Emergency management in patients treated with NOA

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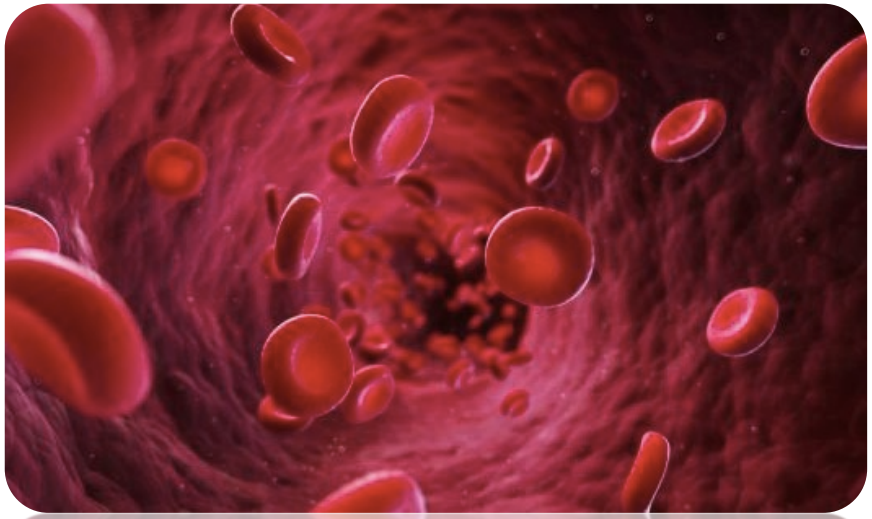
Società Italiana di Medicina d'Emergenza-Urgenza (SIMEU) Lazio

1. Management del reverse nella pratica clinica



Emivita degli anticoagulanti

Table 1: Approximate half-lives of current oral anticoagulants in healthy subjects. Information from respective package inserts.

Agent	Half-life, hours
Warfarin	Mean ~40
Dabigatran	12–17
Rivaroxaban	5–13
Apixaban	12
Edoxaban	10–14

Ageno W et al. Thrombosis and Haemostasis, 2016

Circulation

American Heart Association®

Management and Outcomes of Major Bleeding during Treatment with Dabigatran or Warfarin

Ammar Majeed, Hun-Gyu Hwang, Stuart J. Connolly, John W. Eikelboom, Michael D. Ezekowitz, Lars Wallentin, Martina Brueckmann, Mandy Fraessdorf, Salim Yusuf and Sam Schulman

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Table 3. Hemostatic treatment for all major bleeding events in the RE-LY trial, GEE method*

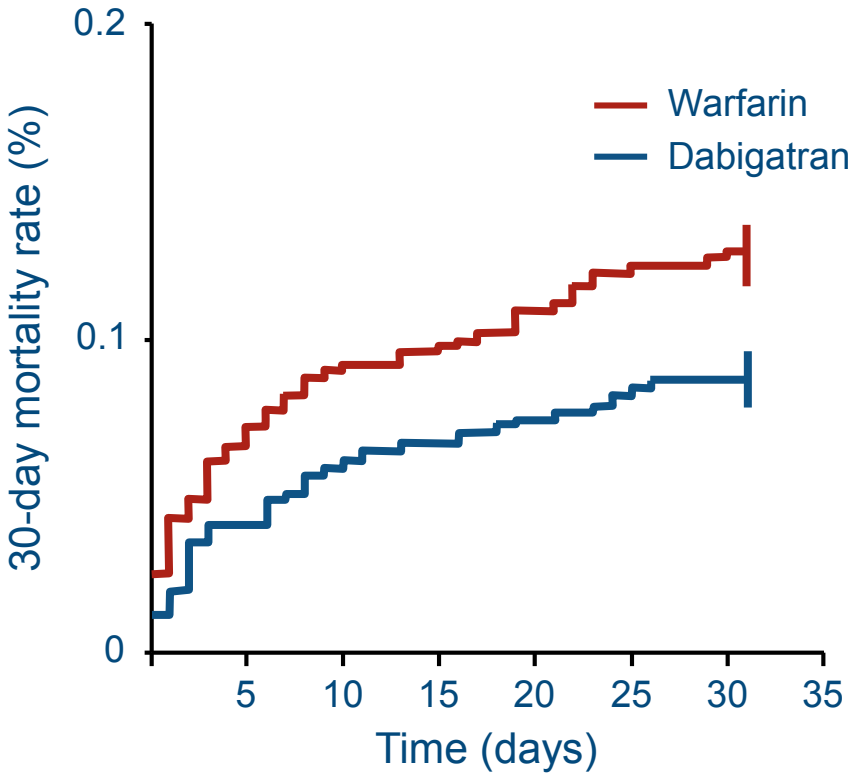
	D 110 mg	D 150 mg	Dabigatran	Warfarin	P-value D 110 vs D 150	P-value D vs Warfarin	P-value D110 vs Warfarin	P-value D 150 vs Warfarin
Fresh frozen plasma, %	18	22	20	30	0.12	<0.001	<0.001	0.01
Cryoprecipitate, %	0.7	1.0	0.9	1.4	0.65	0.36	0.30	0.55
Platelets, %	3.2	3.7	3.5	5.0	0.69	0.17	0.17	0.31
Vitamin K, %	9.1	11	10.2	26	0.34	<0.001	<0.001	<0.001
Prothrombin complex concentrate, %	0.7	0.4	0.6	1.0	0.52	0.36	0.64	0.25
Recombinant factor VIIa, %	0.2	1.4	0.9	0.6	0.05	0.96	0.39	0.21
Coagulation factor replacement, %	0.2	0.6	0.4	1.0	0.39	0.21	0.13	0.47

*The generalized estimating equation for estimation of the parameters of a generalized linear model with a possible unknown correlation between outcomes. Includes events on treatment and up to 3 days after last dose.

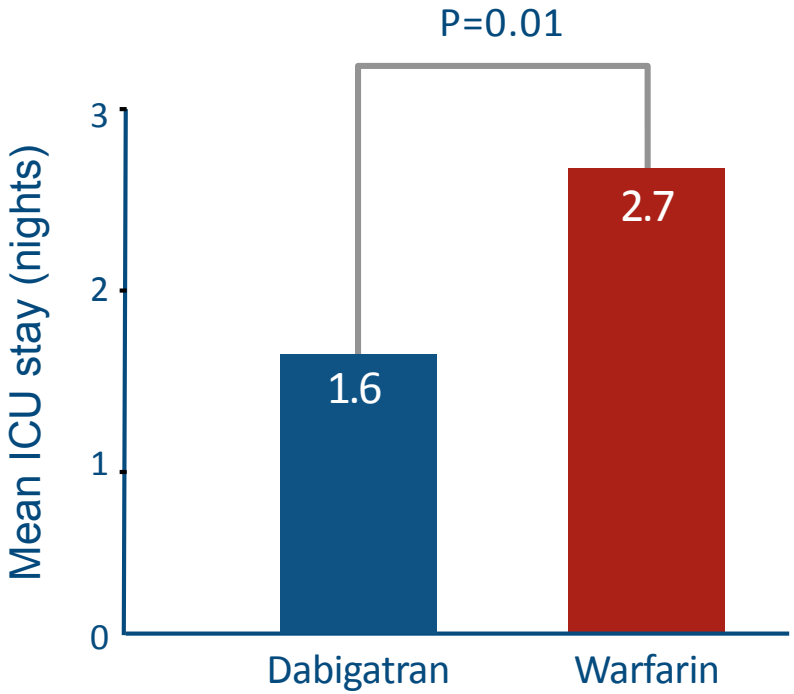
I pazienti con sanguinamenti maggiori da dabigatran erano più anziani, avevano una clearance ridotta e avevano più frequentemente usato NSAID o ASA

If bleeding occurs, lower mortality was seen with dabigatran vs warfarin in the absence of a specific reversal agent

Trend for reduced risk for death with dabigatran vs warfarin during 30 days after a major bleeding event (P=0.052)*



Shorter ICU stay after a major bleed with dabigatran vs warfarin in RE-LY®



For RE-LY® population alone, significant RRR of 44% in mortality rate was evident at 30 days

*Only first major bleed included; analysis not adjusted for covariates. Combined data for dabigatran 150 mg and 110 mg BID treatment groups from five Phase III trial populations with SPAF and DVT/PE; ICU, intensive care unit

Majeed A et al. Circulation 2013;128:2325–32

Vascular Medicine

Periprocedural Bleeding and Thromboembolic Events With Dabigatran Compared With Warfarin

Results From the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Randomized Trial

Jeff S. Healey, MD, MSc; John Eikelboom, MD; James Douketis, MD; Lars Wallentin, MD, PhD; Jonas Oldgren, MD, PhD; Sean Yang, MSc; Ellison Themeles, BA; Hein Heidbuchel, MD; Alvaro Avezum, MD; Paul Reilly, PhD; Stuart J. Connolly, MD; Salim Yusuf, MD, DPhil; Michael Ezekowitz, MB, ChB, DPhil; on behalf of the RE-LY Investigators

Background—Dabigatran reduces ischemic stroke in comparison with warfarin; however, given the lack of antidote, there is concern that it might increase bleeding when surgery or invasive procedures are required.

