EXplore the efficacy and safety of once-daily oral riVaroxaban for the prevention of caRdiovascular events in subjects with non-valvular aTrial fibrillation scheduled for cardioversion: X-VeRT

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On behalf of X-VeRT trial committees and Investigators

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Disclosure

- Consultant to: Boston Scientific; Medtronic; St. Jude; Biosense Webster; ELA Sorin; Boehringer Ingelheim; Bayer HealthCare; Abbott; Pfizer
- Speaker's Bureau: Boston Scientific; Medtronic; St. Jude; Biosense Webster; BARD; Sanofi; Boehringer Ingelheim; Bayer HealthCare; Abbott
- Investigator: Medtronic; Biosense Webster; Sanofi; Cameron Health, BARD; Bayer HealthCare; Abbott; Pfizer
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- Equity and Intellectual Property Rights: Cameron Health

Study Rationale and Background

- Cardioversion is a common procedure worldwide used to restore normal rhythm in patients with AF[1]
- Without adequate anticoagulation, the periprocedural risk of thromboembolism with cardioversion is 5–7%[2] (1% for patients receiving a VKA)[3]
- VKAs are the current standard of care before and after cardioversion,[4] with only post hoc analyses supporting use of novel OACs[5–7]

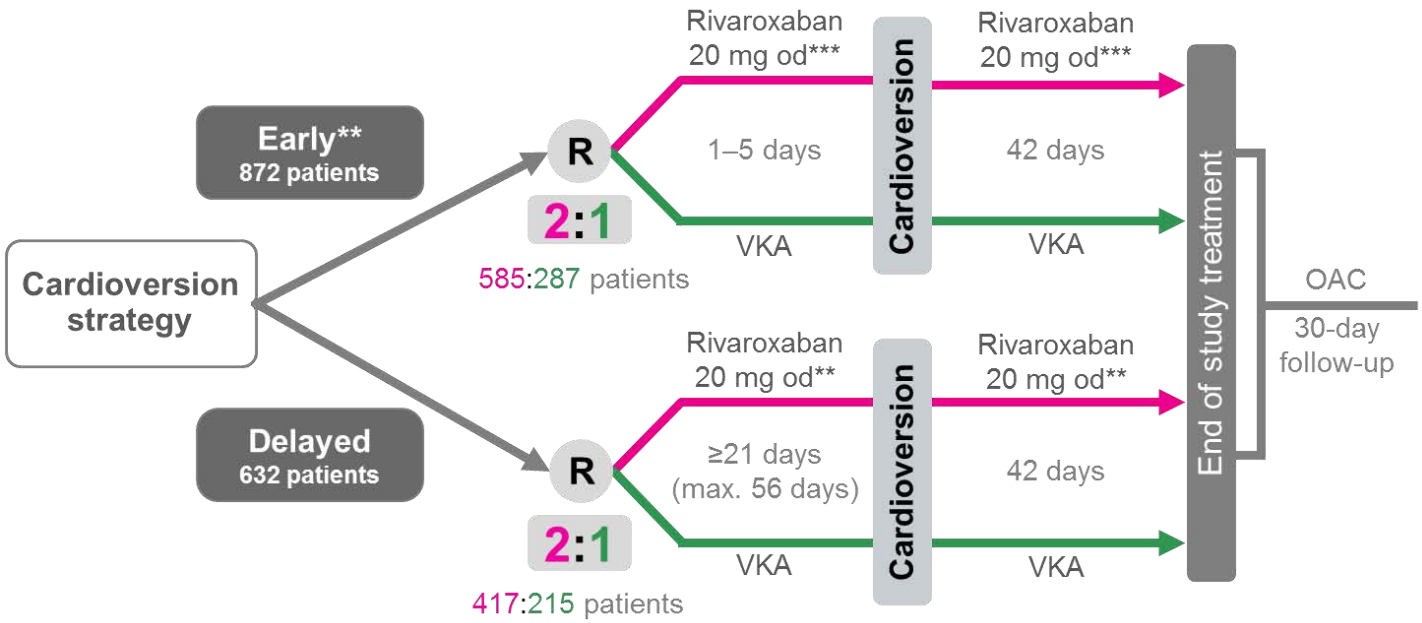
1. Hernandez-Madrid *et al*, 2013; 2. Stellbrink *et al*, 2004; 3. Gallagher *et al*, 2002; 4. Camm *et al*, 2012; 5. Piccini *et al*, 2013; 6. Nagarakanti *et al*, 2011; 7. Flaker *et al*, 2014

X-VeRT: Study Objective and Design

Exploring the efficacy and safety of once-daily rivaroxaban for the prevention of cardiovascular events* in patients with non-valvular AF scheduled for elective cardioversion compared with dose-adjusted VKAs

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

1,504 patients randomized from **141 centres** across **16 countries**



*Composite of stroke and TIA, non-CNS systemic embolism (SE), MI and cardiovascular death; **Protocol recommended only if adequate anticoagulation or immediate TEE; ***15 mg if CrCl 30–49 ml/min; and VKA with INR 2.0–3.0

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

Primary Outcomes

Primary Efficacy Outcome

	Rivaroxaban (N=978)		VKA (N=492)		Risk ratio (95% CI)
	%	n*	%	n*	
Primary efficacy outcome	**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	

