Papel de los nuevos anticoagulantes en la práctica clínica

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Papel de los nuevos anticoagulantes en la práctica clínica

- **Artroplastia de cadera y rodilla**
- **Pacientes encamados**
- **Trombosis venosa y embolia pulmonar**
- **Fibrilación auricular no valvular**

Tromboprofilaxis en artroplastia de cadera y rodilla

DABIGATRAN	Variable principal de eficacia	Variable secundaria de eficacia	Hemorragias graves
RE-NOVATE (prótesis de cadera),			
Dabigatrán 220 mg	6.0%	3,1%	2,0%
Dabigatrán 150 mg	8,6%	4,3%	1,3%
Enoxaparina 40 mg	6,7%	3,9%	1,6%
RE-NOVATE II (prótesis de cadera),			
Dabigatrán 220 mg	7,7%	2,2%*	1,4%
Enoxaparina 40 mg	8,8%	4,2%	0,9%
RE-MODEL (prótesis de rodilla),			
Dabigatrán 220 mg	36,4%	2,6%	1,5%
Dabigatrán 150 mg	40,5%	3,8%	1,3%
Enoxaparina 40 mg	37,7%	3,5%	1,3%

***p <0.05; †p <0.01; ‡p <0.001**

***Variable principal de eficacia*:** combinación de TVP en la flebografía, EP y muerte.
***Variable secundaria de eficacia*:** la suma de EP no fatal, TVP proximal y muerte por ETV.

Tromboprofilaxis en artroplastia de cadera y rodilla

RIVAROXABAN	Variable principal de eficacia	Variable secundaria de eficacia	Hemorragias graves
RECORD 1, (prótesis de cadera)			
Rivaroxabán 10 mg	1,1%‡	0,2%‡	0,3%
Enoxaparina 40 mg	3,7%	2,0%	0,1%
RECORD 3, (prótesis de rodilla)			
Rivaroxabán 10 mg	9,6%‡	1,0%*	0,6%
Enoxaparina 40 mg	18,9%	2,6%	0,5%

*p <0.05; †p <0.01; ‡p <0.001

***Variable principal de eficacia*:** combinación de TVP en la flebografía, EP y muerte.
***Variable secundaria de eficacia*:** la suma de EP no fatal, TVP proximal y muerte por ETV.

Tromboprofilaxis en artroplastia de cadera y rodilla

APIXABAN	Variable principal de eficacia	Variable secundaria de eficacia	Hemorragias graves
ADVANCE-3, (prótesis de cadera)			
Apixabán 2,5 mg 2 veces al día	**1,4%‡**	**0,5%†**	**4,8%**
Enoxaparina 40 mg	**3,9%**	**1,1%**	**5,0%**
ADVANCE-2, (prótesis de rodilla)			
Apixabán 2,5 mg 2 veces al día	**15,1%‡**	**1,1%***	**0,6%**
Enoxaparina 40 mg	**24,4%**	**2,2%**	**0,9%**

***p <0.05; †p <0.01; ‡p <0.001**

***Variable principal de eficacia*:** combinación de TVP en la flebografía, EP y muerte.
***Variable secundaria de eficacia*:** la suma de EP no fatal, TVP proximal y muerte por ETV.

MINISTERIO DE SANIDAD Y CONSUMO

Blood Coagulation, Fibrinolysis and Cellular Haemostasis

Venous thromboembolism and bleeding after total knee and hip arthroplasty

Findings from the Spanish National Discharge Database

Ricardo Guijarro[1]; Julio Montes[2]; Carlos San Roman[3]; Juan Ignacio Arcelus[4]; Giovanni Barillari[5]; Xavier Granero[6]; Manuel Monreal[7]

	ETV	No ETV	Muerte	No muerte
Pacientes, N	436	57.601	54	57.983

Guijarro R, et al. *Thromb Haemost* 2011;105: 610–5.

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	ETV	No ETV	Muerte	No muerte
Pacientes, N	**436**	**57.601**	**54**	**57.983**
Hemorragias,				
Hematoma quirúrgico	**17 (3,4%)**	**583 (1,0%)**	**2 (3,7%)**	**598 (1,0%)**
Gastrointestinal	**2 (0,5%)**	**59 (0,1%)**	**3 (5,6%)**	**58 (0,1%)**
Cerebral	**0**	**2 (0,003%)**	**0**	**2 (0,003%)**
Cualquiera	**22 (5,0%)**	**677 (1,2%)**	**7 (13%)**	**692 (1,2%)**

Guijarro R, et al. *Thromb Haemost* 2011;105: 610–5.

