MultiCare
FIRST EDITION

ANTICOAGULANTI
Trattamento interventistico

GIANLUCA BOTTO
FESC, FEHRA, FAIAC
UO ELETTROFISIOLOGIA

Regione Lombardia
ASST Rhodense

Presenter Disclosure Information

- Research support:
  Boston Scientific, Medtronic; St., Bayer Healthcare, Gilead, Sanofi
- Advisory Board:
  Biotronik, Medtronic; St. Jude Medical, MSD, Sanofi, Bayer Healthcare, Boehringer, BMS, Pfizer, Daiichi/Sankyo
- Speaker Fees:
  Boston Scientific, Medtronic, St. Jude Medical, Sorin Group, Bayer Healthcare, Boehringer, BMS, Cardiome, Meda, MSD, Pfizer, Sanofi, Daiichi/Sankyo

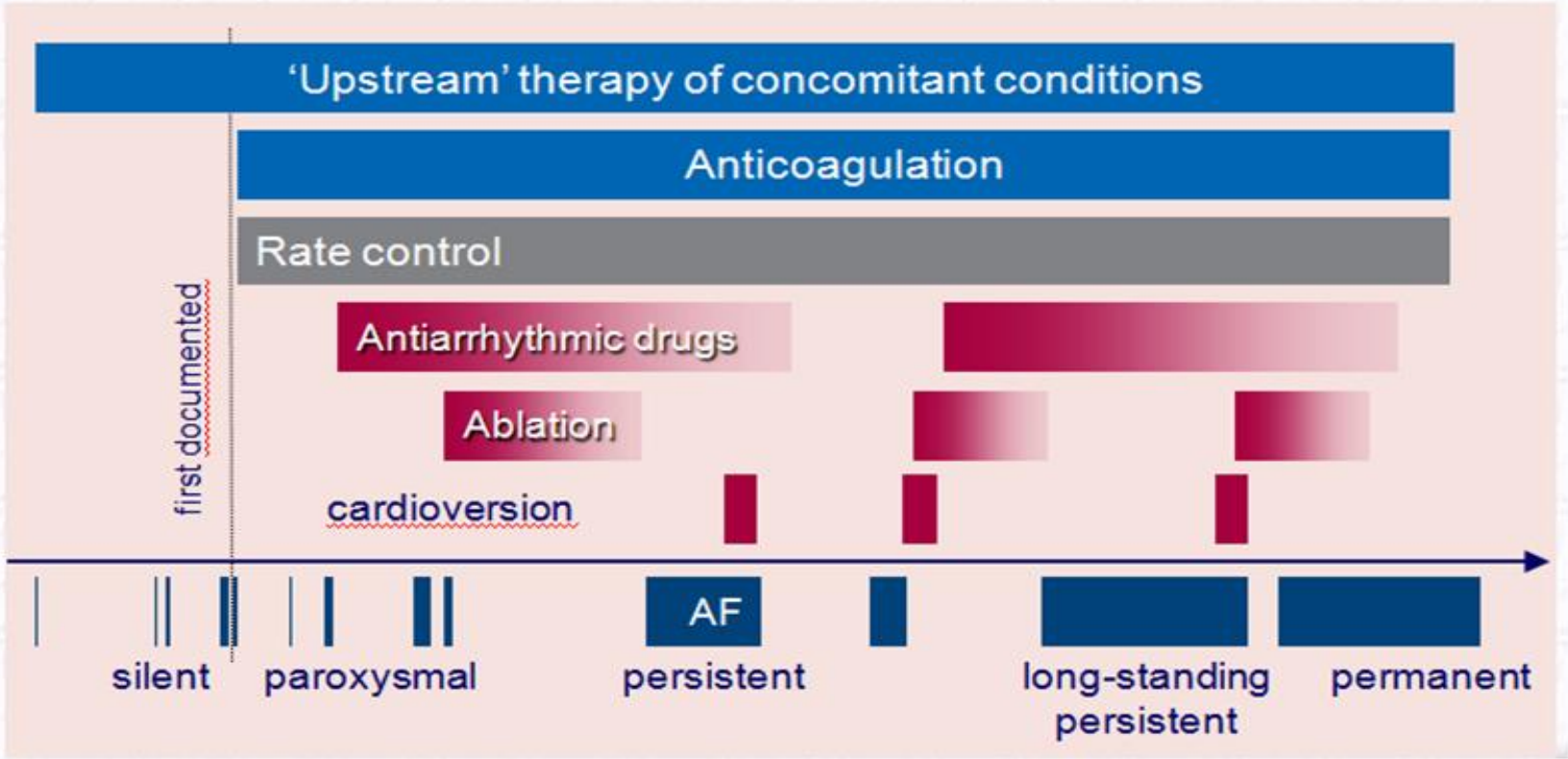
NOACs vs VKAs

Real-World Data & RCTs

Outcome	Real-world data: 10 propensity-score matched studies 494.964 pts		Randomized trials: 4 randomized controlled trials 72.963 pts	
	Risk ratio	95% CI	Risk ratio	95% CI
Major bleeding	**0.91**	0.79–1.05	**0.85**	0.73–1.00
MI	**0.81**	0.60–1.08	**0.95**	0.80–1.14
Stroke or embolism	**0.88**	0.83–0.94	**0.79**	0.72–0.87
Death	**0.71**	0.58–0.87	**0.90**	0.86–0.96

Li G. Eur J Epidemiol 2016; 31: 541-61

Natural time course of AF



AF = atrial fibrillation

European Heart Journal (2010) 31, 2369-2429

Limitations of VKA Therapy

VKA therapy has several limitations that make it difficult to use in practice

- Unpredictable response
- Narrow therapeutic window (INR range 2.0–3.0)
- Slow onset/ offset of action
- Numerous food–drug interactions
- Numerous drug–drug interactions
- Warfarin resistance

Routine coagulation monitoring → Frequent dose adjustments

Ansell J. *Chest* 2008; 133; 160S-198S.
Umer Ushman MH. *J Interv Card Electrophysiol* 2008; 22: 129-137.
Nutescu EA. *Cardiol Clin* 2008; 26: 169-187.

Characteristics of NOACs

Comparison With Warfarin

	WARFARIN	DABIGATRAN	RIVAROXABAN	APIXABAN	EDOXABAN
Target	Vitamin K-dep. clotting factors II, VII, IX,and X	Thrombin	Factor Xa	Factor Xa	Factor Xa
Bioavailability (%)	>95	~6	>80 (with food)	>50	>60 (85 with food)
Intake with food recommended ?	NO	NO	Mandatory	NO	No official recommendation
Absorption with H2B/PPI ?	NO	-12%-30%	NO	NO	NO
Time to peak activity (hs)	72-96	1-3	2,5-4	3-4	1-2
Half life (hs)	40	12-17	5-9 (young healty) 11-13 (elderly)	8-15	9-11
Dosing frequency	OD	BID	OD	BID	OD
Interaction with drugs	Numerous drugs including substrates of CYP2C9, CYP3A4, CYP1A2	Strong P-gp inhibitors and inducers	Strong CYP3A4 inducers, strong inhibitors of both CYP3A4 and P-gp	Strong inhibitors and inducers of both CYP3A4 and P-gp	Strong P-gp inhibitors and inducers
Interaction with food	YES	NO	NO	NO	NO
Renal elim (%)	<1	~80	~33 (66)	~27	~50

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CARDIOVERSIONE ELETTRICA DELLA FIBRILLAZIONE ATRIALE

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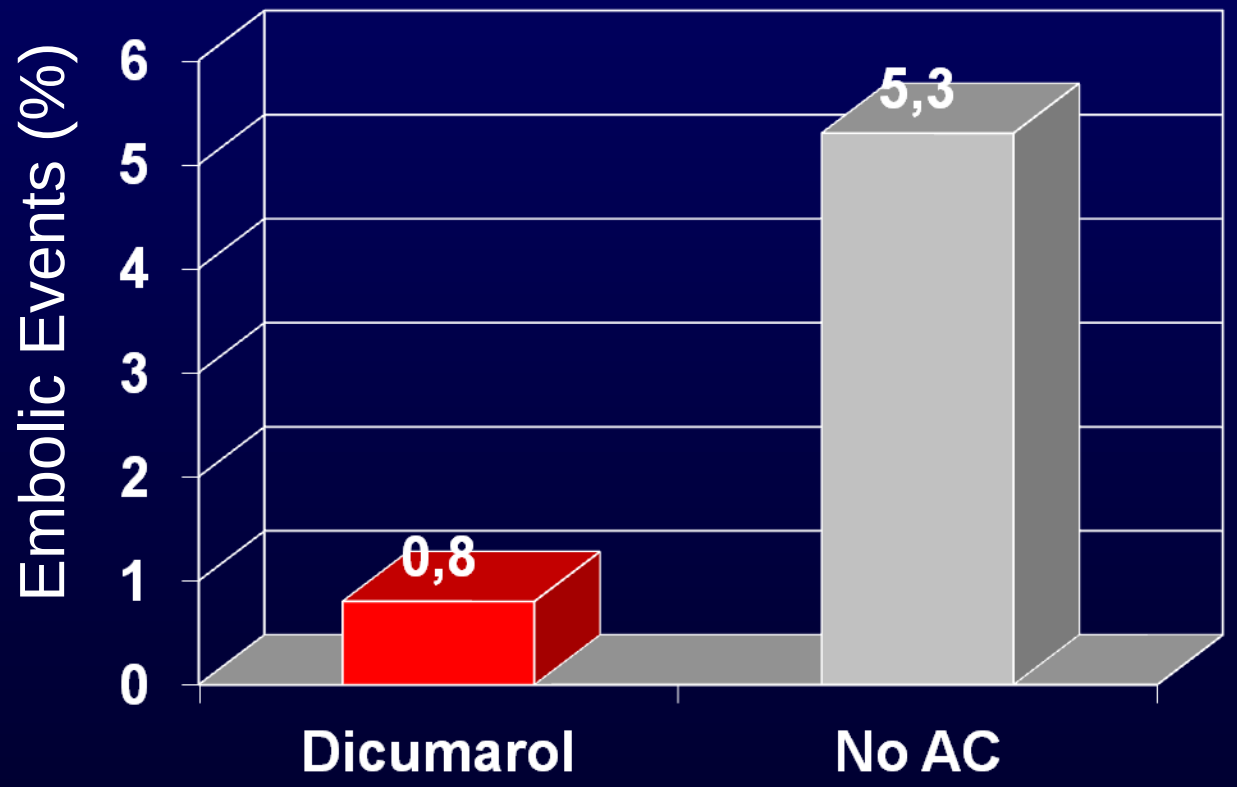
The American Journal of Cardiology

The Efficacy of Anticoagulant Therapy in Preventing Embolism Related to D.C. Electrical Cardioversion of Atrial Fibrillation

CJ. Bjerkelund, MD, OM Orning, MD



VKA reduces the peri-procedural embolic events b/ween 0.5 and 1.6%

- *Weinberg et al. AJC 1989*
- *Arnold et al. JACC 1992*
- *Stellbrink et al. Circul 2004*

Am J Cardiol 1969; 23: 208-16

European Heart Journal Advance Access published September 2, 2014

European Heart Journal
doi:10.1093/eurheartj/ehu367

FASTTRACK
ESC HOT LINE BARCELONA

Rivaroxaban vs. vitamin K antagonists for cardioversion in atrial fibrillation

Riccardo Cappato[1†], Michael D. Ezekowitz[2†*], Allan L. Klein[3], A. John Camm[4], Chang-Sheng Ma[5], Jean-Yves Le Heuzey[6], Mario Talajic[7], Maurício Scanavacca[8], Panos E. Vardas[9], Paulus Kirchhof[10,11,12], Melanie Hemmrich[13], Vivian Lanius[14], Isabelle Ling Meng[13], Peter Wildgoose[15], Martin van Eickels[13], and Stefan H. Hohnloser[16], on behalf of the X-VeRT Investigators

Aims X-VeRT is the first prospective randomized trial of a novel oral anticoagulant in patients with atrial fibrillation undergoing elective cardioversion.

Methods and results We assigned 1504 patients to rivaroxaban (20 mg once daily, 15 mg if creatinine clearance was between 30 and 49 mL/min) or dose-adjusted vitamin K antagonists (VKAs) in a 2:1 ratio. Investigators selected either an early (target period of 1–5 days after randomization) or delayed (3–8 weeks) cardioversion strategy. The primary efficacy outcome was the composite of stroke, transient ischaemic attack, peripheral embolism, myocardial infarction, and cardiovascular death. The primary safety outcome was major bleeding. The primary efficacy outcome occurred in 5 (two strokes) of 978 patients (0.51%) in the rivaroxaban group and in 5 (two strokes) of 492 patients (1.02%) in the VKA group [risk ratio 0.50; 95% confidence interval (CI) 0.15–1.73]. In the rivaroxaban group, four patients experienced primary efficacy events following early cardioversion (0.71%) and one following delayed cardioversion (0.24%). In the VKA group, three patients had primary efficacy events following early cardioversion (1.08%) and two following delayed cardioversion (0.93%). Rivaroxaban was associated with a significantly shorter time to cardioversion compared with VKAs ($P < 0.001$). Major bleeding occurred in six patients (0.6%) in the rivaroxaban group and four patients (0.8%) in the VKA group (risk ratio 0.76; 95% CI 0.21–2.67).

Conclusion Oral rivaroxaban appears to be an effective and safe alternative to VKAs and may allow prompt cardioversion.

