



x congresso nazionale

simeu

NAPOLI 18-20 NOVEMBRE 2016

Pronto Soccorso e NAO

esempi organizzativi e gestionali

Enrico Bernardi

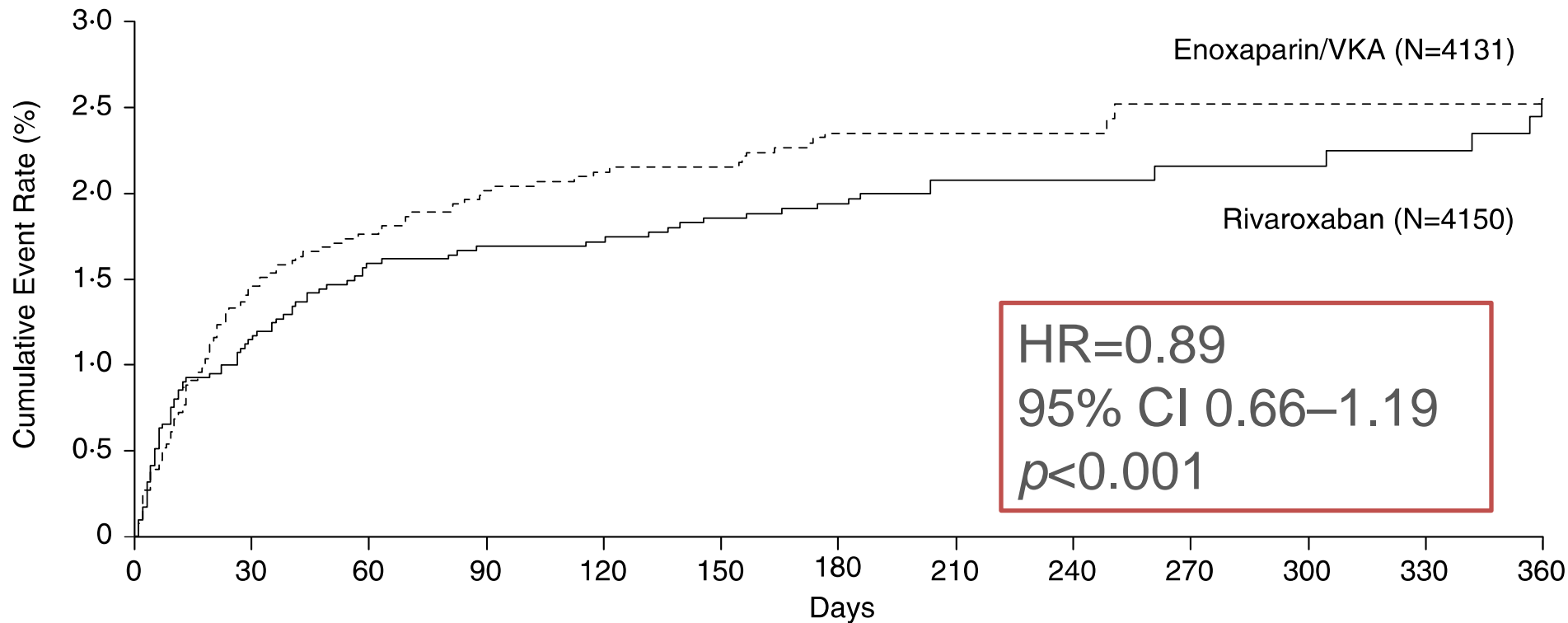


PROVINCIA
DI TREVISO

Setting

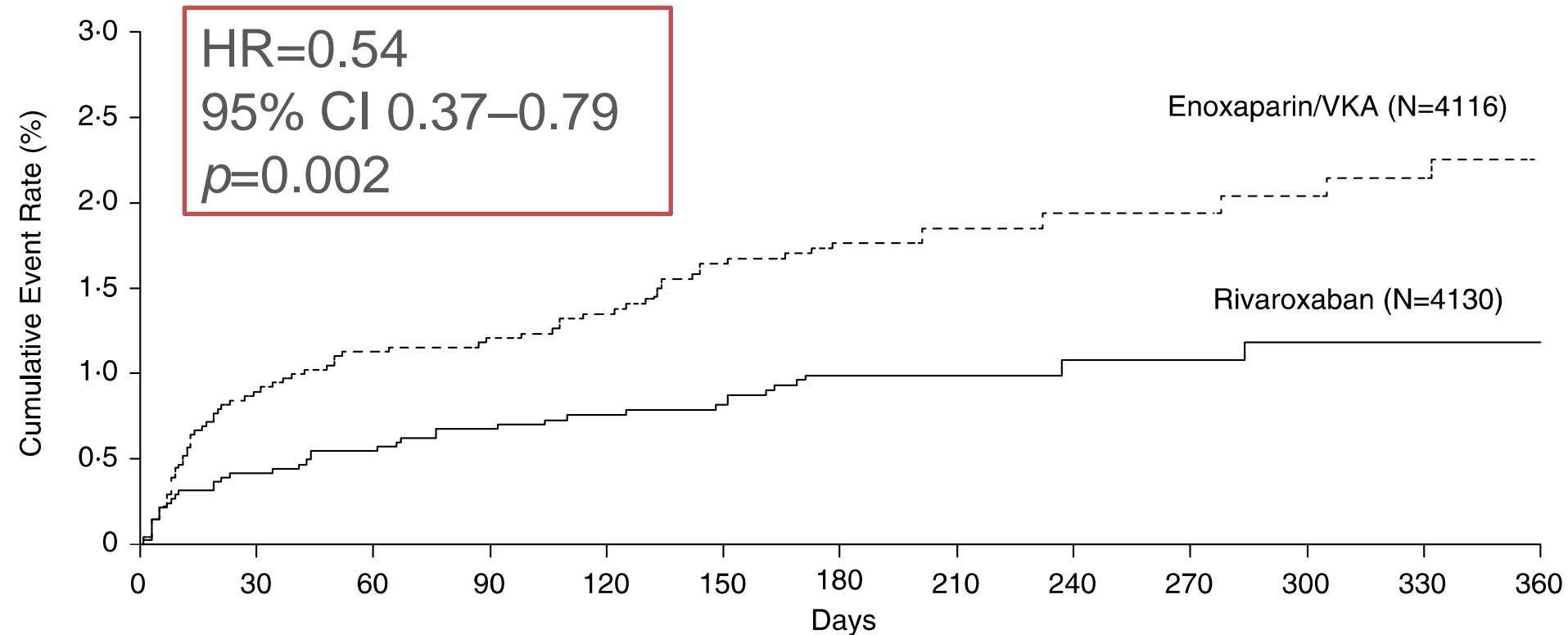
- VTE / FA → accessi in PS (>2% / anno)
- VTE
 - trattamento episodio acuto
 - ricovero / dimissione (letti!!)
 - benefit / risk (recidiva / emorragie)
- FA
 - prevenzione ictus
 - benefit / risk
 - CV(E) sicura

Trattamento TVP/EP efficacy



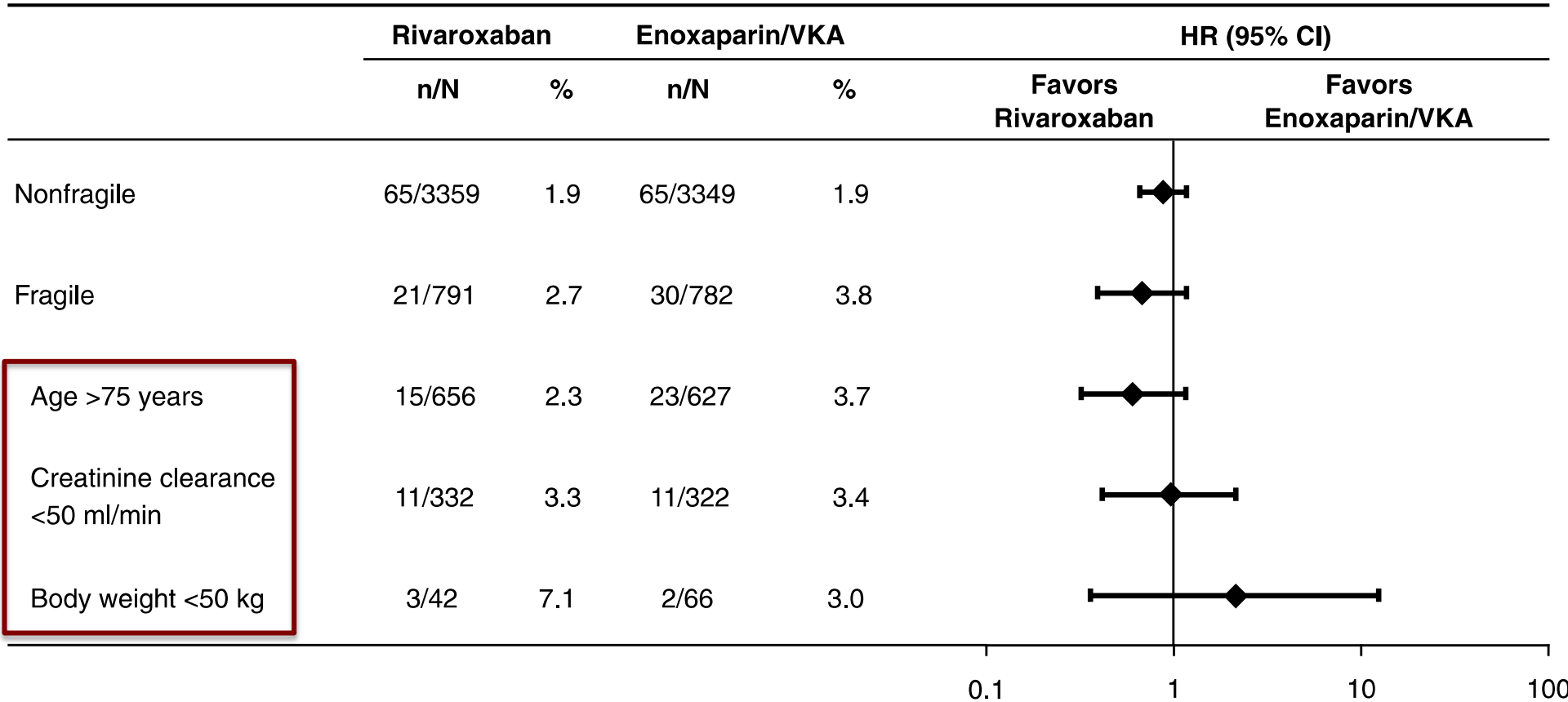
Prins, et al. Thrombosis Journal 2013, 11:21