Blood Coagulation, Fibrinolysis and Cellular Haemostasis

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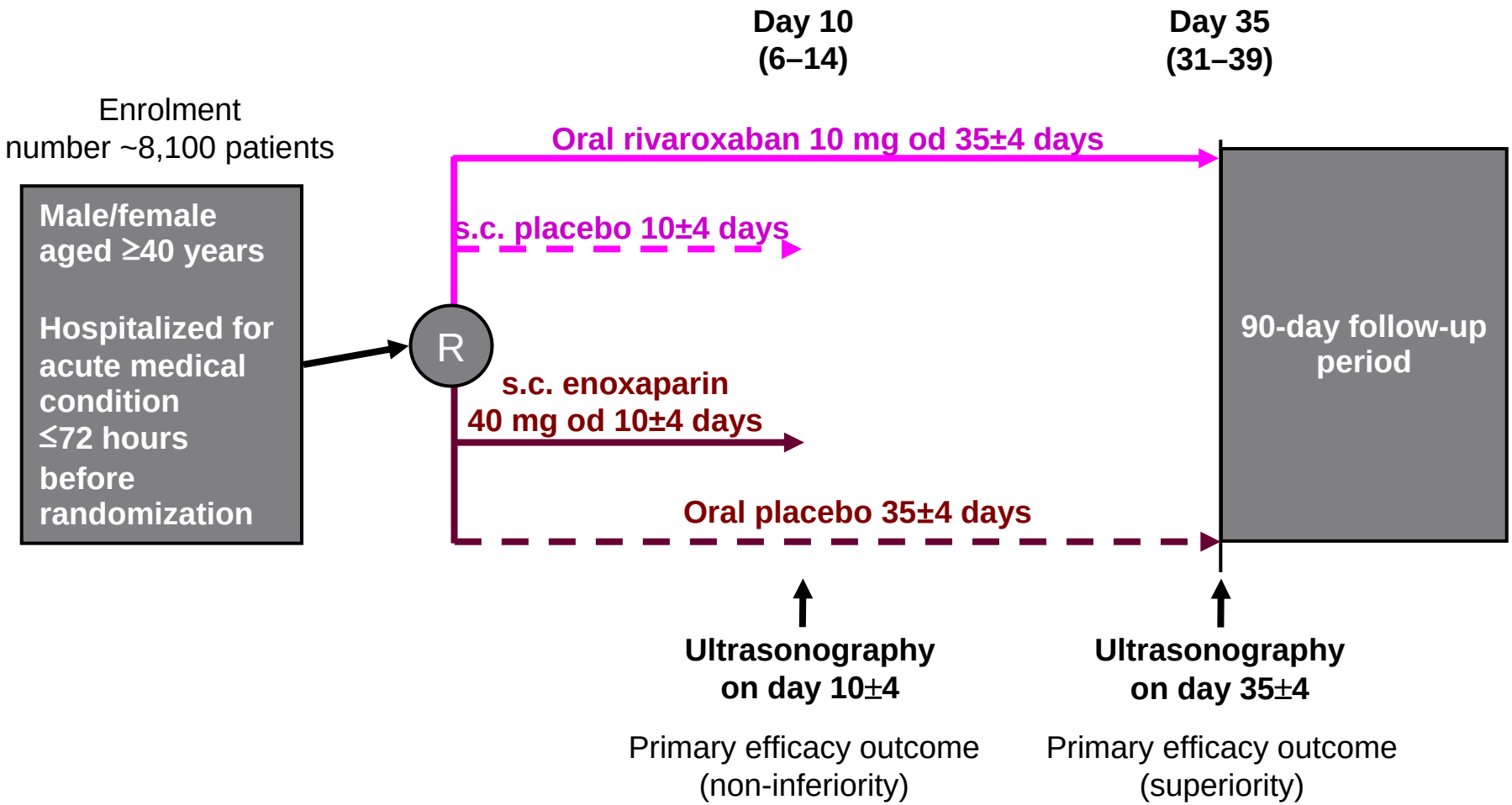
	ETV	No ETV	Muerte	No muerte
Pacientes, N	**436**	**57.601**	**54**	**57.983**
ETV,				
TVP durante el ingreso	**254 (58%)**	**-**	**1 (1,8%)**	**253 (0,4%)**
TVP tras el alta	**76 (17%)**	**-**	**1 (1,8%)**	**75 (0,1%)**
EPdurante el ingreso	**56 (13%)**	**-**	**8 (15%)**	**48 (0,1%)**
EP tras el alta	**50 (11%)**	**-**	**3 (5,5%)**	**47 (0,1%)**
Cualquiera	**436**	**-**	**13 (24%)**	**423 (0,7%)**

Guijarro R, et al. *Thromb Haemost* 2011;105: 610–5.