X-VeRT

Objective & Outcomes

- Objective

  explore efficacy and safety of once-daily rivaroxaban (20 mg) for the prevention of CV events in pts with NV-AF scheduled for elective cardioversion compared with dose-adjusted VKAs

- Primary Efficacy Outcome

  composite of

  - stroke and TIA,
  - non-CNS SE,
  - MI and
  - CV death

- Primary Safety Outcome

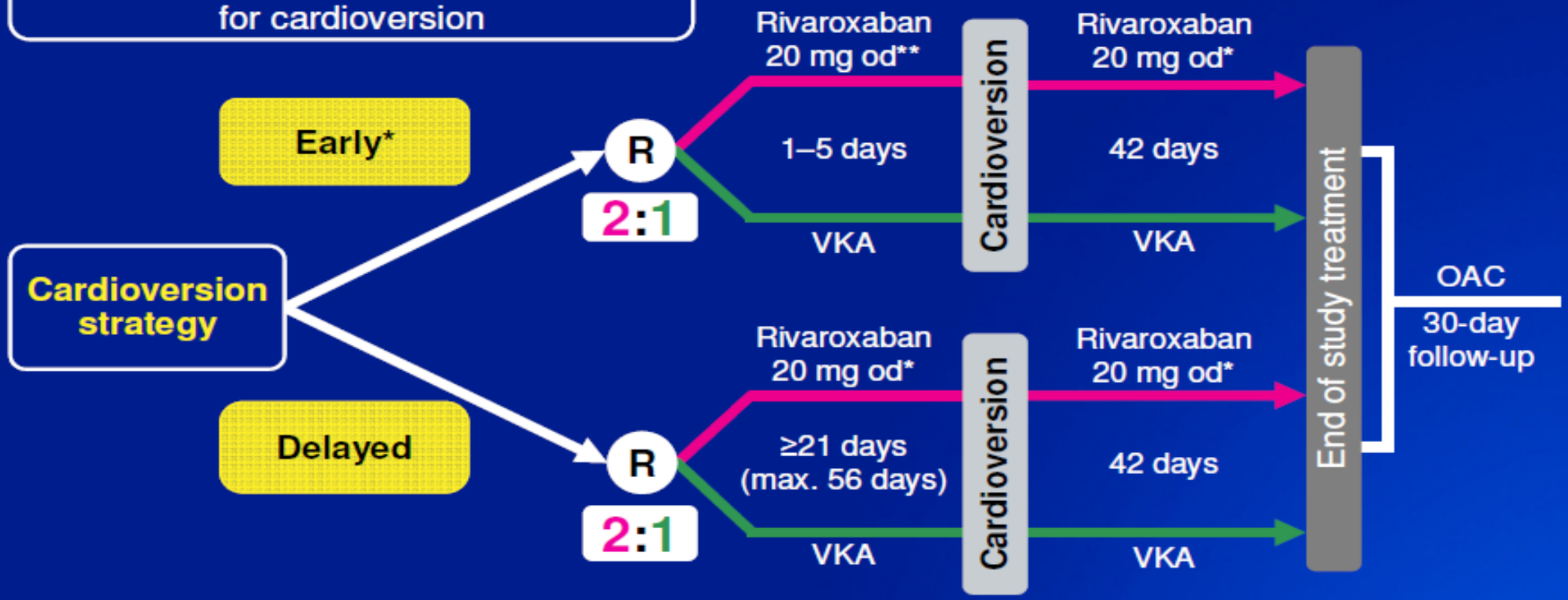
  major bleeding (ISTH definition)

- Enrollment oct 2012 – feb 2014

Design: randomized, open-label, parallel-group, active-controlled multicentre study

Inclusion criteria:
Age ≥18 years, non-valvular AF lasting >48 h or unknown duration, scheduled for cardioversion

1504 pts from 141 centres / 16 countries



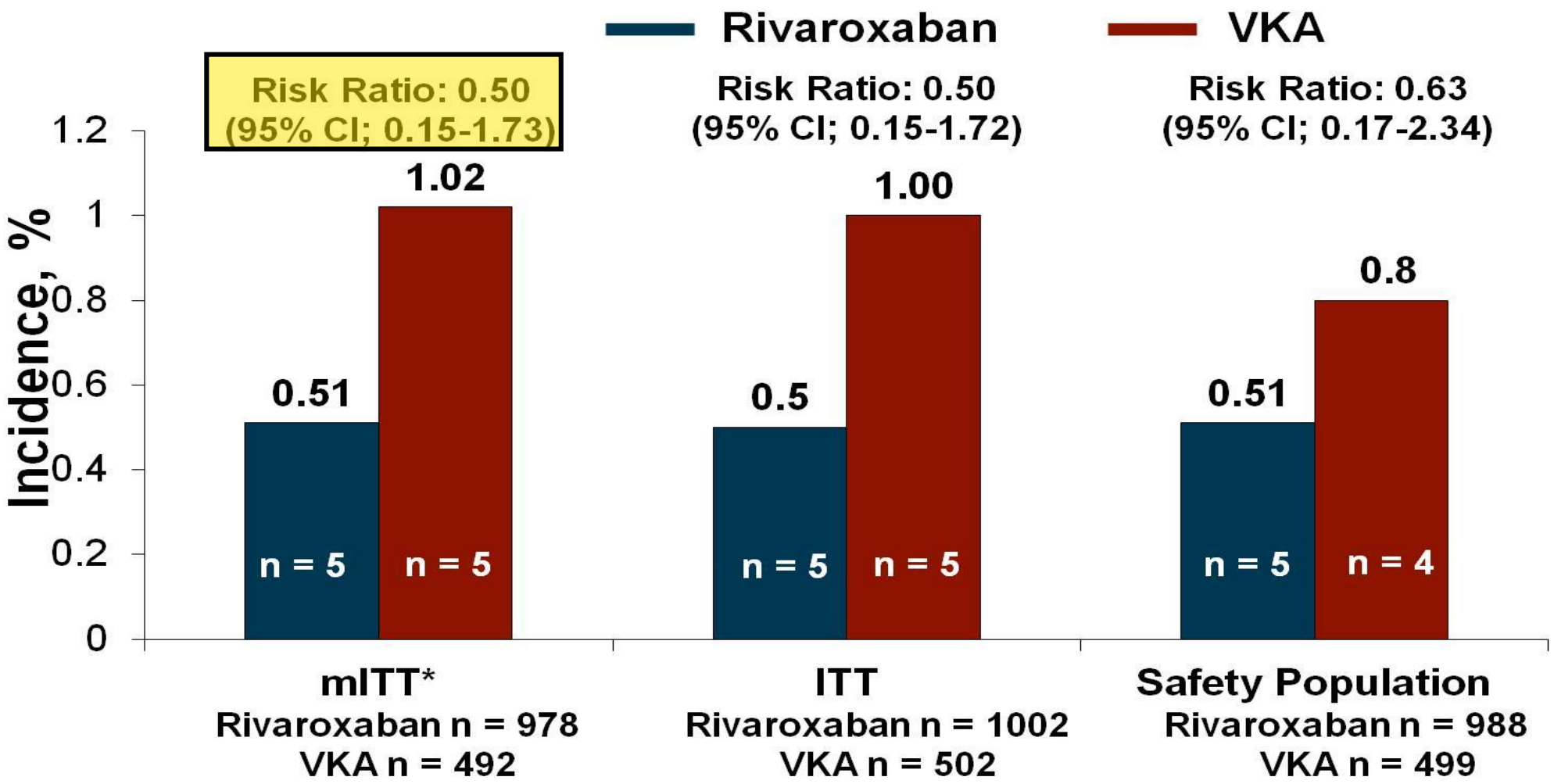
* Protocol recommended only if adequate anticoagulation or immediate TEE;
**15 mg if CrCl 30–49 ml/min; VKA with INR 2.0–3.0

Ezekowitz *et al*, 2014; www.clinicaltrials.gov. NCT01674647

Cappato R. Eur Heart J 2014

X-VeRT
Primary Efficacy

Primary outcome events were experienced in 10/1470 (0.68%; 95%CI 0.36-1.21)

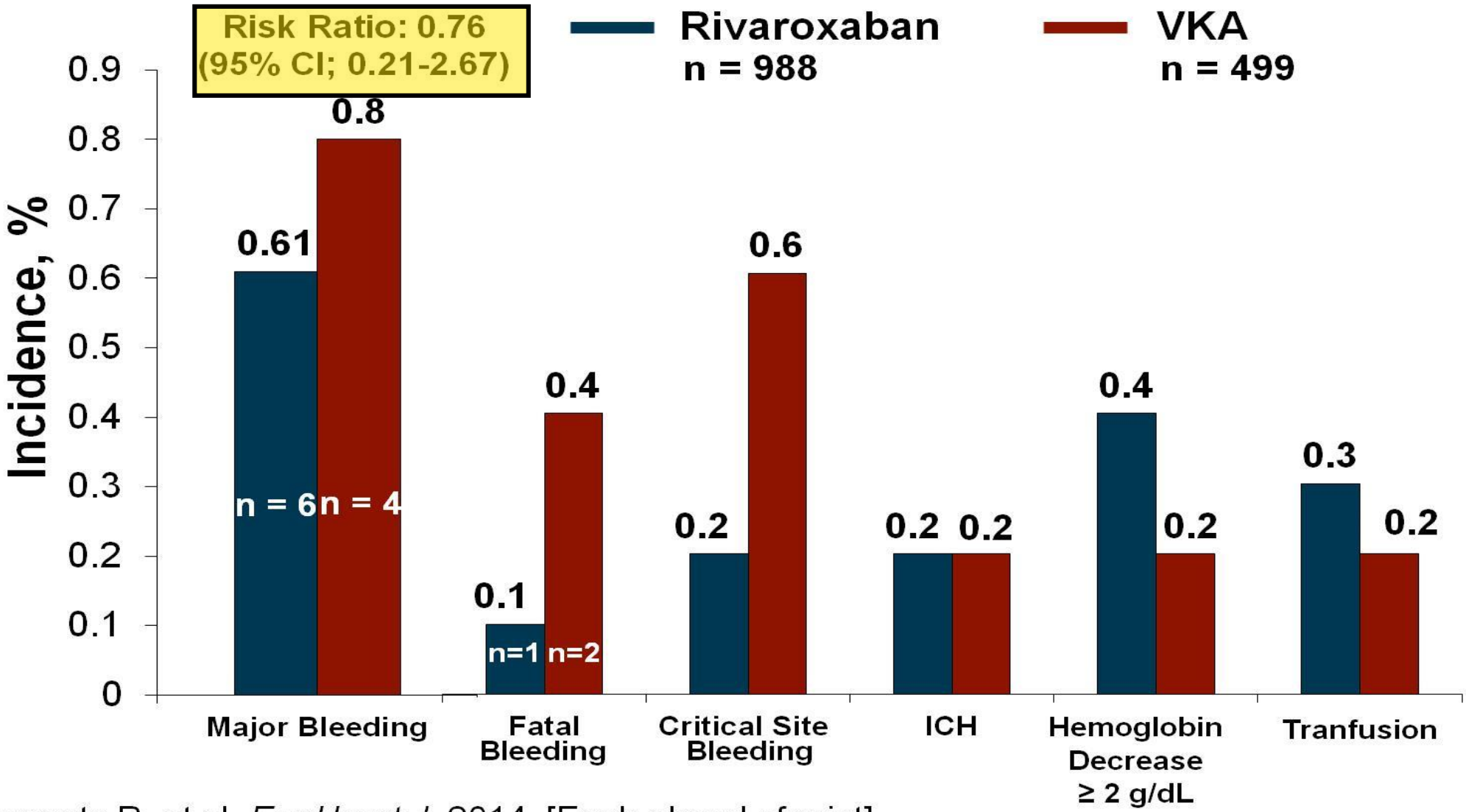


*Excluded patients from the ITT group who were found to have atrial thrombi on TEE.

