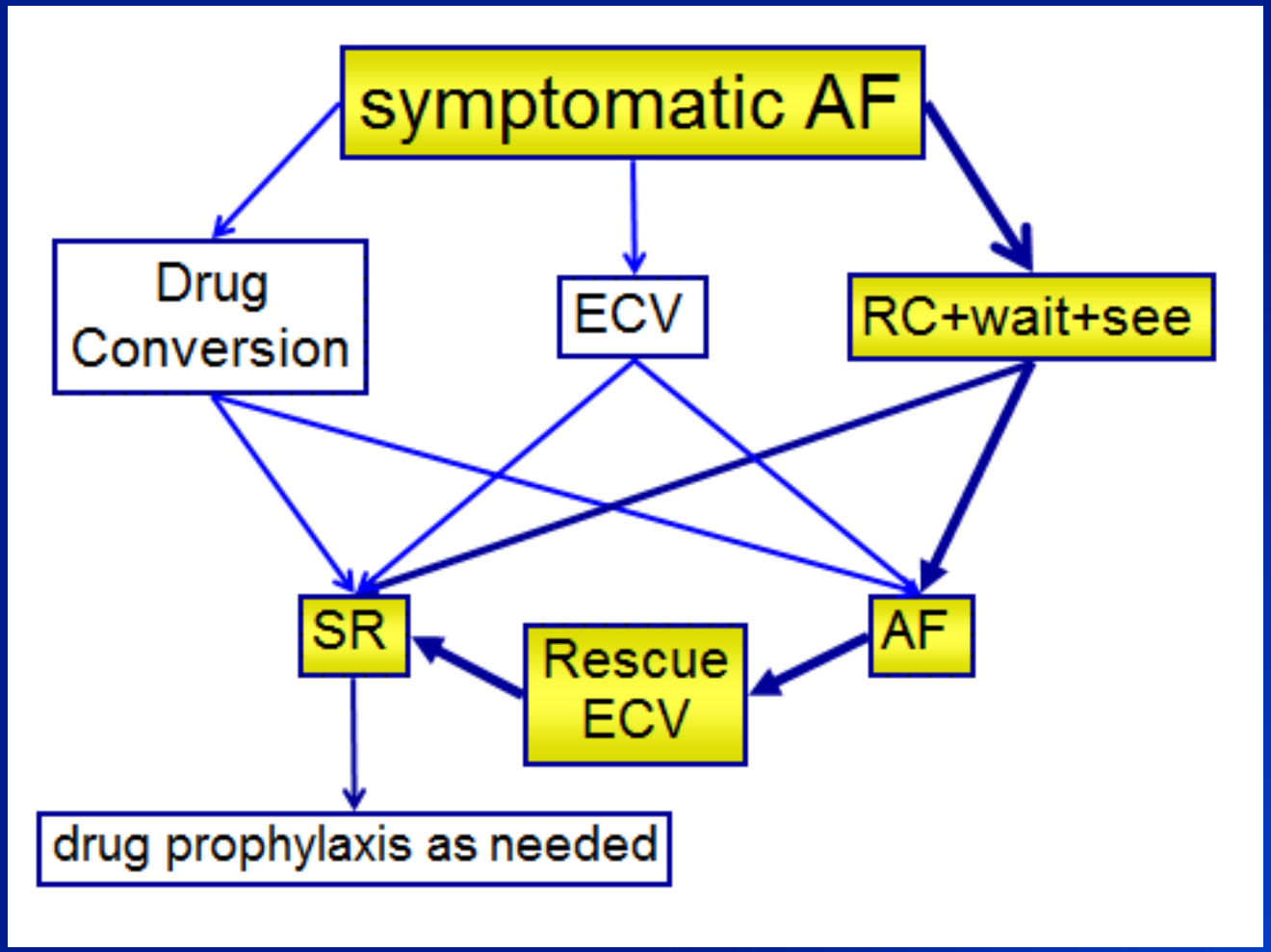
NOACs and cardioversion

Results from the X-vert trial

X-VeRT

Approaches to cardioversion of atrial fibrillation



Boosters of clinical AF research

- String galvanometer
  - Einthoven 1902
- Quinidine for cardioversion
  - Frye 1918
- DC electrical cardioversion
  - Lown 1962
- Electrical atrial remodeling
  - Allessie 1995
- Catheter ablation of focal AF
  - Haissaguerre 1997
- Rhythm versus Rate trials
  - RACE (Van Gelder) / AFFIRM (Wyse) 2002