Tromboprofilaxis en pacientes encamados

MAGELLAN: clinical trial design



www.clinicaltrials.gov

Eficacia y seguridad

	Rivaroxaban n = 3,997	Enoxaparina n = 4,001	p
Días 1-10			
Primary efficacy outcome	78 (2.7%)	82 (2.7%)	
Hemorragia grave	24 (0.6%)	11 (0.3%)	0.032
Días 11-35			
Primary efficacy outcome	131 (4.4%)	175 (5.7%)	
Hemorragia grave	19 (0.5%)	4 (0.1%)	0.0004

Muerte

	Rivaroxaban n = 3,997	Enoxaparina n = 4,001
Días 1-10		
Muerte por tromboembolismo	3 (0.08%)	6 (0.15%)
Muerte por hemorragia	5 (0.13%)	1 (0.02%)
Días 11-35		
Muerte por tromboembolismo	16 (0.40%)	24 (0.60%)
Muerte por hemorragia	2 (0.05%)	0

Causas de muerte a 30 días según el factor de riesgo en 18.028 pacientes con embolia pulmonar.

	N	Muerte	EP fatal	Hemorragia fatal
Pacientes, N	18.028	1.147 (6,4%)	441 (2,4%)	67 (0,4%)
Cirugía reciente	2.212			
Inmovilización ≥4 días	4.169			
Espontáneas,				
Cáncer	2.605			
Tratamiento hormonal	579			
Viaje reciente	343			
Embarazo/puerperio	53			
Idiopática	8.187			

Causes of death at 30 days according to the different risk factors in 18,028 patients with acute pulmonary embolism.

	N	Muerte	EP fatal	Hemorragia fatal
Pacientes, N	18.028	1.147 (6,4%)	441 (2,4%)	67 (0,4%)
Cirugía reciente	2.212	80 (3,6%)	31 (1,4%)	7 (0,3%)
Inmovilización ≥4 días	4.169	496 (12%)	191 (4,6%)	22 (0,5%)
Espontáneas,				
Cáncer	2.605	304 (12%)	99 (3,8%)	15 (0,6%)
Tratamiento hormonal	579	6 (1,0%)	4 (0,7%)	0
Viaje reciente	343	4 (1,2%)	0	1 (0,3%)
Embarazo/puerperio	53	0	0	0
Idiopática	8.187	262 (3,2%)	117 (1,4%)	23 (0,3%)

Pacientes inmovilizados

	N	Edad (años±DS)	Trombo-profilaxis	Muerte a 30 días	EP fatal a 30 días
Pacientes, N	**4.169**	**71±16**	**1.054 (25%)**	**496 (12%)**	**191 (4,6%)**
Duración,					
<7 días	**1.062**				
1-4 semanas	**1.820**				
>4 semanas	**1.217**				
Lugar,					
Hospital	**913**				
Centro crónicos	**235**				
Domicilio	**1.999**				
No datos	**1.022**				