Trattamento TVP/EP safety



Prins, et al. Thrombosis Journal 2013, 11:21

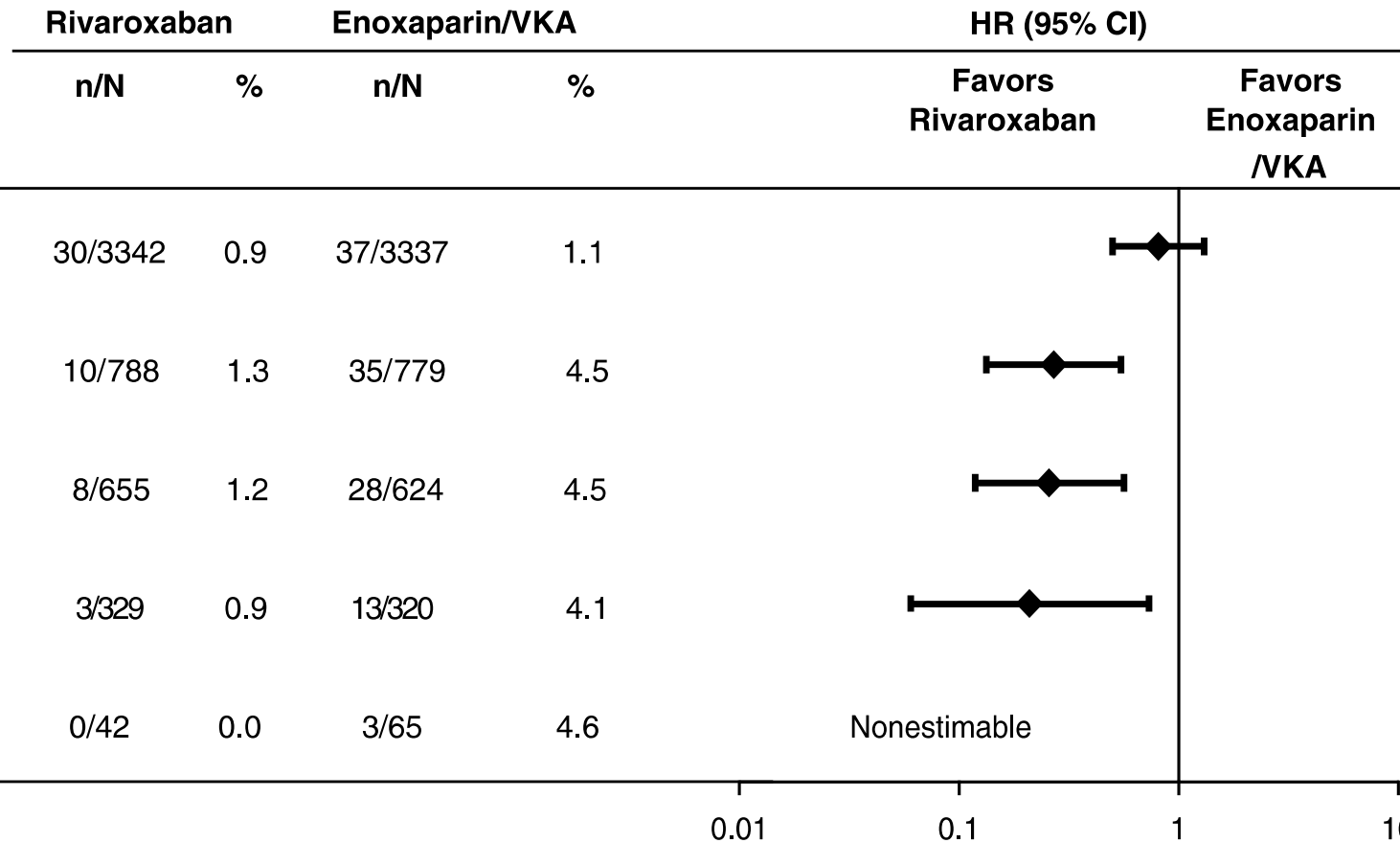
Trattamento TVP/EP efficacy



Prins, et al. Thrombosis Journal 2013, 11:21

Trattamento TVP/EP

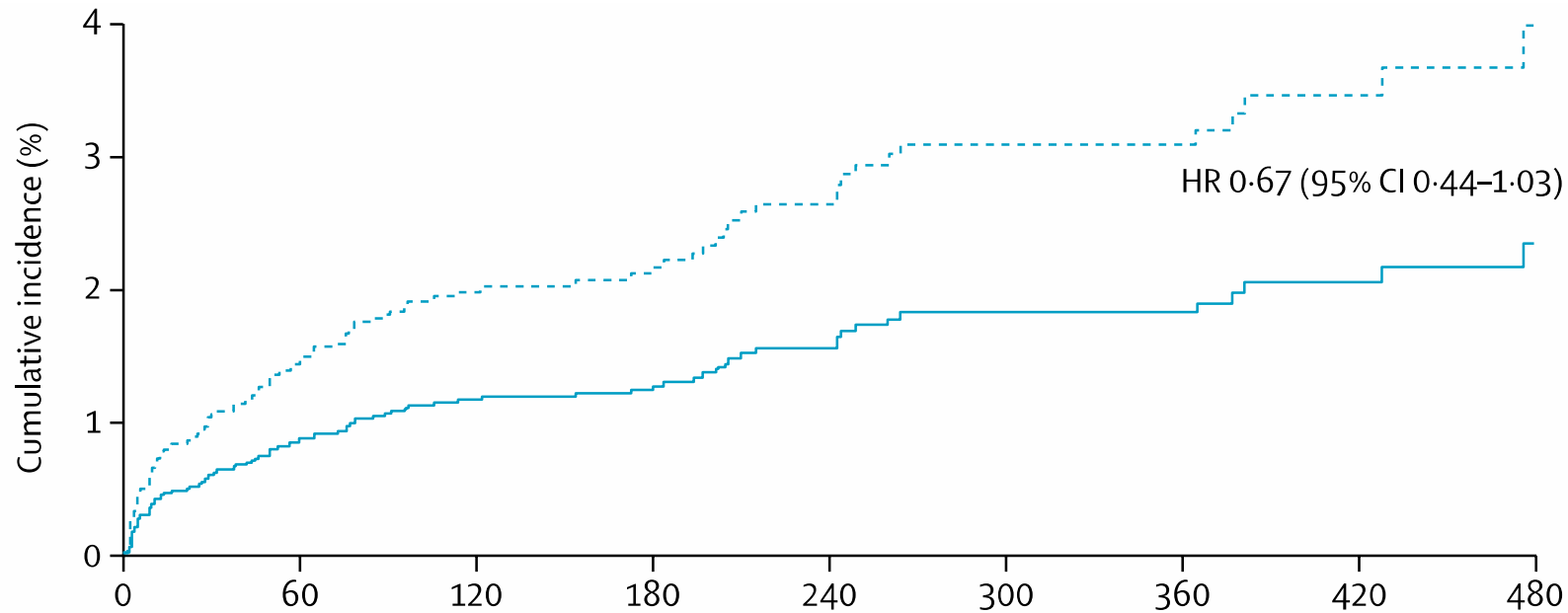
safety



Prins, et al. Thrombosis Journal 2013, 11:21

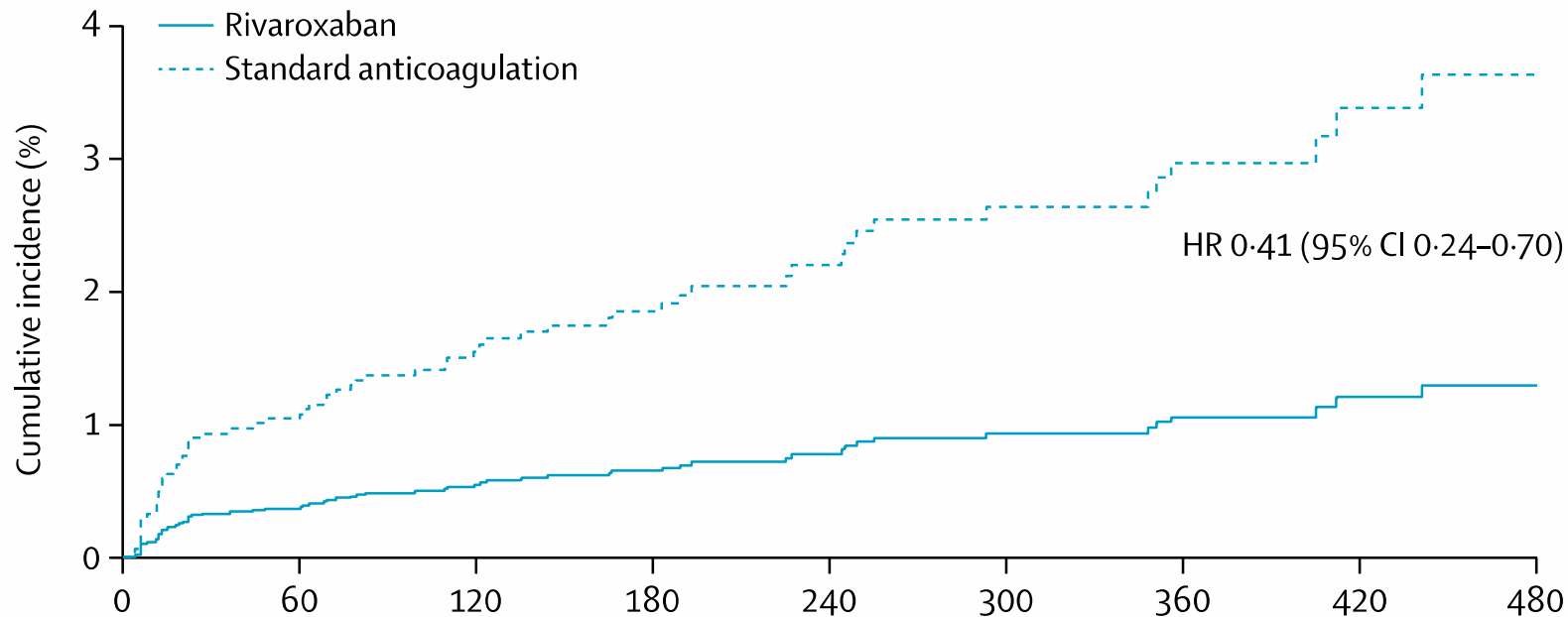
Trattamento TVP/EP efficacy

XOLIA



Rivaroxaban									
Patients at risk	2619	2380	1642	1340	789	658	560	263	174
Patients with events	0	23	31	32	34	34	34	36	37
Standard anticoagulation									
Patients at risk	2149	1858	1444	1212	828	695	603	313	193
Patients with events	0	30	37	40	46	52	52	53	54