Bernard Lown, 1962

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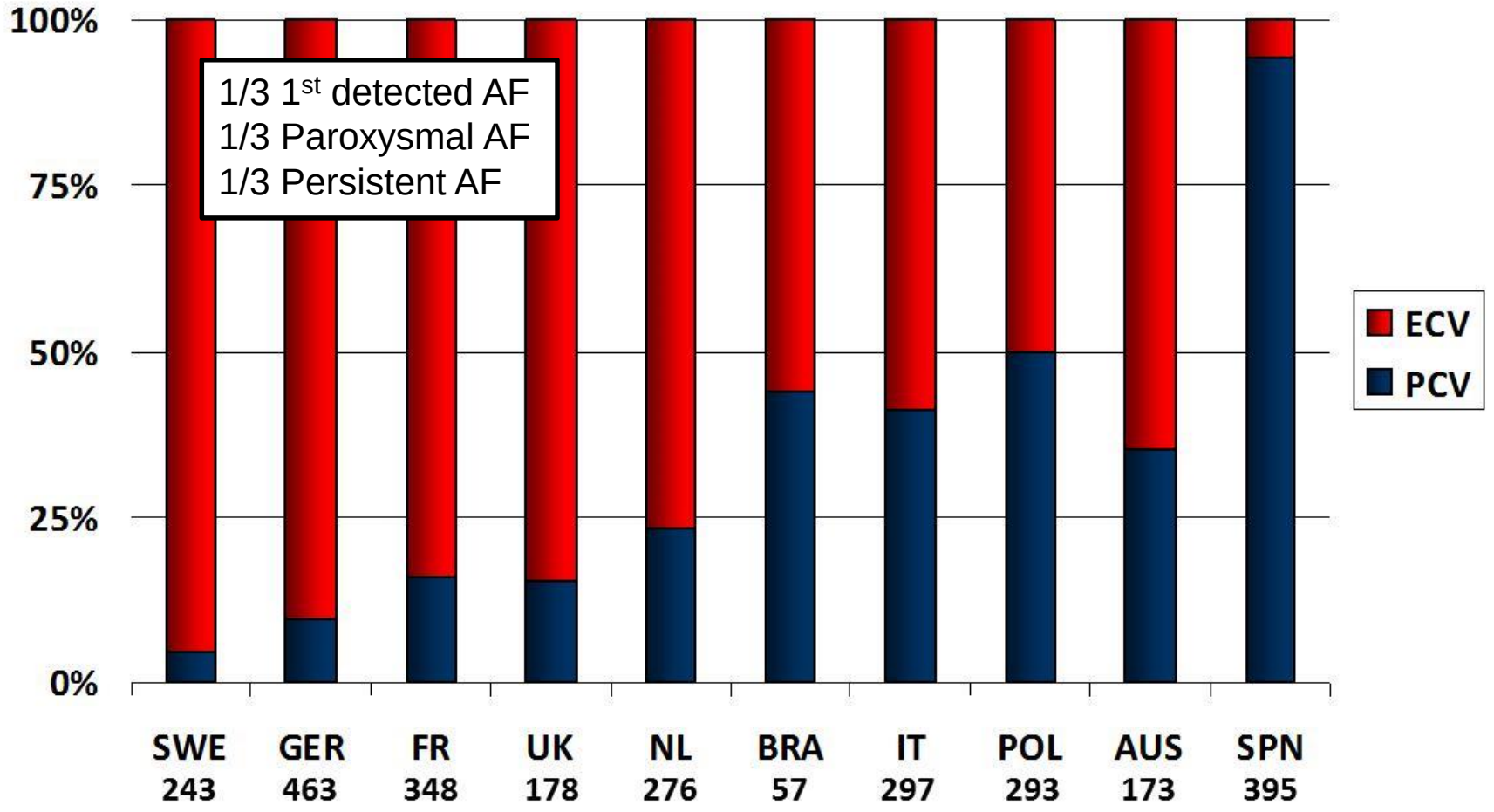
Distribution of type of cardioversion differs by country – cultural differences



Crijns HJ et al. Int J Cardiol 2014

RHYTHMAF
International Registry on Cardioversion for Atrial Fibrillation

Risk of Thrombo embolic event peri-cardioversion?

