Clinical data for stroke prevention in patients with non-valvular atrial fibrillation

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Disclosures

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Session Overview

- Patient management for stroke prevention in NVAF
- Overview on NOACs NVAF Randomized Controlled Trial results
- Review NOAC Real World Data on NVAF stroke prevention

NVAF-related stroke is associated with significant morbidity and mortality[1,2]

Morbidity

NVAF **increases risk of stroke** by approximately **5-fold**[1]

NVAF-related stroke is associated with **increased severity and disability**[2]

Mortality

30-day mortality rate of **~33%** (vs 16% for non-AF strokes)[2]

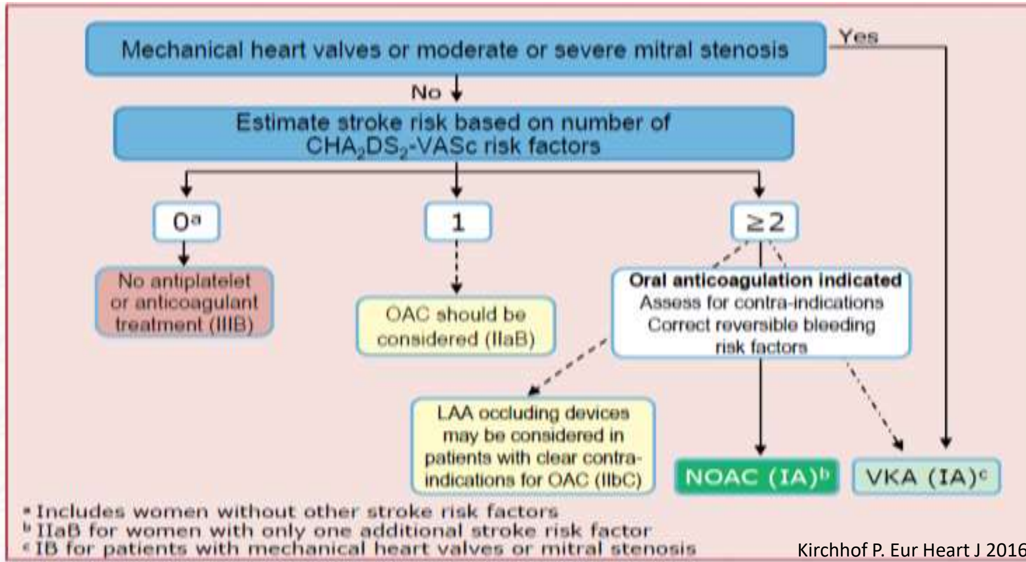
1-year mortality rate of **~50%** (vs 27% for patients without AF)[2]

20% of all strokes in the general population are due to AF[2]

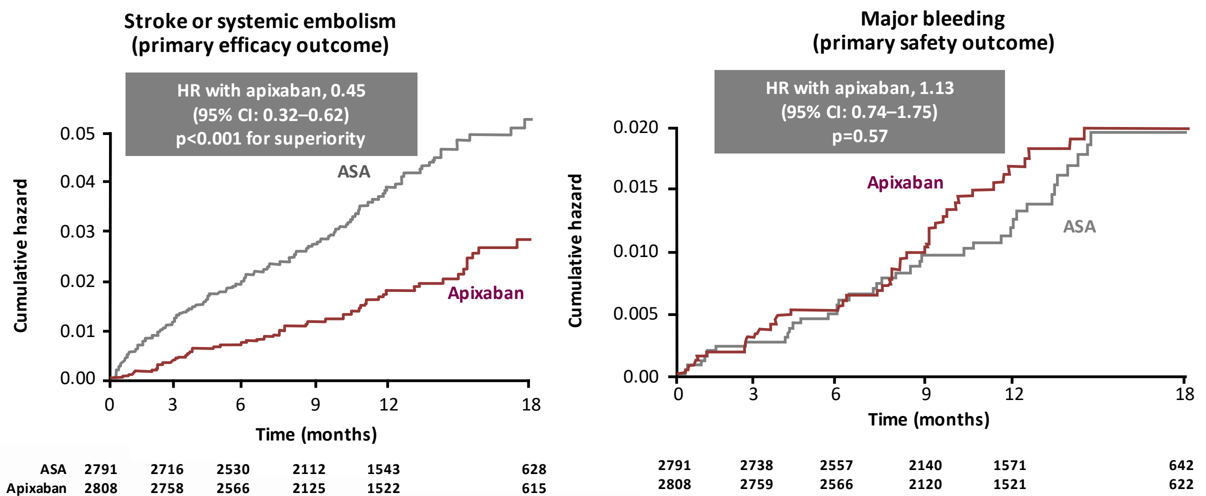
AF: atrial fibrillation.