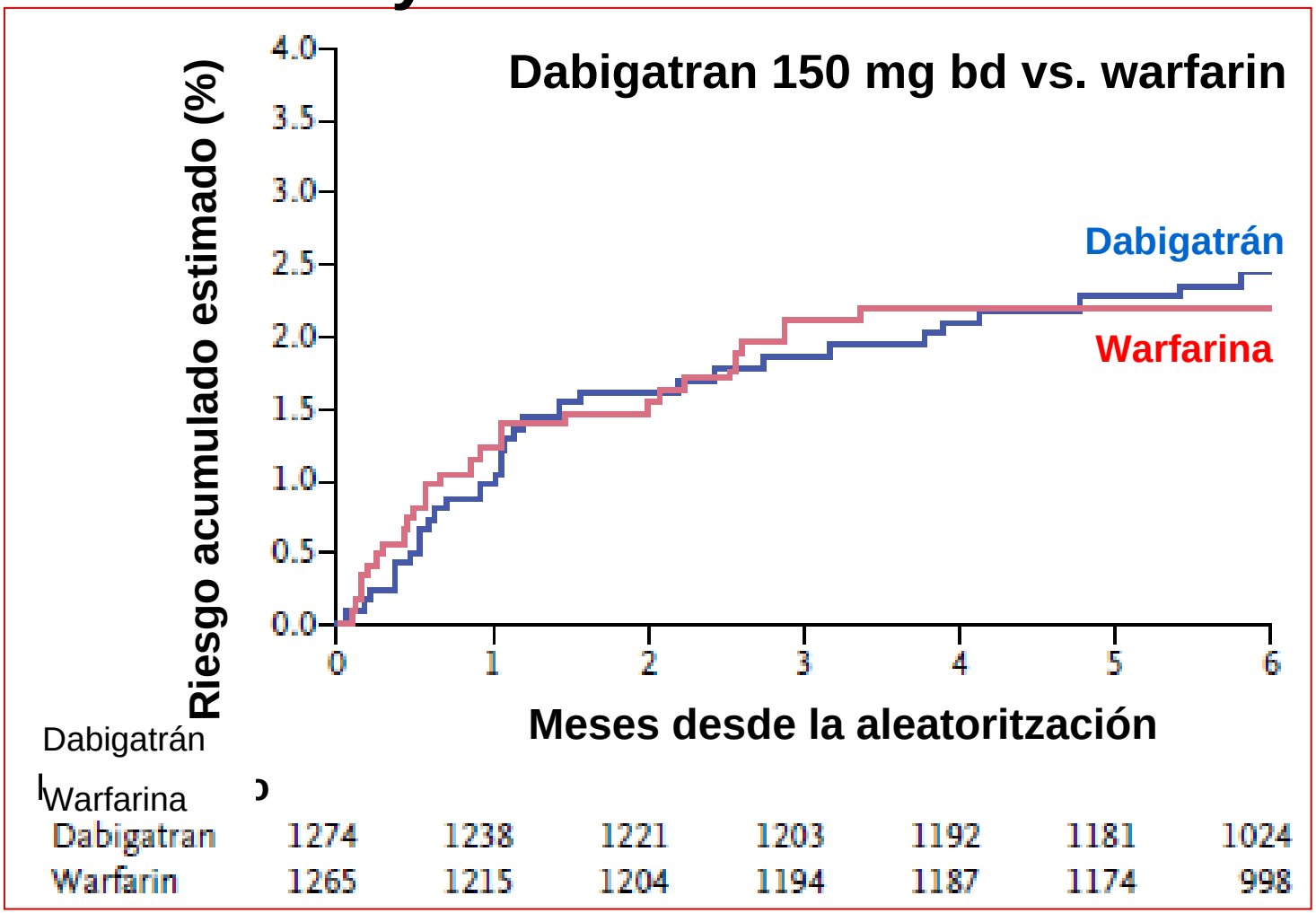
Pacientes inmovilizados

	N	Edad (años±DS)	Trombo-profilaxis	Muerte a 30 días	EP fatal a 30 días
Pacientes, N	**4.169**	**71±16**	**1.054 (25%)**	**496 (12%)**	**191 (4,6%)**
Duración,					
<7 días	**1.062**	**70±16**	**281 (27%)**	**90 (8.5%)**	**39 (3,7%)**
1-4 semanas	**1.820**	**69±17**	**583 (32%)**	**214 (12%)**	**78 (4,3%)**
>4 semanas	**1.217**	**75±16**	**168 (14%)**	**183 (15%)**	**71 (5,8%)**
Lugar,					