- NO anticoagulation: 5–7%[1]
- With VKA: 1%[2]

1. Stellbrink C *et al. Circulation* 2004;109:997–1003;
2. Gallagher M *et al. J Am Coll Cardiol* 2002;4:926–9333

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Guidelines for pericardioversion anticoagulation

ESC[1]

If AF > 48 hours or unknown duration: VKA >3 weeks before and >4 weeks after CV

Life long VKA if stroke risk factors, irrespective of outcome of CV

EHRA[2]

If compliance with NOAC intake can be reliably confirmed, cardioversion with NOAC seems acceptably safe.

Prior TEE should be considered if there is doubt about compliance

1. Camm AJ, et al. EHJ 2012 2. Heidbuchel H.. et al. Europace 2013.

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Post-hoc data analyses on cardioversion from the large NOAC trials

- RE-LY, ARISTOTLE, ROCKET AF retrospective subanalyses CV: clinical outcomes were similar to the overall study populations[3,4,5]
- … with extremely low event rates

1. Camm AJ *et al. Eur Heart J* 2012;33:2719–2747;
3. Piccini JP *et al. J Am Coll Cardiol* 2013;61:1998–2006; 4. Nagarakanti R *et al. Circulation* 2011;123:13[illegible]36
5. Flaker G *et al. J Am Coll Cardiol* 2014;63:1082–1087