Cappato R, et al. *Eur Heart J.* 2014. [Epub ahead of print]

X-VeRT
Safety Outcomes

Major bleeding occurred in 6/988 (0.61%; 95%CI 0.66-1.27)

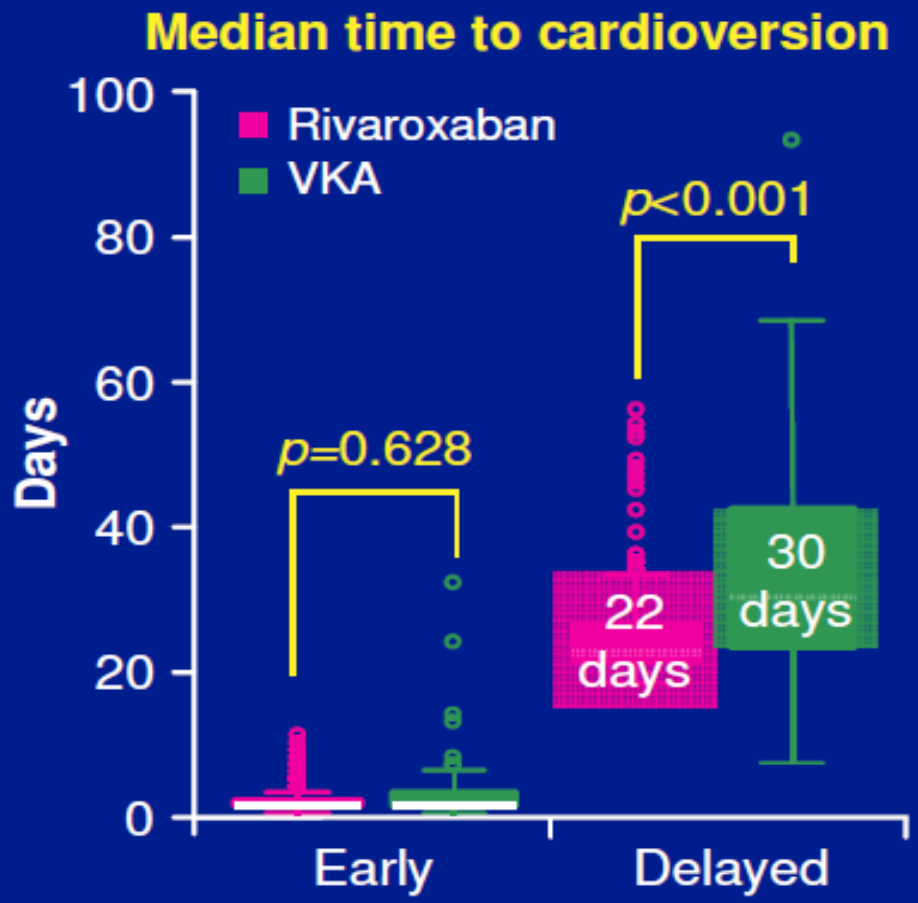


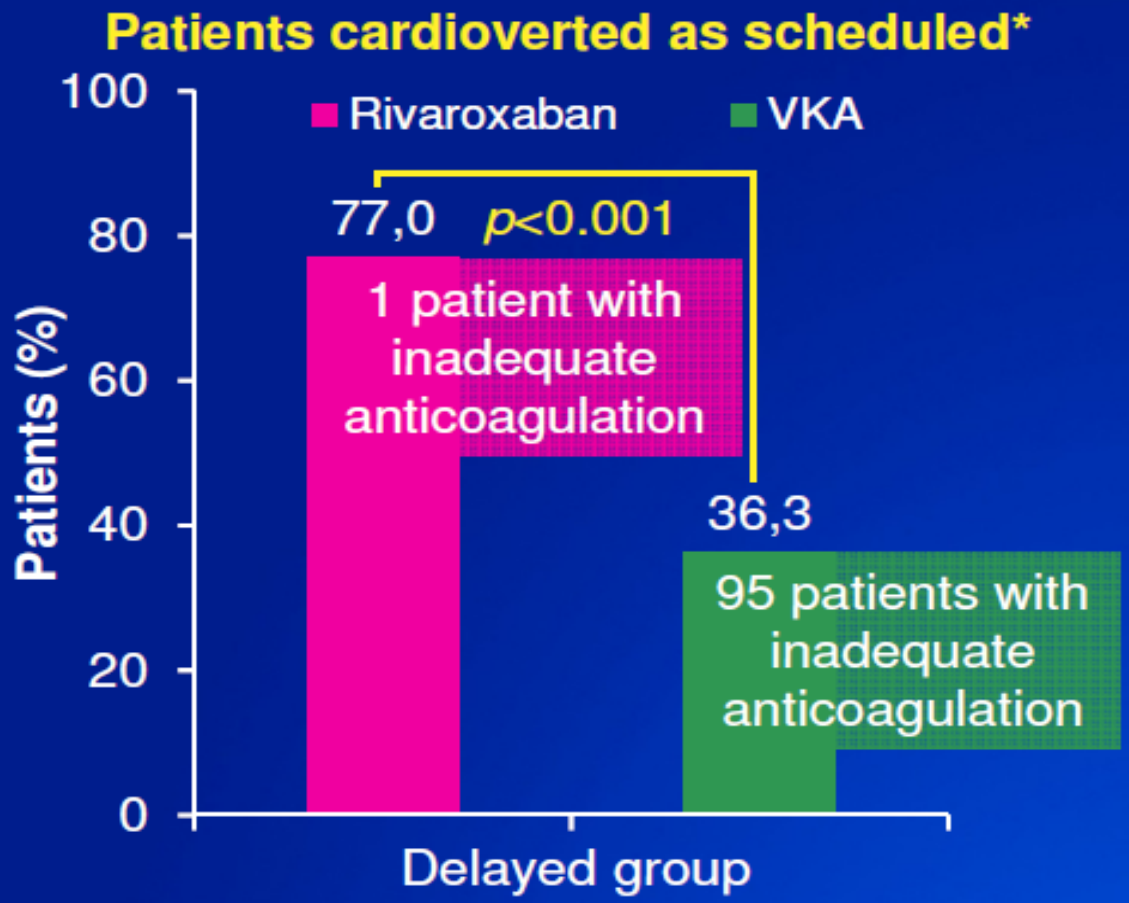
Cappato R, et al. *Eur Heart J.* 2014. [Epub ahead of print]

X-VeRT

Cappato R. Eur Heart J 2014

Time to cardioversion by cardioversion strategy





*Reason for not performing cardioversion as first scheduled from 21–25 days primarily due to inadequate anticoagulation (indicated by drug compliance <80% for rivaroxaban or weekly INRs outside the range of 2.0–3.0 for 3 consecutive weeks before cardioversion for VKA)

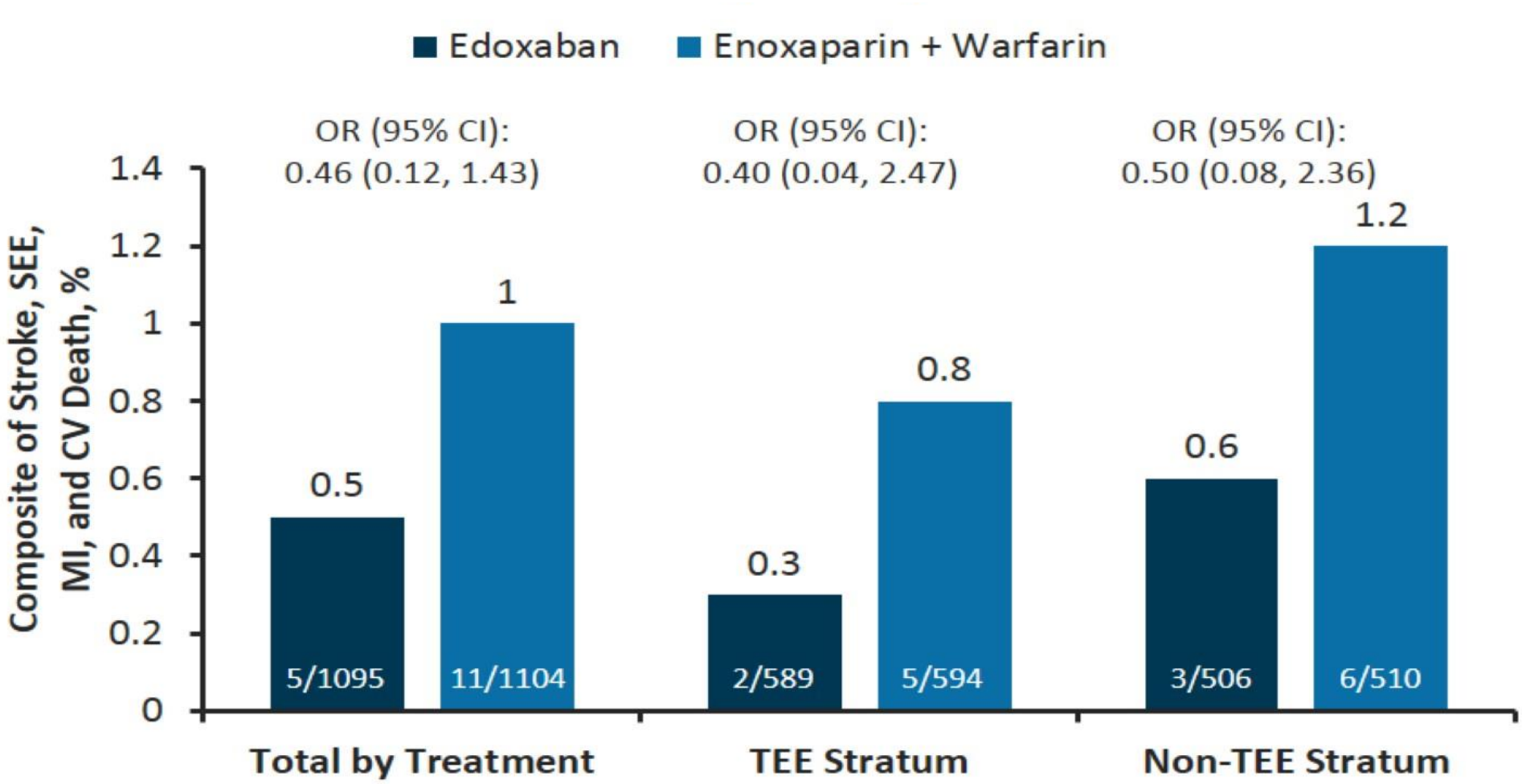
Procedure Cost Calculations Per Patient Based On Inputs

	Italy	
	Rivaroxaban	Warfarin
Drug cost for 63 days	€132[12]	€4[13]
INR monitoring (63 days)	N/A	€271
Cost of cardioversion	€676	€662
Additional booked cardioversion procedures per patient—when rescheduled on the scheduled day	0.172	0.477
Additional booked cardioversion procedures per patient—when rescheduled prior to the scheduled day	0.058	0.161
Cost of nurse specialist per reschedule[b]	N/A	N/A
Cost of rescheduling on the scheduled day	€116	€316
Cost of rescheduling prior to the scheduled day	N/A	N/A
Cost of additional waiting time for patients on warfarin	N/A	€35
Total procedure cost per patient	€924	€1289

ENSURE-AF

*Primary Efficacy**

**Stroke, SE, MI, CV death*



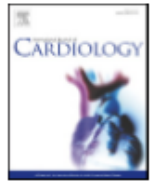
Goette A, et al. *Lancet.* 2016.

International Journal of Cardiology 185 (2015) 72–77

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard



2015
3+1 trials
3635 pts – 4517 CV

Efficacy and safety of direct oral anticoagulants in patients undergoing cardioversion for atrial fibrillation: A systematic review and meta-analysis of the literature ☆

Francesco Dentali [a,*], Giovanni Luca Botto [b], Monica Gianni [c], Pasquale Ambrosino [d], Matteo Nicola Dario Di Minno [e]

Clin Res Cardiol (2015) 104:582–590
DOI 10.1007/s00392-015-0821-8

ORIGINAL PAPER

2015
3+1 trials
3512 pts – 4471 CV

Non-vitamin K antagonist oral anticoagulants in the cardioversion of patients with atrial fibrillation: systematic review and meta-analysis

Daniel Caldeira · João Costa · Joaquim J. Ferreira · Gregory Y. H. Lip · Fausto J. Pinto

Am J Cardiovasc Drugs (2016) 16:33–41
DOI 10.1007/s40256-015-0136-1

SYSTEMATIC REVIEW

Outcomes After Cardioversion in Atrial Fibrillation Patients Treated with Non-Vitamin K Antagonist Oral Anticoagulants (NOACs): Insights from a Meta-Analysis

Parijat Sen[1] · Amartya Kundu[2] · Partha Sardar[3] · Saurav Chatterjee[4] · Ramez Nairooz[5] · Hossam Amin[6] · Wilbert S. Aronow[7]

2016
3+1 trials
3512 pts – 4257 CV

THE AMERICAN JOURNAL of MEDICINE®

2016
4+1 trials
3949 pts – 4900 CV

Efficacy and Safety of Non-Vitamin K Antagonist Oral Anticoagulants After Cardioversion for Nonvalvular Atrial Fibrillation

Giulia Renda, MD, PhD,[a] Marco Zimarino, MD, PhD,[a] Fabrizio Ricci, MD,[a] Jonathan P. Piccini, MD,[b] Michael D. Ezekowitz, MD, PhD,[c] Manesh R. Patel, MD, PhD,[b] Riccardo Cappato, MD,[d] Robert P. Giugliano, MD,[e] Raffaele De Caterina, MD, PhD[a]

NOACs for Cardioversion in Atrial Fibrillation

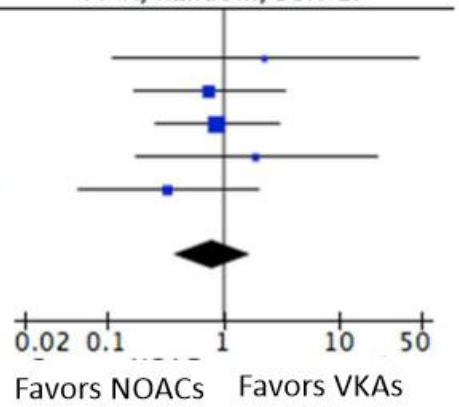
An Updated Meta-analysis

STROKE/SE

Study or Subgroup	NOACs Events	NOACs Total	WARFARIN Events	WARFARIN Total	Weight	Risk Ratio M-H, Random, 95% CI
ARISTOTLE	0	331	0	412		Not estimable
ENGAGE-AF	2	251	0	114	6.4%	2.28 [0.11, 47.15]
ENSURE-AF	3	1095	4	1104	26.1%	0.76 [0.17, 3.37]
RE-LY	7	1319	4	664	38.9%	0.88 [0.26, 3.00]
ROCKET-AF	2	138	1	132	10.2%	1.91 [0.18, 20.85]
X-VeRT	2	1002	3	502	18.3%	0.33 [0.06, 1.99]
Total (95% CI)		**4136**		**2928**	**100.0%**	**0.82 [0.38, 1.75]**
Total events	16		12			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.92$, df = 4 (P = 0.75); $I^2 = 0\%$