Trattamento TVP/EP safety



Rivaroxaban

	0	60	120	180	240	300	360	420	480
Patients at risk	2619	2386	1650	1348	797	664	566	262	173
Patients with events	0	10	14	17	18	18	18	19	19

Standard anticoagulation

	0	60	120	180	240	300	360	420	480
Patients at risk	2149	1870	1458	1226	842	710	612	317	197
Patients with events	0	22	30	33	37	42	45	46	47

Linee guida

Recommendations

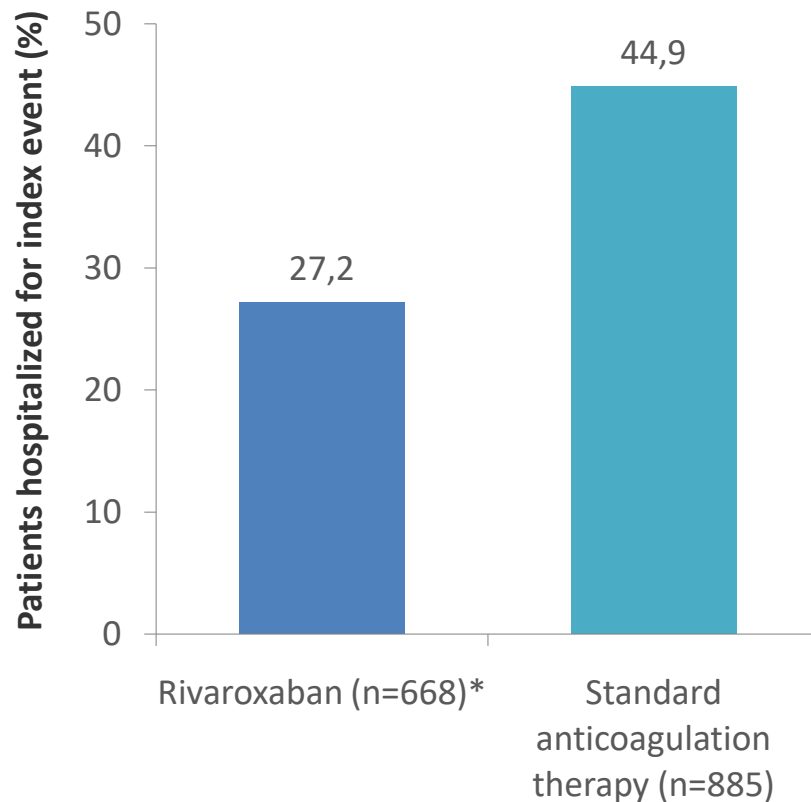
In patients with DVT of the leg or PE and **NO CANCER**, as long-term (first 3 months) anticoagulant therapy, we suggest **DABIGATRAN, RIVAROXABAN, APIXABAN OR EDOXABAN** over **VKA** therapy (all Grade 2B)*.

Kearon C, et al. Chest 2016; 149(2):315-352

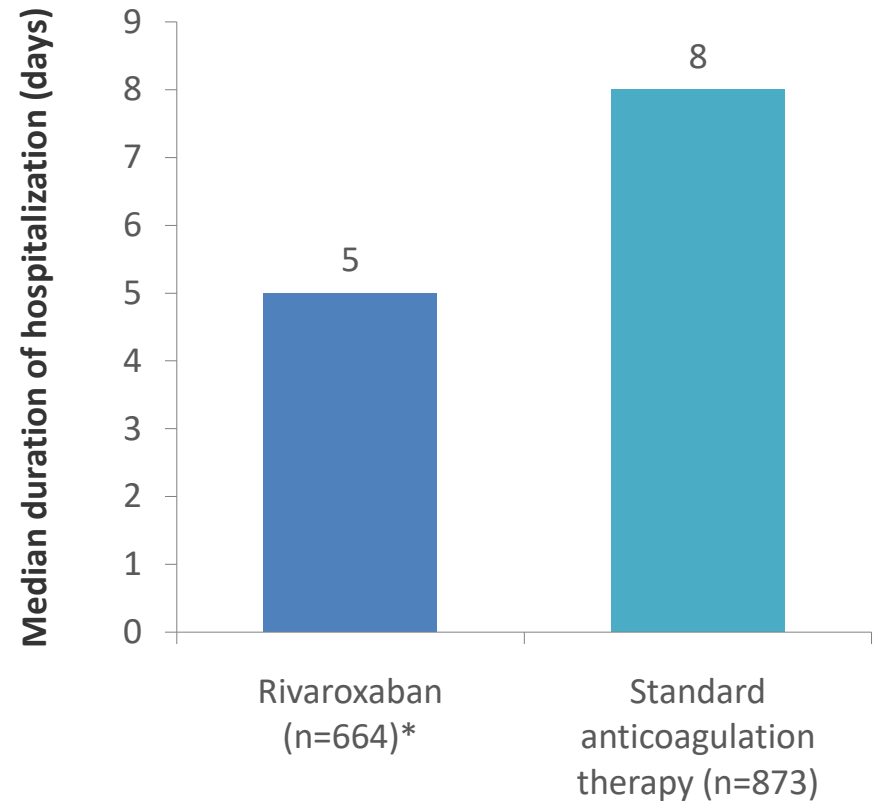
Reduced hospitalization



Proportion of patients hospitalized



Median duration of hospitalization



Turpie A et al. ISTH 2015 (Poster PO607-TUE)

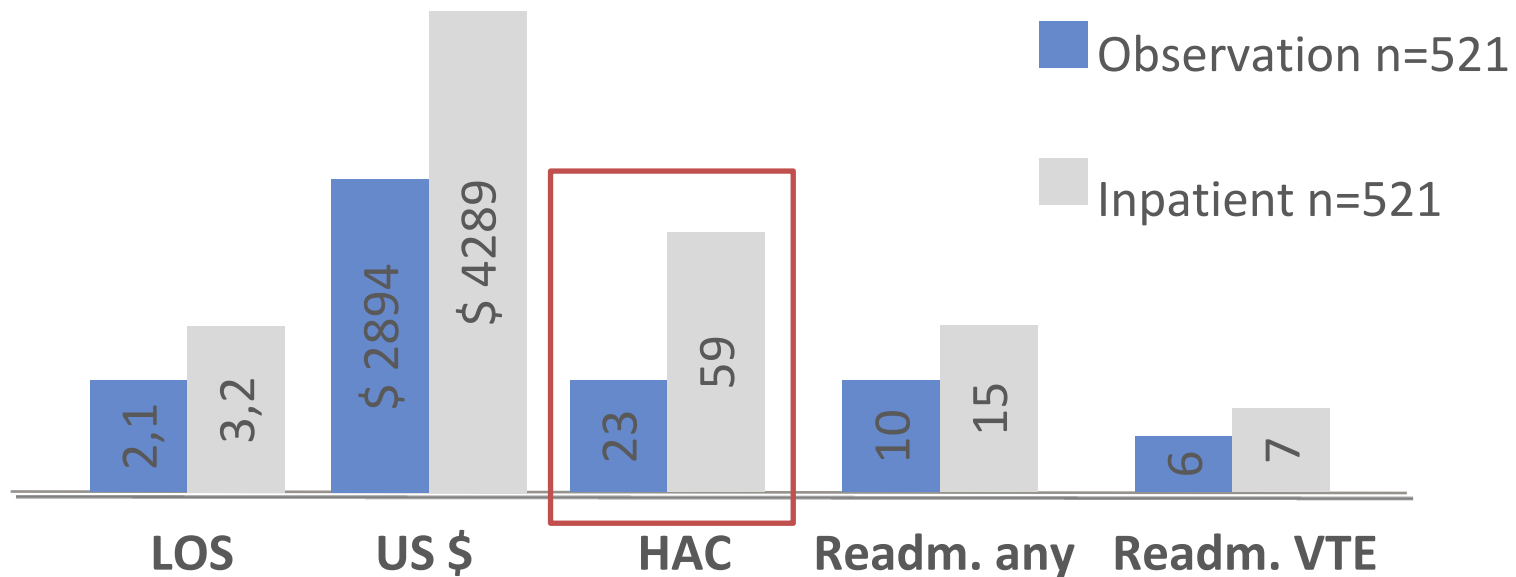


Immediate Discharge and Home Treatment With Rivaroxaban of Low-risk Venous Thromboembolism Diagnosed in Two U.S. Emergency Departments: A One-year Preplanned Analysis

- n = 101 (30% low-risk PE [Hestia])
- 51% of all DVT and 27% of all PE
- Mean follow-up: 389 (213 to 594)
- While on treatment
 - No VTE recurrence
 - No major or clinically relevant bleeding

Outcomes associated with observation status versus inpatient management of pulmonary embolism patients anticoagulated with rivaroxaban

- Retrospective (Premier Hospital DB)
- Observation (< 2 gg) vs admission
- No readmission due to MB



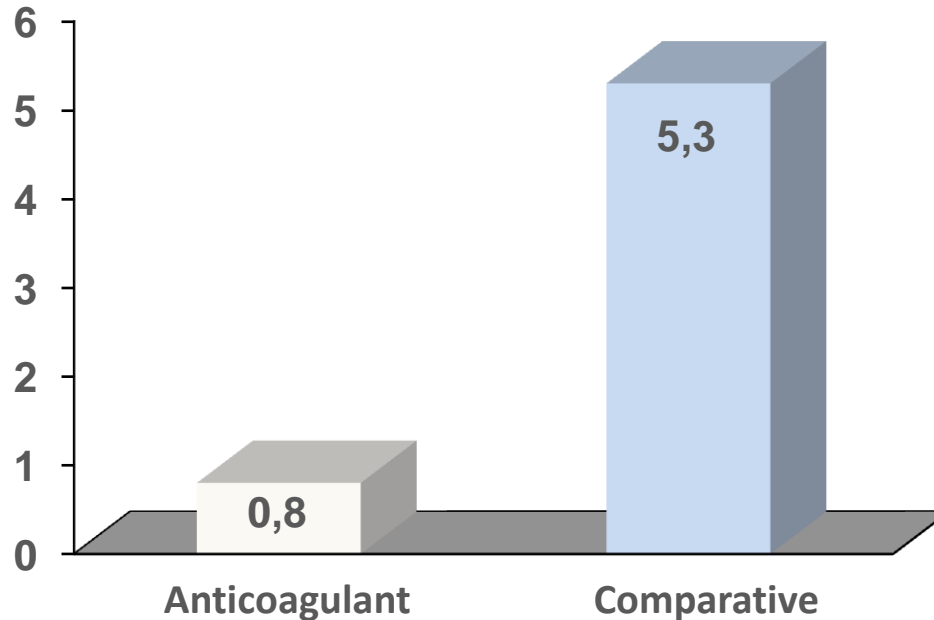
Weeda ER, et al. Acad Emerg Med 2015;22(7):788-95