Methods and Results—The current analysis was undertaken to compare the periprocedural bleeding risk of patients in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial treated with dabigatran and warfarin. Bleeding rates were evaluated from 7 days before until 30 days after invasive procedures, considering only the first procedure for each patient. A total of 4591 patients underwent at least 1 invasive procedure: 24.7% of patients received dabigatran 110 mg, 25.4% received dabigatran 150 mg, and 25.9% received warfarin, $P=0.34$. Procedures included: pacemaker/defibrillator insertion (10.3%), dental procedures (10.0%), diagnostic procedures (10.0%), cataract removal (9.3%), colonoscopy (8.6%), and joint replacement (6.2%). Among patients assigned to either dabigatran dose, the last dose of study drug was given 49 (35–85) hours before the procedure on comparison with 114 (87–144) hours in patients receiving warfarin, $P<0.001$. There was no significant difference in the rates of periprocedural major bleeding between patients receiving dabigatran 110 mg (3.8%) or dabigatran 150 mg (5.1%) or warfarin (4.6%); dabigatran 110 mg versus warfarin: relative risk, 0.83; 95% CI, 0.59 to 1.17; $P=0.28$; dabigatran 150 mg versus warfarin: relative risk, 1.09; 95% CI, 0.80 to 1.49; $P=0.58$. Among patients having urgent surgery, major bleeding occurred in 17.8% with dabigatran 110 mg, 17.7% with dabigatran 150 mg, and 21.6% with warfarin: dabigatran 110 mg; relative risk, 0.82; 95% CI, 0.48 to 1.41; $P=0.47$; dabigatran 150 mg: relative risk, 0.82; 95% CI, 0.50 to 1.35; $P=0.44$.

Conclusions—Dabigatran and warfarin were associated with similar rates of periprocedural bleeding, including patients having urgent surgery. Dabigatran facilitated a shorter interruption of oral anticoagulation.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00262600.

(*Circulation*. 2012;126:343-348.)

RE-LY® demonstrated no significant difference in major bleeding with dabigatran vs warfarin for urgent and elective procedures

	% patients (n/N)			D150 vs warfarin		D110 vs warfarin	
	D150	**D110**	**Warfarin**	**RR (95% CI)**	**P value**	**RR (95% CI)**	**P value**
Urgent surgery	**17.7** (25/141)	**17.8** (19/107)	**21.6** (24/111)	0.82 (0.50–1.35)	0.43	0.82 (0.48–1.41)	0.47
% of total surgeries	9.2	7.2	7.1				
Elective surgery	**3.8** (53/1405)	**2.8** (38/1380)	**3.3** (48/1447)	1.14 (0.77–1.67)	0.51	0.83 (0.55–1.26)	0.38
% of total surgeries	90.1	92.8	92.9				
P (interaction)					0.31		0.90

In RE-LY®, major bleeding was 5–6 times more common after urgent vs elective surgery (P<0.001) regardless of the OAC used

In RE-LY®, 4591/12091 patients underwent at least one invasive procedure. Surgeries were classified as urgent according to the judgment of the local investigator

Healey JS et al. Circulation 2012;126:343–48

Caso clinico: L'esperienza nell'A.O. San Giovanni Addolorata di Roma

Caso clinico:
motivo dell'accesso in PS

ore 13.00:
Donna di 79 anni
entra in sala d'emergenza con codice di accesso in PS: ROSSO

Motivo dell'accesso: RETTORRAGIA e IPOTENSIONE GRAVE (PA 80/40 mmHg). La paziente presentava già da qualche giorno vomito e diarrea.

In anamnesi: ipertensione arteriosa, pregressi episodi di FA (CHA_2DS_2 VAS_c: 4; HAS-BLED: 2).

TERAPIA:
ANTICOAGULANTE Amiodarone una cp, Valsartan 80 mg, Pantoprazolo 20 mg una cp.
Assunzione dell'anticoagulante due ore prima.

Caso clinico: esami di laboratorio

ora	crea	Hb	GR	GB	INR	PT	aPTT	aPTT Ratio
13.00	1,31	12,8	4,450,000	21,000	1,49	54	49 sec	1,54
16.00	(31 ml/hr)	8,0	3,000,000	12,630	**2,0**	**35**	**70 sec**	**2,2**

Caso clinico:
Terapia effettuata in PS

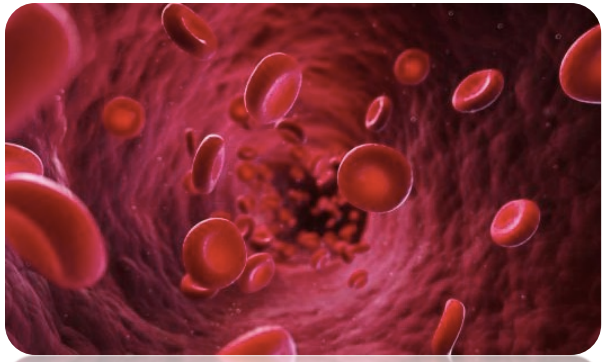
- Si pratica terapia con Colloidi (Hydroxyethyl starch, 1000 cc), Cristalloidi (sodio cloruro), Pantoprazolo 80 mg ev; Dopamina due fiale in pompa peristaltica. Si richiedono due unità di emazie che effettua nel pomeriggio.

- I valori di PA si mantengono costantemente bassi; la rettorragia non si arresta.

Endoscopia d'urgente

Rettosigmoidoscopia:

A livello del sigma assenza di lesioni; il retto appare completamente repleto di coaguli e materiale brunastro. A livello del retto distale pare apprezzarsi rilievo di 15 mm ricoperto di feci e coaguli (polipo?). Non segni di sanguinamento attivo in corso d'esame. Si consiglia look appena possibile preparazione del viscere.



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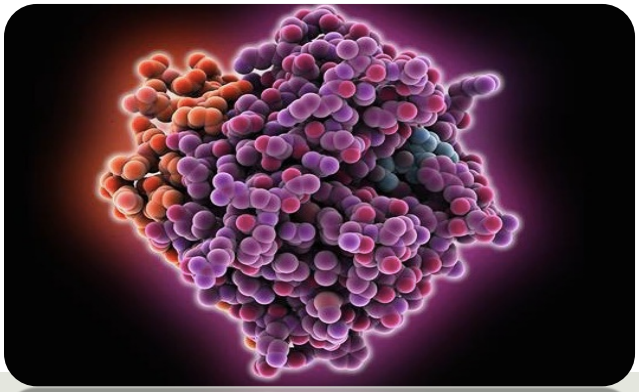
Assunzione dell'anticoagulante due ore prima.