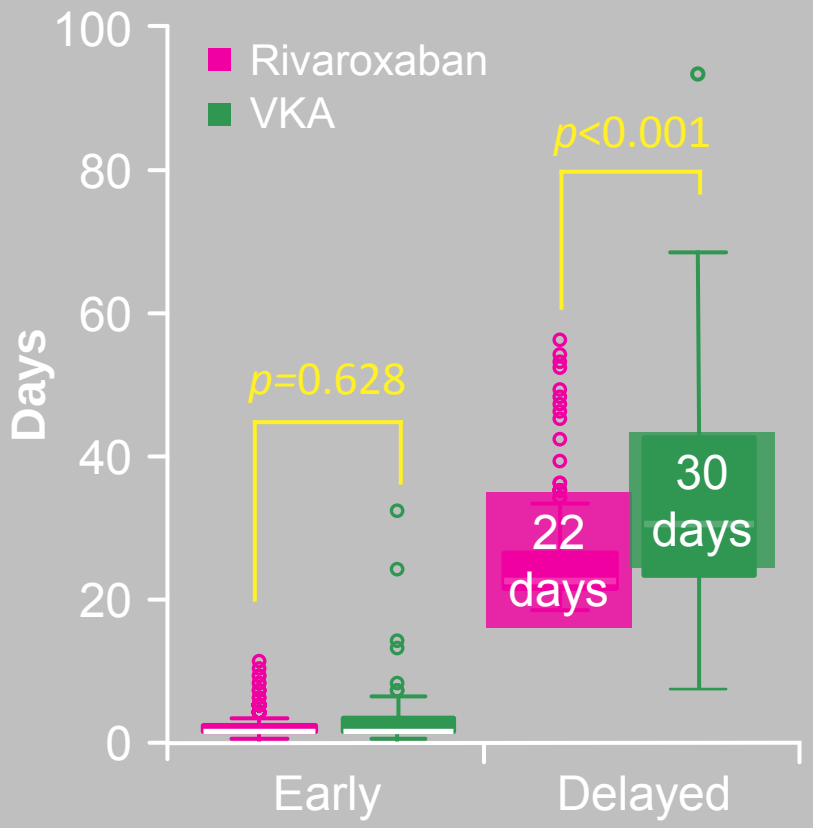
*Number of patients with events; patients may have experienced more than one primary efficacy event mITT population

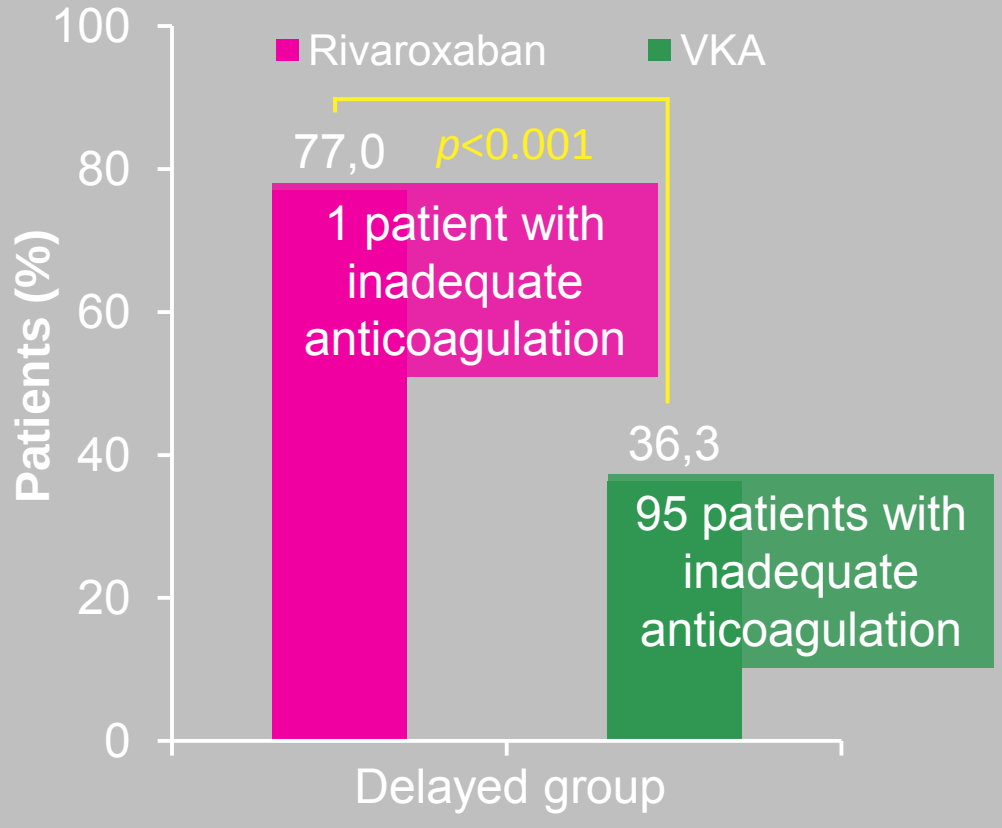
Primary Safety Outcome

	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

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)

Conclusion

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- First prospective, randomized trial of a novel OAC in patients with AF undergoing elective cardioversion
- Low and similar incidence of primary efficacy outcome events between the treatment groups
- Similar incidence of major bleeding
- Time to cardioversion was similar (early strategy) or significantly shorter (delayed strategy) using rivaroxaban compared with VKA

Oral rivaroxaban 20 mg once daily appears to be an effective and safe alternative to VKA, and allows prompt elective cardioversion in patients with AF