OSPEDALE SANTA CORONA
PIETRA LIGURE (SV)

AZIENDA SANITARIA LOCALE N. 2 SAVONESE

I NAO tra studi controllati e vita reale

Riunione congiunta SIN – SNO Triregionale
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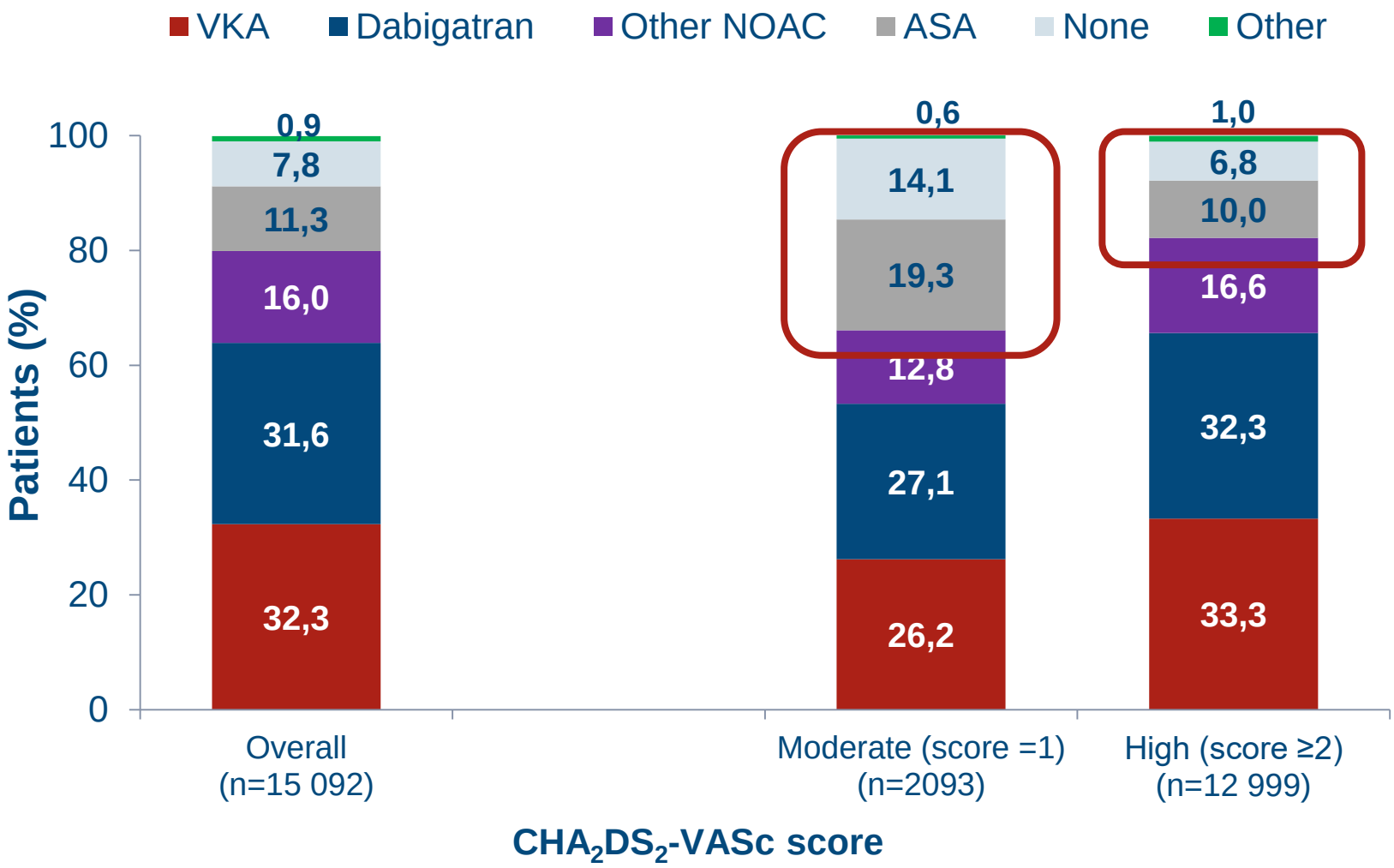
Four NOACs to choose from

	Dabigatran 150 mg	Dabigatran 110 mg	Apixaban 5/2.5 mg	Rivaroxaban 20/15 mg	Edoxaban 60/30 mg
Dosing frequency	BID		BID	OD	OD
RCTs: major bleeding vs warfarin[1–4]	Not significant	↓ 20%	↓ 31%	Not significant	↓ 20%
RCTs: stroke/SE vs warfarin[1–4]	↓ 35%	Not significant	↓ 21%	Not significant	Not significant
Superior safety profile reinforced by comparative real-world data[5,6]	✓		✓	✗	✗
Specific reversal agent available	✓		✗	✗	✗

No head-to-head RCT comparison. Head-to-head data available from observational studies. RCT, randomized controlled trial

1. Connolly et al. N Engl J Med 2014; 2. Patel et al. N Engl J Med 2011; 3. Granger et al. N Engl J Med 2011; 4. Giugliano et al. N Engl J Med 2013; 5. Larsen et al. BMJ 2016; 6. Lin et al. Presented at ESC 2015

GLORIA™-AF Phase II: 34% of patients at moderate risk and 18% at high risk of stroke did not receive any OAC



'Other NOAC': rivaroxaban or apixaban; 'Other': includes antiplatelets other than ASA and combination of OACs

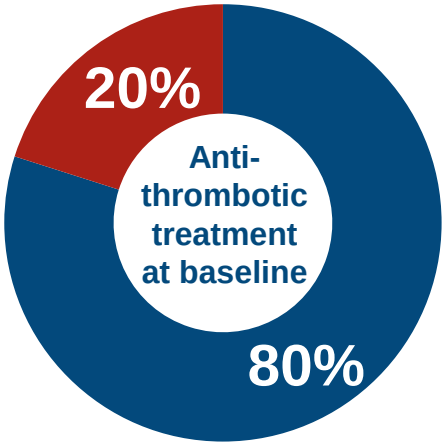
ASA, acetylsalicylic acid; CHA_2DS_2-VASc, score for evaluating ischaemic stroke risk in patients with AF

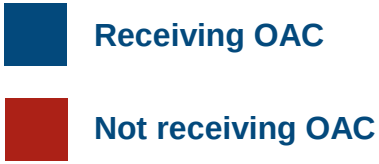
1. Huisman MV et al. Presented at ESC 2015

Despite the demonstrated safety and efficacy of NOACs, many patients at risk of stroke do not receive OACs

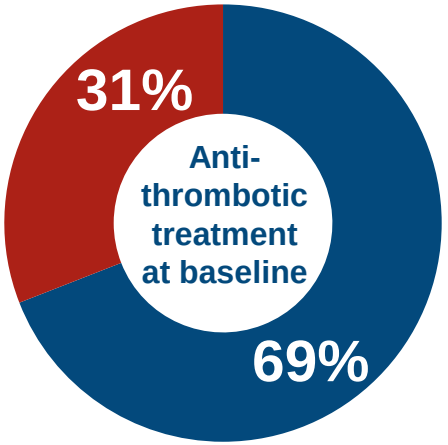
Analysis of data from global and European prospective, observational registries has shown an increasing uptake of NOACs, but many patients with AF who are at risk of stroke do not receive OACs[1–4]