Hospital	**913**	**70±16**	**523 (57%)**	**110 (12%)**	**31 (3,4%)**
Centro crónicos	**235**	**79±12**	**33 (14%)**	**46 (20%)**	**20 (8,5%)**
Domicilio	**1.999**	**71±17**	**253 (13%)**	**217 (11%)**	**81 (4,1%)**
No datos	**1.022**	**71±16**	**245 (24%)**	**123 (12%)**	**59 (5,8%)**

Tratamiento de la trombosis venosa profunda y le embolia pulmonar

RECOVER™
Study of treatment of venous thromboembolism

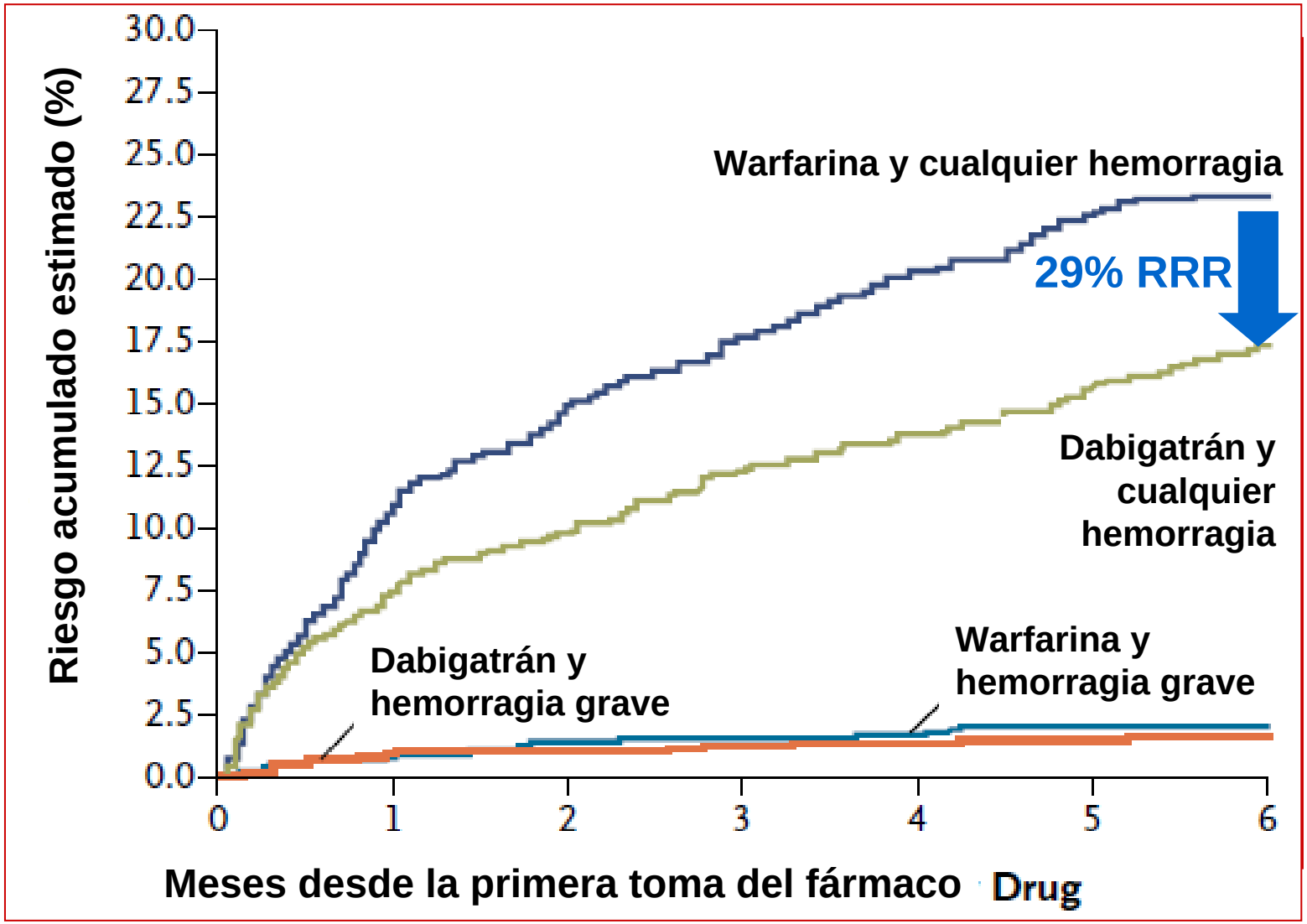
Riesgo acumulado de recurrencias y muerte relacionada