The first published prospective RCT on NOAC and CV

European Heart Journal Advance Access published September 2, 2014

European Heart Journal
doi:10.1093/eurheartj/ehu367

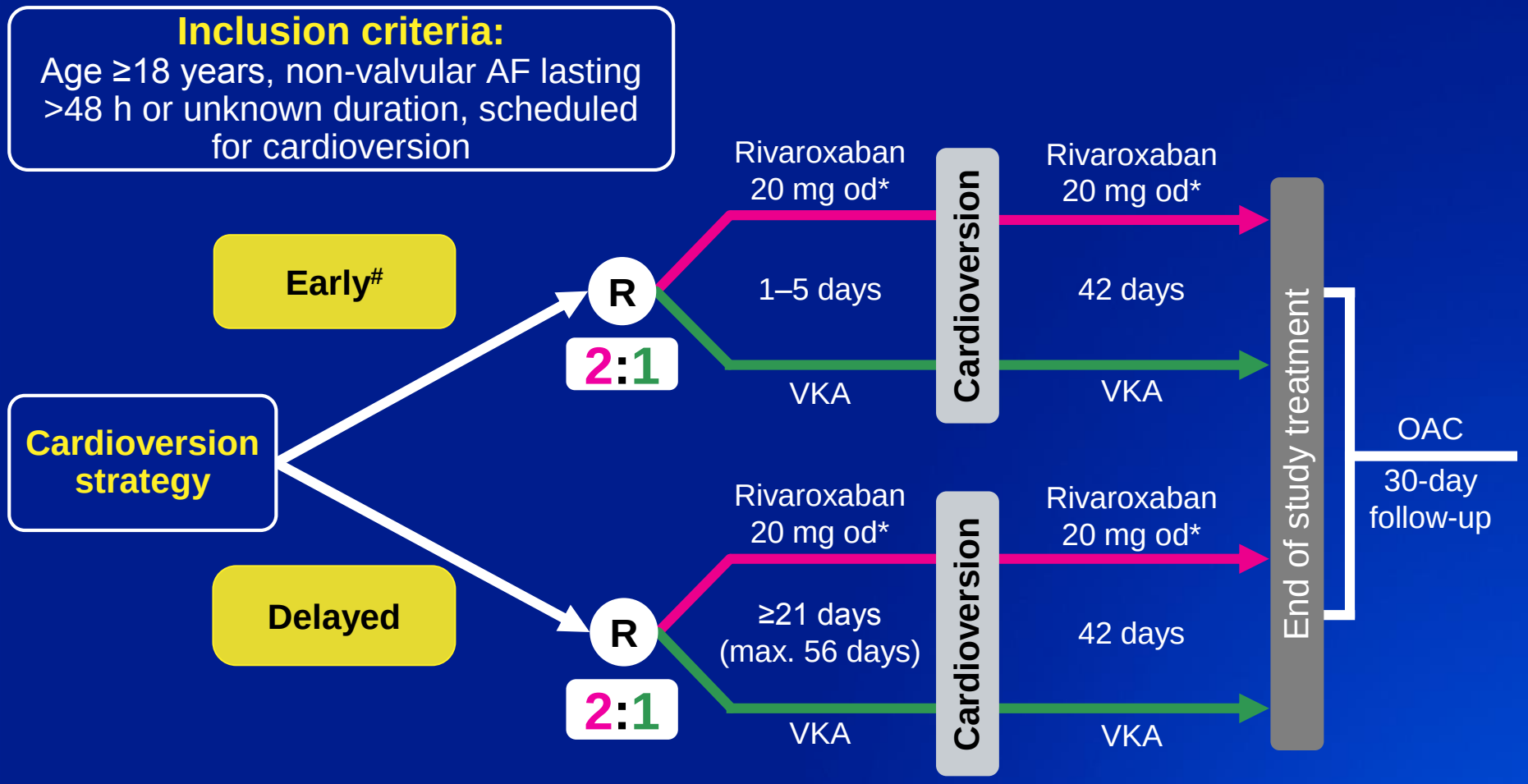
FASTTRACK
ESC HOT LINE BARCELONA

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

X-VeRT

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



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

Ezekowitz MD *et al. Am Heart J* 2014;167:646–652; www.clinicaltrials.gov. NCT01674647

X-VeRT

X-VeRT: primary endpoints

Primary efficacy endpoints[1]	Primary safety endpoint[1]
A composite of: • Stroke and TIA • Non-CNS systemic embolism • Myocardial infarction • Cardiovascular death	• Major bleeding (ISTH definition)[2]

All endpoints adjudicated by treatment assignment-blinded Clinical Endpoint Committee

1. Cappato R et al. *Eur Heart J* 2014: doi: 10.1093/eurheartj/ehu367;
2. Schulman S *et al*. *J Thromb Haemost* 2005;3:692–694

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X-VeRT: baseline demographics

	Rivaroxaban (n=1,002)	VKA (n=502)	Total (N=1,504)
Age, mean (SD), years	64.9 (10.6)	64.7 (10.5)	64.9 (10.5)
Female, %	27.4	26.9	27.3
$CHADS_2$ score, mean (SD)	1.3 (1.0)	1.4 (1.0)	1.4 (1.1)
CHA_2DS_2VASc score, mean (SD)	2.3 (1.6)	2.3 (1.6)	2.3 (1.6)
Hypertension, %	65.0	68.7	66.2
Congestive heart failure, %	19.7	14.9	18.1
Previous stroke/TIA or SE, %	6.7	9.8	7.7
Diabetes mellitus, %	20.3	20.5	20.3
Type of AF, %*			
First-diagnosed	23.8	21.1	22.9
Paroxysmal	17.2	22.7	19.0
Persistent	55.9	50.0	53.9
Long-standing persistent	3.0	5.2	3.7

*Data missing in 7 patients. Renal function: 92.5% of patients had CrCl ≥50 ml/min
ITT population

Cappato R *et al. Eur Heart J* 2014: doi: 10.1093/eurheartj/ehu367

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X-VeRT: primary efficacy endpoints (randomisation - 42 days follow-up)

	Rivaroxaban (N=978)		VKA (N=492)		Risk ratio (95% CI)
	%	n*	%	n*	
Primary efficacy endpoint	**0.51**	**5**	**1.02**	**5**	**0.50 (0.15–1.73)**
Stroke	0.20	2	0.41	2	
Haemorrhagic stroke	0.20	2		0	
Ischaemic stroke		0	0.41	2	
TIA		0		0	
Non-CNS SE		0	0.20	1	
MI	0.10	1	0.20	1	
Cardiovascular death	0.41	4	0.41	2	

*Number of patients with events; patients may have experienced more than one primary efficacy event
mITT population

Cappato R *et al. Eur Heart J* 2014: doi: 10.1093/eurheartj/ehu367

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X-VeRT: primary safety endpoints (randomisation - 42 days follow-up)

