

	RE-LY	ROCKET-AF	ARISTOTLE	ENGAGE-AF
Comparison	Dabigatran 150 mg bd, 110 mg bd vs warfarin	Rivaroxaban 20 mg od vs warfarin	Apixaban 5 mg bd vs warfarin	Edoxban 60 mg od, 30 mg od vs warfarin
Patients, n	18,113	14,264	18,201	21,105
Study design	Double blind, open-label with blinded endpoint evaluation	Double blind, double dummy	Double blind, double dummy	Double blind, double dummy
Reduced dose for selected patients	–	15 mg od: CrCl 30–49 mL/min	2.5 mg bd where two of: ➤ serum creatinine ≥1.5 mg/dL ➤ age ≥80 years ➤ body weight ≤60 kg	Dose halved (30 mg, 15 mg) where one of: ➤ CrCl 30–50 mL/min, ➤ body weight ≤60 kg ➤ concomitant verapamil, quinidine or dronedarone
Mean patient age, years	71	73	70 (median)	72
Mean CHADS ₂ score	2.1	3.5	2.1	2.8
Mean time in therapeutic range, %	64.0	55.0	62.2	64.9
Valve exclusion	Severe valve disorder	Significant MS; any prosthesis	Moderate/Severe MS; mechanical	Moderate/Severe MS; mechanical
Paroxysmal AF, %	32	18	15	25
Primary endpoint SSE HR (95 % CI)*	150 mg: 0.65 (0.52–0.81) ^S 110 mg: 0.90 (0.74–1.10)	0.88 (0.75–1.03)	0.79 (0.66–0.95) ^S	60 mg: 0.79 (0.63–0.99) 30 mg: 1.07 (0.87–1.31)
Ischaemic stroke HR (95 % CI)*	150 mg: 0.76 (0.60–0.98) ^S 110 mg: 1.11 (0.89–1.40)	0.94 (0.75–1.17)	0.92 (0.74–1.13)	60 mg: 1.00 (0.83–1.19) 30 mg: 1.41 (1.19–1.67)
Major bleeding HR (95 % CI)*	150 mg: 0.93 (0.81–1.07) 110 mg: 0.80 (0.70–0.93) ^S	1.04 (0.90–1.20)	0.69 (0.60–0.80) ^S	60 mg: 0.80 (0.71–0.91) 30 mg: 0.47 (0.41–0.55)
Major gastrointestinal bleeding HR (95 % CI)*	150 mg: 1.48 (1.18–1.85) 110 mg: 1.08 (0.85–1.38)	1.61 (1.30–1.99)	0.89 (0.70–1.15)	60 mg: 1.23 (1.02–1.50) 30 mg: 0.67 (0.53–0.83) ^S
Intracranial bleeding HR (95 % CI)*	150 mg: 0.40 (0.27–0.60) ^S 110 mg: 0.31 (0.20–0.47) ^S	0.67 (0.47–0.93) ^S	0.42 (0.30–0.58) ^S	60 mg: 0.47 (0.34–0.63) ^S 30 mg: 0.30 (0.21–0.43) ^S
Reduction in all-cause mortality	150 mg: 0.88 (0.77–1.00) 110 mg: 0.91 (0.80–1.03)	0.85 (0.70–1.02)	0.89 (0.80–0.99)	60 mg: No 30 mg: Yes
All comparisons versus warfarin and reached non-inferiority, unless otherwise stated.				
*Data for dabigatran are presented as relative risk (95 % CI)				
^S Superior				
AF = atrial fibrillation; CHADS ₂ = congestive heart failure, hypertension history, age≥75 years, diabetes mellitus history, stroke or symptoms of transient ischaemic attack; CI = confidence interval; CrCl = creatinine clearance; HR = hazard ratio; MS = mitral stenosis; NOAC = non-vitamin K oral anticoagulant; SSE = stroke or systemic embolism				