GLORIA™-AF (10 675 patients)[1]





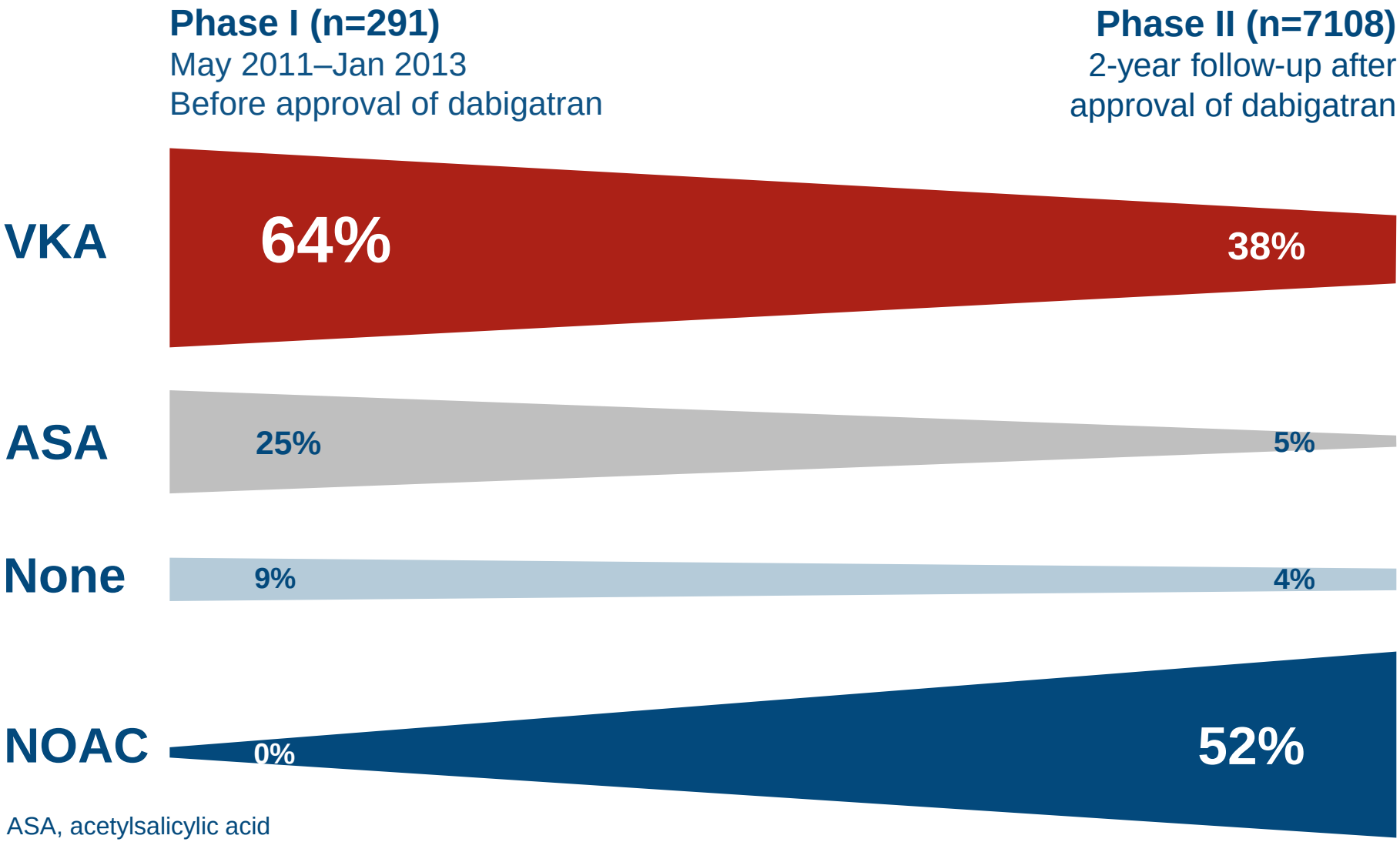
GARFIELD-AF (17 475 European patients)[2]



Similar proportions of patients did not receive OACs in the PREFER in AF (17.7%) and EORP-AF (20.0%) registries[3,4]

1. Huisman MV et al. Am J Med 2015; 2. Camm AJ et al. Poster P85323, ESC 2015; 3. Kirchhof P et al. Europace 2014; 4. Lip GHY et al. Europace 2014

GLORIA™-AF Phase II (Europe): clear shift away from VKAs and ASA following introduction of the NOACs



ASA, acetylsalicylic acid

1. Huisman MV et al. Presented at ESC 2015

Considerazioni Anno 2014

- Liguria Trattamenti avviati NAO = n. 5805
- Liguria Trattamenti avviati totali = n. 134.926
- Incidenza % dei PT NAO = 4,3 %

- Italia Trattamenti avviati NAO = 10.965
- Italia Trattamenti avviati totali = 266.204
- Incidenza % dei PT NAO = 4, 1%

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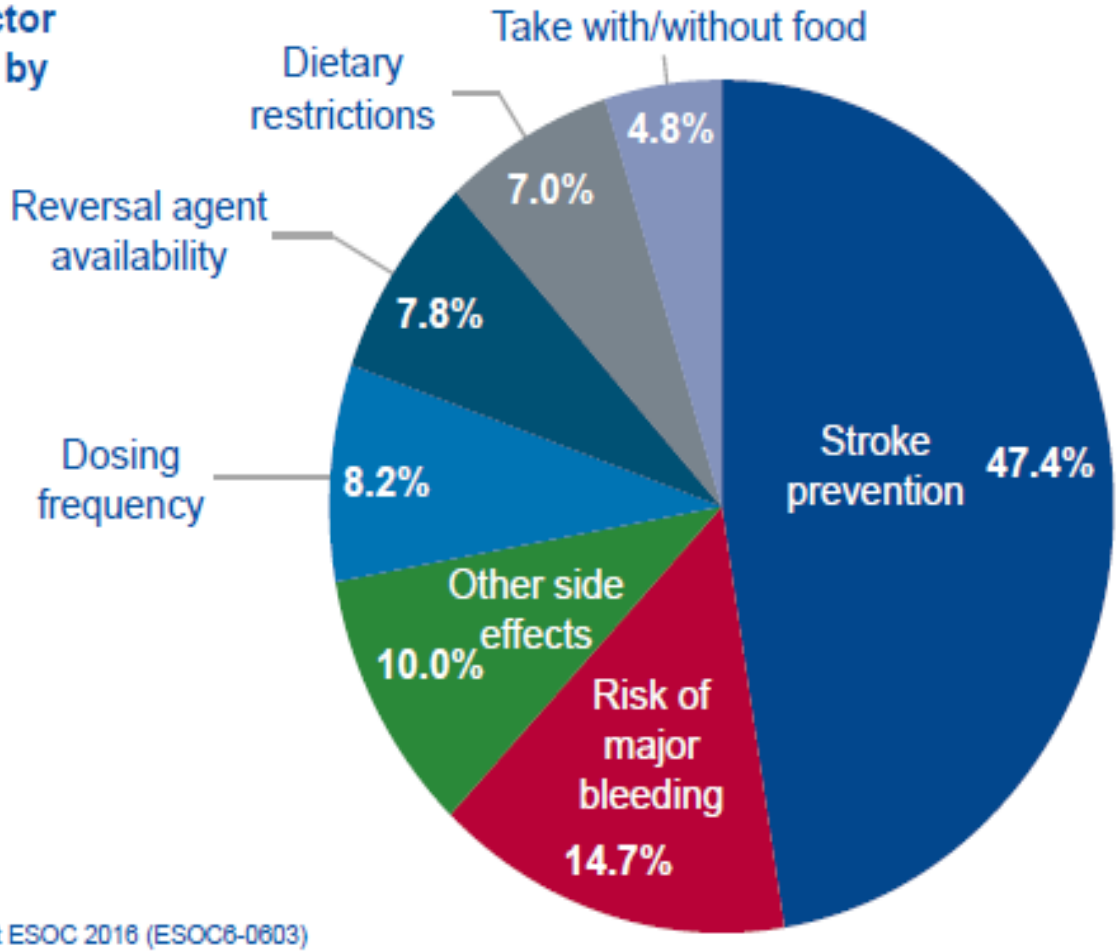
Perché