Home Treatment of Patients with Low-Risk PE with the Oral Factor Xa Inhibitor Rivaroxaban: Prospective Management Trial (HoT-PE)

- n= 1100 low-risk PE
 - absence (echo or CT) of RV enlargement or dysfunction, and of free floating thrombi
- Rivaroxaban standard (15 x 2 + 20)
- Follow-up 3 months
- End-point: symptomatic recurrent (VTE) or death related to PE @ 3 months

Fibrillazione atriale

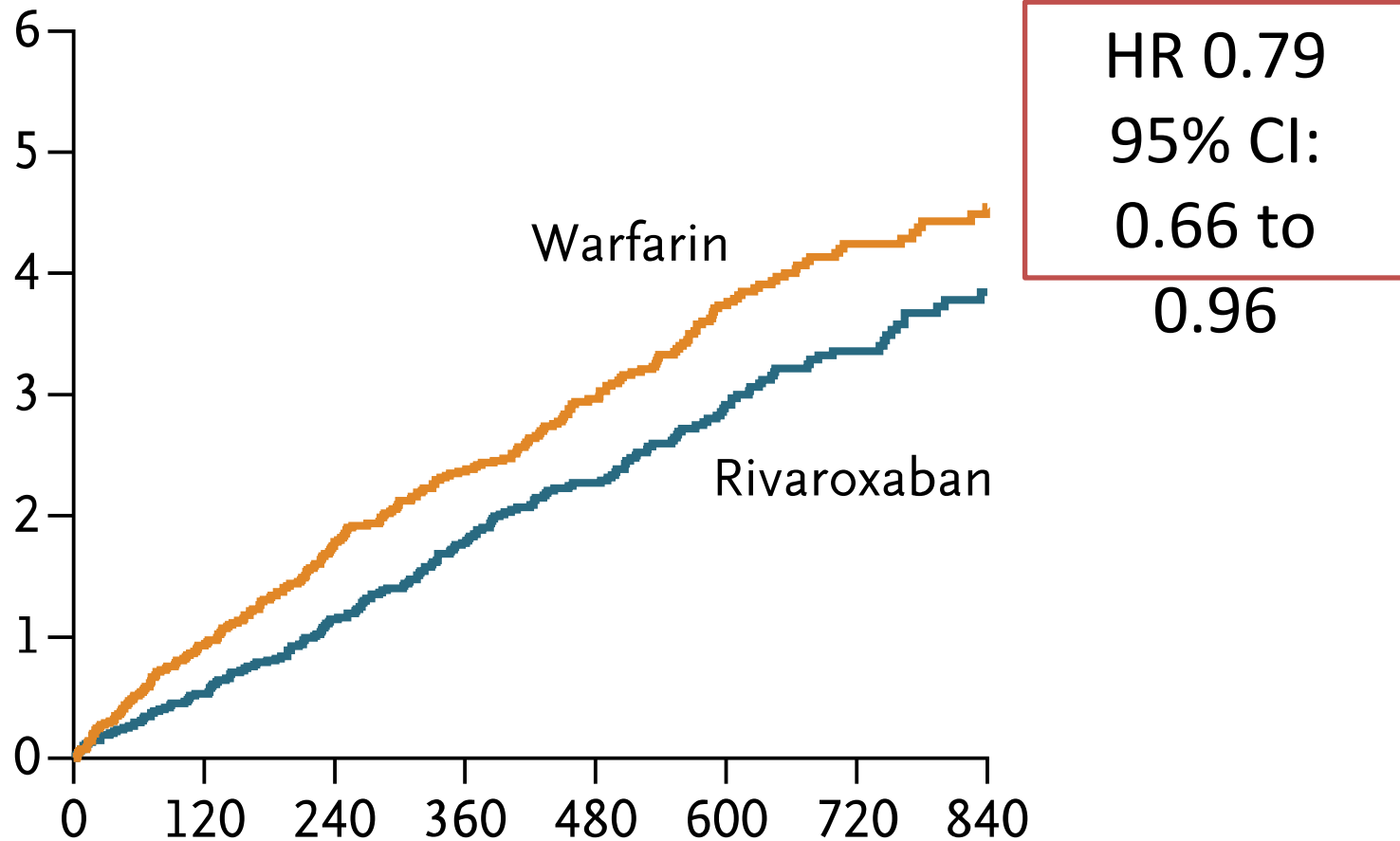
The efficacy of anticoagulant prophylaxis in connection with electrical cardioversion of AF



Is anticoagulation indicated before and after electrical cardioversion of AF?

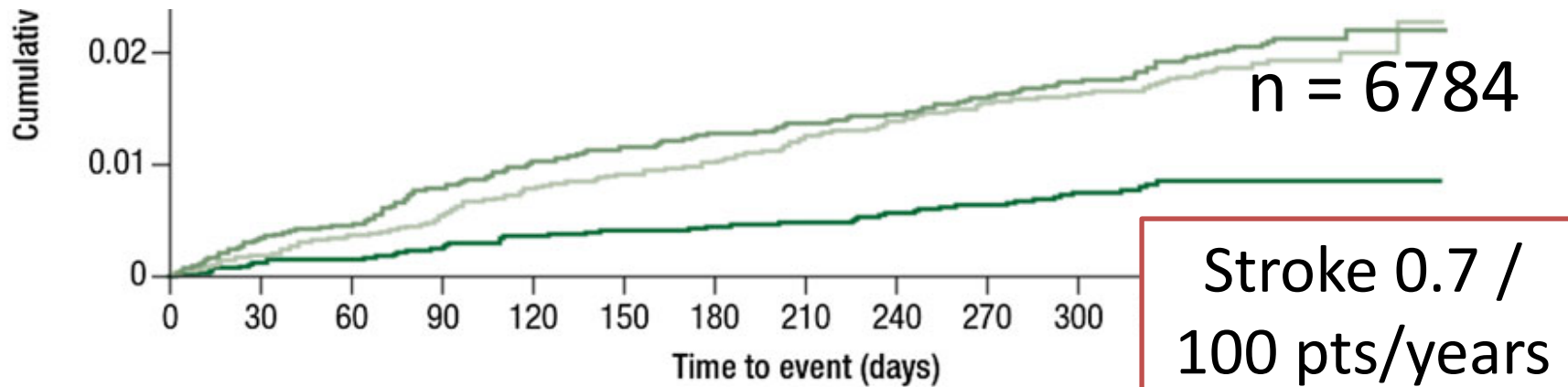
Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation

- $n = 14,264$



Patel RM, et al. N Engl J Med 2011;365:883-91

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



s at risk:

se death	6784	6530	6349	6211	6054	5938	5853	5754	5679	5597	5512	5295	4307	1153	514
bleeding	6784	6522	6340	6197	6033	5909	5824	5726	5649	5559	5471	5256	4273	1144	513
'systemic sm	6784	6532	6353	6216	6053	5933	5848	5752	5674	5587	5499	5282	4296	1149	513

Camm AJ, et al. European Heart Journal
doi:10.1093/eurheartj/ehv466

Ribaroxaban e MB

ROCKET AF 

Patel MR et al,
NEJM 2011

Dresden
NOAC Register

Beyer-Westendorf
BLOOD, 7 AUGUST 2014



Tamayo S.
Clin Cardiology 2015

XANTUS

Camm AJ et al,
Eur Heart J 2015

n	7.111	1.775	27.467	6.784
CHADS2	3.5	2.4	3.0/2.2	2.1
MB	3.6	3.1	2.86	2.1
Fatal B	0.2	0.3	0.08	0.2

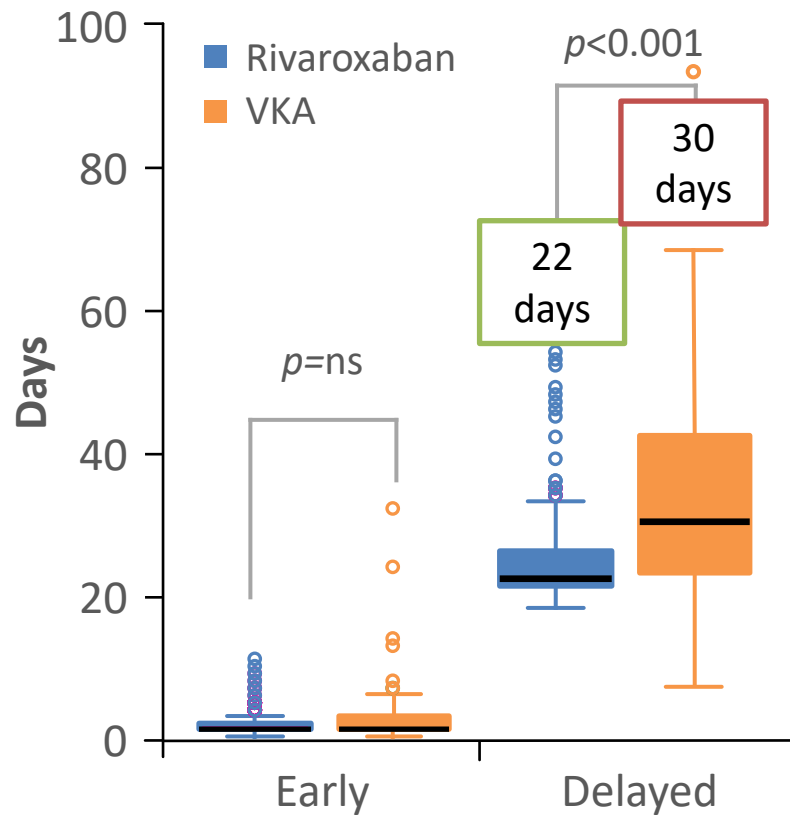
Quality and Outcomes

Characterizing Major Bleeding in Patients
With Nonvalvular Atrial Fibrillation: A
Pharmacovigilance Study of 27 467 Patients
Taking Rivaroxaban