Schulman S, et al. N Engl J Med 2009;361:2342–2352

RECOVER™
Study of treatment of venous thromboembolism

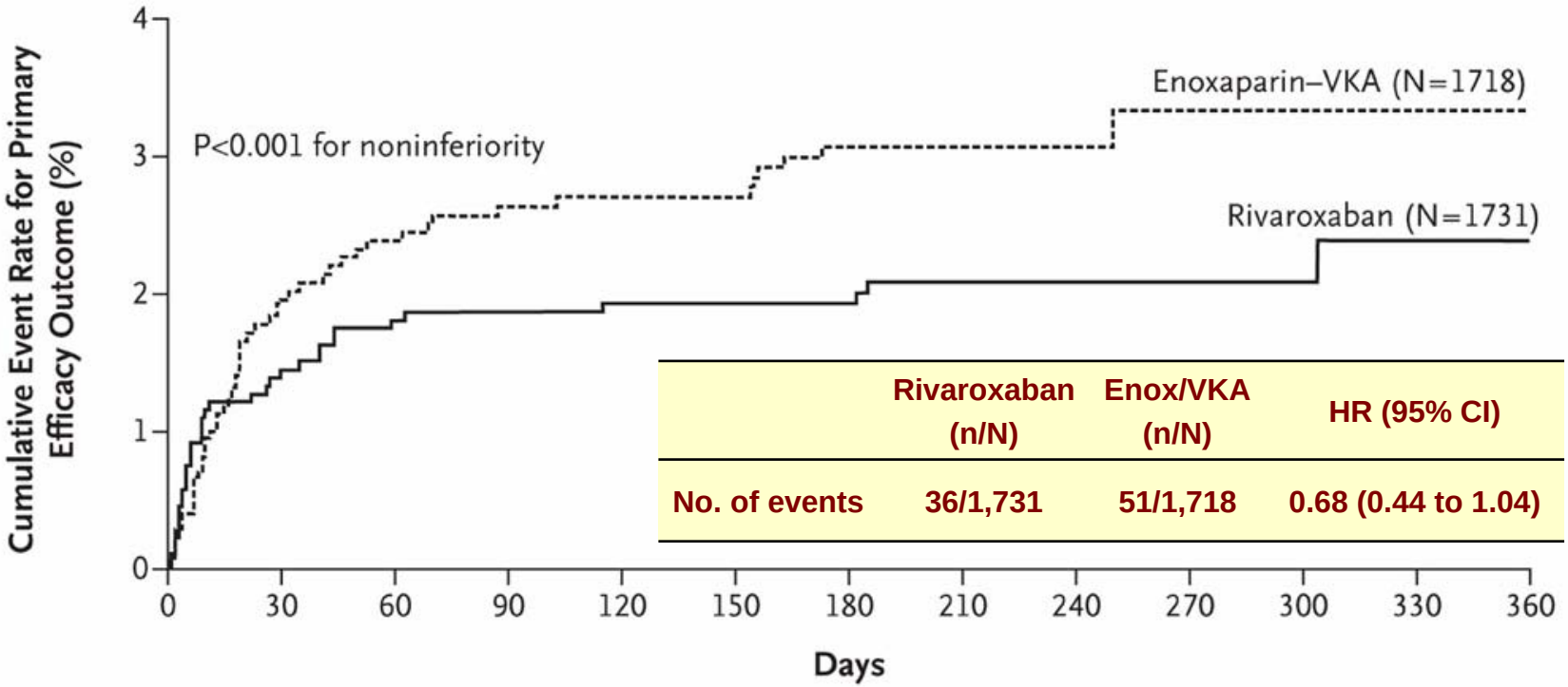
Riesgo acumulado de hemorragia



Schulman S, et al. N Engl J Med 2009;361:2342–2352

The NEW ENGLAND JOURNAL of MEDICINE

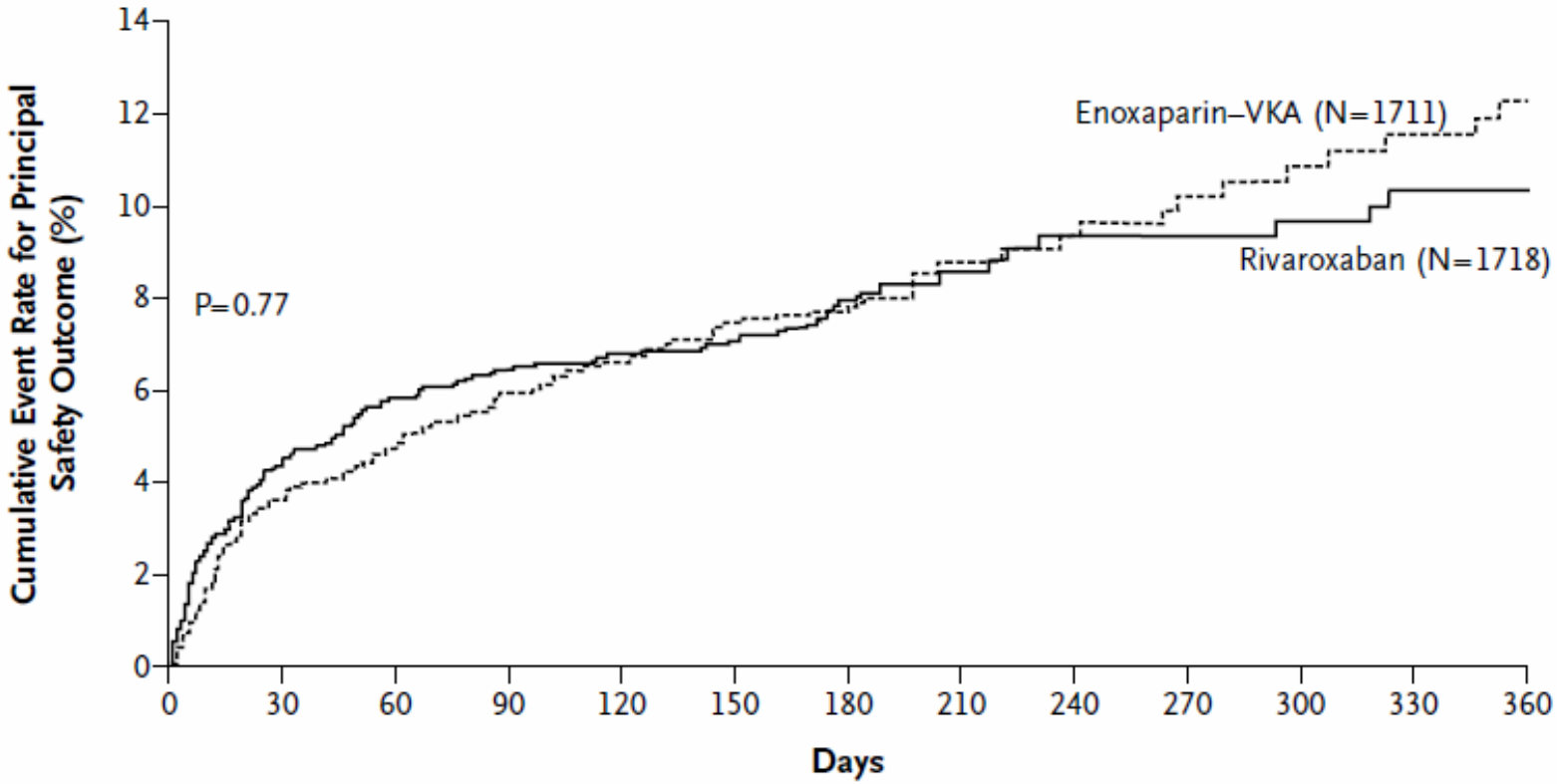
Acute DVT Study



	Rivaroxaban (n/N)	Enox/VKA (n/N)	HR (95% CI)
No. of events	36/1,731	51/1,718	0.68 (0.44 to 1.04)