Test for overall effect: Z = 0.52 (P = 0.60)

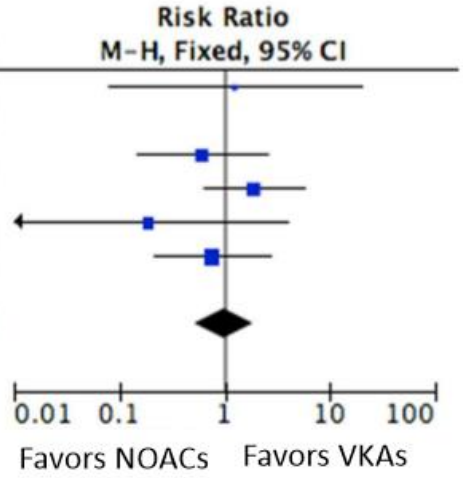


MAJOR BLEEDING

Study or Subgroup	NOACs Events	NOACs Total	VKAs Events	VKAs Total	Weight	Risk Ratio M-H, Fixed, 95% CI
ARISTOTLE	1	331	1	412	4.7%	1.24 [0.08, 19.82]
ENGAGE-AF	0	251	0	114		Not estimable
ENSURE-AF	3	1067	5	1082	26.1%	0.61 [0.15, 2.54]
RE-LY	15	1319	4	664	27.9%	1.89 [0.63, 5.67]
ROCKET-AF	0	138	2	132	13.4%	0.19 [0.01, 3.95]
X-VeRT	6	988	4	499	27.9%	0.76 [0.21, 2.67]
Total (95% CI)		**4094**		**2903**	**100.0%**	**0.98 [0.51, 1.87]**
Total events	25		16			

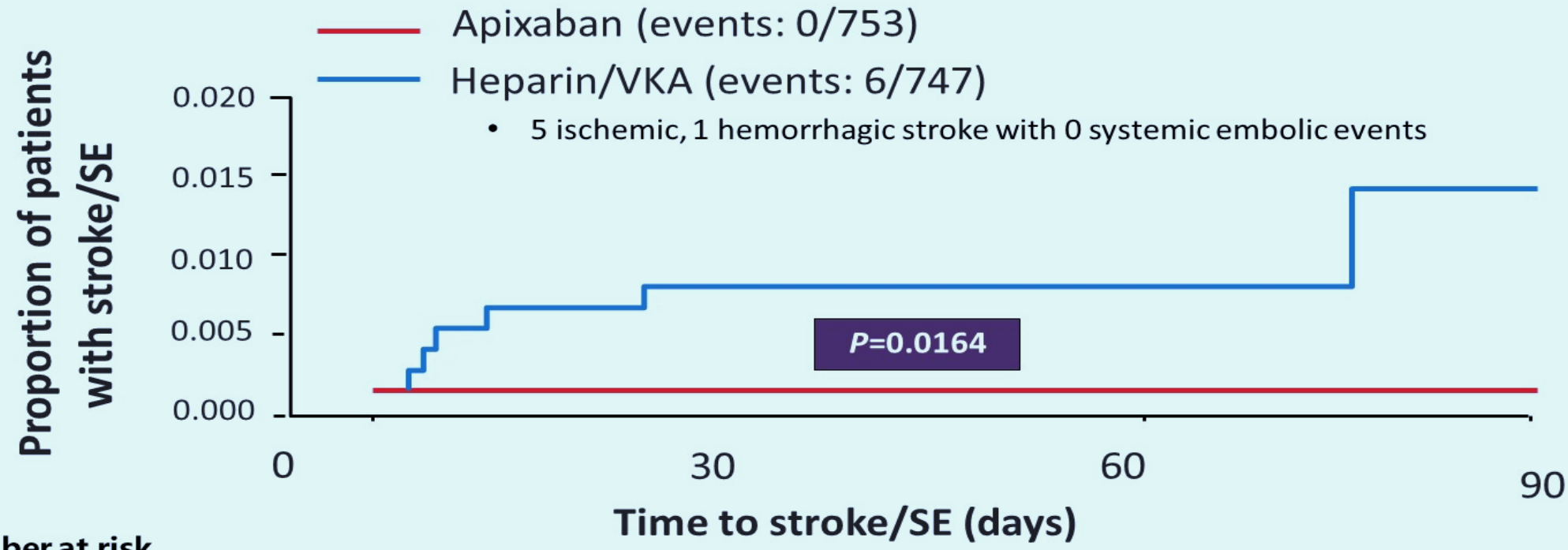
Heterogeneity: $Chi^2 = 3.10$, df = 4 (P = 0.54); $I^2 = 0\%$

Test for overall effect: Z = 0.06 (P = 0.95)



Renda G., De Caterina R.
Am J Med 2016

Stroke/Systemic Embolic Outcomes



Number at risk				
Apixaban	752	614	199	55
Heparin/VKA	747	655	231	88

One patient's adjudicated stroke date was one day prior to randomization; thus at Day 0, only 1499 were at risk for stroke. No patients had SE. ITT population. SE = systemic embolism

Ezekowitz M, ESC 2017

EMANATE Safety Outcomes

Safety Population: N=1456*

*Randomized and received ≥ 1 dose of study medication (by treatment received).

	Apixaban Total (n=735)	Apixaban Loading Dose (n=342)	Hep/VKA Total (n=721)
Major bleeds	3	(1)	6
Clinically Relevant Non-Major bleeds	11	(4)	13

In pts randomized to apixaban, cardioversion could be performed 2 hours after a loading dose of 10 mg

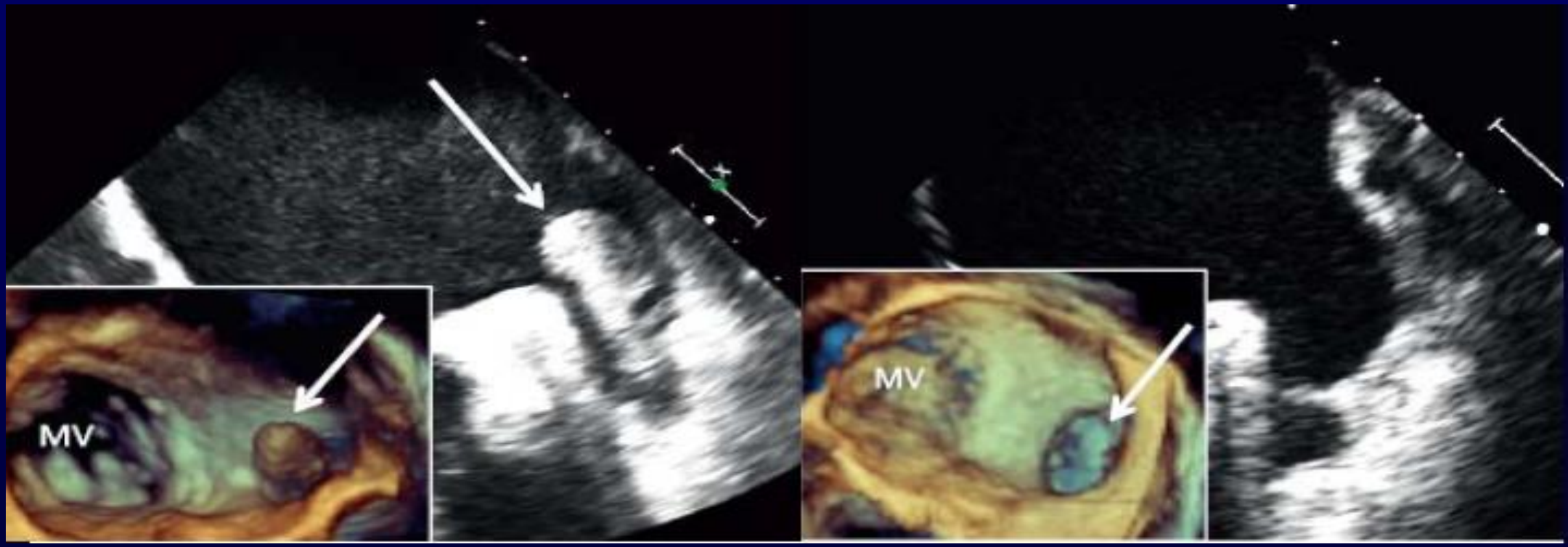
Ezekowitz M, ESC 2017

NOACs

TEE or No TEE

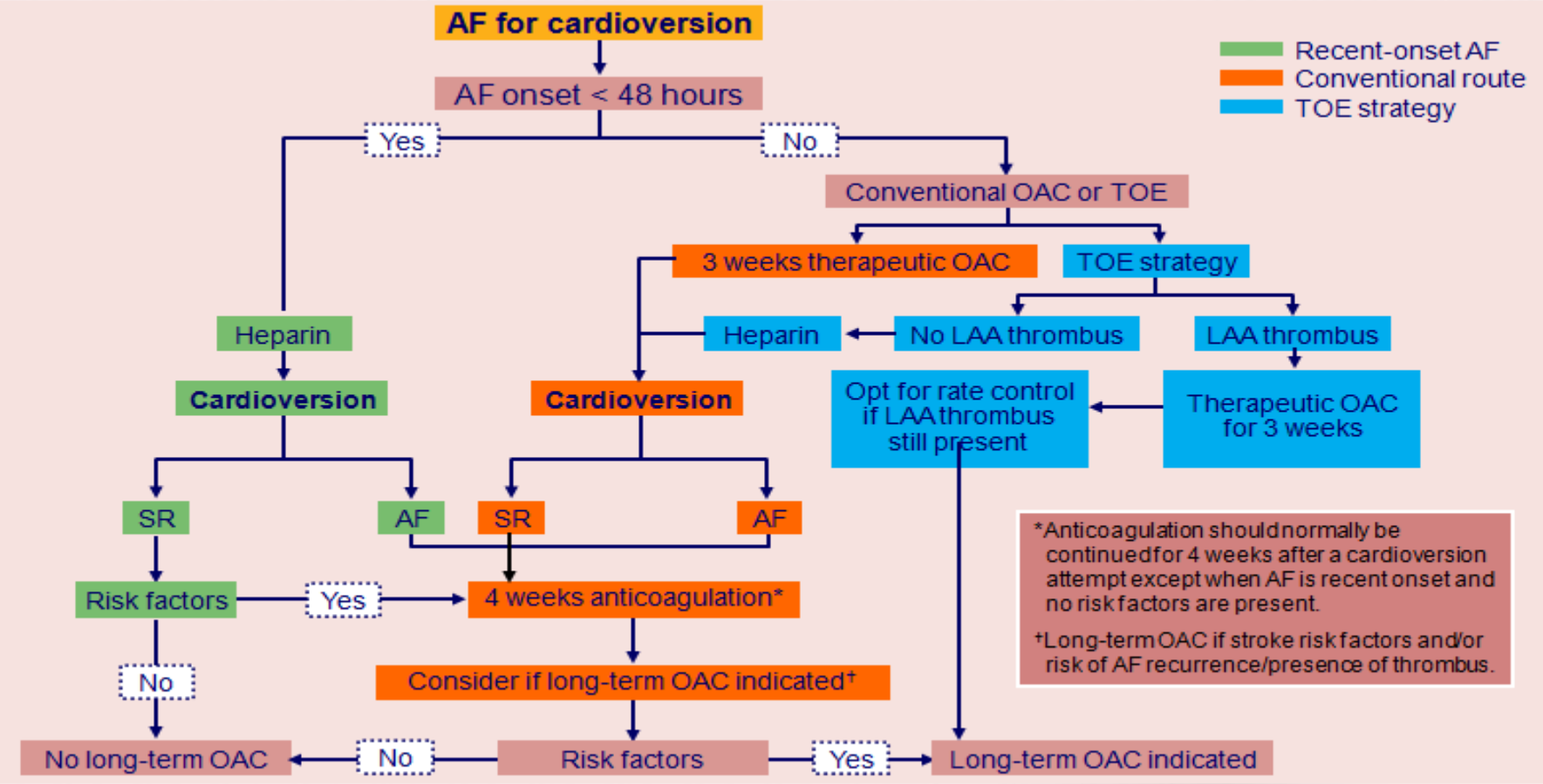
This is the Dilemma

TEE Should Be Performed To Rule Out Left Atrial Thrombi



Klein AL. N Engl J Med 2001; 344: 1411-1420.

Cardioversion, TOE and anticoagulation



AF = atrial fibrillation; DCC = direct current cardioversion; LA = left atrium; LAA = left atrial appendage; OAC = oral anticoagulant; SR= sinus rhythm; TOE= transoesophageal echocardiography.