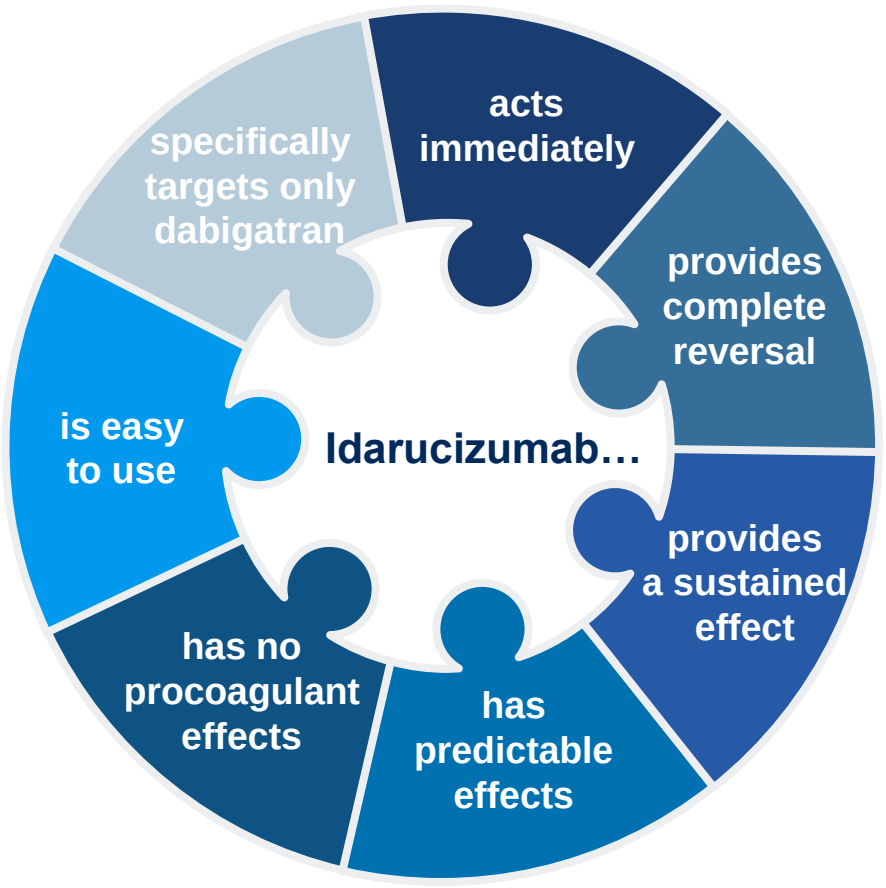
In 2016, what factors should be considered in the patient–physician dialogue regarding NOAC choice?

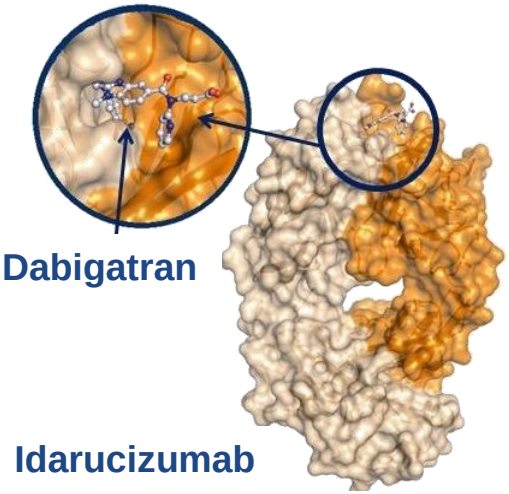
The most important factor in choice of OAC rated by patients (N=937)



Adapted from Lane et al. Presented at ESOC 2016 (ESOC6-0603)