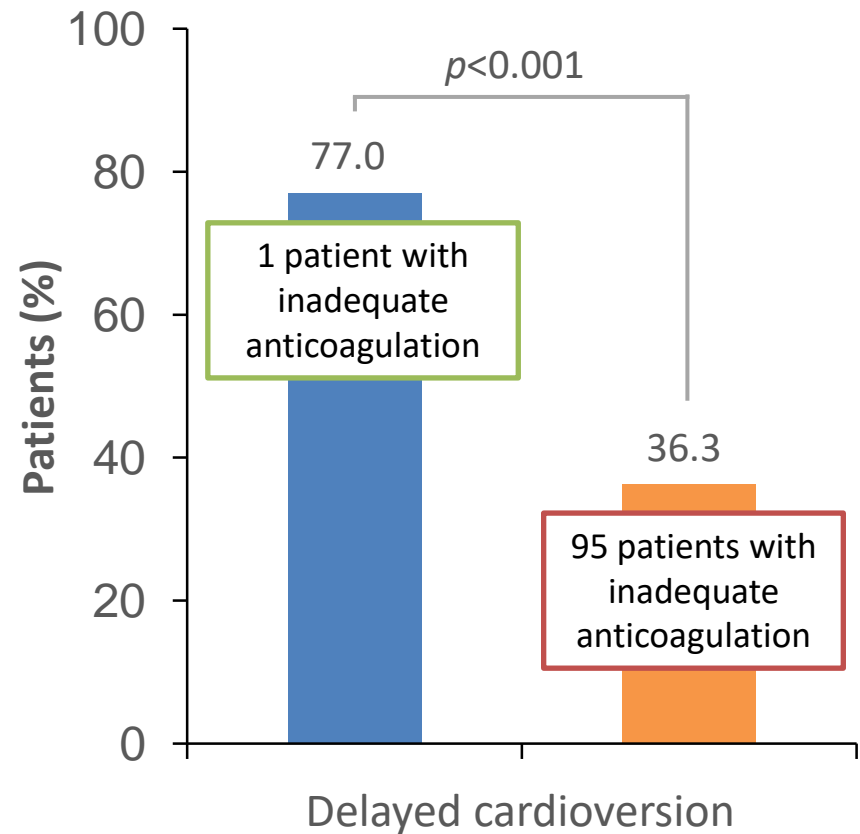
- USA Dep. of Defense electronic health care DB
- $n = 27.467$
- MB = 2.86/100 pts-yrs, 95% CI: 2.61-3.13
- 88.5% gastrointestinal
- FB = 0.08 /100 pts-yrs, 95% CI: 0.05-0.14

Time to Cardioversion by strategy

Median time to cardioversion



Patients cardioverted as scheduled*



Cappato R et al, Eur Heart J 2014;35:3346–3355

Gestione sanguinamenti

1. Assess exact time and amount of last rivaroxaban intake

If recent ingestion (< 2 h) consider charcoal (30–50 g for adults), as well as gastric lavage.

Consider that:

- maximal effect is expected 2–4 h after ingestion
- for doses ≥ 50 mg, a ceiling effect, with no further increase in average plasma levels, is expected
- normalization of hemostasis is expected at 16–24 h after ingestion (unless severe renal insufficiency: $\text{CrCl} < 15$ ml/min)

2. Order blood tests

- Venous blood gas analysis: if low hemoglobin, order CBC, group and cross-match
- Renal and liver function
- PT or, if available, anti-FXa chromogenic assay. PT values exceeding the upper normal limit at trough (9–12 h from

last intake) may indicate high bleeding risk. If possible use Neoplastin Plus, TriniCLOT PT, Excel S or Neoplastin R

- Before urgent surgery: request CBC instead of venous blood gas analysis

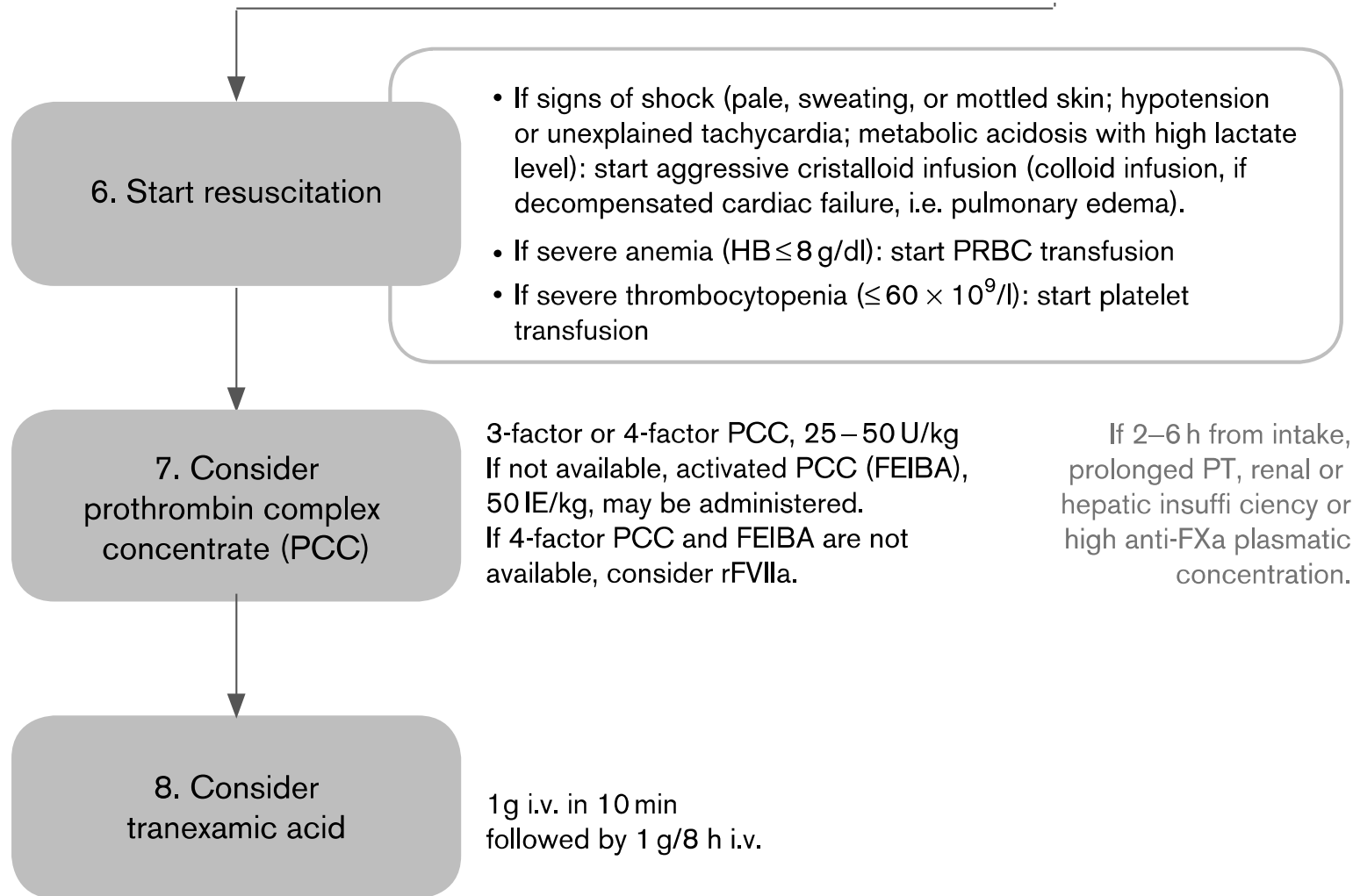
3. If applicable, start mechanical compression or local/surgical hemostatic measures

4. Consider tranexamic acid (0.5–1 g orally, 3-times daily, for several days)

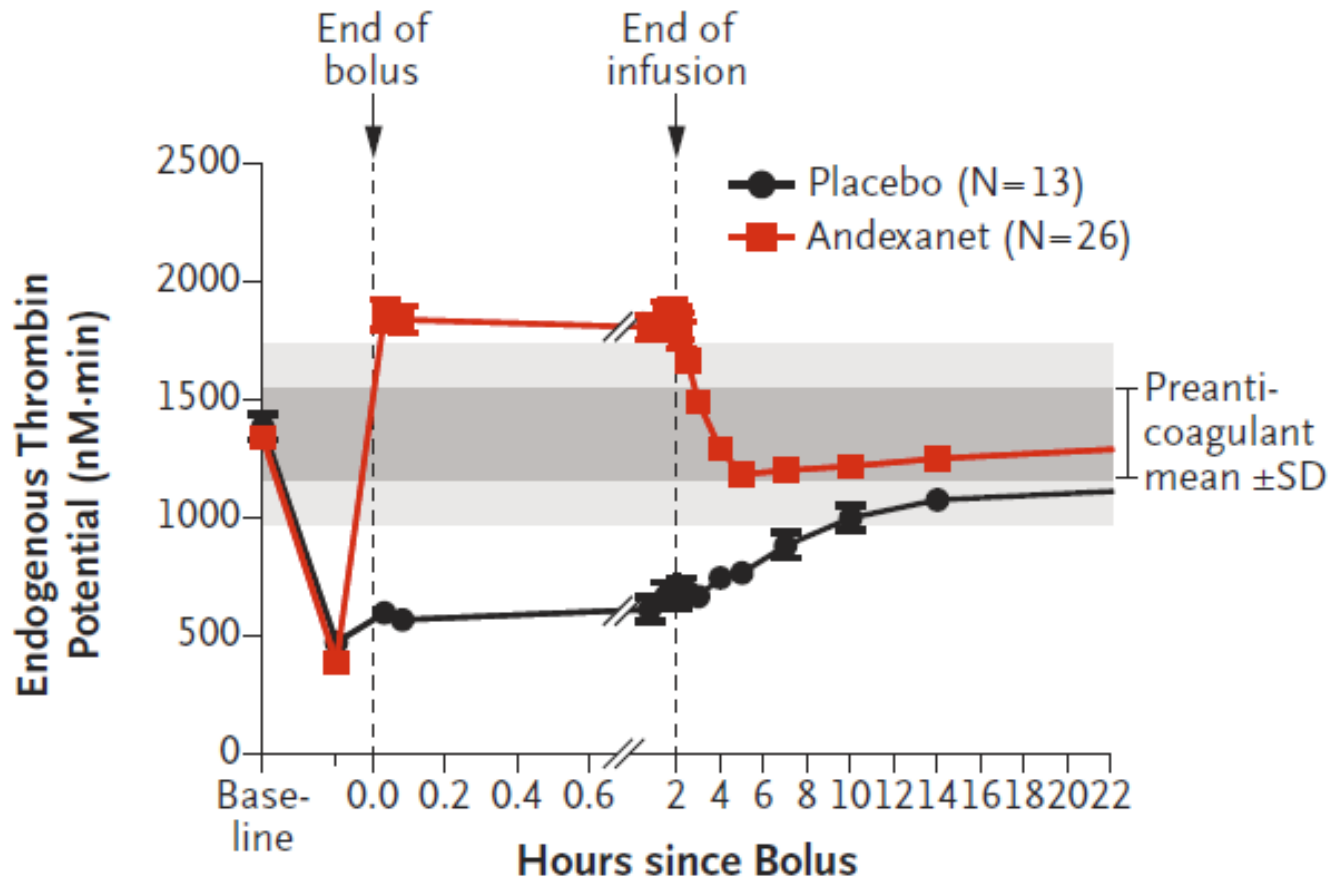
Delay for 12 h if rivaroxaban dosage is once daily
Skip the next dose if dosage is twice daily.