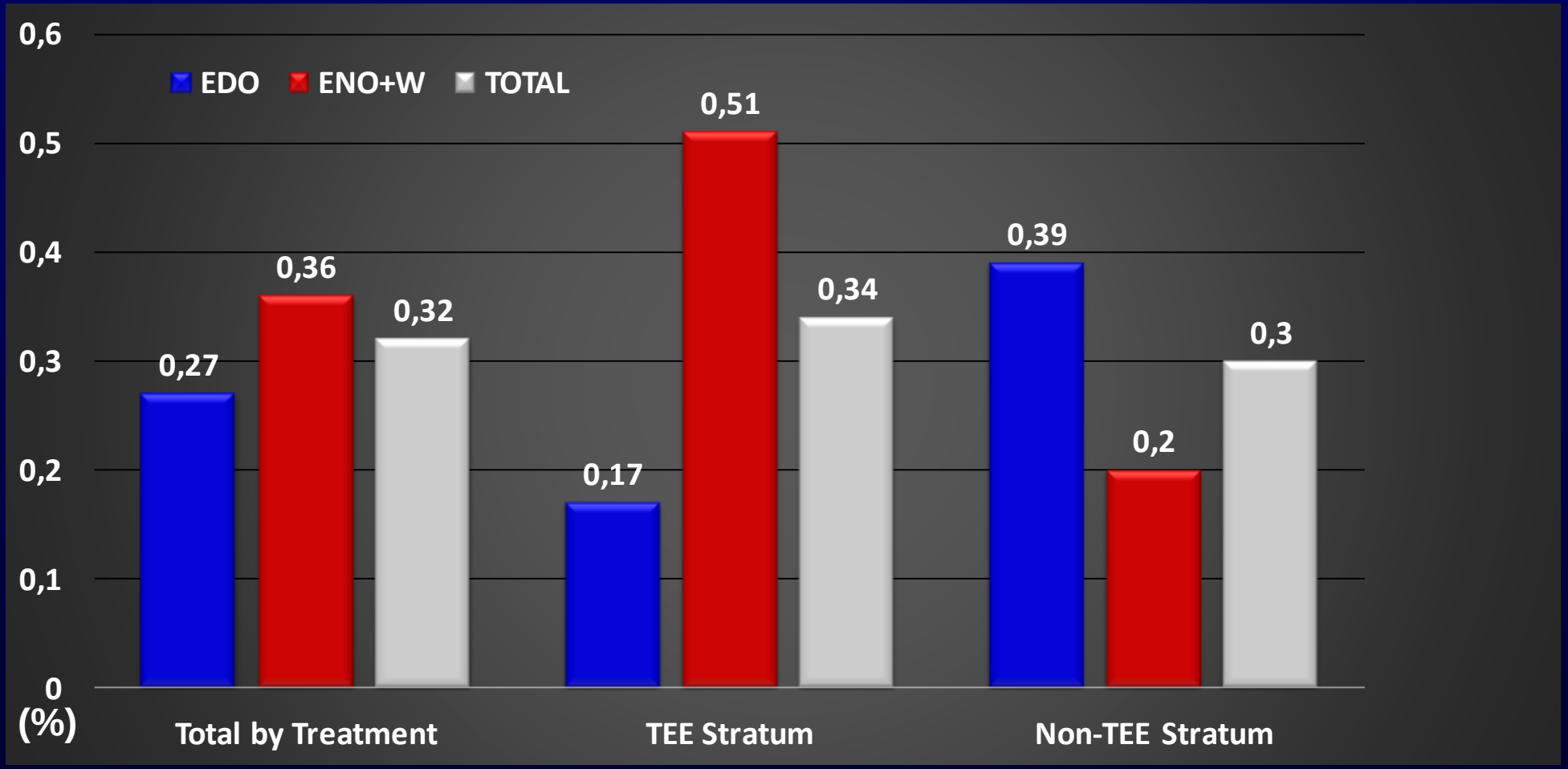
www.escardio.org/guidelines

European Heart Journal (2010) 31, 2369-2429

EUROPEAN SOCIETY OF CARDIOLOGY®

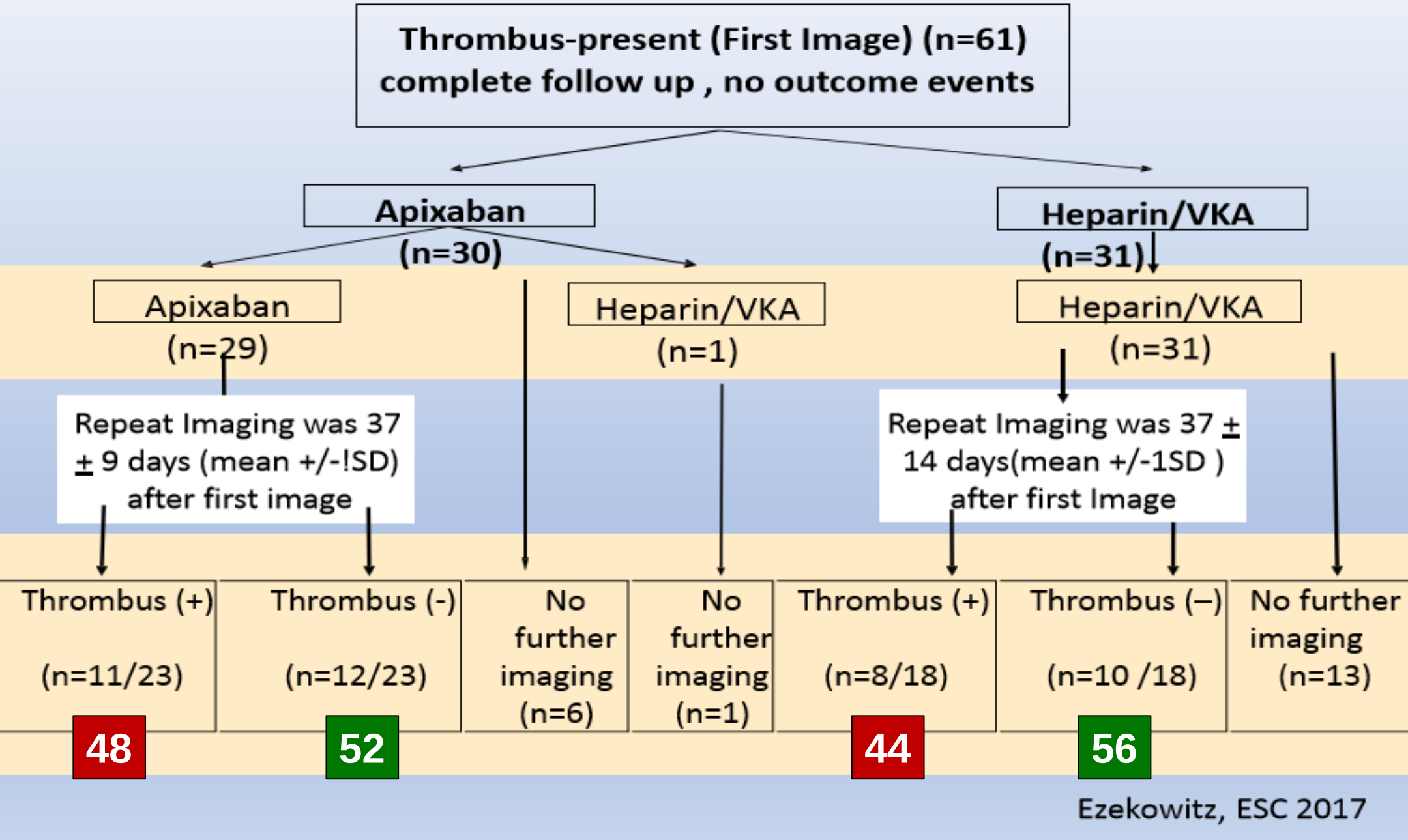
ENSURE-AF

Stroke + Systemic Embolism only



Goette A. Lancet 2016: 388: 1995-2003 (modif)

Image-Guided Strategy (n=840)



Ezekowitz, ESC 2017

NOAC Use in AF Pts Undergoing CV

- CV is a common procedure often performed by cardiologist or ED physicians
  - the requirement of OAC peri-CV pertain to both electrical and pharmacological CV
- NOACs are reasonable alternatives to Warfarin in pts undergoimg CV
- When considering CV in a NV-AF pts taking NOACs is mandatory to assess pts compliance
  - there is no coagulation assay available for NOCAs that provides information on anticoagulation intensity
- If NOACs compliance can be reliably confirmed, CV should be safe.
- Consider TEE as first option if doubt about compliance

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ABLAZIONE TRANSCATETERE DELLA FIBRILLAZIONE ATRIALE

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Risk of AF Ablation Procedure

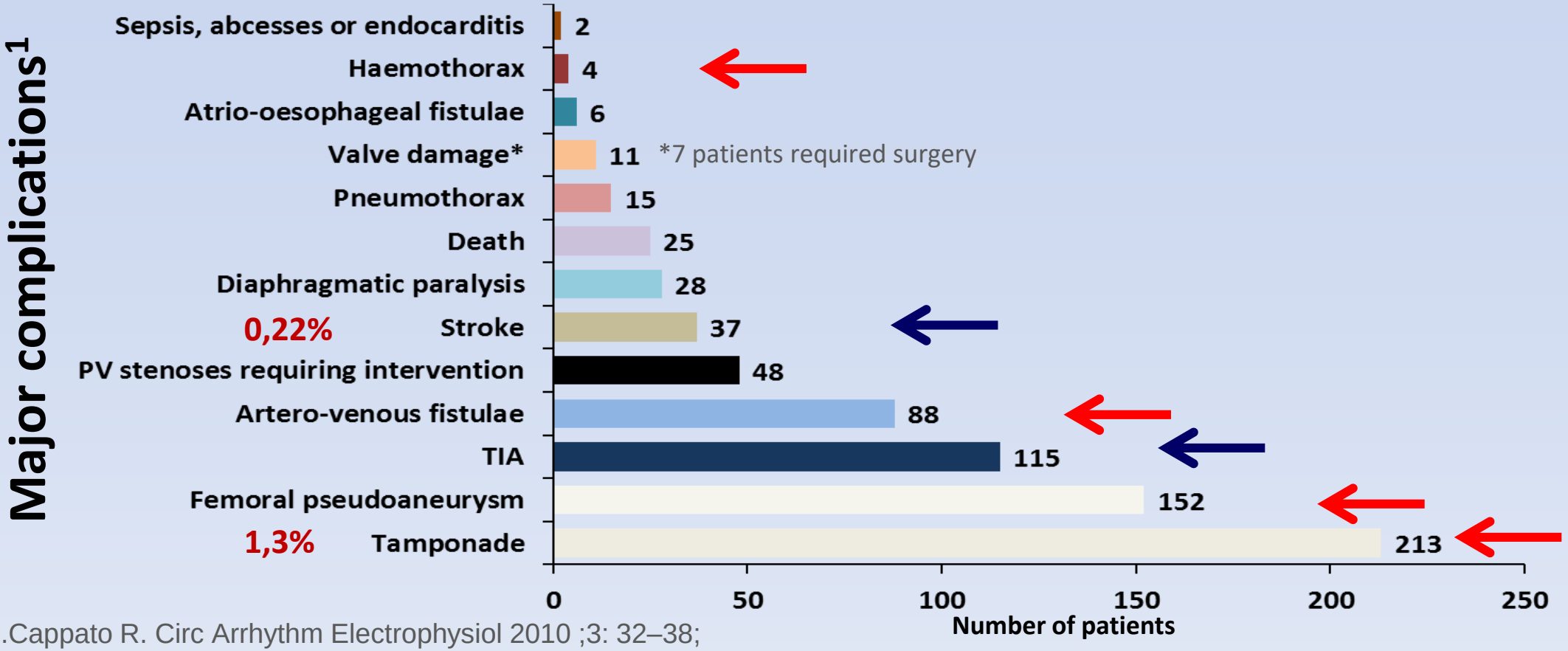
- Pts with AF are usually receiving OAC Rx to reduce stroke risk
- Requirement of an extra AC at the time of ablation procedure to reduced embolic risk associated to catheter manipulation
- Pts are therefore exposed to bleeding risk associated with extra AC
- Uninterrupted VKA Rx is actually the gold standard
- NOACs can simplify the management of AC by overcoming limitations associated with the use of VKAs

Worldwide Report on the Ablation-Related Peri-procedural Complications

4.5% Major complications reported by 741 patients[1]

25 deaths, 37 strokes, 115 TIAs and 213 episodes of tamponade[1]

Tamponade, atrio-oesophageal fistulas, stroke and MI are the most common fatal complications[2]