Idarucizumab fulfils the characteristics of an ideal reversal agent





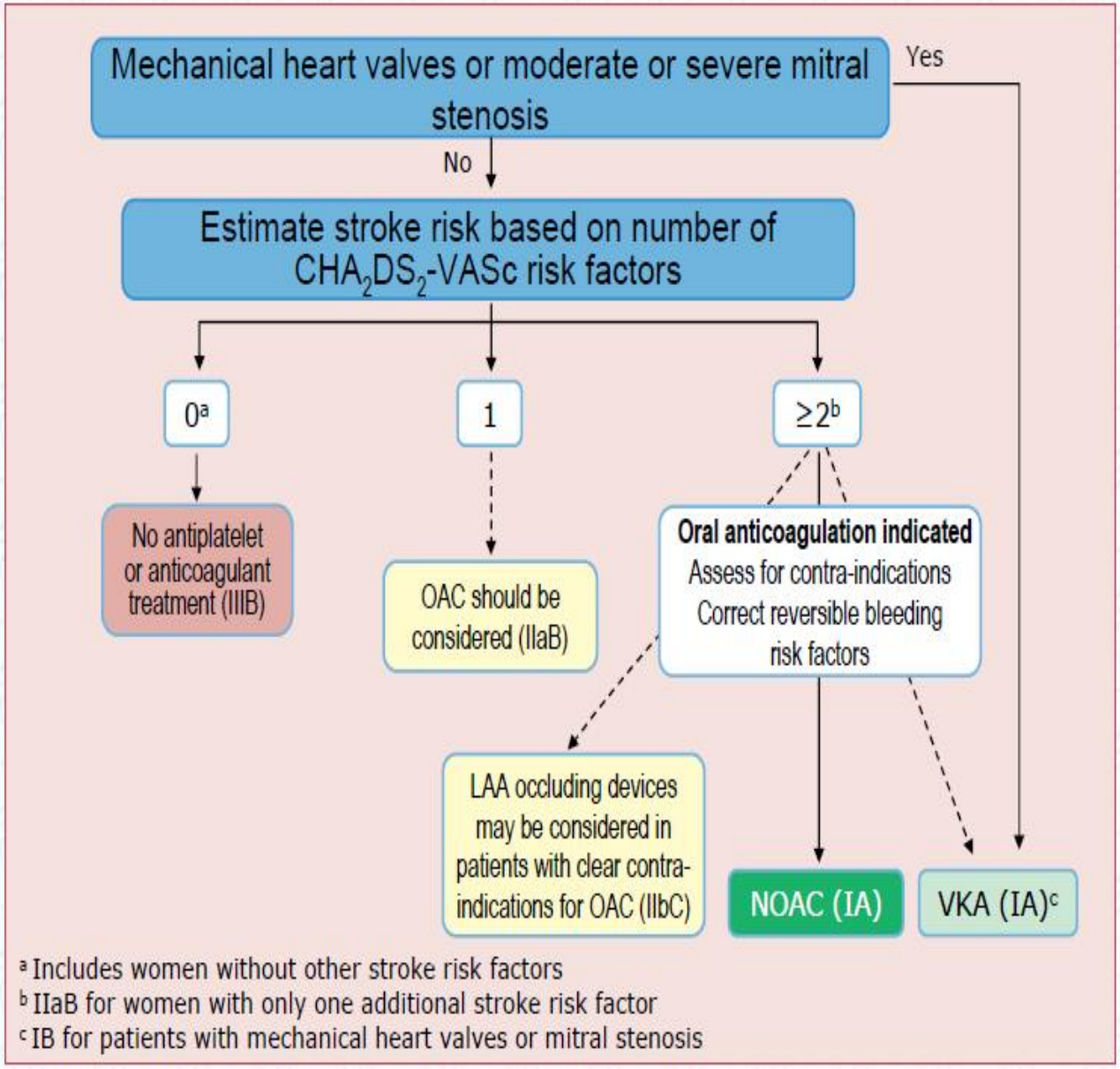
- Humanized Fab fragment
- Binding affinity for dabigatran ~350× higher than dabigatran to thrombin
- Short half life

Idarucizumab takes dabigatran out of the equation, helping physicians to concentrate on other vital aspects of emergency management

Idarucizumab is not approved in all countries. Please check your local prescribing information for details

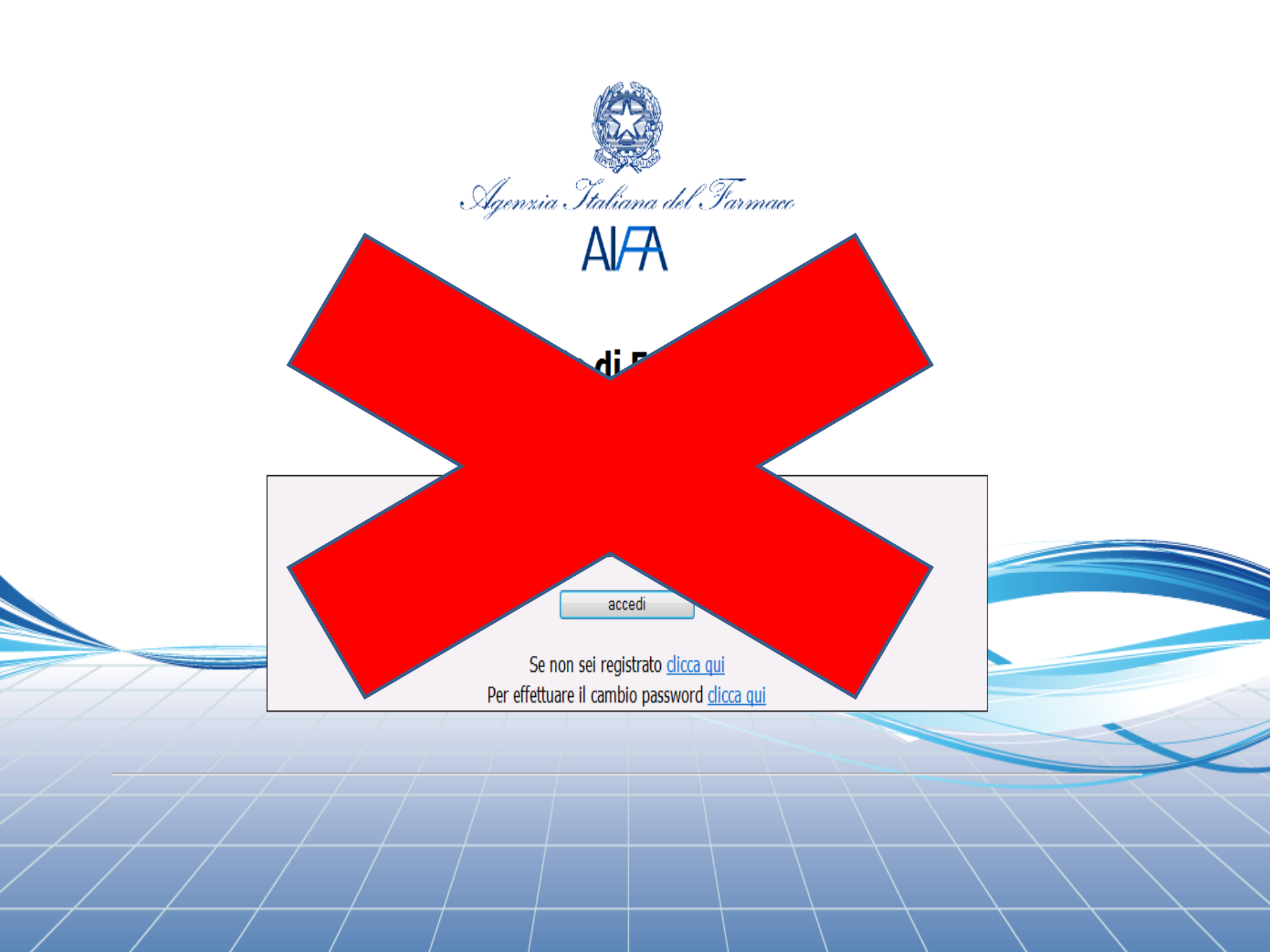
1. Pollack C. ISTH 2015; 2. Schiele F et al. Blood 2013; 3. Stangier J et al. ISTH 2015

Initiation of stroke prevention therapy in atrial fibrillation



[a] Includes women without other stroke risk factors
[b] IIaB for women with only one additional stroke risk factor
[c] IB for patients with mechanical heart valves or mitral stenosis