	Rivaroxaban (N=988)		VKA (N=499)		Risk ratio (95% CI)
	%	n*	%	n*	
Major bleeding	**0.61**	**6**	**0.80**	**4**	**0.76 (0.21–2.67)**
Fatal	0.1	1	0.4	2	
Critical-site bleeding	0.2	2	0.6	3	
Intracranial haemorrhage	0.2	2	0.2	1	
Hb decrease ≥2 g/dl	0.4	4	0.2	1	
Transfusion of ≥2 units of packed RBCs or whole blood	0.3	3	0.2	1	

*Number of patients with events; patients may have experienced more than one primary safety event
Safety population

Cappato R *et al. Eur Heart J* 2014: doi: 10.1093/eurheartj/ehu367

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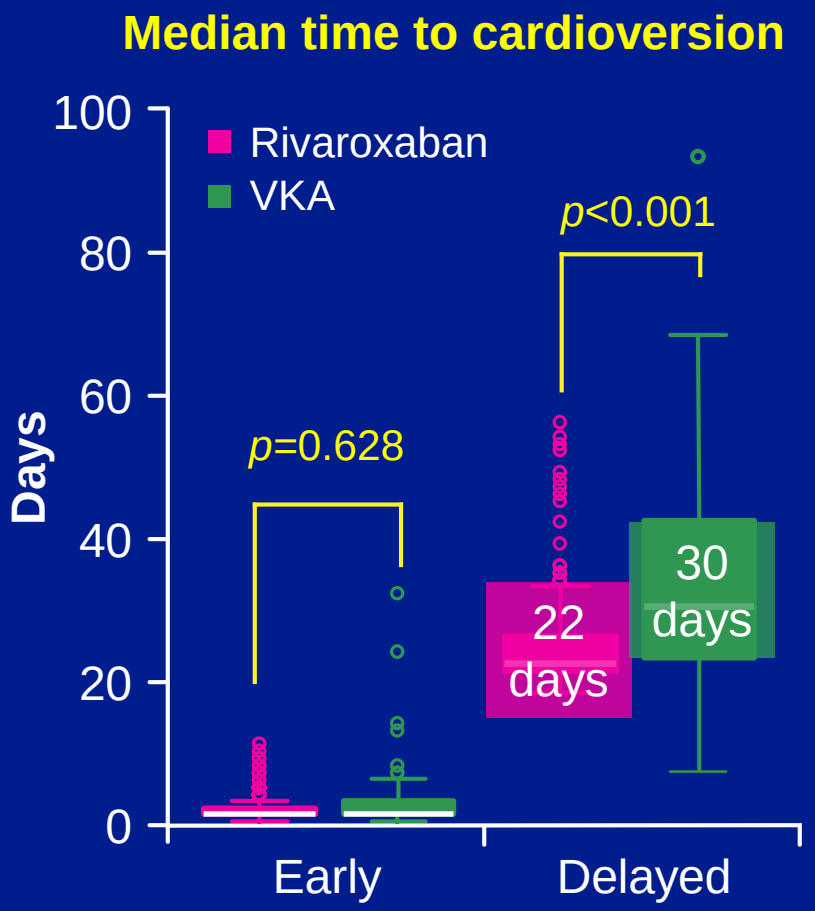
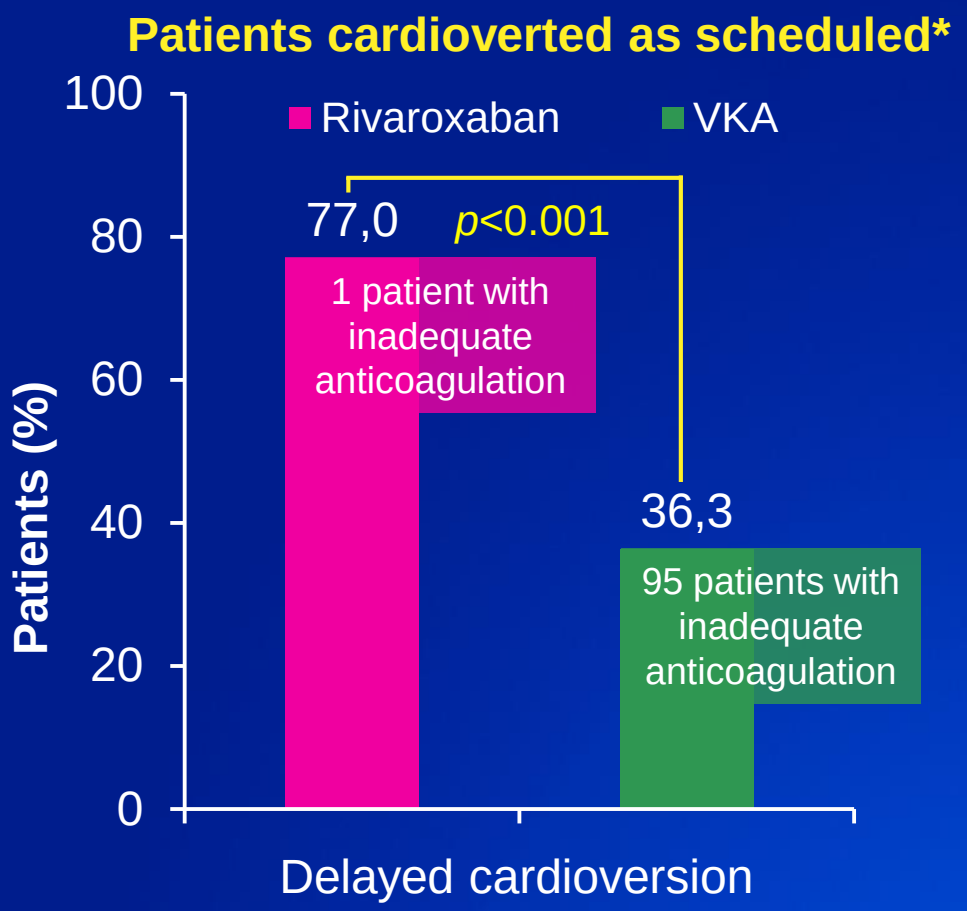
X-VeRT: time to cardioversion by cardioversion strategy