Arruolamento studio RE-VERSE

Ore 20.30:
inizia, previo consenso informato:
PROTOCOLLO IDARUCIZUMAB

Ore 20.45, PA 80/60, si pratica prima fiala **Idarucizumab 2,5 gr e si esegue prelievo per fattori della coagulazione**
Ore 20.55, PA 90/55
Ore 21.00 si pratica seconda fiala **Idarucizumab 2,5 gr**
Ore 23.00 PA **100/60**. Paziente asintomatica per rettorragia



Caso clinico: esami di laboratorio

ora	Hb	GR	GB	INR	PT	aPTT	aPTT Ratio
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16.00	**8,0**	3,000,000	12,630	**2,0**	**35**	**70**	**2,2**
21.00	9,1*	3,140,000	11,190	**1,2**	**68**	**33**	**1,06**

*Hb dopo due sacche di emazie concentrate

Caso clinico: Conclusioni

- La paziente viene dimessa in settima giornata
- Colonscopia ambulatoriale: diverticolosi del colon
- Dabigatran inserito in terapia dopo 20 giorni dalla dimissione, al dosaggio di 110 mgx2
- Follow-up per i successivi 6 mesi, valori di Hb stabili (13 gr/dl)
- **Conclusioni: emorragia digestiva in paziente con diverticolite acuta, disidratazione, in terapia con Amiodarone (possibile interazione farmacologica)**

Quali sono le emergenze emorragiche?

- Necessaria una classificazione precisa e uniforme degli eventi emorragici per poter attuare i provvedimenti terapeutici più appropriati

- Il Subcommittee on control of Anticoagulation della Società Internazionale di Trombosi ed Emostasi ha definito, nel 2005, le "emorragie maggiori", come le emorragie che presentano una delle seguenti caratteristiche:

ISth International Society on Thrombosis and Haemostasis

Table 2: Definitions of bleeding used in pivotal NOAC trials.

Major bleeding	Life-threatening bleeding
• Decrease in haemoglobin of ≥ 2 g/dl, or • Transfusion of ≥ 2 units of packed RBCs, or • Bleeding into a critical site (intracranial, intra-spinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, retroperitoneal)	• Fatal bleeding, or • Symptomatic intra-cranial bleeding, or • Bleeding with decrease of haemoglobin of ≥ 5 g/dl, or • Bleeding requiring inotropic support, or • Bleeding requiring surgery, or • Transfusion of ≥ 4 units of packed RBCs

Thromb Haemost 2013; 110: 205–212

Europace Advance Access published August 31, 2015

Europace
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EHRA PRACTICAL GUIDE

Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation

Hein Heidbuchel[1*], Peter Verhamme[2], Marco Alings[3], Matthias Antz[4], Hans-Christoph Diener[5], Werner Hacke[6], Jonas Oldgren[7], Peter Sinnaeve[2], A. John Camm[8], and Paulus Kirchhof[9,10]

Advisors:, Azhar Ahmad, M.D. (Boehringer Ingelheim Pharma), Jutta Heinrich-Nols, M.D. (Boehringer Ingelheim Pharma), Susanne Hess, M.D. (Bayer Healthcare Pharmaceuticals), Markus Müller, M.D., Ph.D. (Pfizer Pharma), Felix Münzel, Ph.D. (Daiichi-Sankyo Europe), Markus Schwertfeger, M.D. (Daiichi-Sankyo Europe), Martin Van Eickels, M.D. (Bayer Healthcare Pharmaceuticals), and Isabelle Richard-Lordereau, M.D. (Bristol Myers Squibb/Pfizer)

Document reviewers:, Gregory Y.H. Lip, (Reviewer Coordinator; UK), Chern-En Chiang, (Taiwan), Jonathan Piccini, (USA), Tatjana Potpara, (Serbia), Laurent Fauchier, (France), Deirdre Lane, (UK), Alvaro Avezum, (Brazil), Torben Bjerregaard Larsen, (Denmark), Guiseppe Boriani, (Italy), Vanessa Roldan-Schilling, (Spain), Bulent Gorenek, (Turkey), and Irene Savelieva, (UK, on behalf of EP-Europace)

[1]Department of Cardiology – Arrhythmology, Hasselt University and Heart Center, Jessa Hospital, Stadsomvaart 11, 3500 Hasselt, Belgium; [2]Department of Cardiovascular Sciences, University of Leuven, Belgium; [3]Department of Cardiology, Amphia Ziekenhuis, Breda, Netherlands; [4]Department of Cardiology, Klinikum Oldenburg, Oldenburg, Germany; [5]Department of Neurology, University Hospital Essen, University Duisburg-Essen, Germany; [6]Department of Neurology, Ruprecht Karls Universität, Heidelberg, Germany; [7]Uppsala Clinical Research Center and Department of Medical Sciences, Uppsala University, Uppsala, Sweden; [8]Clinical Cardiology, St George's University, London, UK; [9]University of Birmingham Centre for Cardiovascular Sciences, Birmingham, UK; and [10]Department of Cardiology and Angiology, University of Münster, Germany

The current manuscript is an update of the original Practical Guide, published in June 2013[Heidbuchel H, Verhamme P, Alings M, Antz M, Hacke W, Oldgren J, *et al.* European Heart Rhythm Association Practical Guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation. *Europace* 2013;15:625–51; Heidbuchel H, Verhamme P, Alings M, Antz M, Hacke W, Oldgren J, *et al.* EHRA practical guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation: executive summary. *Eur Heart J* 2013;34:2094–106]. Non-vitamin K antagonist oral anticoagulants (NOACs) are an alternative for vitamin K antagonists (VKAs) to prevent stroke in patients with non-valvular atrial fibrillation (AF). Both physicians and patients have to learn how to use these drugs effectively and safely in clinical practice. Many unresolved questions on how to optimally use these drugs in specific clinical situations remain. The European Heart Rhythm Association set out to coordinate a unified way of informing physicians on the use of the different NOACs. A writing group defined what needs to be considered as 'non-valvular AF' and listed 15 topics of concrete clinical scenarios for which practical answers were formulated, based on available evidence. The 15 topics are (i) practical start-up and follow-up scheme for patients on NOACs; (ii) how to measure the anticoagulant effect of

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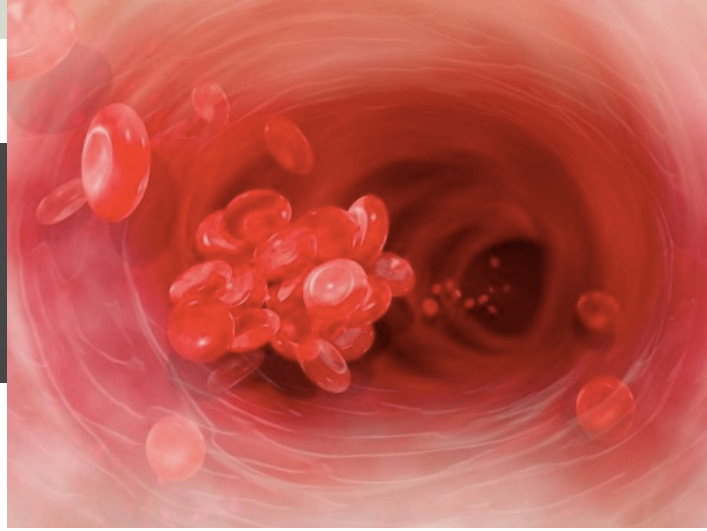
Gestione dei sanguinamenti



- Le indicazioni rilevabili in letteratura non vanno oltre il consenso di esperti

- I dati non derivano da studi clinici ma da studi in vitro e in vivo su parametri di laboratorio in esseri umani (volontari sani) o modelli animali di sanguinamento