European Heart Journal - doi:10.1093/eurheartj/ehw 210


Agenzia Italiana del Farmaco
AIFA
accedi
Se non sei registrato clicca qui
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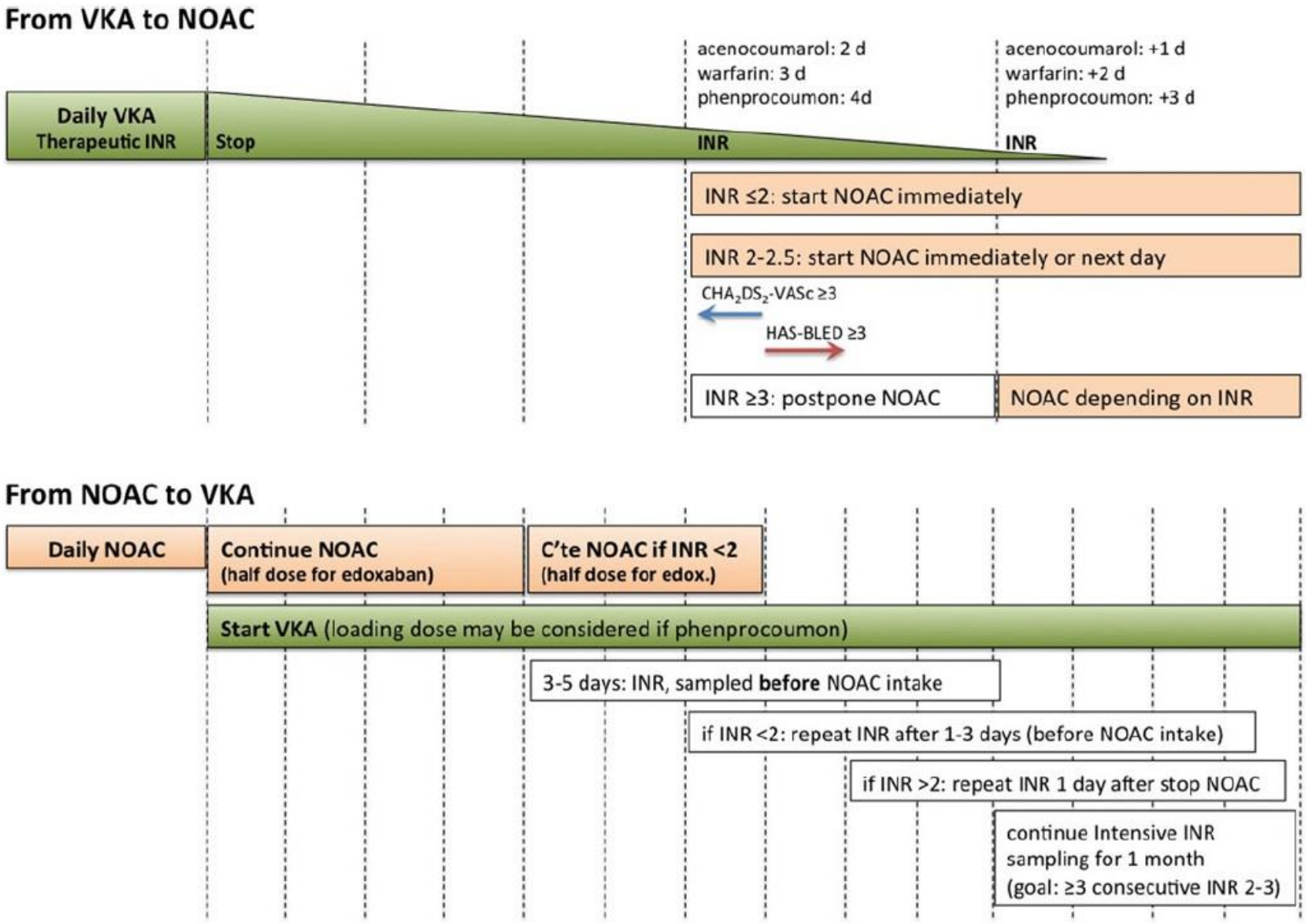


Switching between vitamin-K antagonists (VKA) and non-VKA oral anticoagulants (NOACs) and vice versa.

Last intake of drug before elective surgical intervention

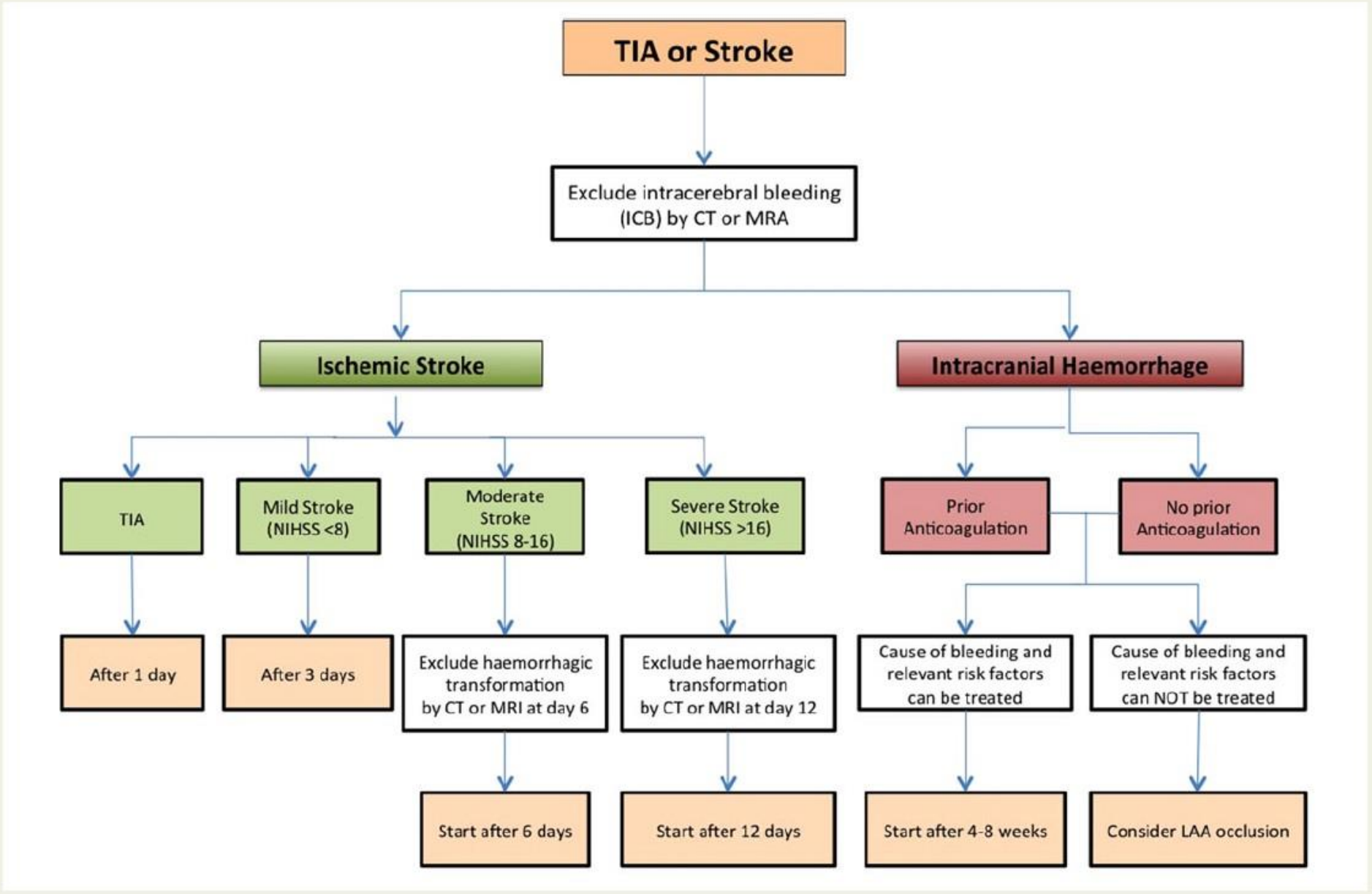
	Dabigatran		Apixaban–Edoxaban–Rivaroxaban	
	No important bleeding risk and/or adequate local haemostasis possible: perform at trough level (i.e. ≥12 or 24 h after last intake)			
	Low risk	High risk	Low risk	High risk
CrCl ≥80 mL/min	≥24 h	≥48 h	≥24 h	≥48 h
CrCl 50–80 mL/min	**≥36 h**	**≥72 h**	≥24 h	≥48 h
CrCl 30–50 mL/min[a]	**≥48 h**	**≥96 h**	≥24 h	≥48 h
CrCl 15–30 mL/min[a]	Not indicated	Not indicated	**≥36 h**	**≥48 h**
CrCl <15 mL/min	No official indication for use			
	There is no need for pre-operative bridging with LMWH/UFH			