*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)

Cappato R *et al. Eur Heart J* 2014: doi: 10.1093/eurheartj/ehu367

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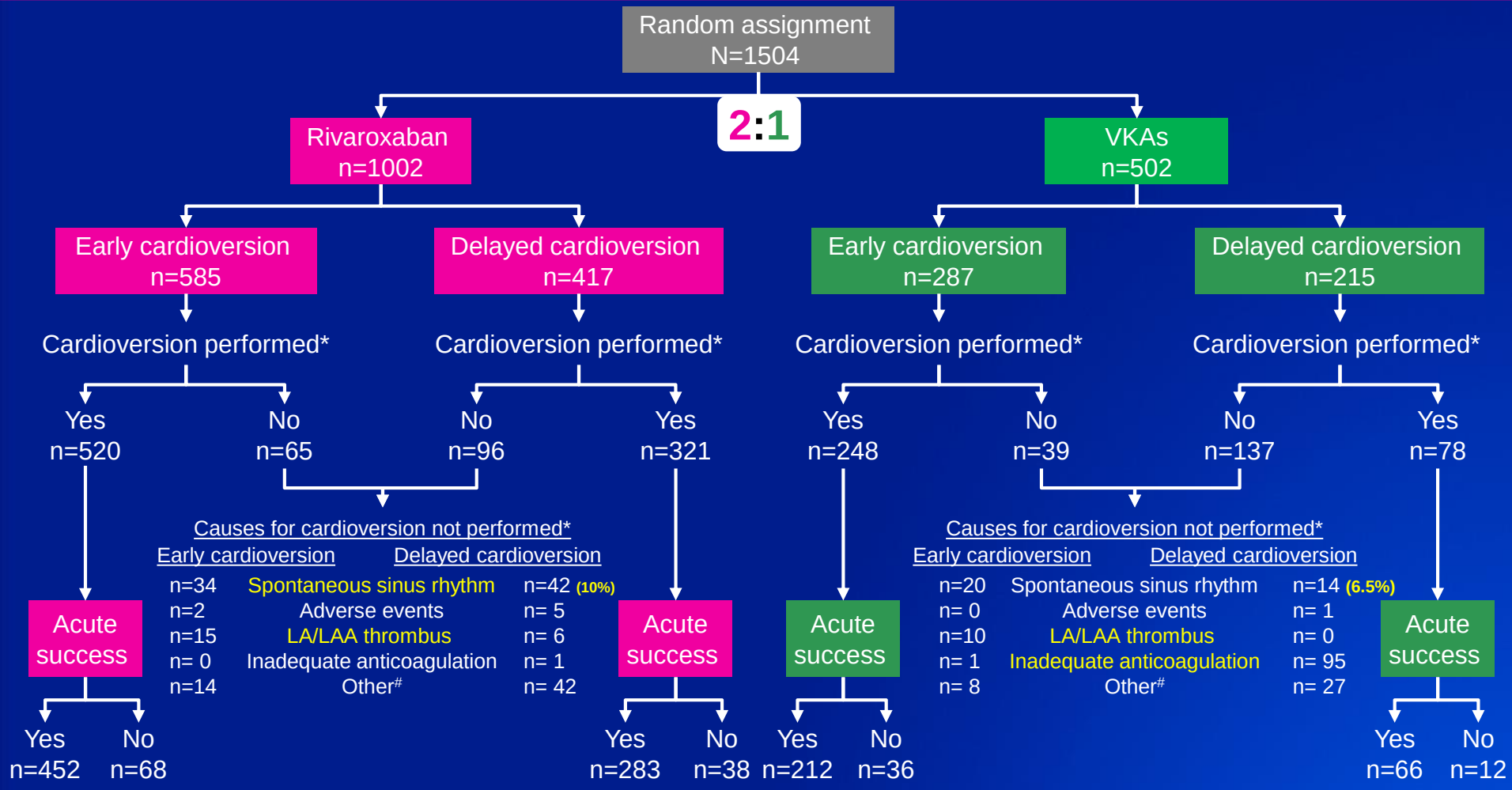
X-VeRT: study patient flow of scheduled cardioversion (ITT population)