5. Delay or skip next dose of rivaroxaban

.....

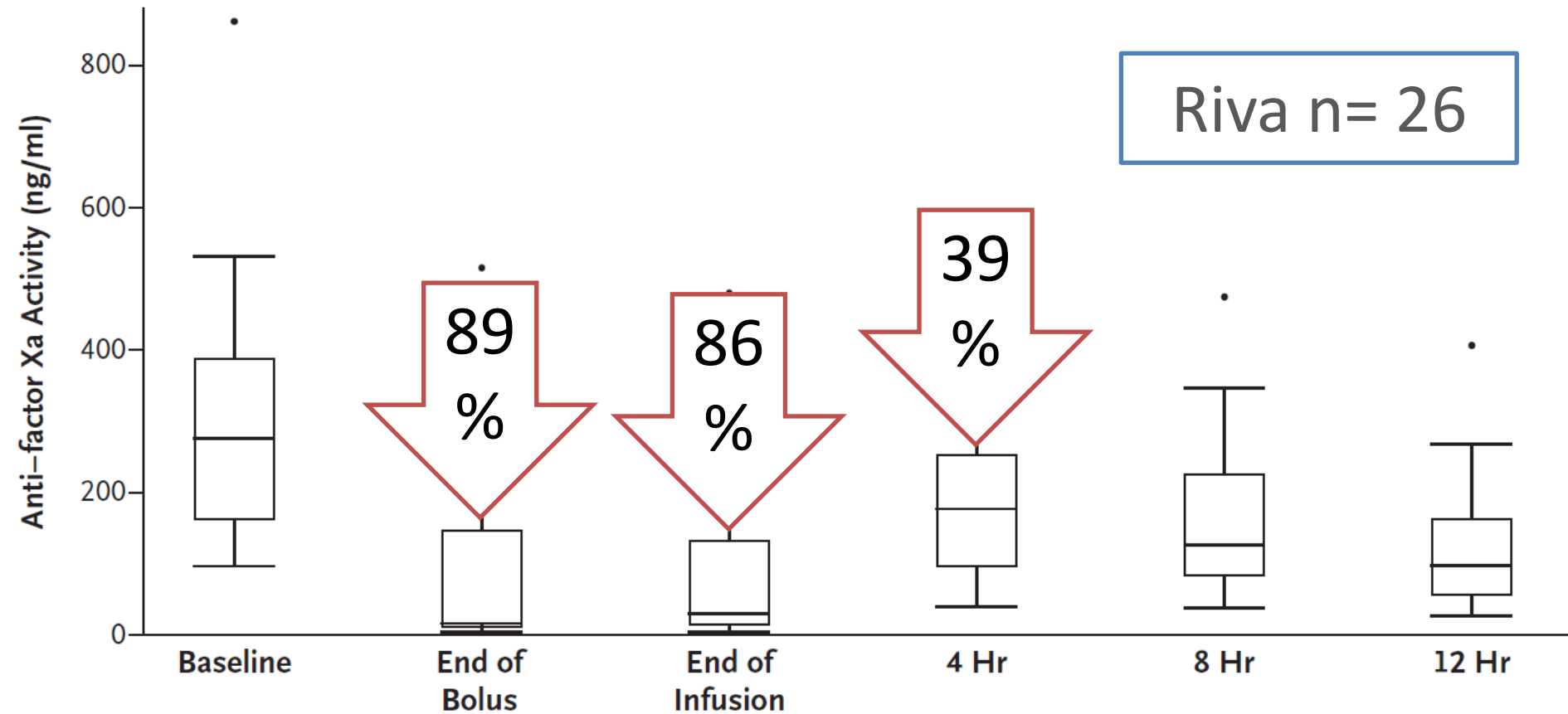


Andexanet alfa for the reversal of factor Xa inhibitor activity



Siegal DM et al. NEJM 2015;373:2413-24

Andexanet Alfa for Acute Major Bleeding Associated with Factor Xa Inhibitors



Connolly SJ et al. NEJM 2016;375:1131-41

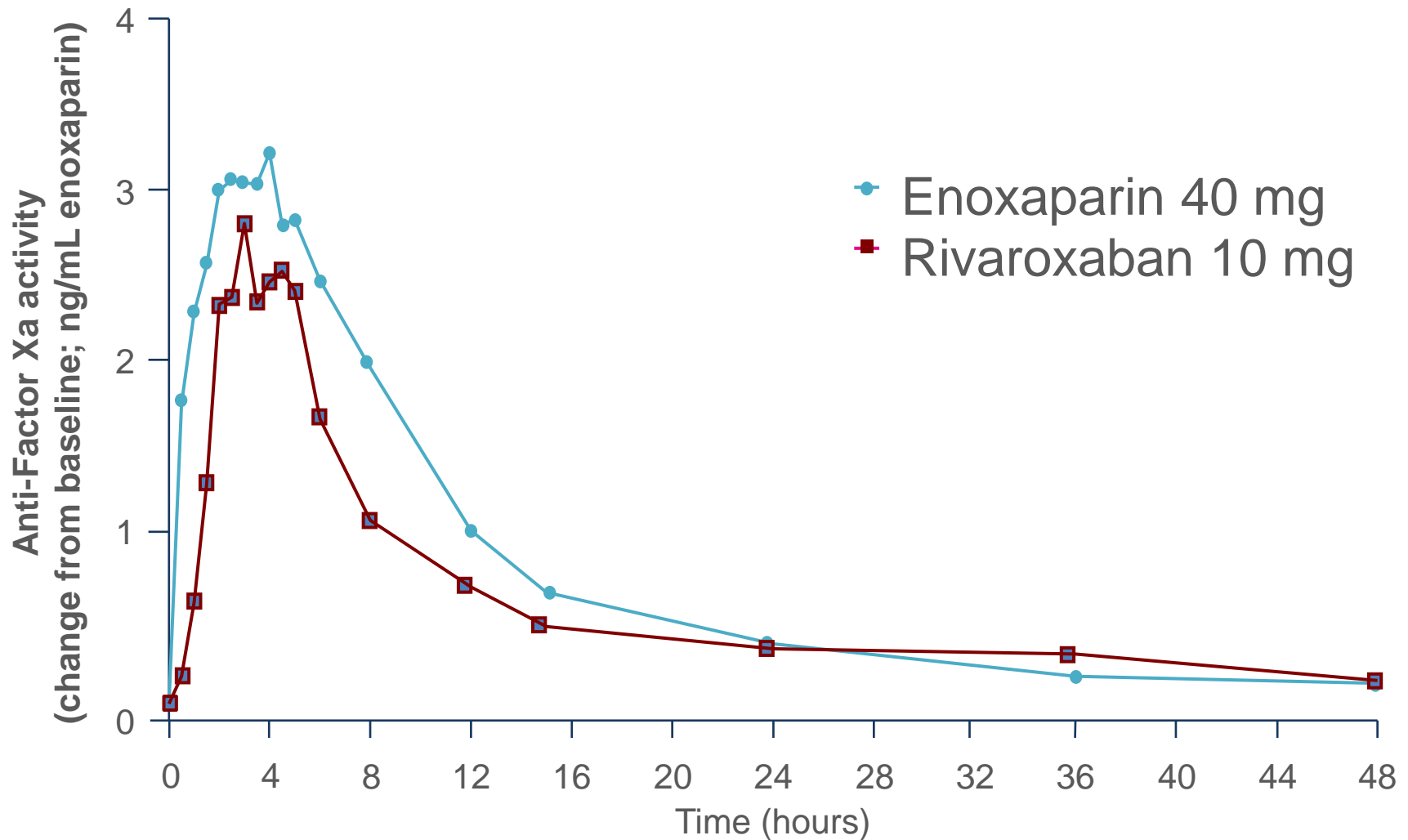
Do we need an antidote?

	Patients	MB	PCC
ROCKET AF	7.131	395	5
DRESDEN	1.775	66	6
XANTUS	6.784	128	2

- Of 15.690 treated, *only* 589 had MB
- Only **13** needed coagulation factors

Patel MR et al. N Engl J Med. 2011;365(10):883–891
Beyer-Westendorf J et al. Blood. 2014;124(6):955–962
Camm AJ et al. Eur Heart J 2016;37:1145-53

Time!



Kubitza D et al. Clinical Pharm in Drug Dev. 2013;2(3):270–277

Stroke Rivaroxaban e trombolisi

Intravenous thrombolysis in a patient using factor Xa inhibitor

Daniel Korya, MD^{*}, Haitham Dababneh, MD[†], Mohammad Moussavi, MD^{*}, Spozhmy Panezai, MD,
Emad Noor, MD, and Jawad F Kirmani, MD

Stroke Note

Neurol Sci
DOI 10.1007/s10072-015-2336-5

LETTER TO THE EDITOR

**Intravenous Thrombolysis in a Stroke
Patient Receiving Rivaroxaban**

Felix Fluri Florian Heinen Christoph Kleinschnitz

**Intravenous thrombolysis for acute stroke in a patient
on treatment with rivaroxaban**

Lucia Nardetto¹ · Simone Tonello² · Luigi Zuliani² · Bruno Giometto¹

**Intravenous thrombolysis with recombinant tis-
sue plasminogen activator for acute ischemic
stroke in a patient treated with rivaroxaban**