Bold values deviate from the common stopping rule of ≥24 h low risk, ≥48 h high risk.

Low risk: with a low frequency of bleeding and/or minor impact of a bleeding; high risk with a high frequency of bleeding and/or important clinical impact.

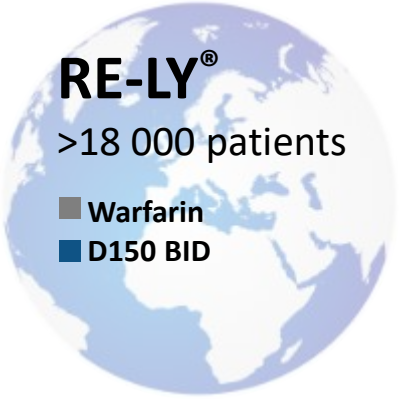
CrCl, creatinine clearance.

[a]Many of these patients may be on the lower dose of dabigatran (i.e. 110 mg BID) or apixaban (i.e. 2.5 mg BID), or have to be on the lower dose of rivaroxaban (i.e. 15 mg OD) or edoxaban (i.e. 30 mg OD).



Flowchart for the initiation or re-initiation of anticoagulation after transient ischaemic attack (TIA)/stroke or intracerebral haemorrhage.

Independent FDA study of Medicare patients mirrors the favourable benefit–risk profile of dabigatran from RE-LY®