1. Wolf et al. *Stroke.* 1991;22:983–988; 2. Marini et al. *Stroke.* 2005;36:1115–1119.

Stroke prevention in NVAF. 2016 ESC Guidelines recommendations

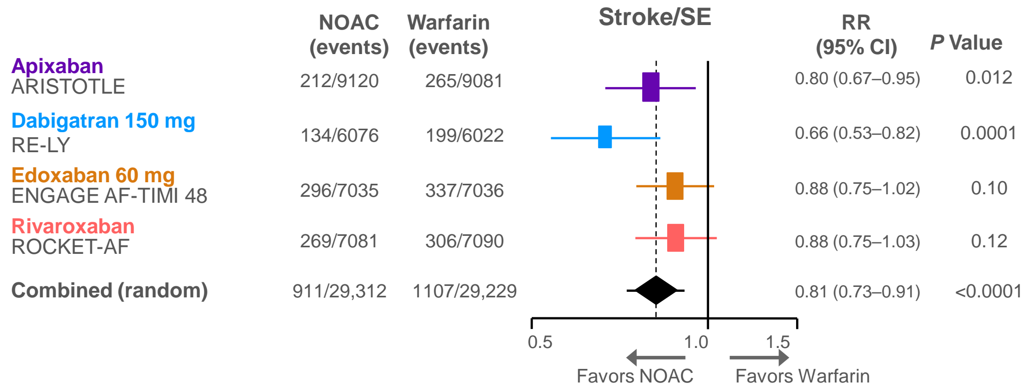


AVERROES: apixaban vs. ASA – reduction in stroke or systemic embolism without increased bleeding[1]



1. Connolly et al. *N Engl J Med* 2011;364:806–817.

NOACs Significantly Reduced Stroke/SE vs Warfarin



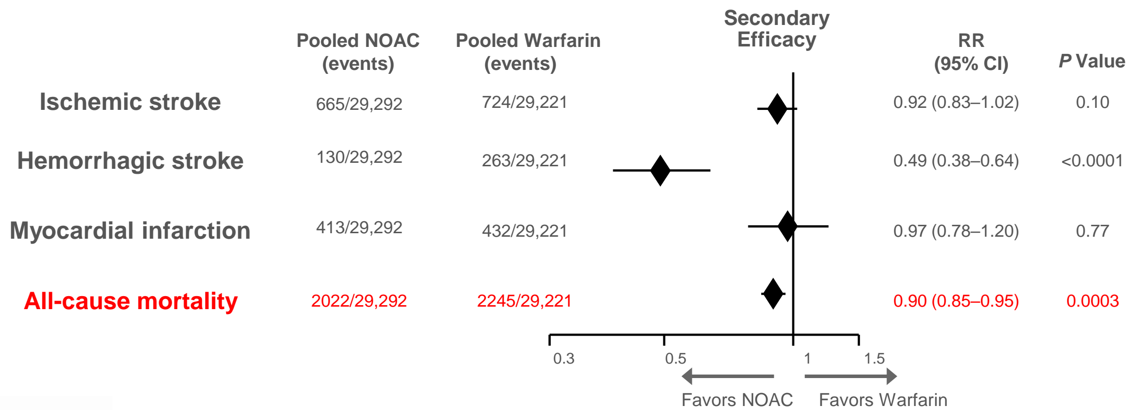
Meta-analysis included **71,683 patients** enrolled in ARISTOTLE, RE-LY, ENGAGE-AF TIMI 48, and ROCKET-AF

- 42,411 patients received a NOAC
- 29,272 patients received warfarin

CI=confidence interval; RR=relative risk; SE=systemic embolism.