Case Report

**Intravenous Thrombolysis with Recombinant Tissue
Plasminogen Activator in a Stroke Patient Treated
with Rivaroxaban**

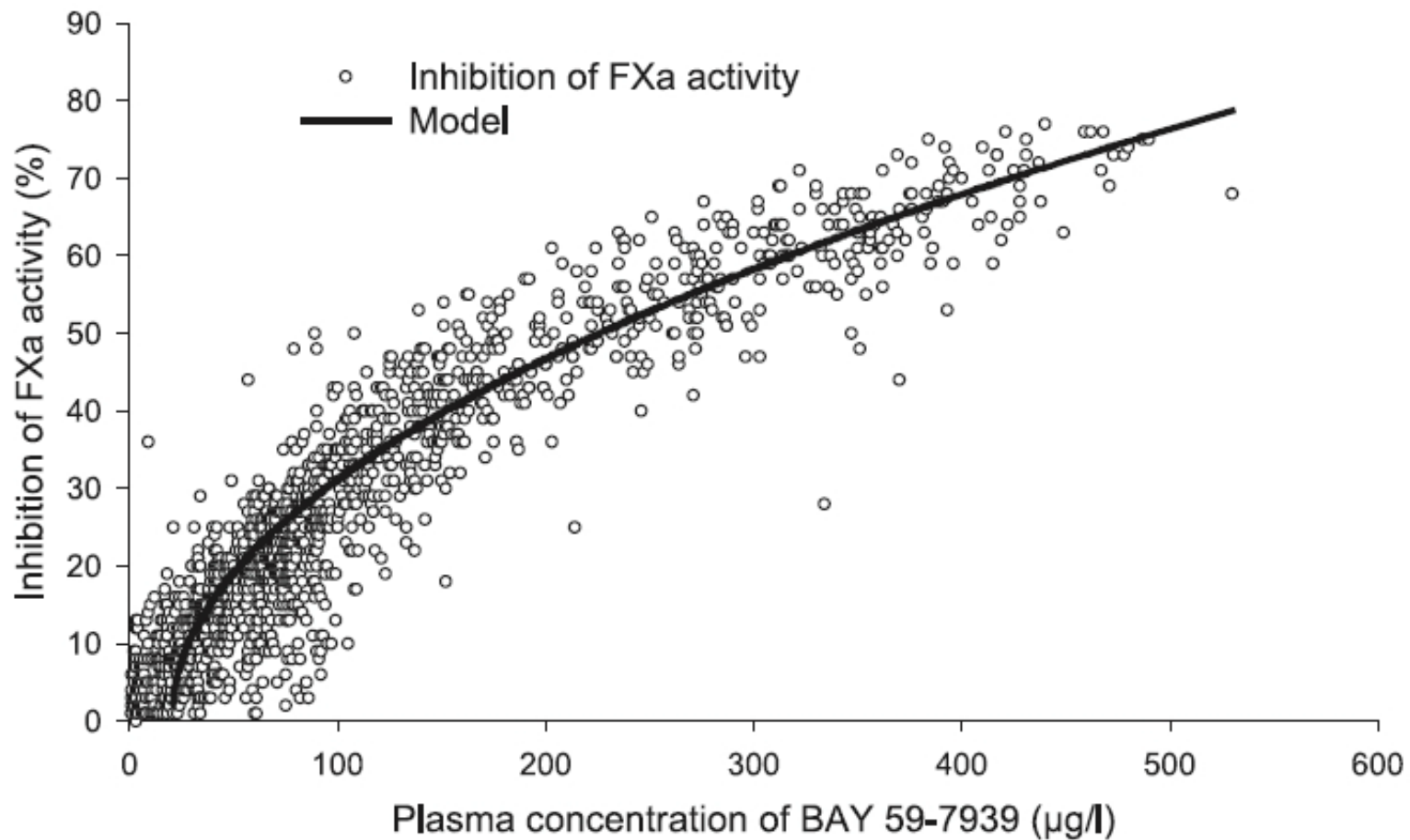
Hideyuki Ishihara, MD, PhD, Hiroaki Torii, MD, PhD, Hirochika Imoto, MD, PhD,
Fumiaki Oka, MD, PhD, Hirokazu Sadahiro, MD, PhD, and Michiyasu Suzuki, MD, PhD

?

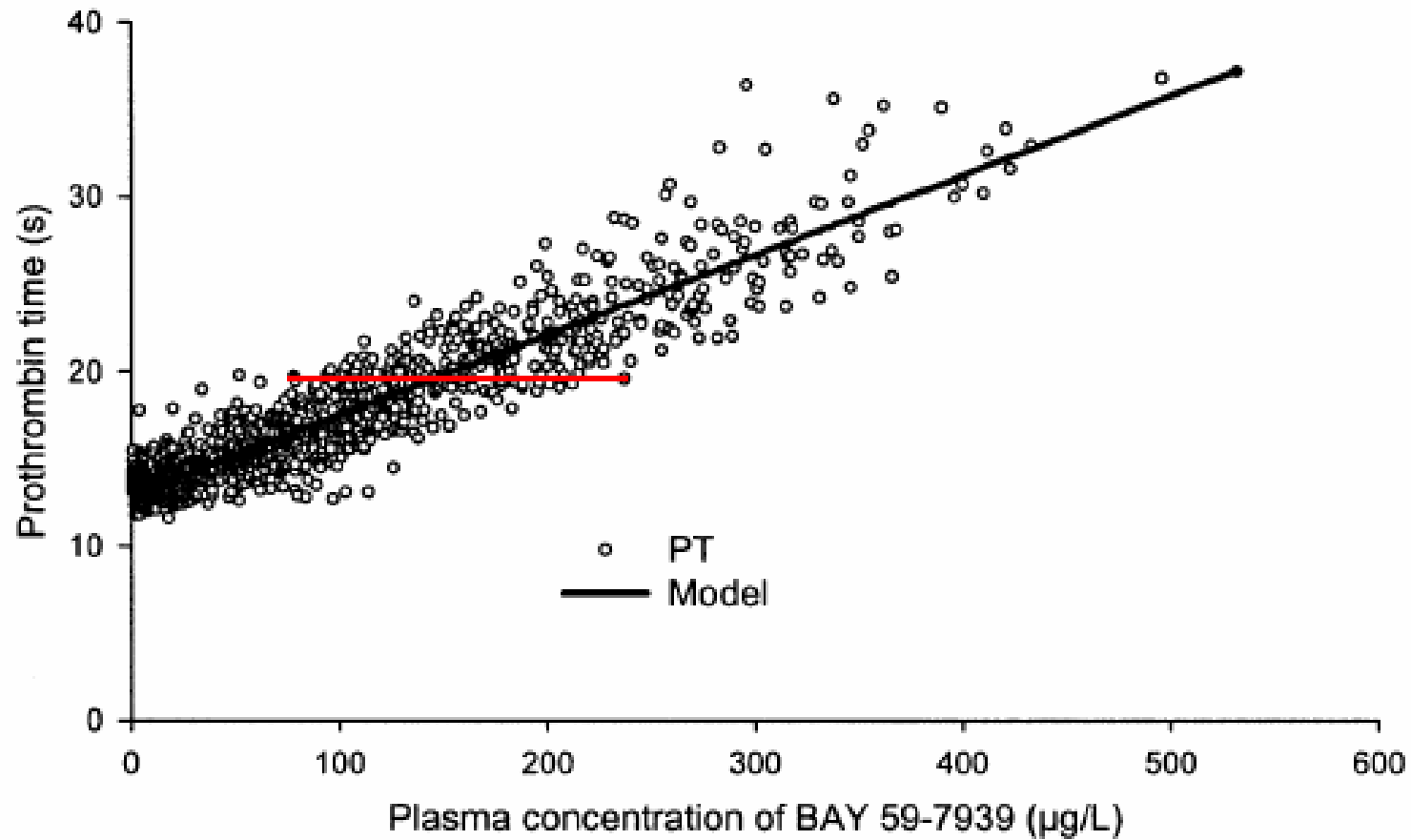
Test della coagulazione

- Anti-Xa (10 studi) → **QUANTITATIVO**
 - con calibratori specifici → correlazione **lineare** ($r^2 = 0.95$ to 1.00) meno robusta se [<100 ng/mL]
- PT (11 studi) → **QUALITATIVO**
 - prolungato, ma ampia variabilità tra reagenti
 - possibile standardizzazione con INR specifico
- aPTT → **NON UTILIZZABILE**
 - correlazione non lineare, ampia variabilità tra reagenti

Rivaroxaban e FXa



Rivaroxaban e PT



Anti-Xa / PT (INR)

Anti-Xa negativo → esclude
[Rivaroxaban] clinicamente rilevanti

PT prolungato → indica presenza di
Rivaroxaban (*qualitativamente*)

Cucker A, J Am Coll Cardiol 2014;64:1128–39

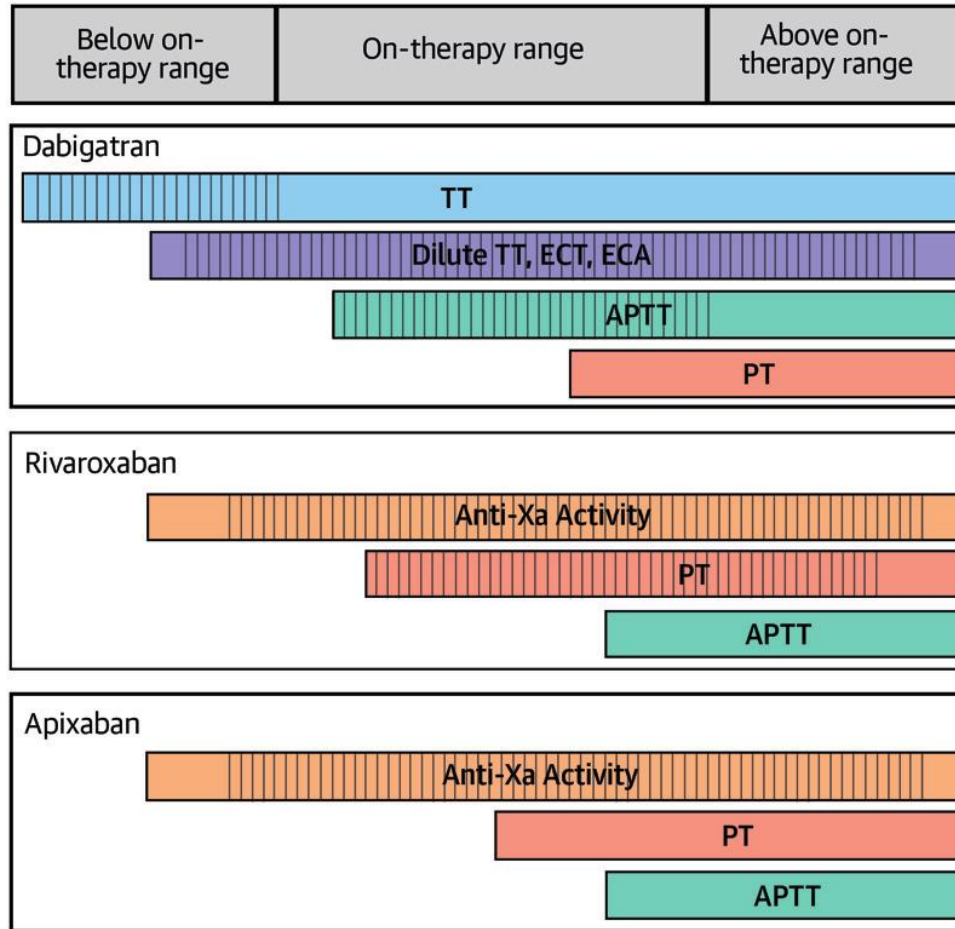
Anti-Xa / PT (INR)