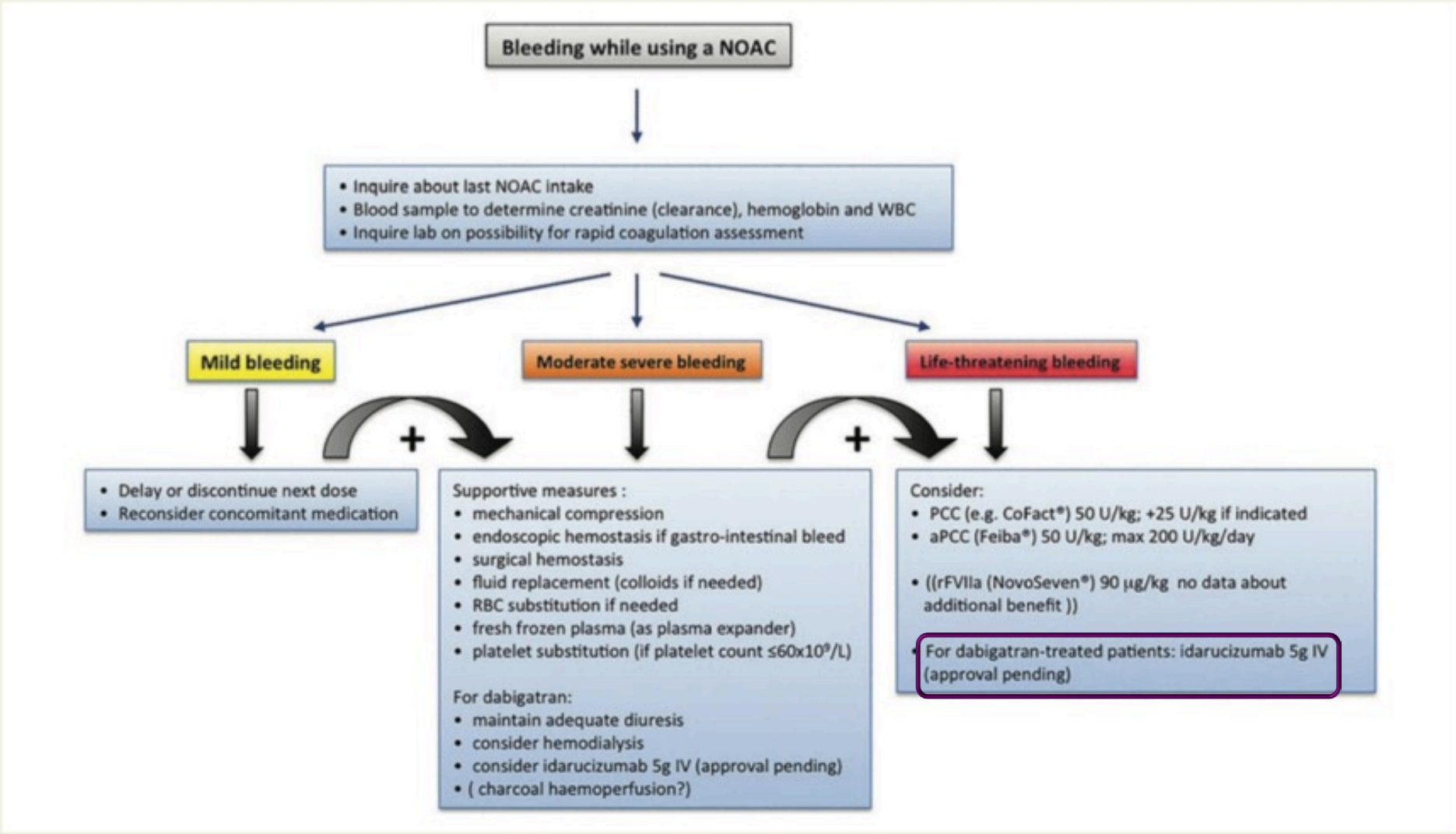


Figure 5 Management of bleeding in patients taking NOACs. Possible therapeutic measures in case of minor or severe bleeding in patients on NOAC therapy. Based on van Ryn *et al.*[39]

Dabigatran Reverse: IDARUCIZUMAB

Idarucizumab (Humanized Fab fragment)

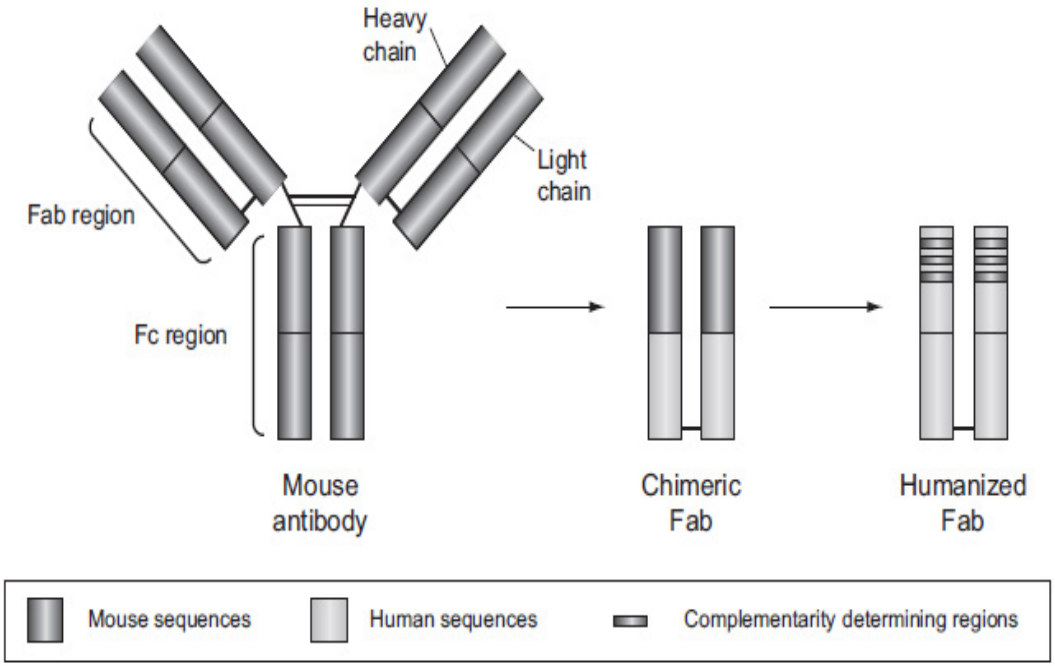


Figure 1. Development of idarucizumab. The fragment antigen-binding (Fab) region is composed of a light and heavy chain and contains the part of the antibody that binds to dabigatran. It also contains a constant region, which, when murine sequences are replaced with human ones, is called a chimeric Fab. The fragment constant (Fc) region interacts directly with the immune system; however, such non-specific binding is avoided by removal of the Fc region.

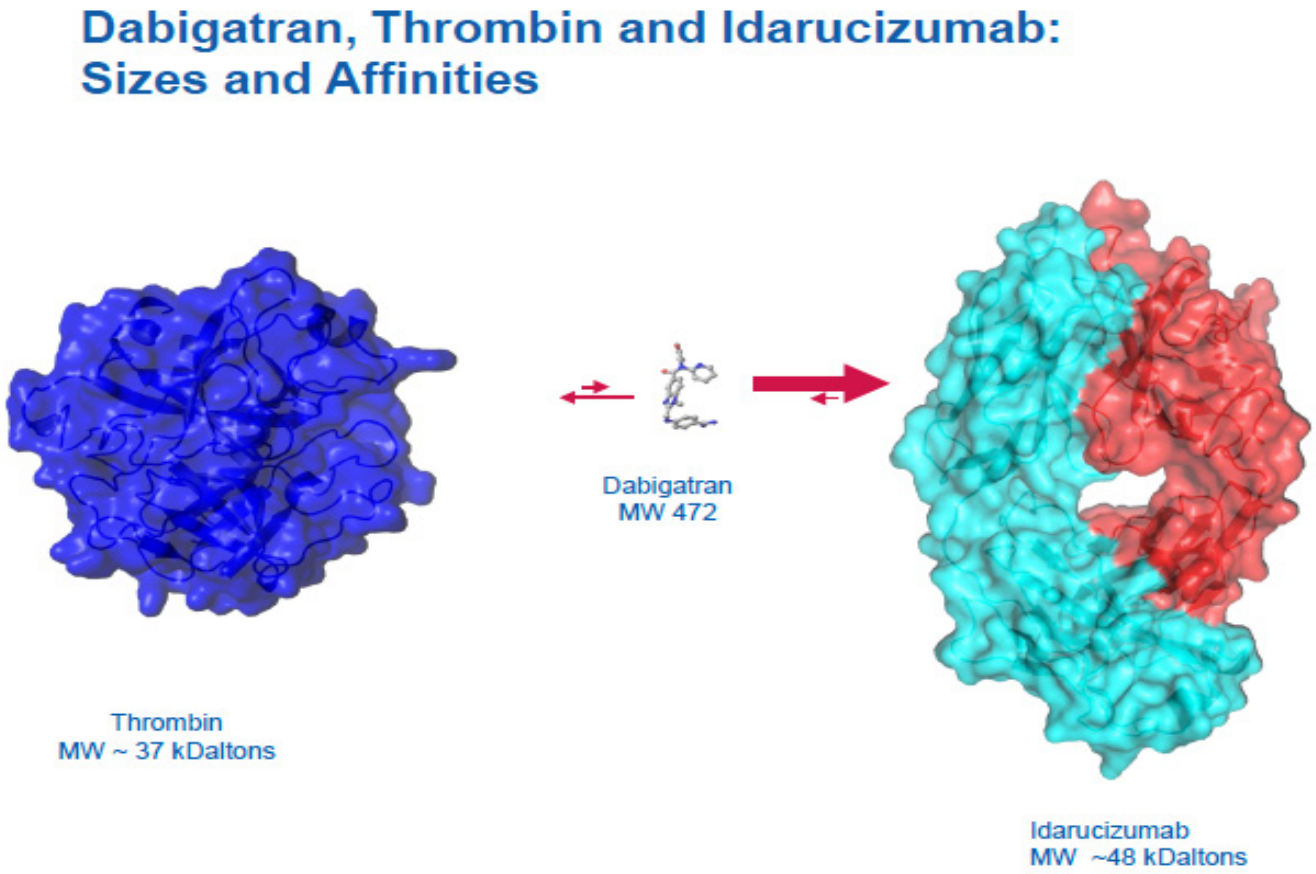
Immunization of mice with dabigatran derived aptens coupled to carrier proteins