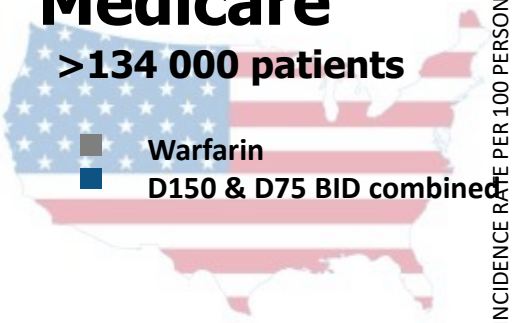


RE-LY®

>18 000 patients

Warfarin

D150 BID

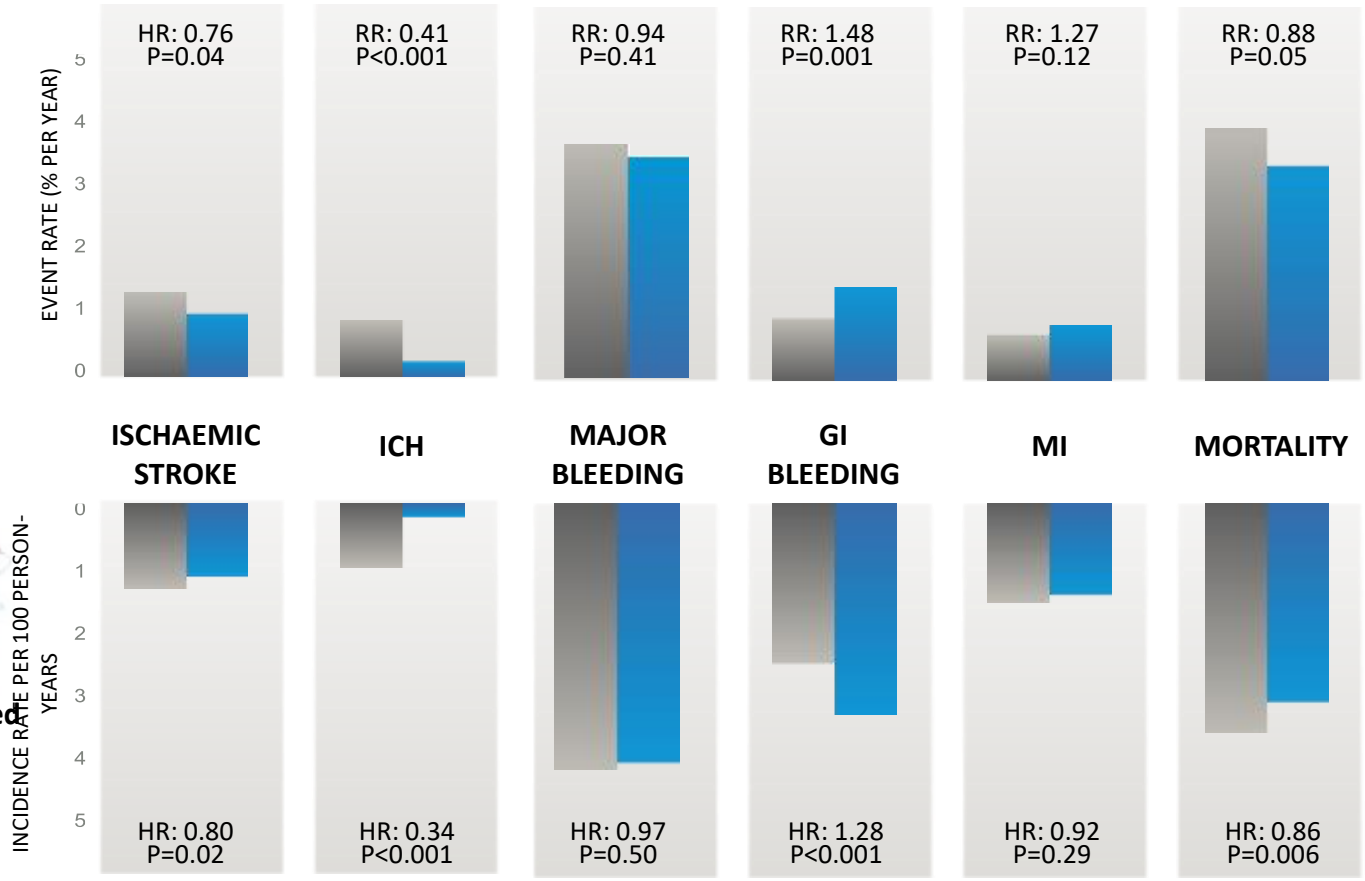


Medicare

>134 000 patients

Warfarin

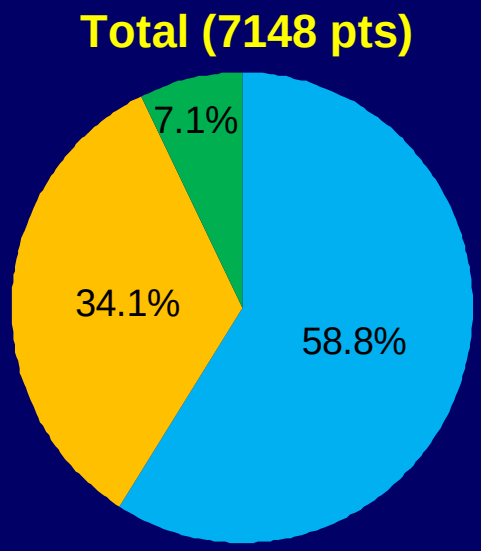
D150 & D75 BID combined



In the USA, the licensed doses for Pradaxa® are: 150 mg BID and 75 mg BID for the prevention of stroke and systemic embolism in adult patients with NVAF. In the EU, dabigatran 110 mg BID is indicated for certain patients, and was shown to be as effective vs VKA for prevention of stroke/SE. RE-LY® was a PROBE (prospective, randomized, open-label with blinded endpoint evaluation) study

*Primary findings for dabigatran are based on analysis of both 75 mg and 150 mg together without stratification by dose. **1.** Graham et al. Circulation 2015; **2.** Connolly et al. NEJM 2009; **3.** Connolly et al. NEJM 2010; **4.** Pradaxa®· EU SPC, 2015; **5.** Connolly S et al. NEJM 2014

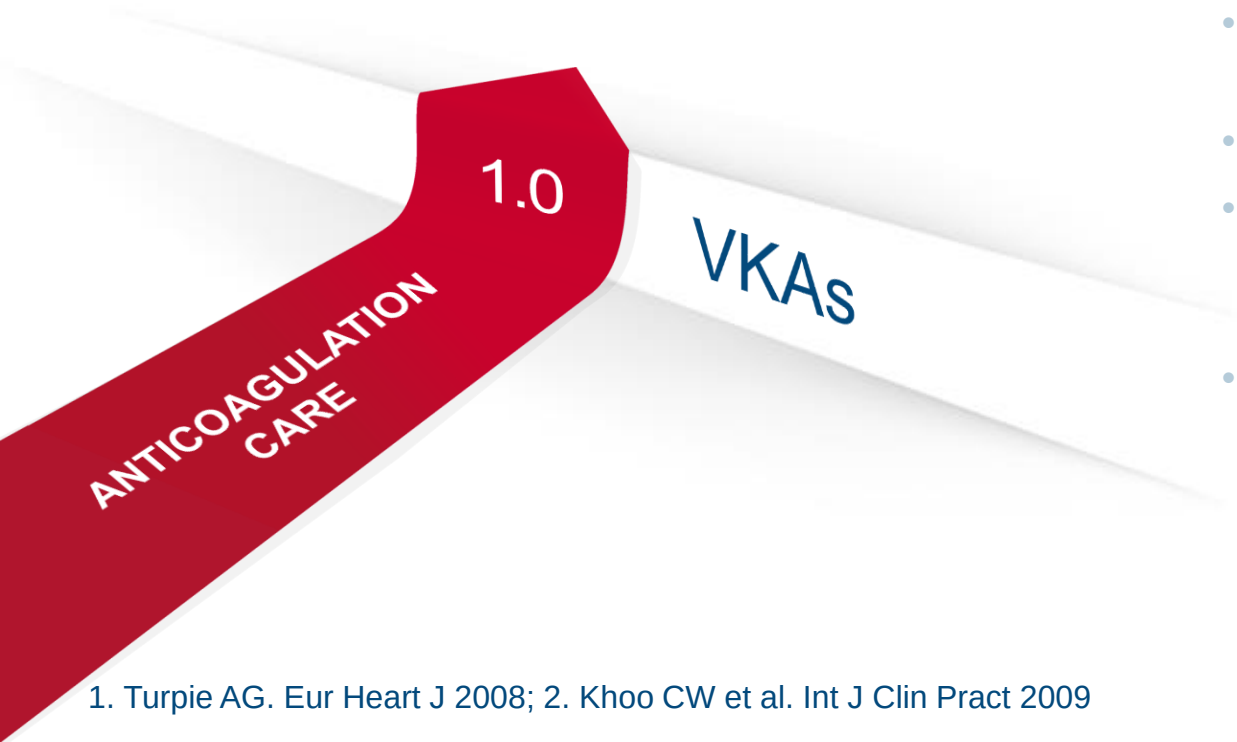
Antithrombotic Treatment (7.148 pts) and ATT by Type of AF (evaluated in 6.910 pts)