*As scheduled; for early cardioversion: 1–5 days after randomization; for delayed cardioversion: 21–25 days after randomization; #not further specified

Cappato R *et al. Eur Heart J* 2014: doi: 10.1093/eurheartj/ehu367

X-VeRT

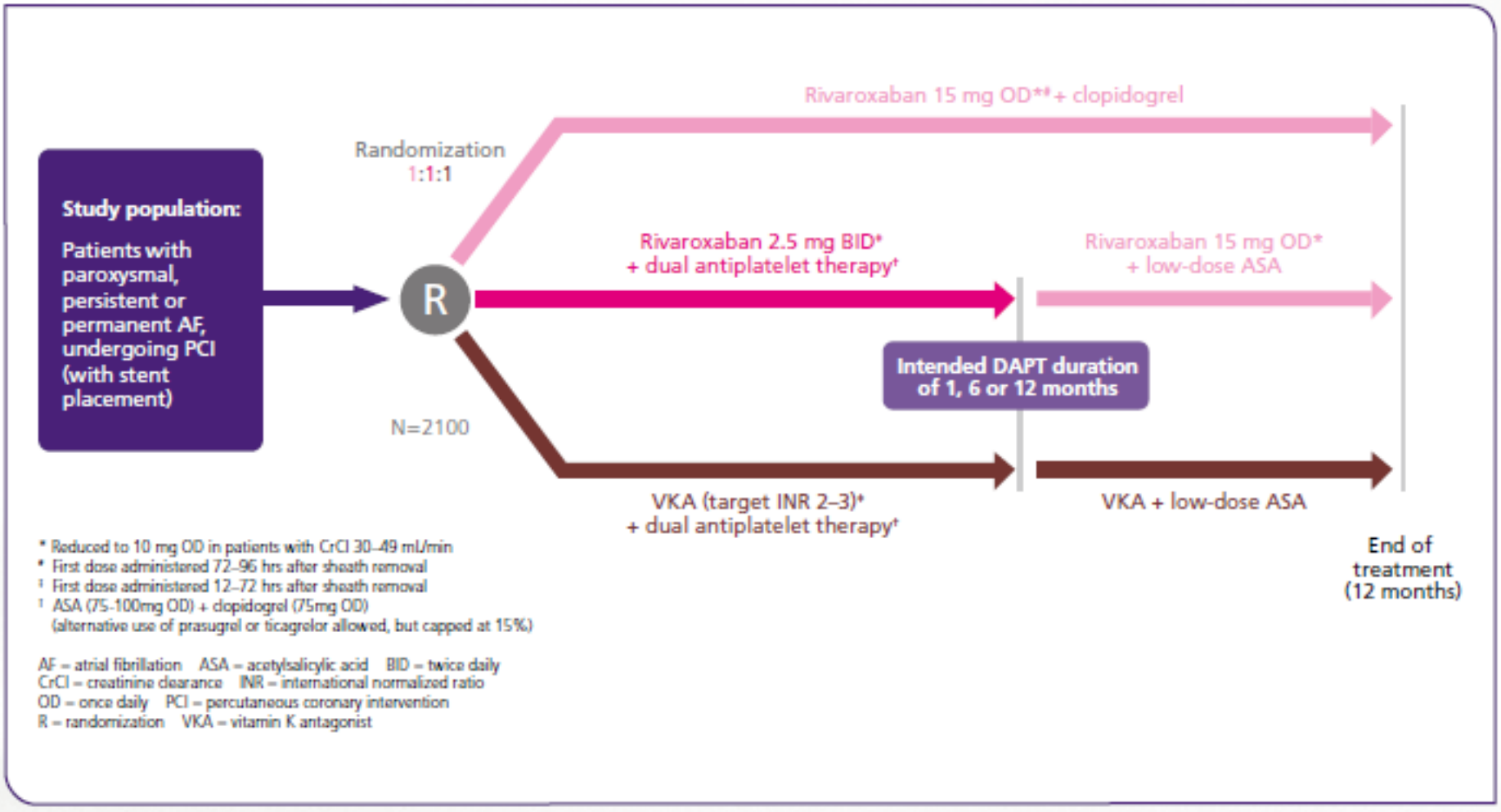
X-VeRT conclusions

- First completed prospective RCT of a NOAC in patients with AF undergoing elective cardioversion
- Rivaroxaban = VKA (effectiveness and safety)
- Time to delayed cardioversion significantly shorter with rivaroxaban