Isolation of Antigen Binding Fragment (FAB) from Monoclonal Antibodies exhibiting the highest affinity for dabigatran

Murine protein sequences were replaced with human sequences

The use of humanized Fab instead of an intact antibody results in a shorter half-life and a reduced potential for immunologic reactions

Idarucizumab is a FAB fragment antibody that binds dabigatran with a 300 – fold higher affinity than dabigatran binds to thrombin



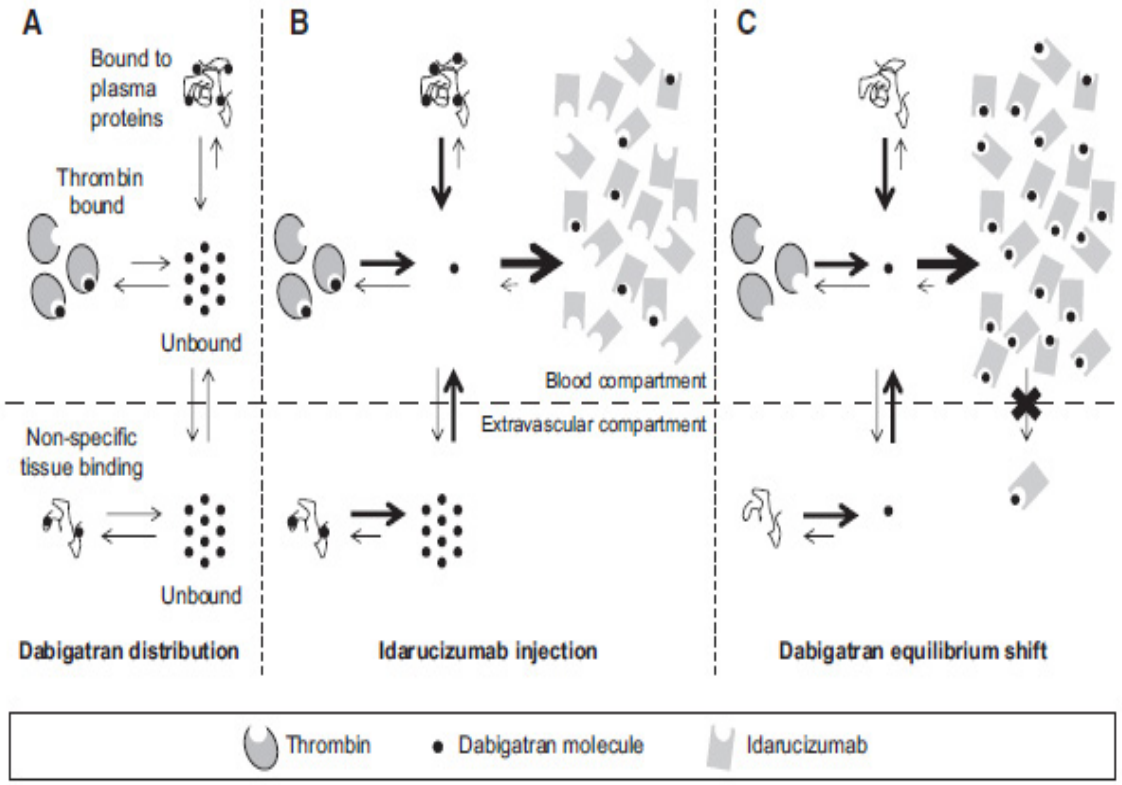
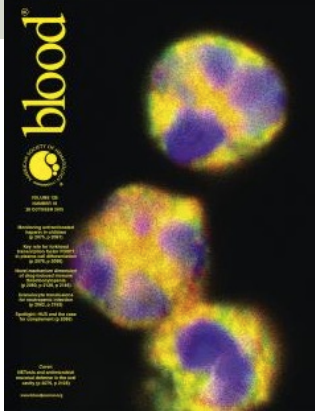


Figure 3. Changes in the distribution of dabigatran after idarucizumab administration. **A**, Circulating dabigatran exists in a state of equilibrium between the plasma and the extravascular compartments. Only unbound dabigatran in the plasma is able to bind thrombin and to inhibit coagulation. **B**, Idarucizumab rapidly binds dabigatran in the plasma. This alters the equilibrium, causing dabigatran in the extravascular compartment to move into the plasma and to potentially dissociate from thrombin (larger arrows). **C**, Because of the high affinity of idarucizumab for dabigatran, thrombin is no longer inhibited, and it regains its capacity to trigger clotting.