No. at Risk

Rivaroxaban	1731	1668	1648	1621	1424	1412	1220	400	369	363	345	309	266
Enoxaparin–VKA	1718	1616	1581	1553	1368	1358	1186	380	362	337	325	297	264



No. at Risk

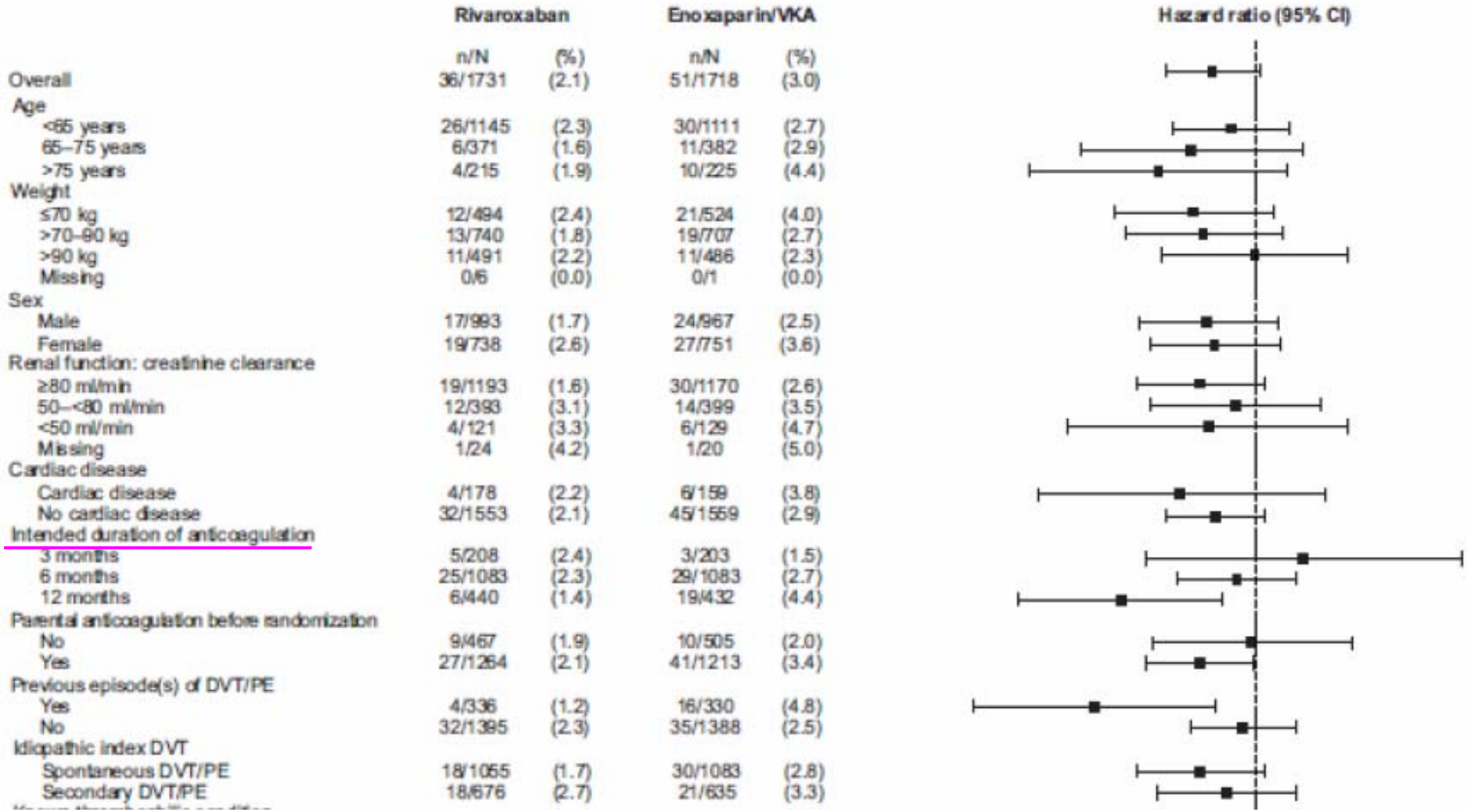
Rivaroxaban	1718	1585	1538	1382	1317	1297	715	355	338	304	278	265	140
Enoxaparin–VKA	1711	1554	1503	1340	1263	1238	619	338	321	287	268	249	118

Figure 3. Kaplan–Meier Cumulative Event Rates for the Principal Safety Outcome in the Acute DVT Study.

VKA denotes vitamin K antagonist.

Figures Supplemental Appendix

Appendix Figure 1. Relative efficacy in the pre-specified subgroups



Prevención de embolia cerebral y sistémica en la fibrilación auricular

What do the RE-LY, AVERROES and ROCKET-AF trials tell us for stroke prevention in atrial fibrillation?