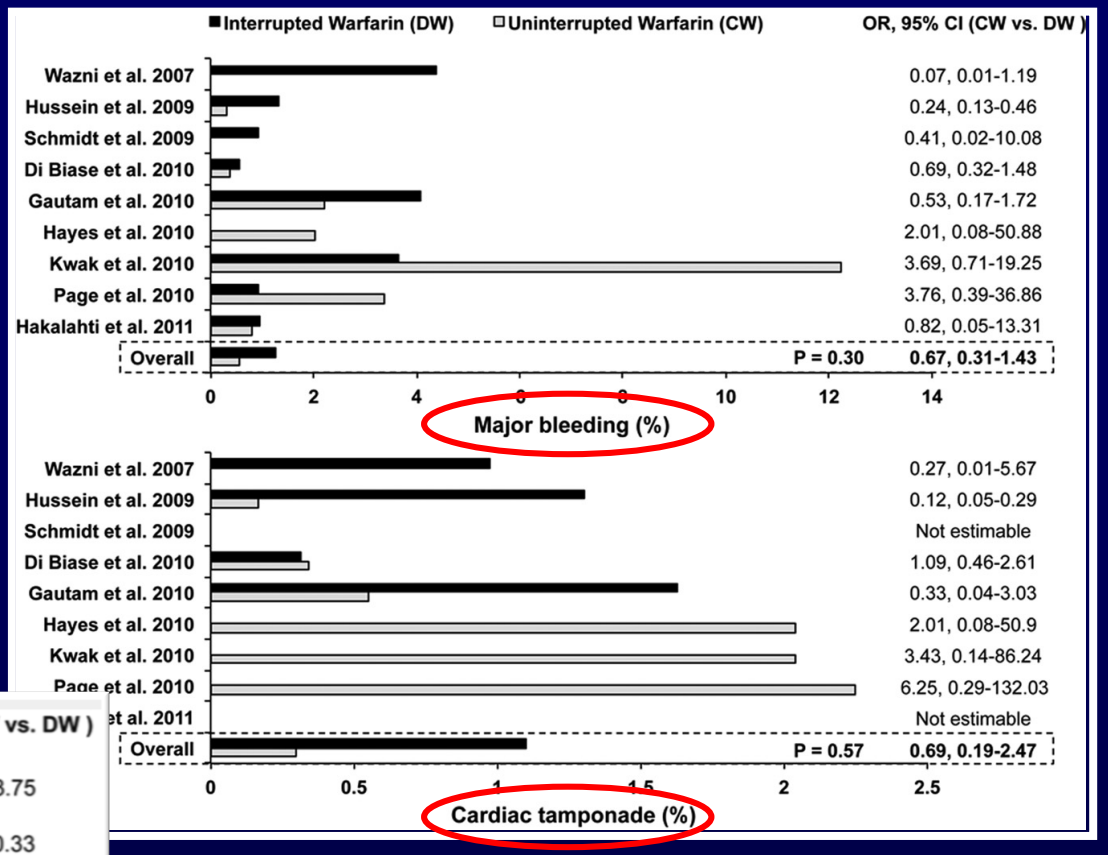


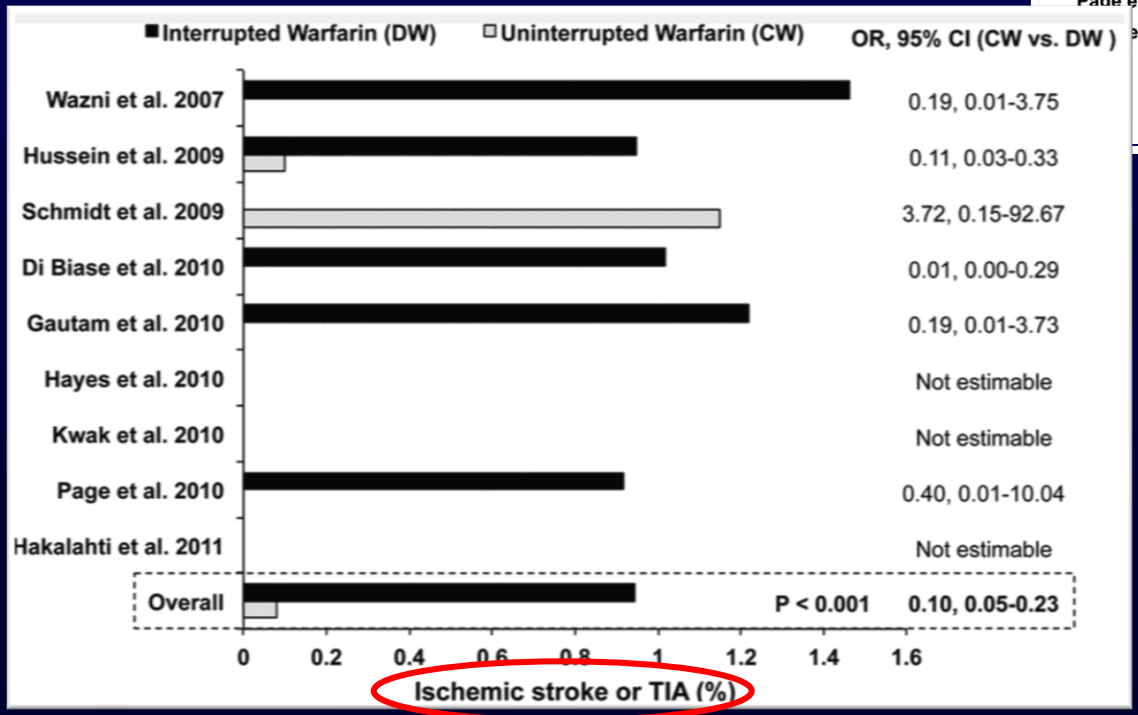
1.Cappato R. Circ Arrhythm Electrophysiol 2010 ;3: 32–38;

2.Cappato R. J Am Coll Cardiol 2009; 53: 1798–1803

Courtesy of Grimaldi M.

AF Ablation Under Therapeutic Warfarin Reduce Complications





Evidence From a Meta-Analysis

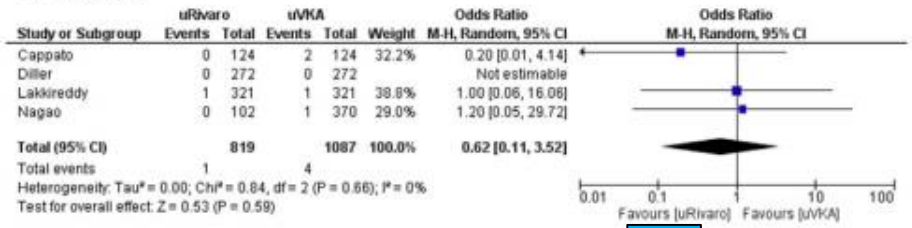
Santangeli P.
Circ Arrhthm Electrophysiol
2012; 5: 302-11

Uninterrupted New Oral Anticoagulants Compared With Uninterrupted Vitamin K Antagonists in Ablation of Atrial Fibrillation: A Meta-analysis

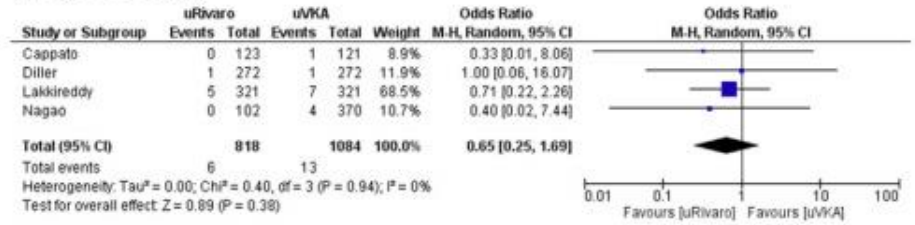
Uninterrupted Rivaroxaban vs uninterrupted VKA

R

Stroke/TIA



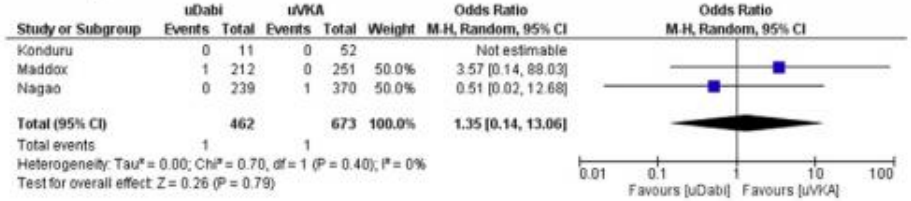
Major bleeding



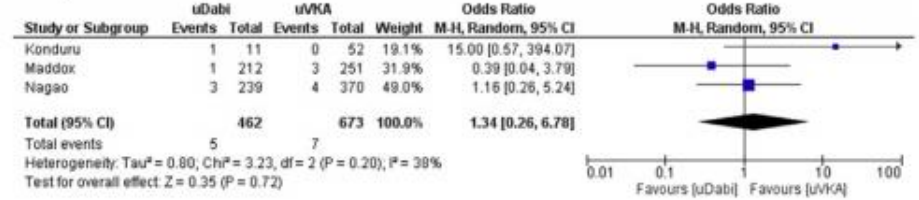
Uninterrupted Dabigatran vs uninterrupted VKA

D

Stroke/TIA



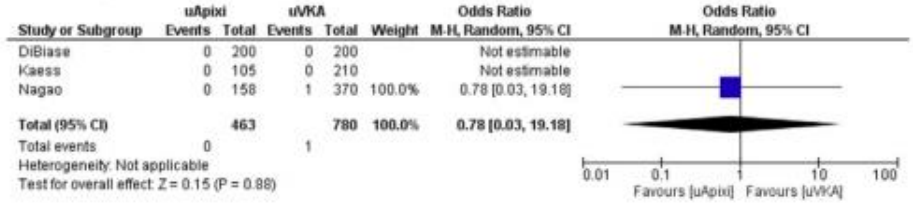
Major bleeding



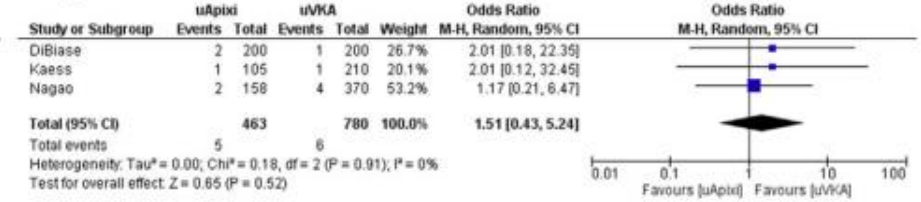
Uninterrupted Apixaban vs uninterrupted VKA

A

Stroke/TIA



Major bleeding



Nairooz R. Canadian J Cardiology 2016; 32: 814e 823e

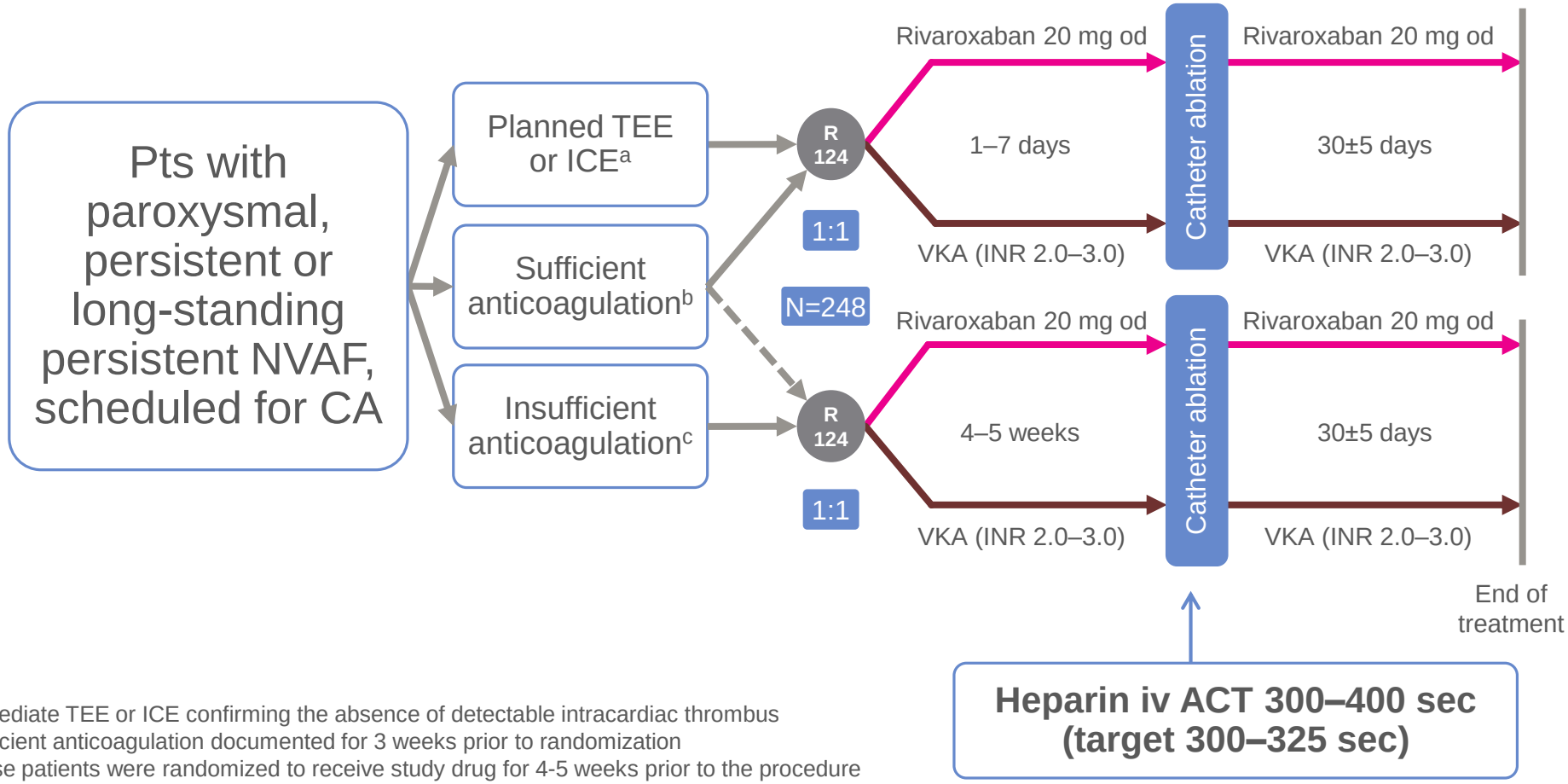
European Heart Journal
doi:10.1093/eurheartj/ehv177

Uninterrupted rivaroxaban vs. uninterrupted vitamin K antagonists for catheter ablation in non-valvular atrial fibrillation

Riccardo Cappato[1,2], Francis E. Marchlinski[3], Stefan H. Hohnloser[4], Gerald V. Naccarelli[5], Jim Xiang[6], David J. Wilber[7], Chang-Sheng Ma[8], Susanne Hess[9], Darryl S. Wells[10], George Juang[11], Johan Vijgen[12], Burkhard J. Hügl[13], Richard Balasubramaniam[14], Christian De Chillou[15], D. Wyn Davies[16], L. Eugene Fields[17], and Andrea Natale[18]*, on behalf of the VENTURE-AF Investigators