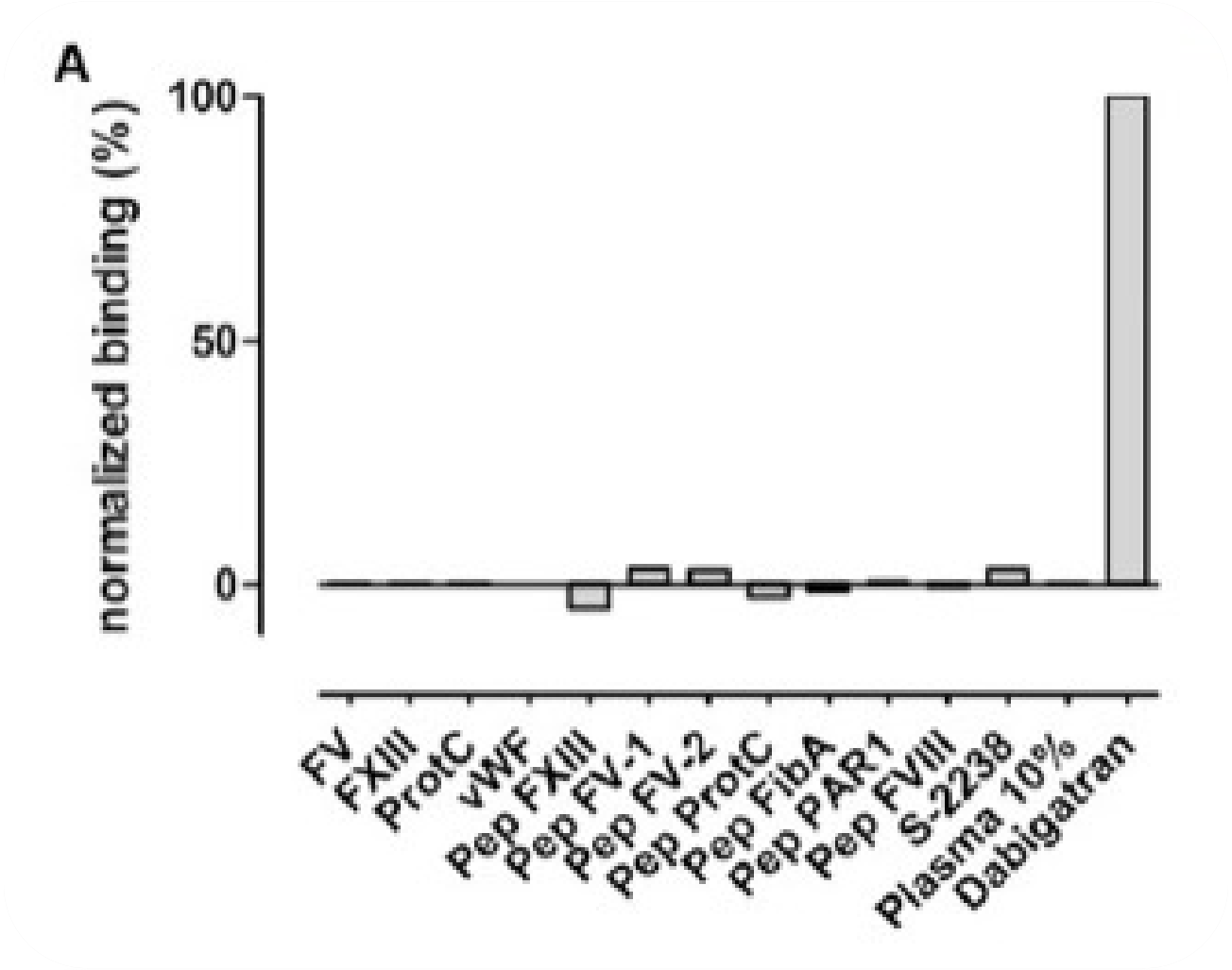
Idarucizumab (Humanized Fab fragment)

- Is specific for dabigatran
- Does not bind thrombin or its substrates
- Does not promote or attenuate thrombin generation
- Does not activate platelets or convert fibrinogen to fibrin

IDARUCIZUMAB HAS NO INTRINSIC ANTICOAGULANT OR PROCOAGULANT EFFECTS



Schiele F, Blood 2013



Idarucizumab (Humanized Fab fragment)

- Idarucizumab is eliminated mainly renally
- Idarucizumab clearance is attenuated in patients with renal impairment, resulting in increased plasma concentrations of idarucizumab
- However, because patients with renal impairment often have elevated dabigatran plasma concentrations, the higher idarucizumab exposure may be advantageous

Praxbind® sviluppo clinico

IDARUCIZUMAB - Animal studies

- Rats → reverse of the anticoagulant effect of dabigatran
- Pigs with crush injury of the liver who received high doses of dabigatran → reduction of blood loss in a dose dependent manner and improvement of survival up to 100%
- Compared with saline idarucizumab significantly attenuated intracerebral hematoma expansion in dabigatran – treated mice

THE PRECLINICAL STUDIES SUPPORT THE POTENTIAL OF IDARUCIZUMAB TO ATTENUATE DABIGATRAN-INDUCED BLEEDING

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Idarucizumab for Dabigatran Reversal

Charles V. Pollack, Jr., M.D., Paul A. Reilly, Ph.D., John Eikelboom, M.B., B.S., Stephan Glund, Ph.D., Peter Verhamme, M.D., Richard A. Bernstein, M.D., Ph.D., Robert Dubiel, Pharm.D., Menno V. Huisman, M.D., Ph.D., Elaine M. Hylek, M.D., Pieter W. Kamphuisen, M.D., Ph.D., Jörg Kreuzer, M.D., Jerrold H. Levy, M.D., Frank W. Sellke, M.D., Joachim Stangier, Ph.D., Thorsten Steiner, M.D., M.M.E., Bushi Wang, Ph.D., Chak-Wah Kam, M.D., and Jeffrey I. Weitz, M.D.

RE-VERSE®

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- Studio prospettico che ha indagato la capacità di 5 gr ev di Idarucizumab di ripristinare la coagulazione in pazienti in trattamento con Dabigatran, che presentavano sanguinamenti maggiori (gruppo A) o che dovevano essere sottoposti a procedure urgenti (gruppo B)

- Endopoint primario: la percentuale di antagonizzazione del dabigatran entro 4 ore dalla somministrazione dell'antidoto sulla base della misurazione del tempo di trombina diluito e dell'ecarin clotting time e endopoint secondario 2. ripristino della normale coagulazione

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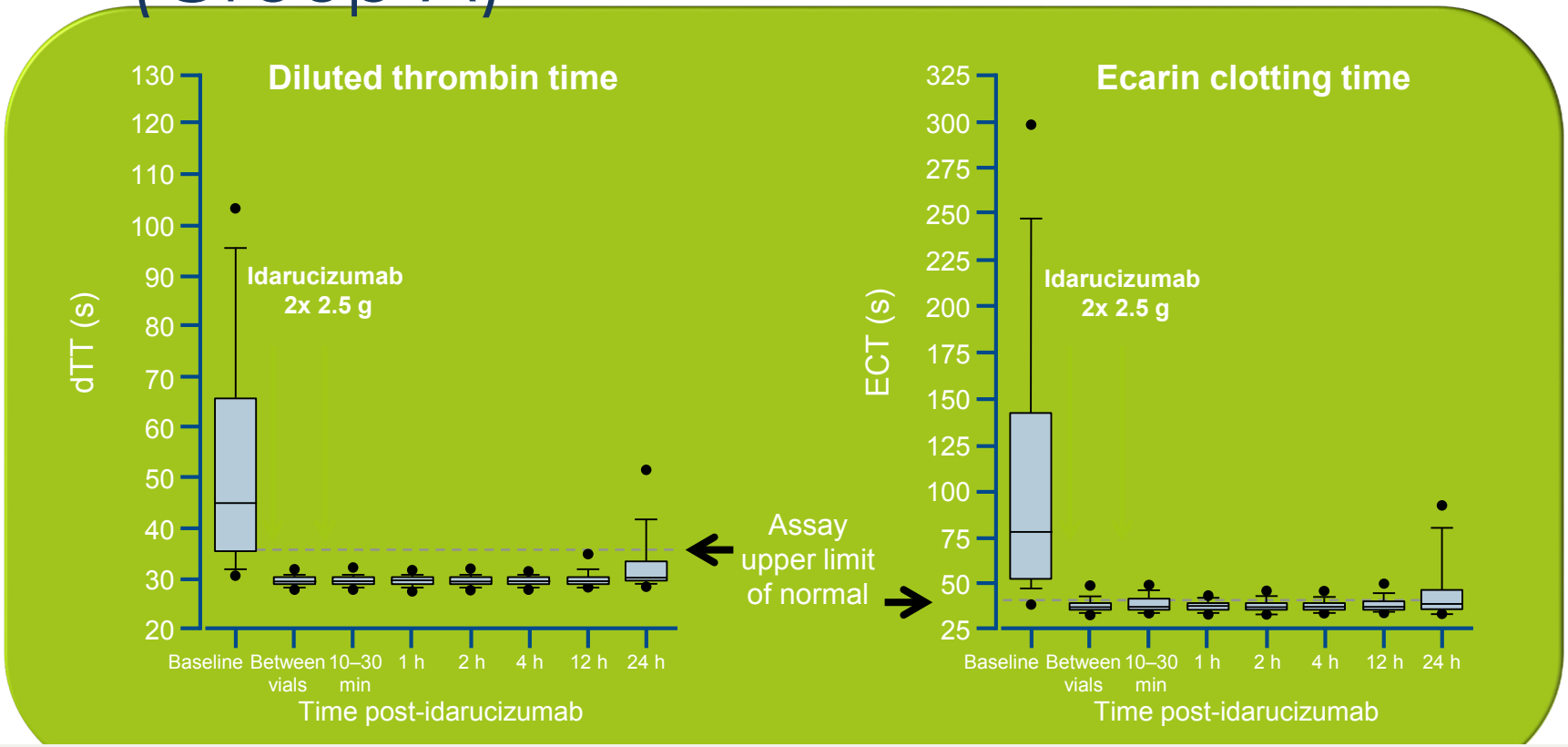
Charles V. Pollack, Jr., M.D., Paul A. Reilly, Ph.D., John Eikelboom, M.B., B.S., Stephan Glund, Ph.D., Peter Verhamme, M.D., Richard A. Bernstein, M.D., Ph.D., Robert Dubiel, Pharm.D., Menno V. Huisman, M.D., Ph.D., Elaine M. Hylek, M.D., Pieter W. Kamphuisen, M.D., Ph.D., Jörg Kreuzer, M.D., Jerrold H. Levy, M.D., Frank W. Sellke, M.D., Joachim Stangier, Ph.D., Thorsten Steiner, M.D., M.M.E., Bushi Wang, Ph.D., Chak-Wah Kam, M.D., and Jeffrey I. Weitz, M.D.