Ingo Ahrens[1]; Gregory Y. H. Lip[2]; Karlheinz Peter[3]

[1]Innere Medizin III, Kardiologie und Angiologie, Universitätsklinik Freiburg, Germany; [2]University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, UK; [3]Atherothrombosis & Vascular Biology, Baker IDI Heart and Diabetes Institute, Melbourne,Victoria, Australia

Table 1: The RE-LY, AVERROES and ROCKET-AF trials compared. The table is based on preliminary data presented for AVERROES and ROCKET-AF (8, 9).

Trial	RE-LY	AVERROES	ROCKET-AF
Drug and doses	Dabigatran etexilate 150 mg BID or 110 mg BID	Apixaban 5 mg BID	Rivaroxaban 20 mg QD (15 mg QD in patients with creatinine clearance 30–49 ml/min)
Number of patients	18,113	5,600	14,000
Design	Randomised, open label	Randomised, double-blind	Randomised double-blind, double dummy
Condition	AF within 6 months prior randomisation + 1 risk factor	AF within 6 months prior randomisation + 1 risk factor	AF within 6 months prior randomisation + 2 risk factors

Thromb Haemost 2011; 105: 574-578

Limitaciones al uso de los nuevos anticoagulantes

- **Coste económico**
- **Adherencia**

TO THE EDITOR: The editorial by Gage that accompanies the report by Connolly et al. highlights the difficulties associated with the use of warfarin therapy in the treatment of patients with atrial fibrillation and considers the use of the new thrombin inhibitor dabigatran.[1] But the author failed to highlight the significant difference in price between warfarin and dabigatran. In Ireland, a month's supply of warfarin in a dose of 5 mg per day costs approximately €2.13 (about $3.55), whereas a month's supply of dabigatran (Pradaxa, Boehringer Ingelheim) in a dose of 110 mg twice daily costs €143.70 (about $239.55). Warfarin has regularly been in the top 15 most frequently prescribed medicines, and more than 32,400 patients in Ireland take it. If just 50% of these patients were to switch to dabigatran, the drug acquisition cost would be roughly €27 million (about $45 million) per year, or about 10% of the total cost of cardiovascular medicines. Clearly, there will be cost offsets, since anticoagulation monitoring will not be necessary and the rate of clinical events will be reduced. Many countries will conduct a formal health technology assessment before providing reimbursement for the drug in the treatment of atrial fibrillation. The editorial suggests that we can rely on RE-LY, but many decision makers will ask, can we afford RE-LY?

Michael Barry, M.B., Ph.D.
Trinity College Dublin

THE EDITORIALIST REPLIES: Thank you for providing the cost of dabigatran in Ireland and for raising the issue of affordability. Dabigatran is not available in the United States, but a 1-month supply of dabigatran can be purchased through Canadian pharmacies for $339 (U.S. dollars) — about 10 times the monthly cost of warfarin therapy (including the cost of monitoring). For a typical participant in the RE-LY trial, the number needed to treat to prevent 1 (nonhemorrhagic) stroke with dabigatran (150 mg twice daily) is 357. Using these estimates, the cost per stroke averted with dabigatran (rather than warfarin) averages approximately $1.3 million (U.S. dollars). For patients with twice the average risk of stroke (e.g., CHADS2 score[1] of 3 to 4), the number needed to treat and the cost per stroke averted would be halved.

However, these calculations do not take into account the costs and morbidity associated with stroke. The cost of care for a stroke patient averages $28,500 in the initial 12 months,[2,3] and the lifetime cost of stroke is several times greater.[3] Thus, although dabigatran is unlikely to be cost-saving, it might be cost-effective, at least in carefully selected patients.

Brian F. Gage, M.D.
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St. Louis, MO

ATENCIÓ PRIMARIA

HOSPITAL TRIAS I PUJOL

Llista de VISITES (de més recent a més antiga)

Data	test / result. / fàrmac. / dosis / partic. / accidents					
11/11/10	INR	1.70	SI	27.50	27.50	
14/10/10	INR	2.50	SI	27.50	27.50	
16/09/10	INR	2.70	SI	27.50	27.50	
26/08/10	INR	2.40	SI	27.50	27.50	
12/08/10	INR	1.80	SI	27.50	27.50	
22/07/10	INR	2.10	SI	27.00	27.00	
09/07/10	INR	2.20	SI	27.00	27.00	
05/07/10	INR	1.60	SI	27.00	27.00	
01/07/10	INR	0.80	SI	27.00	27.00	
03/02/10	INR	2.70	SI	18.00	18.00	
29/01/10	INR	1.90	SI	18.00	18.00	
25/01/10	INR	2.10	SI	18.00	18.00	
21/01/10	INR	1.4 OT	SI	19.00	19.00	