OAC
Other ATT
None

1.0 The first oral anticoagulants

VKAs offered much-needed protection from thromboembolic events



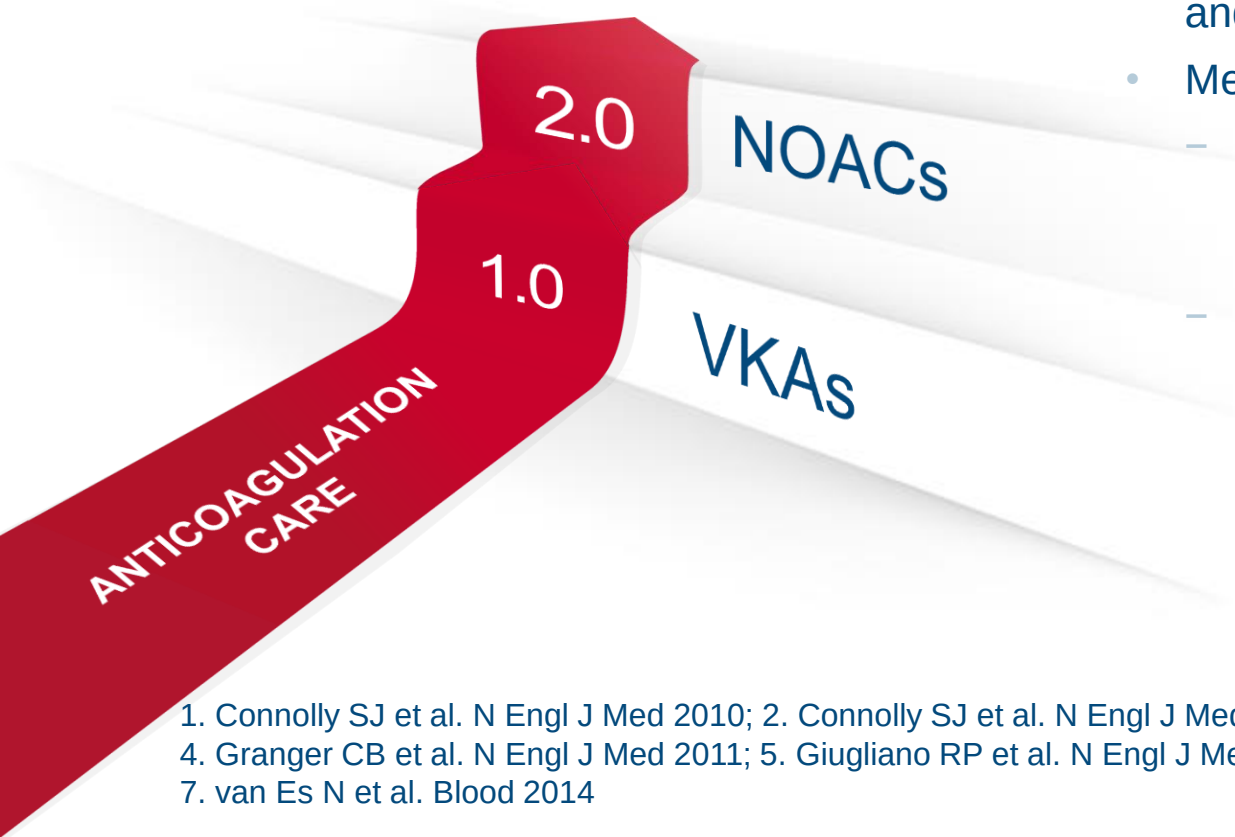
However, VKAs are associated with major limitations:[1,2]

- Narrow therapeutic window
- Variable and unpredictable PK/PD
- Drug and food interactions
- Need for regular anticoagulation monitoring and dose adjustments
- Slow onset and offset of action

1. Turpie AG. Eur Heart J 2008; 2. Khoo CW et al. Int J Clin Pract 2009

2.0 50 years later

NOACs address many of the limitations of traditional therapies

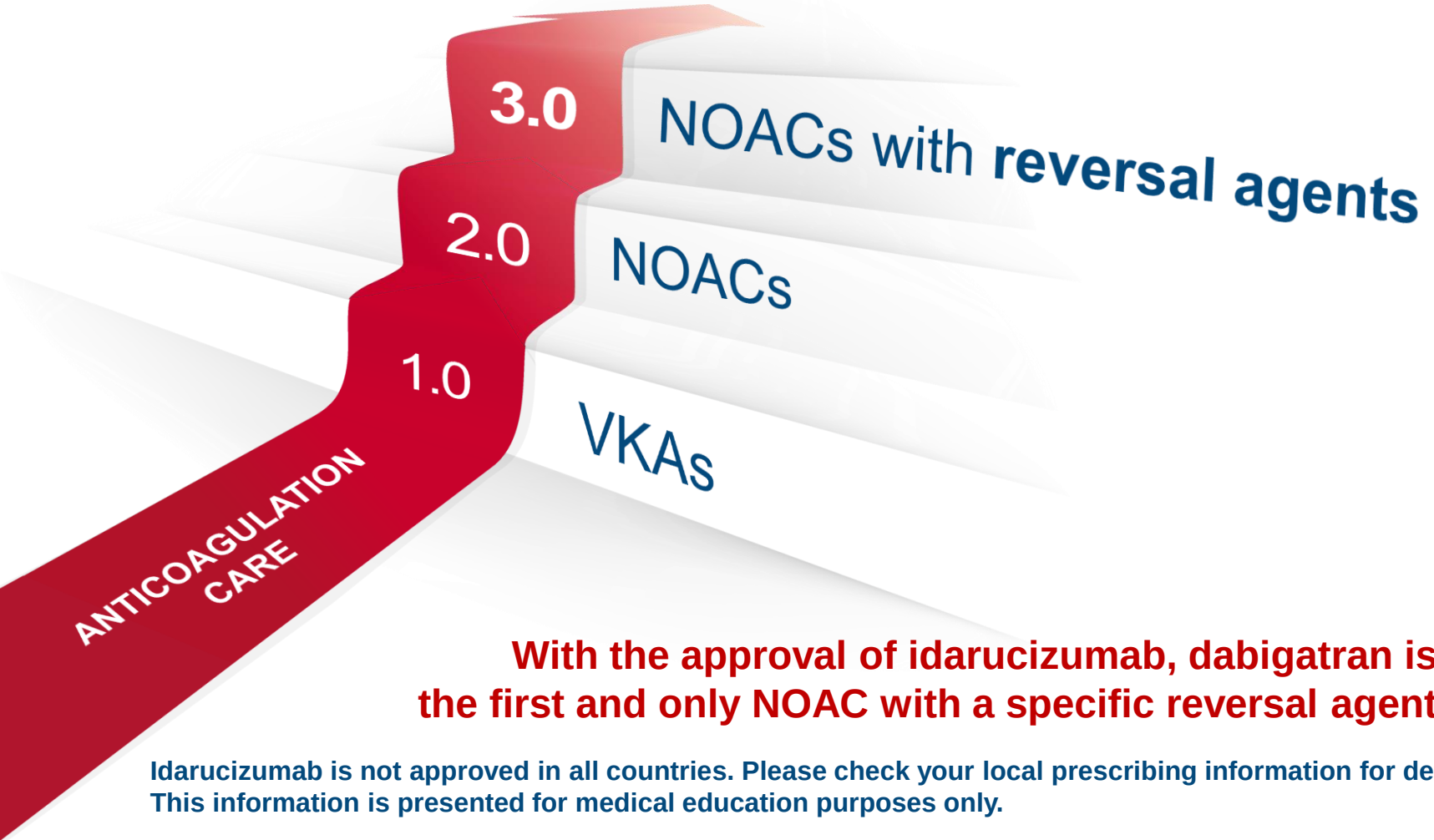


- In clinical trials, NOACs have demonstrated favourable safety and efficacy profiles vs warfarin[1–5]
- Meta-analysis of trial data shows:
  - Reduced risk of stroke or SE, major bleeding, and ICH in SPAF[6]
  - Similar efficacy and reduced risk of major bleeding in acute VTE treatment[7]

1. Connolly SJ et al. N Engl J Med 2010; 2. Connolly SJ et al. N Engl J Med 2014; 3. Patel MR et al. N Engl J Med 2011; 4. Granger CB et al. N Engl J Med 2011; 5. Giugliano RP et al. N Engl J Med 2013; 6. Ruff CT et al. Lancet 2013; 7. van Es N et al. Blood 2014

3.0 Innovation

Specific reversal agents mark the next phase in anticoagulation care



With the approval of idarucizumab, dabigatran is the first and only NOAC with a specific reversal agent

Idarucizumab is not approved in all countries. Please check your local prescribing information for details. This information is presented for medical education purposes only.