PT → “SCREENING”

Anti-Xa → RIFERIMENTO

Cucker A, J Am Coll Cardiol 2014;64:1128–39

Test della coagulazione



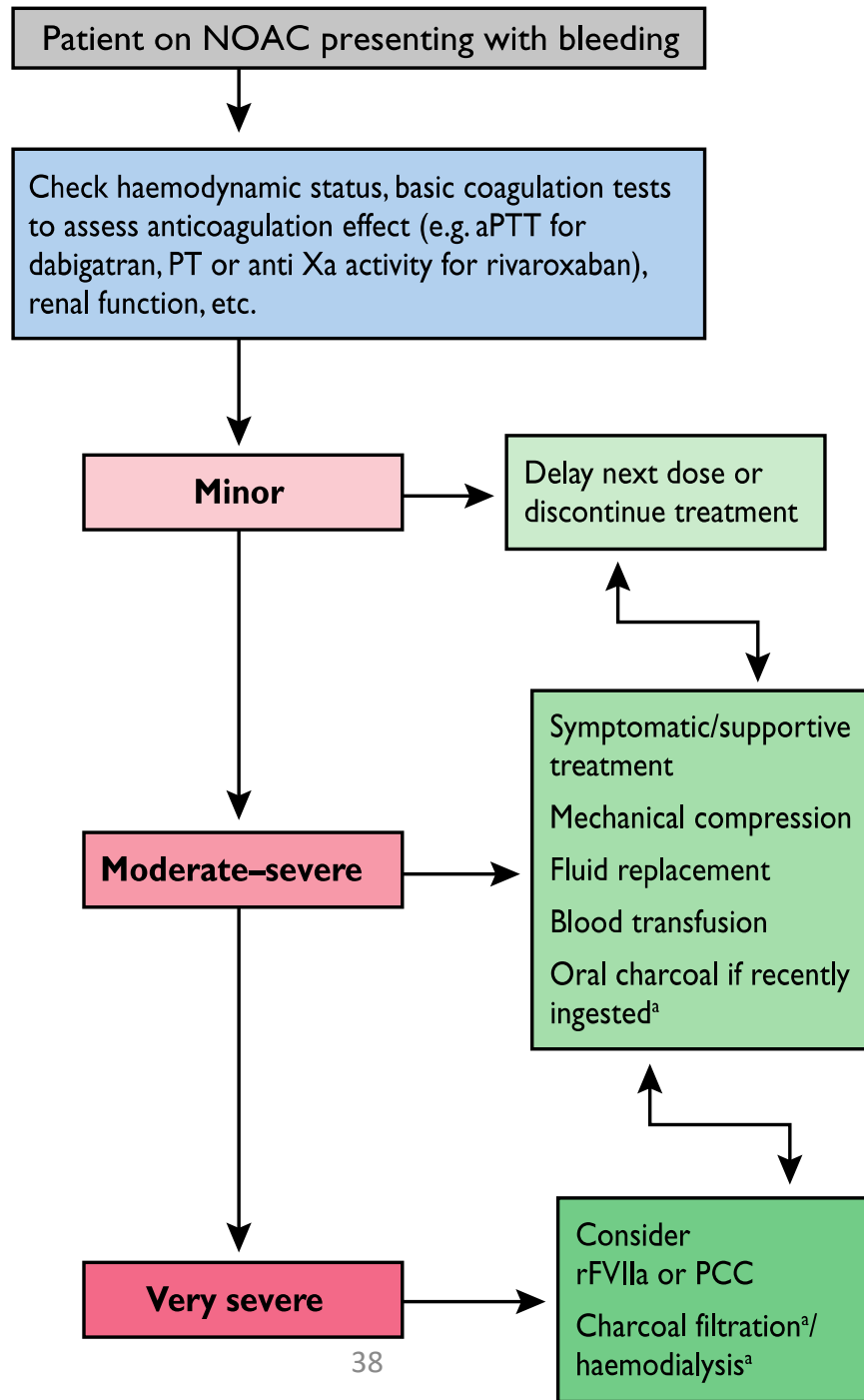
Cucker A, J Am Coll Cardiol 2014;64:1128–39

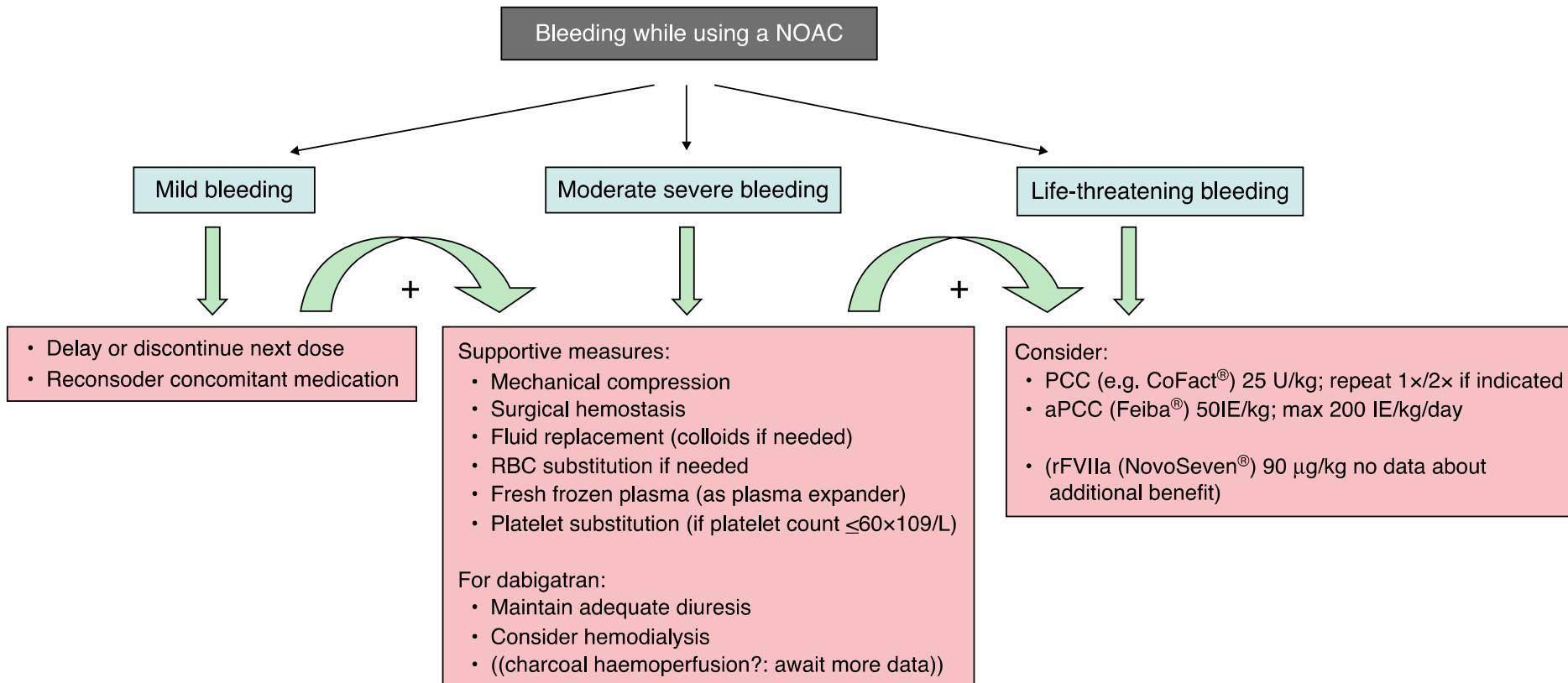
Test anti-Fxa / PT

Anti-Xa	Distributore	Test	CE
Diagnostica Stago	Stago Italia (MI)	STA [®] Rotachrom [®]	SI
Hyphen Biomed	Cabru (MI)	Biophen DiXal [®]	SI
Technoclone	Alifax (PD)	Technochrom [®] anti-Xa	Si

Autore	Test
Dale, et al JTH 2014	TriniCLOT PT Excel S
Douxflis, et al. Thromb Res 2012	Triniclot PT Excel S
Van Bierk,et al. Thromb Haemost 2014	Neoplastin R

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





Europace (2013) 15, 625–651
doi:10.1093/europace/eut083

EHRA PRACTICAL GUIDE

European Heart Rhythm Association Practical Guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation

Emorragie minori

- Solo trattamento di supporto:
 - compressione diretta (se possibile)
 - anti-Xa (PT), funzione renale
 - ritardare la successiva dose (\uparrow PT)
 - sospendere (se emorragia non controllata)

European Heart Rhythm Association Practical
Guide on the use of new oral anticoagulants in
patients with non-valvular atrial fibrillation

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



Emorragie severe

- Come “minore” + sintomatico:
 - compressione, intervento chirurgico
 - supporto (cristalloidi, PRBC / emoderivati)
 - acido tranexamico EV
 - considera CCP

European Heart Rhythm Association Practical
Guide on the use of new oral anticoagulants in
patients with non-valvular atrial fibrillation

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



Emorragie minacciose per la vita

- Somministrazione di:
 - concentrati complesso protrombinico (CCP)
- Considera:
 - concentrato complesso protrombinico attivato (aPCC) [FEIBA[®]]
 - fattore VII attivato ricombinante (rFVIIa)

European Heart Rhythm Association Practical
Guide on the use of new oral anticoagulants in
patients with non-valvular atrial fibrillation

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



Evidenze a supporto

- L'uso dei CCP, dell'aCCP e del rFVII è sostenuto da studi:
 - su volontari sani
 - ex-vivo
 - su modelli animali

Marlu R, et al. Thromb Haemost 2012; 108(2): 217-24

Eerenberg ES, et al. Circulation 2011; 124: 1573–1579

Zhou W, et al. Stroke 2013; 44: 771-778

Khoo TL, et al. Int J Lab Hematol 2013;35(2):222-4

Gruber A, et al. Blood 2008;112:1307

Perzborn E, et al. Haemost Thromb 2008;36:A40

Dinkelaar J, et al. JTH 2013 doi: 10.1111/jth.12236

Perzborn E, et al. Thromb Haemost 2013;110(1)