Cappato R. *Eur Heart* J 2015;36:1805-11

VENTURE AF Design: Randomized, Open-label, Active-controlled Multicentre Study



[a]Immediate TEE or ICE confirming the absence of detectable intracardiac thrombus
[b]Sufficient anticoagulation documented for 3 weeks prior to randomization
[c]These patients were randomized to receive study drug for 4-5 weeks prior to the procedure

Naccarelli GV. *J Interv Card Electrophysiol* 2014;41:107–116

VENTURE AF

VENTURE AF: Patient Demographics*

ITT Population	Rivaroxaban (n=124)	VKA (n=124)
Age, years, mean (SD)	58.6 (9.9)	60.5 (10.5)
Male, n (%)	86 (69.4)	90 (72.6)
Paroxysmal AF, n (%)	95 (76.6)	87 (70.2)
Prior cardioversion, n (%)	47 (37.9)	54 (43.5)
Prior catheter ablation, n (%)	11 (8.9)	11 (8.9)
CHF, n (%)	12 (9.7)	9 (7.3)
Hypertension, n (%)	59 (47.6)	57 (46.0)
Diabetes mellitus, n (%)	8 (6.5)	14 (11.3)
Prior stroke/TIA/embolism, n (%)	0	3 (2.4)
Vascular disease, n (%)	22 (17.7)	25 (20.2)
$CHADS_2$ score, mean (SD)	0.7 (0.7)	0.8 (0.9)
CHA_2DS_2-VASc score, mean (SD)	1.5 (1.3)	1.7 (1.4)
Beta-blocker, selective, n (%)	65 (52.4)	61 (49.2)
Antiarrhythmic, class IC, n (%)	51 (41.1)	49 (39.5)
Antiarrhythmic, class III, n (%)	30 (24.2)	39 (31.5)
Previous VKA use, n (%)	36 (29.0)	37 (29.8)
Previous Rivaroxaban use, n (%)	23 (18.5)	29 (23.4)
Previous Dabigatran use, n (%)	12 (9.7)	10 (8.1)

Cappato R. *Eur Heart* J 2015;36:1805-11

VENTURE AF

VENTURE AF: Complications During the Study Period

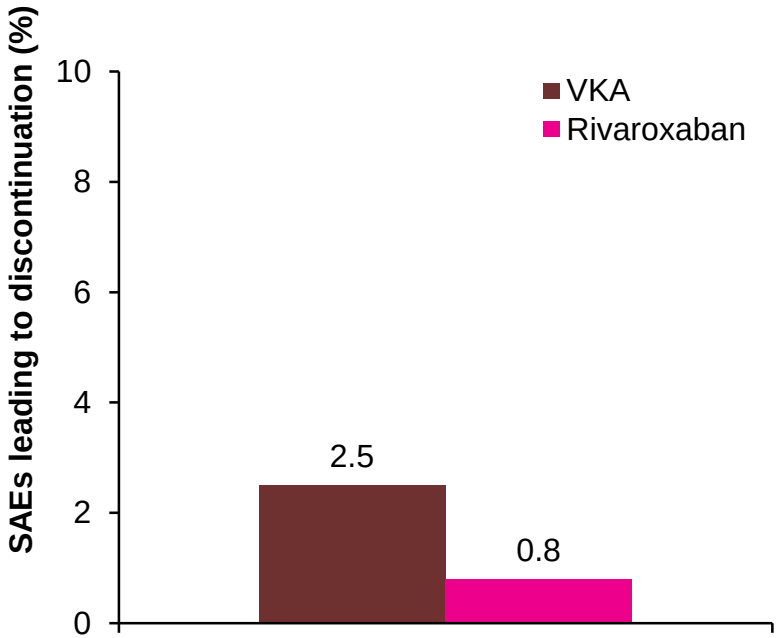
	Riva	VKA	Total
Any bleeding event*	21	18	39
Major bleeding event	**0**	**1**	**1**
Vascular pseudoaneurysm	0	1	1
Non-major bleeding event	**21**	**17**	**38**
Any TEs (composite)#	0	2	2
Ischaemic stroke	0	1	1
Vascular death	0	1	1
Any other procedure-attributable event†	5	5	10
Pericardial effusion (w/out tamponade)	0	1	1

*safety population; #ITT population; †per-protocol population

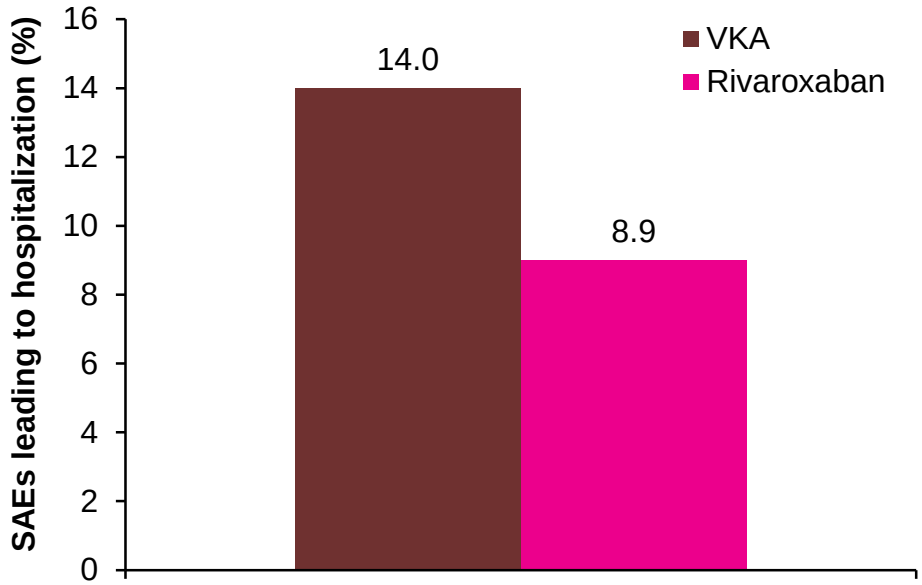
Cappato R. *Eur Heart* J 2015;36:1805-11

VENTURE AF: Serious Adverse Events Leading to…

- …drug discontinuation



- …hospitalization



The number of SAEs leading to drug discontinuation or hospitalization were very low and similar across the treatment groups

Cappato R. *Eur Heart* J 2015;36:1805-11

VENTURE-AF Summary

- VENTURE-AF is the first prospective randomized study of a NOAC in pts with AF undergoing CA
- *Due to expected low event rates and an unfeasible large calculated sample size,* VENTURE-AF was intentionally designed as an exploratory study *and thus no formal statistical superiority or non-inferiority analysis was planned*
- Major complication rates were low and similar, validating study design assumptions
  - *The incidence of primary safety events (major bleeding) was low and similar (**0.4%**; 1 event in a VKA pt and none in rivaroxaban pts)*
  - *The incidence of composite TE events was low and similar **(0.8%**; 2 events, in VKA pts and none in rivaroxaban pts)*
- The overall complication rate was 20.6%

Cappato R. *Eur Heart* J 2015;36:1805-11

RE-CIRCUIT

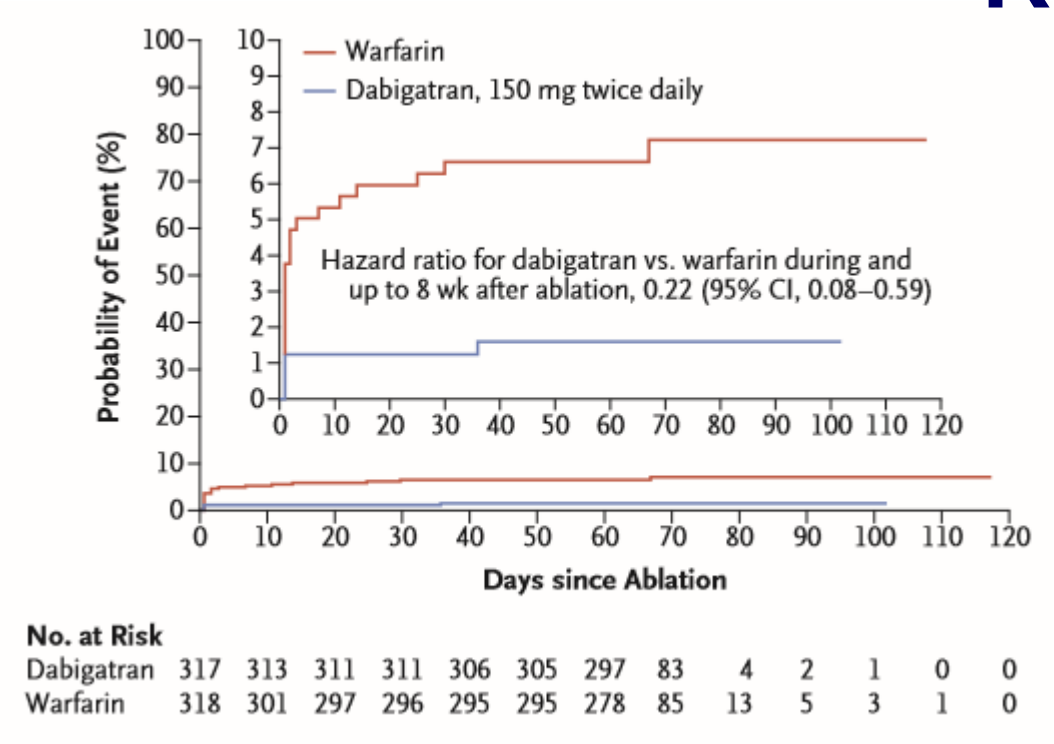
Dabigatran vs Warfarin

- N°=610
- Primary E-P:
  - *ISTH major bleeding @ 90d*
- Secondary E-Ps:
  - *stroke/TIA @ 30/90d*
  - *ISTH major mleeding @ 30d*
  - *net clinical benefit @ 30/90d*
  - *vascular access complications*
  - *pericardial effusion, pericardial tamponade*
  - *all cause mortality*

ClinicalTrials.org NCT 02348723

RE-CIRCUIT Study

Major Bleedings

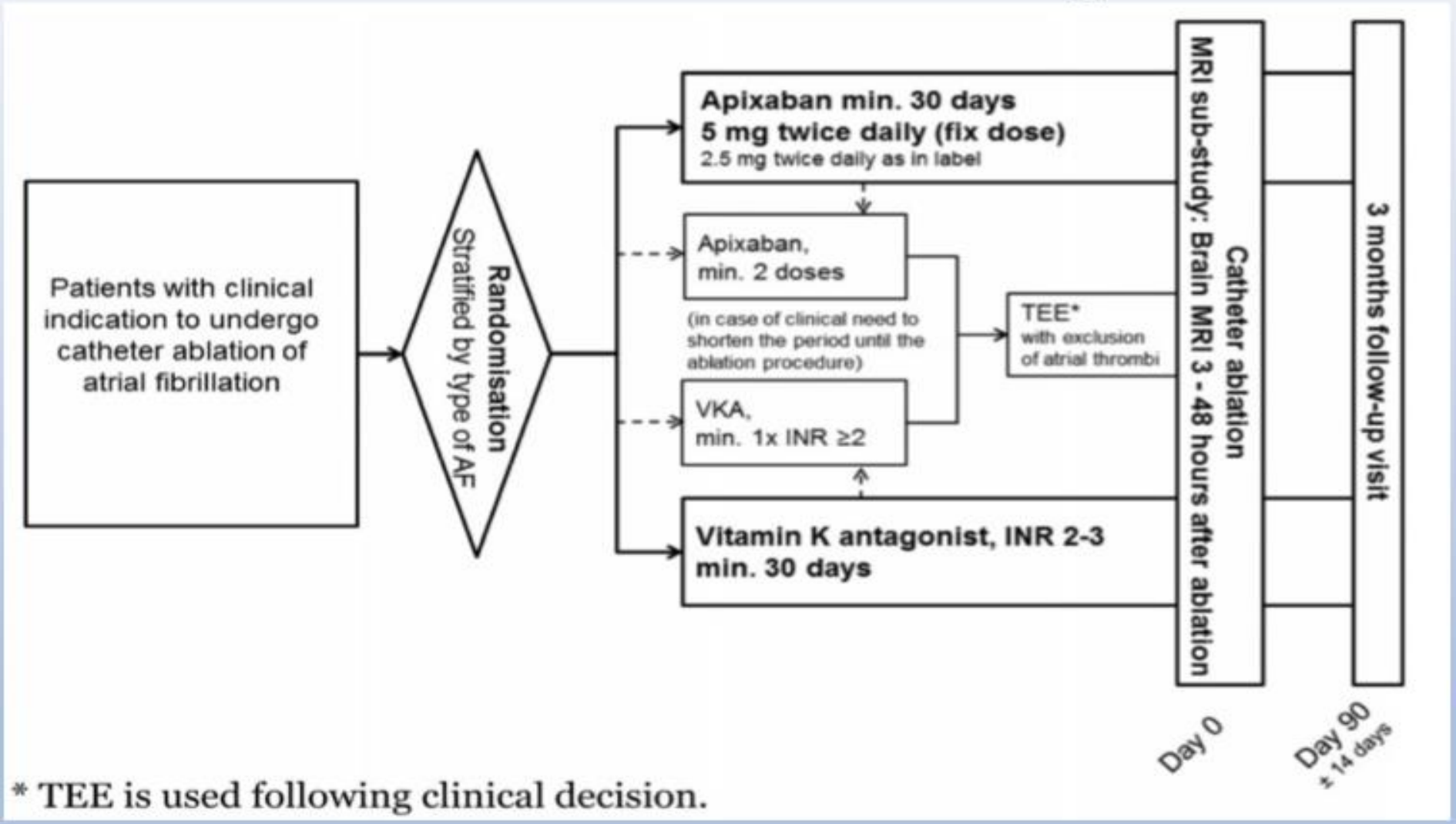


Adverse Events

Event	Dabigatran, 150 mg Twice Daily (N=338)	Warfarin (N=338)	Total (N=676)
		number (percent)	
Any adverse event	225 (66.6)	242 (71.6)	467 (69.1)
Severe adverse event†	11 (3.3)	21 (6.2)	32 (4.7)
Adverse event leading to treatment discontinuation	19 (5.6)	8 (2.4)	27 (4.0)
Serious adverse event	63 (18.6)	75 (22.2)	138 (20.4)
Fatal adverse event	0	0	0
Immediately life-threatening event	1 (0.3)	2 (0.6)	3 (0.4)
Event that resulted in clinically significant or persistent disability or incapacity	0	1 (0.3)	1 (0.1)
Event that required hospitalization	26 (7.7)	34 (10.1)	60 (8.9)
Event that prolonged hospitalization	13 (3.8)	22 (6.5)	35 (5.2)
Other‡	29 (8.6)	27 (8.0)	56 (8.3)