- 90 pazienti che hanno ricevuto Idarucizumab (51 gruppo A e 39 guppo B).
- Il 100% dei pazienti che avevano un allungamento del tempo di trombina (68 pz) e dell'ECT (81) dopo 5 minuti presentavano una normalizzazione dei test della coagulazione (95% CI)
- Idarucizumab normalizza la coagulazione con una percentuale di successo vicina al 98% e il suo effetto è evidente in alcuni minuti.

Patients with uncontrolled bleeding (Group A)



(51 patients) Median maximum reversal within 4 hours was 100% (95% CI: 100–100)

dTT normalized in 98% and ECT in 89% of patients with elevated values at baseline*

Pazienti che necessitano di intervento chirurgico urgente

Intervento chirurgico urgente

Prima di un intervento:
Valutazione del test di coagulazione comuni (aPTT per Inibitori diretti della Trombina; PT per gli inibitori del fattore Xa) o specifici test di coagulazione (DTT per DTI; test cromogenici per gli inibitori FXa)

Aneddotiche segnalazioni di interventi effettuati solo con la semplice dimostrazione dell'aPTT normale, in terapia con dabigatran. Non è una strategia consigliabile (vedi aPTT normale nonostante DTT allungato)

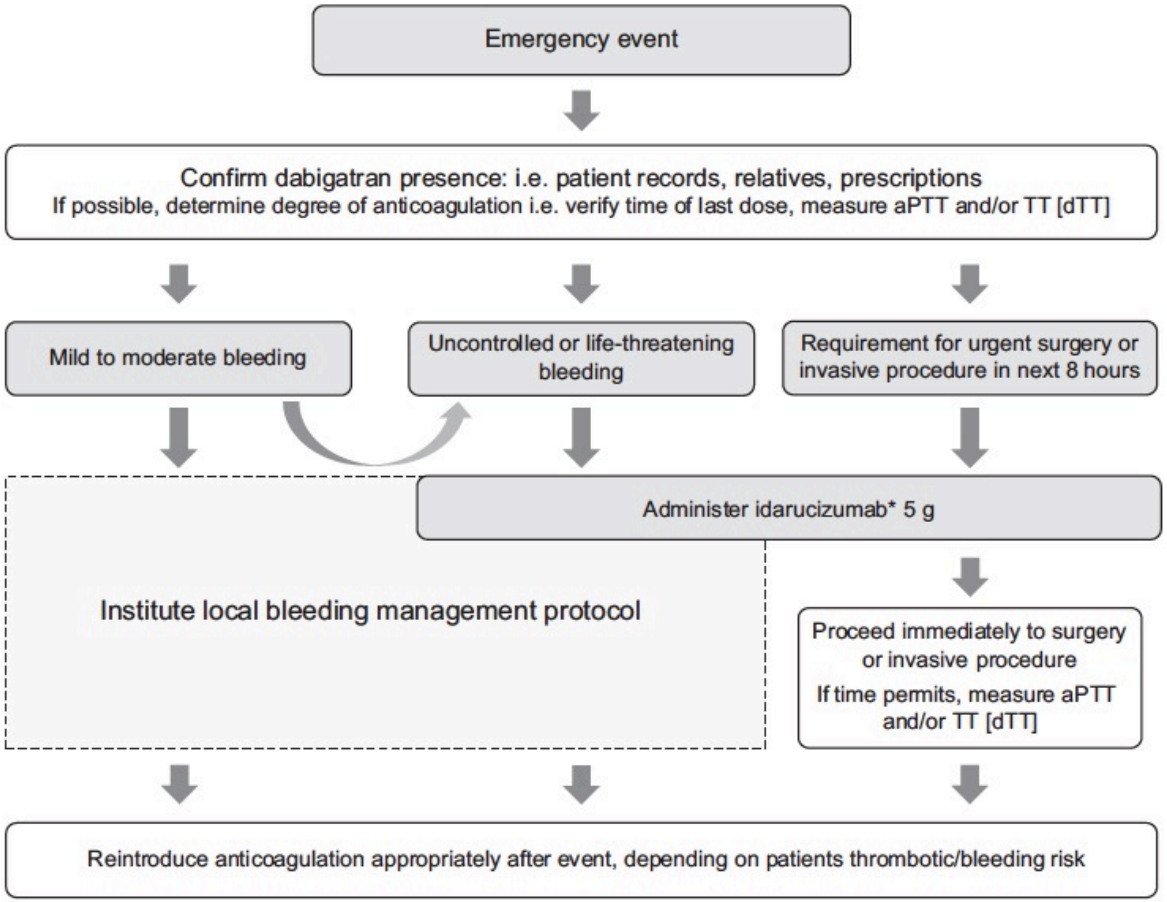


Figure 7. Proposed algorithm for management of patients treated with dabigatran who present with bleeding episodes or require urgent surgery/invasive procedures. *Administer two 50-mL vials of idarucizumab (each containing 2.5 g) intravenously. In rare cases when dabigatran anticoagulation remains present after idarucizumab and bleeding continues in the patient, a second 5-g dose of idarucizumab may be considered. aPTT indicates activated partial thromboplastin time; dTT, diluted thrombin time; and TT, thrombin time.

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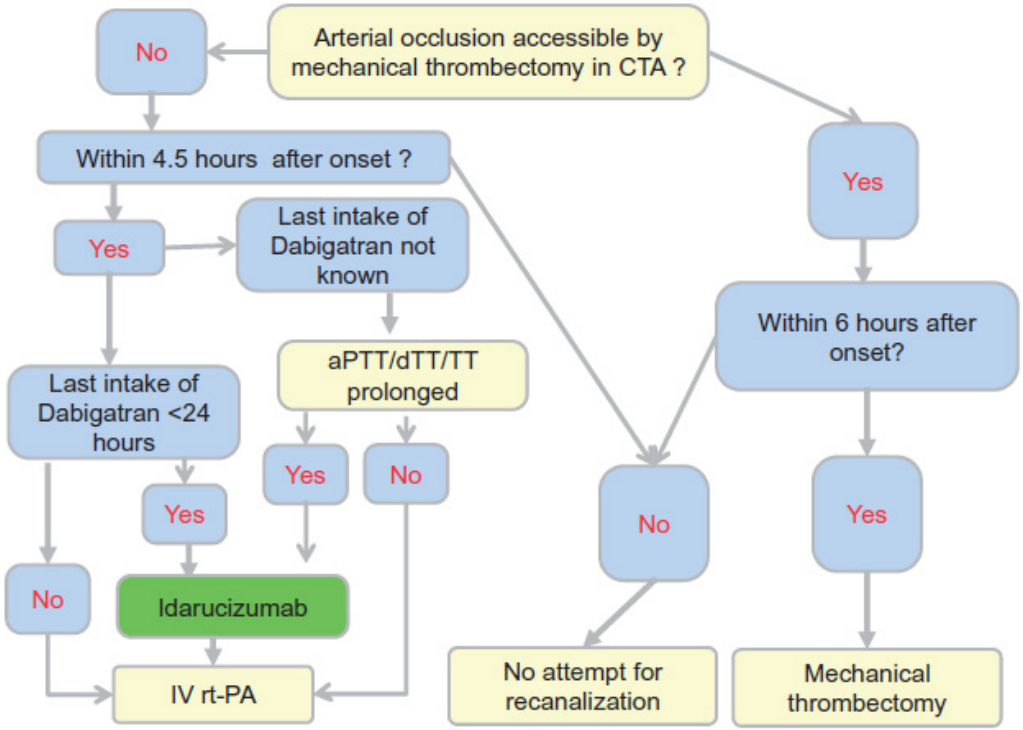
Figure 1. Flow diagram for thrombolysis or thrombectomy inpatients treated with Dabigatran



aPPT, activated partial thromboplastin time; CTA, computerized tomography angiography; dTT, diluted thrombin time; IV, intravenous; rt-PA, recombinant tissue plasminogen activator

Chi dovrebbe ricevere un reversal agent?