Cappato R *et al. Eur Heart J* 2014: doi: 10.1093/eurheartj/ehu367;
Cappato R. ESC Congress 2014. Oral presentation 4945

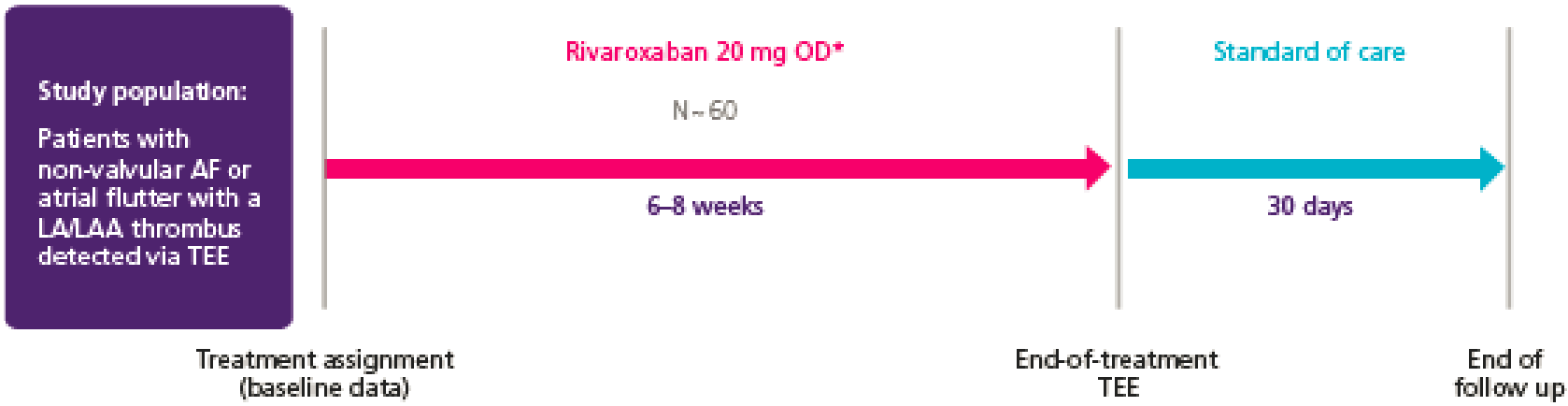
X-VeRT

Rivaroxaban & PCI (IIIb)



Rivaroxaban & LAA thrombus (IIIb)

Study Design



* CrCl 15–49 ml/min: 15 mg OD

AF = atrial fibrillation CrCl = creatinine clearance
LA = left atrial LAA = left atrial appendage
OD = once daily TEE = transesophageal echocardiogram

Thank you

X-VERT