Calkins H.
N Engl J Med 2017;376:1627-36

AXAFA – AFNET 5 design

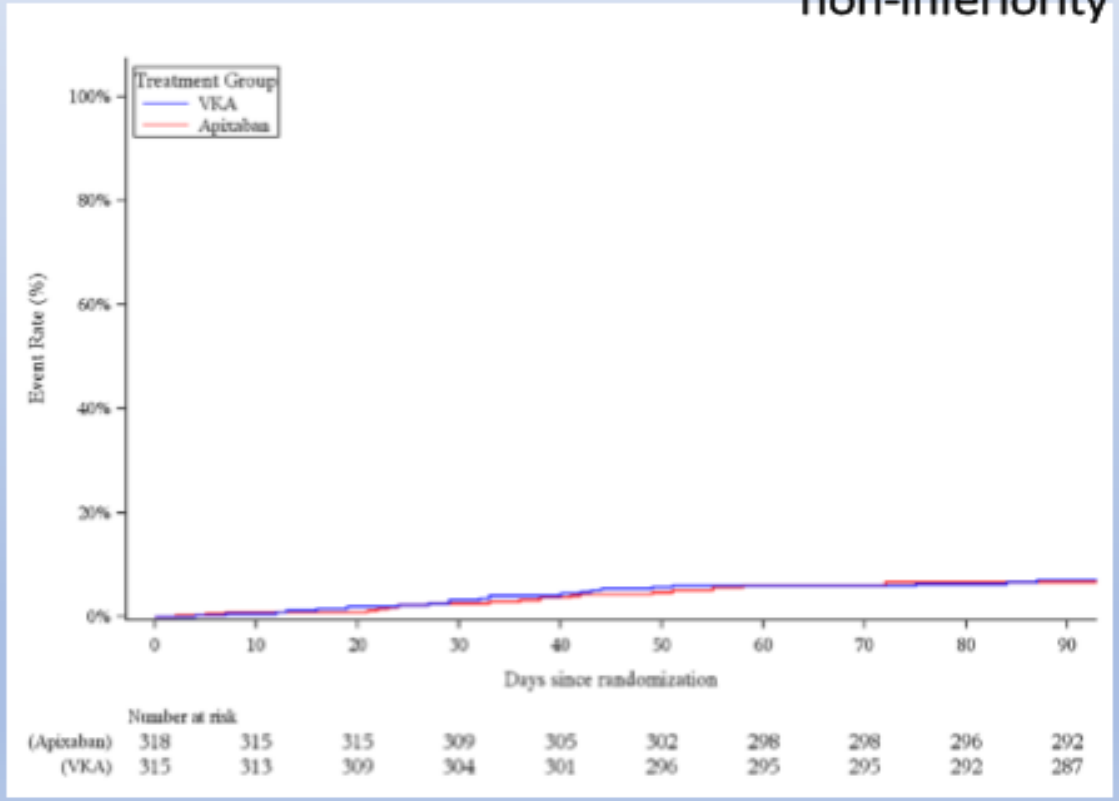


* TEE is used following clinical decision.

www.axafa.af-net.eu, Di Biase L, et al. *Europace* 19: 132-138. (2017)

Primary outcome

Difference in primary outcome rate -0.38%
90% confidence interval -4.0%, %-3.3%
non-inferiority p=0.0002



	Apixaban	VKA
Composite of all-cause death, stroke or major bleeding	22/318 (6.9%), non-inferiority p=0.0002	23/315 (7.3%)
Death	1 (0.3%)	1 (0.3%)
Stroke or TIA	2 (0.6%)	0
Intracranial hemorrhage	0	1 (0.3%, fatal)
TIMI major bleeding	1 (0.3%)	3 (1%)
ISTH major bleeding	10 (3.1%)	14 (4.4%)
Tamponade	2 (0.6%)	5 (1.6%)

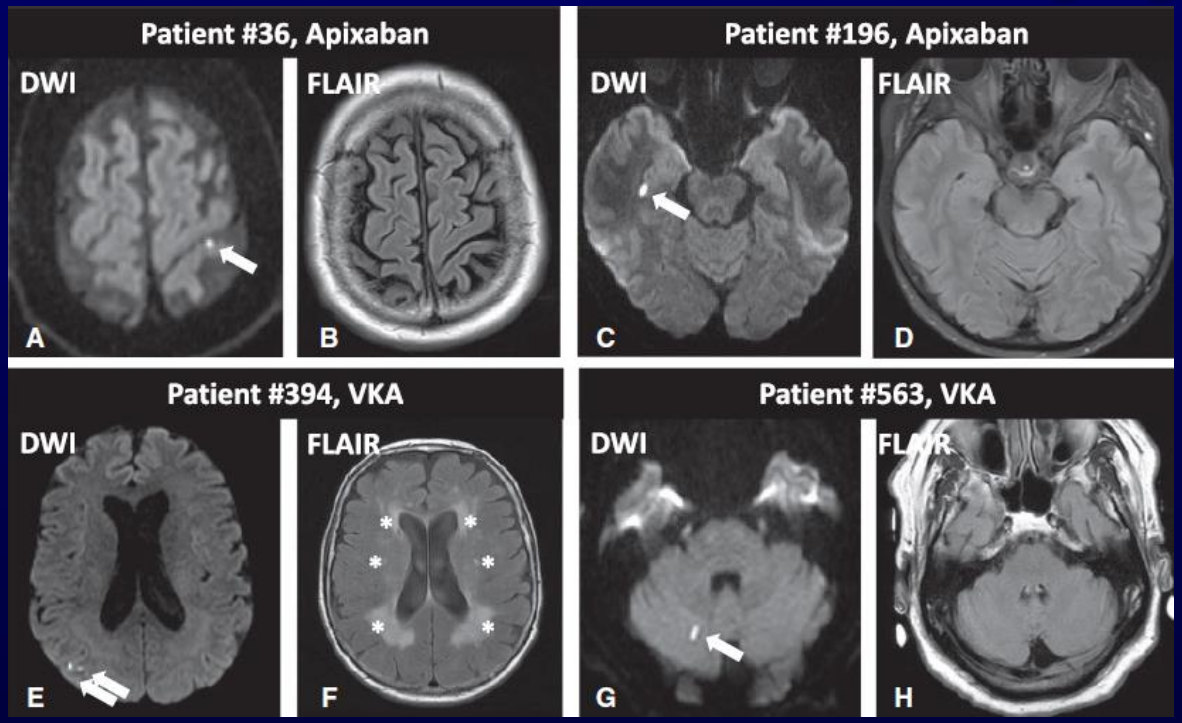
AXAFA - AFNET 5

Primary Outcome

Kirchhof P.
EHJ 2018;
39: 2942–2955

AXAFA - AFNET 5

High-Resolution Diffusion-Weighted Brain Magnetic Resonance Imaging Substudy



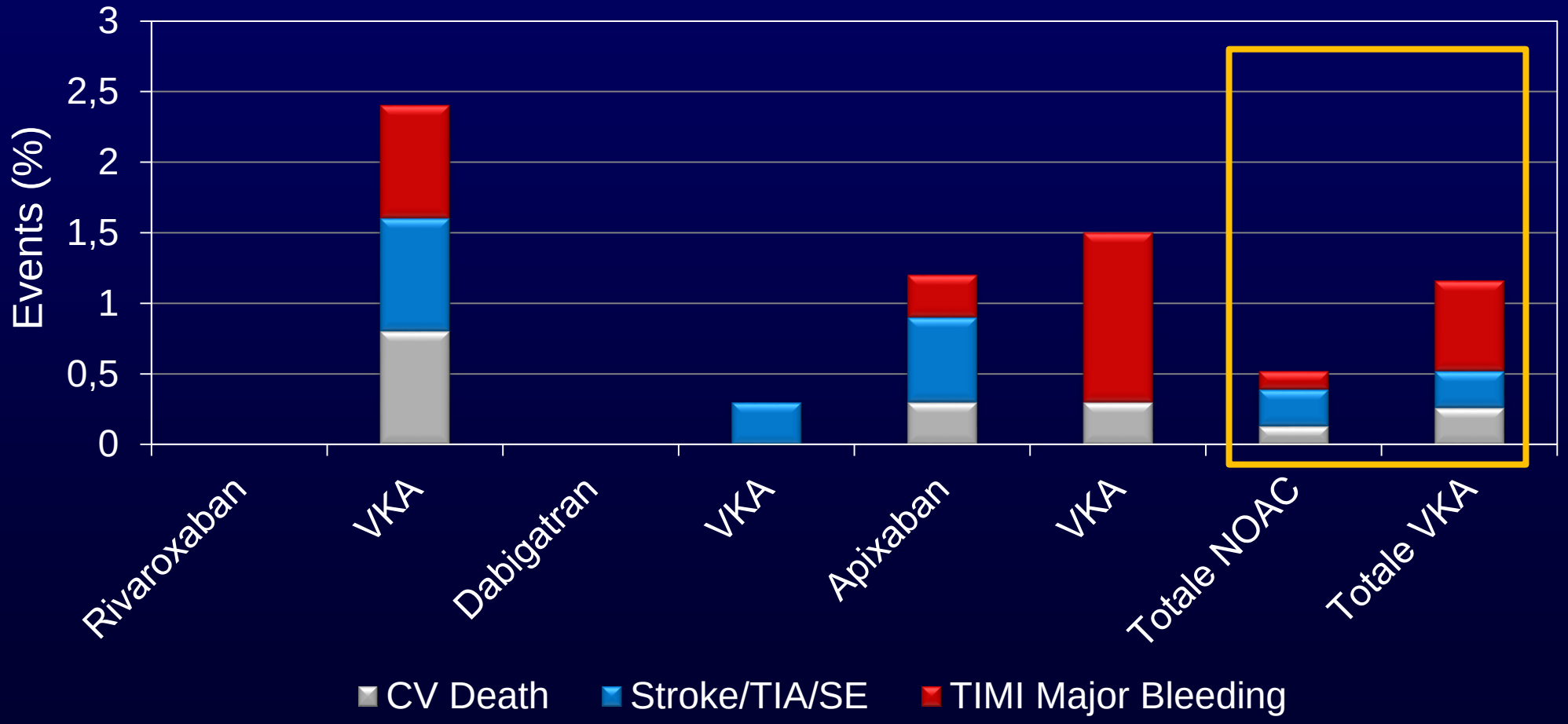
acute brain lesions detected in the brain MRI sub-study

	All patients ($n = 323$)	Apixaban ($n = 162$)	VKA ($n = 161$)	*P*-value
No lesion	239 (74.0%)	118 (72.8%)	121 (75.2%)	0.635
Exactly one lesion	46 (14.2%)	27 (16.7%)	19 (11.8%)	0.211
Exactly two lesions	21 (6.5%)	7 (4.3%)	14 (8.7%)	0.111
More than two lesions	17 (5.3%)	10 (6.2%)	7 (4.3%)	0.463

Kirchhof P.
EHJ 2018;
39: 2942–2955

VENTURE-AF, RE-CIRCUIT, AXAFA-AFNET 5

Event Rate in 1547 Pts



AEIOU Study Advances Uninterrupted NOAC Strategy in AF Ablation

	Apixaban uninterrupted N 150 ®	**Apixaban dose withheld N 150 ®**	**Warfarin uninterrupted N 295 retro**
NMCS bleeding (%)	11.3	9.7	9.8
Major bleeding (%)	1.3	2.1	1.4
TE event (TIA) (N°)	1	1	2
Death (N°)	-	-	-

Reynolds M. J Am Coll Cardiol EP 2018; 4: 580–8)

Anticoagulation Peri-AF Ablation

Summary

- During peri-procedural phase there is an increased risk for TE events
- CA peri-procedural phase: NOACs can continue to be used
  - *last dose is given the day before procedure*
  - *restart the evening of the procedure*
  - *eliminate the need for bridging*
- *After CA pts continue receiving OAC for at least two months to allow for healing, then the need for OAC can be assessed*