala CHA2DS2VASc para evaluación riesgo tromboembólico y escala SAMeTT2R2->2 para tratamiento inicio.	
Galicia	Si	Si	Si	Si	Si	Si	Si		
Madrid	Si	No	No	No	No	No	No	Una de las diferencias más relevantes es la imposibilidad de prescripción inicial en pacientes con alto riesgo de hemorragia intracraneal	
Murcia	No	Si	No	Si	Si	Si	Si		
Navarra	Si	Si	Si	Si	Si	Si	Si		
País Vasco	Si	Si	Si	Si	Si	Si	Si		
La Rioja	No	Si	No	No	Si	Si	Si		
Ceuta y Melilla	Si	Si	Si	Si	Si	Si	Si	Mal control: Tener durante los 6 últimos meses: <60% de controles en rango de anticoagulación ó 4 o más determinaciones de INR por encima de 5	

ETHAN HAWKE EMMA WATSON

REGRESIÓN

UNA PELÍCULA DE ALEJANDRO AMENÁBAR

EL MAL
SIEMPRE ENCUENTRA
SU VÍCTIMA

EL PAÍS

ARCHIVO

EDICIÓN
IMPRESA



PORTADAS A LA CARTA

Regala algo diferente, regala una portada

Hemeroteca

LUNES, 31 de agosto de 2009

Un fármaco más eficaz para el corazón puede sustituir al Sintrom

EL PAÍS

ESPAÑA

ANDALUCÍA CATALUÑA C. VALENCIANA GALICIA MADRID

Más de 120.000 personas no reciben los anticoagulantes que necesitan

EL PAÍS

PORTADA

INTERNACIONAL

POLÍTICA

SOCIEDAD

EDUCACIÓN SALUD CIENCIA MEDIO AMBIENTE IGUALDAD CONSUMO COMUNICACIÓN

ESTÁ PASANDO La epidemia del ébola Homofobia Acoso escolar Reforma del aborto

Nuevas barreras en el acceso a los nuevos anticoagulantes

PRÓXIMAMENTE

#REGRESION





GEORGE CLOONEY

TOMORROWLAND





Evaluation of medical costs associated with use of new oral anticoagulants compared with standard therapy among venous thromboembolism patients

informa
healthcare

JME
Journal of Medical Economics
A SAGE journal

Just Accepted by *Journal of Medical Economics*

Original Research

Comparison of differences in medical costs when new oral anticoagulants are used for the treatment of patients with non-valvular atrial fibrillation and venous thromboembolism versus warfarin or placebo in the US

J Thromb Thrombolysis (2015) 40:131–138
DOI 10.1007/s11239-014-1158-2



COSTE - EFECTIVOS

Evaluation of medical costs avoided when new oral anticoagulants are used for extended treatment of venous thromboembolism based on clinical trial results

Real-World Medical Cost Avoidance When New Oral Anticoagulants are Used Versus Warfarin for Venous Thromboembolism in the United States

Clinical and Applied
Thrombosis/Hemostasis
1-7

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DOI: 10.1177/11076029615585991
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J Med Econ 2014;17:763-70.

J Med Econ 2015;18:399-409.

J Thromb Thrombolysis 2015;40:131-138.



Direct Comparison of Dabigatran, Rivaroxaban, and Apixaban for Effectiveness and Safety in Nonvalvular Atrial Fibrillation

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April 3rd, 2016



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ORIGINAL ARTICLE

Extended Thromboprophylaxis with Betrixaban in Acutely Ill Medical Patients

Alexander T. Cohen, M.D., Robert A. Harrington, M.D., Samuel Z. Goldhaber, M.D., Russell D. Hull, M.B., B.S., Brian L. Wiens, Ph.D., Alex Gold, M.D., Adrian F. Hernandez, M.D., and C. Michael Gibson, M.D., for the APEX Investigators*

May 27, 2016 | DOI: 10.1056/NEJMoa1601747

Conclusiones



LEONARDO
SBARAGLIA

PABLO
ECHARRI

Y CLARA
LAGO

ELLOS TENÍAN UN PLAN, ÉL UNA OPORTUNIDAD.

AL FINAL DEL TÚNEL

ESCRITA Y
DIRIGIDA POR RODRIGO GRANDE

21 DE ABRIL - SOLO EN CINES

- NACOS son una realidad.
- Resultados mundo real = Ensayos clínicos.
- Eficaces & Seguros.
- Coste-Efectivos.
- A la cola de Europa en utilización
- Dabigatran ya tiene Antídoto.

The End