Managing reversal of direct oral anticoagulants in emergency situations

Anticoagulation Education Task Force White Paper

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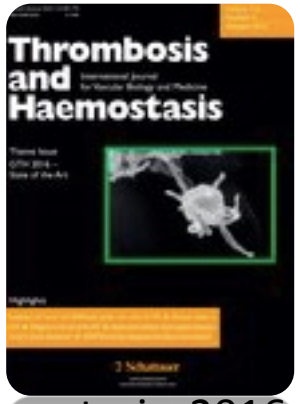


Thrombosis and Haemostasis, 2016

quando e come utilizzare il reverse in urgenza?

Table 2: Situations in which to consider use of a reversal agent.

Clinical situation	Definite need for a reversal agent	Reversal agent possibly helpful (patient-dependent)	Reversal agent generally not needed
Life-threatening bleeding (e.g., intracranial haemorrhage, symptomatic or expanding extradural haemorrhage, or uncontrollable haemorrhage)	X		
Bleeding in a closed space or critical organ (e.g., intracranial, intraspinal, intraocular, pericardial, pulmonary, retroperitoneal, or intramuscular with compartment syndrome)	X		
Persistent major bleeding despite local haemostatic measures, or risk of recurrent bleeding because of delayed DOAC clearance or DOAC overdose	X		
Need for urgent intervention that is associated with a high risk of bleeding and that cannot be delayed to allow for drug clearance	X		
Emergency surgery or intervention in patients at high risk for procedural bleeding: neurosurgery (intracranial, extradural, or spinal), lumbar puncture, cardiac, or vascular surgery (aortic dissection/aneurysm repair), hepatic, or other major organ surgery	X		
Need for urgent surgery or intervention in patients with acute renal failure		X	
Elective surgery			X
Gastrointestinal bleeds that respond to supportive measures			X
High drug levels or excessive anticoagulation without associated bleeding			X
Need for surgery or intervention that can be delayed long enough to permit drug clearance			X

DOACs, non-Vitamin K oral anticoagulants. Adapted from Levy et al. 2015 (31).

Protocol Development

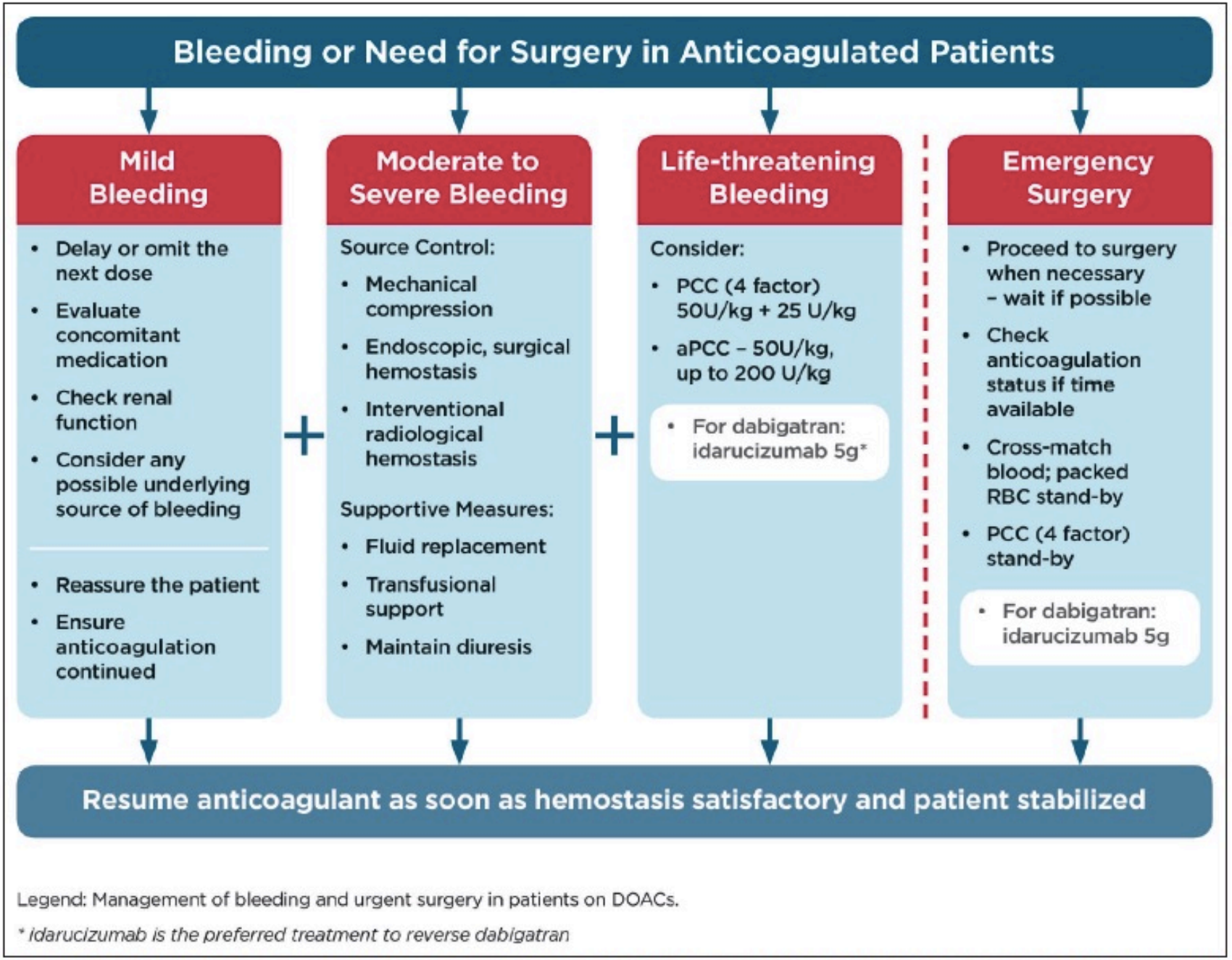
Sviluppo di un protocollo

- Gli attori principali interessati al reverse di una terapia anticoagulante possono variare da un ospedale all'altro: sviluppare protocolli locali per definire la reverse strategy.

- E' fondamentale sviluppare protocolli specifici al fine di garantire l'uso appropriato di questi farmaci.

- Team multidisciplinare (urgentisti, specialisti in coagulazione, cardiologi e neurologi).

- Nel protocollo specificare le misure generali da adottare in caso di sanguinamento.



Legend: Management of bleeding and urgent surgery in patients on DOACs.

** idarucizumab is the preferred treatment to reverse dabigatran*

Figure 1: An algorithm for management of patients treated with a DOAC who present with mild, moderate to severe, or life-threatening bleeding or who require emergency surgery. DOAC, direct oral anticoagulant.

Take Home message

- La sicurezza del paziente deve essere la priorità quando si introduce un nuovo anticoagulante.
- L'arrivo dei reverse dei NAO può aumentare la confidenza, facilitando la gestione delle emorragie pericolose per la vita.
- L'uso dei reverse non potrà mai prescindere dalle altre misure di supporto.

Grazie per l'attenzione!