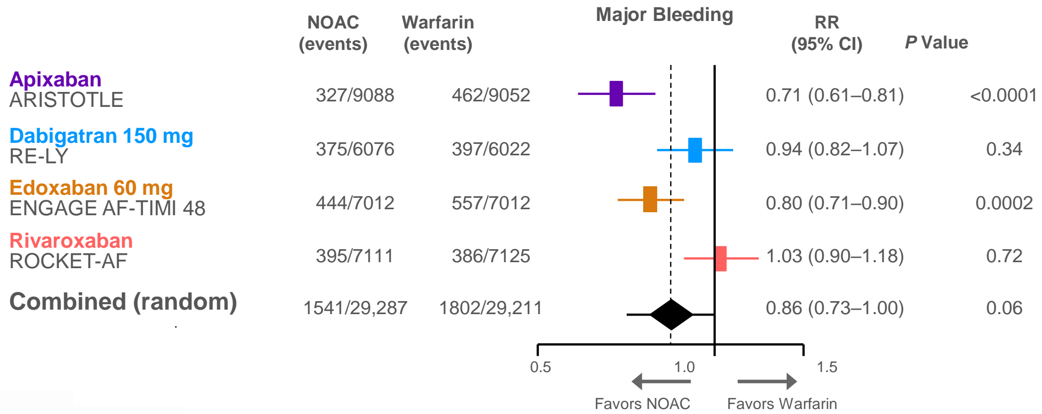
Ruff CT et al. Lancet. 2014;383:955-962.

NOACs Significantly Reduced Hemorrhagic Stroke and All-cause Mortality vs Warfarin



Ruff CT et al. *Lancet.* 2014;383:955-962.

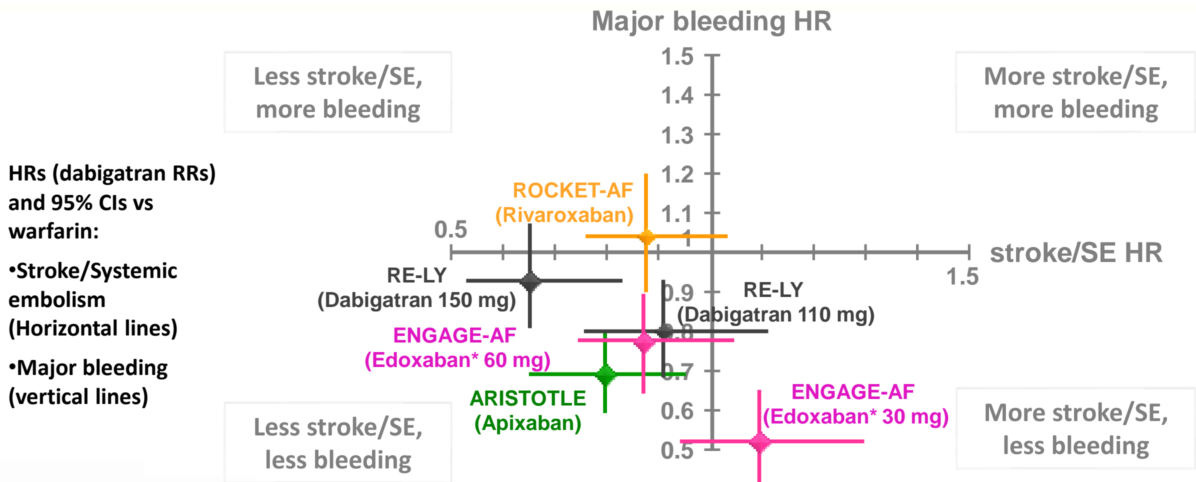
NOACs Are at Least as Safe as Warfarin With Respect to Major Bleeding



	NOAC (events)	Warfarin (events)	RR (95% CI)	*P* Value
Apixaban ARISTOTLE	327/9088	462/9052	0.71 (0.61–0.81)	<0.0001
Dabigatran 150 mg RE-LY	375/6076	397/6022	0.94 (0.82–1.07)	0.34
Edoxaban 60 mg ENGAGE AF-TIMI 48	444/7012	557/7012	0.80 (0.71–0.90)	0.0002
Rivaroxaban ROCKET-AF	395/7111	386/7125	1.03 (0.90–1.18)	0.72
Combined (random)	1541/29,287	1802/29,211	0.86 (0.73–1.00)	0.06

Ruff CT et al. *Lancet*. 2014;383:955-962.

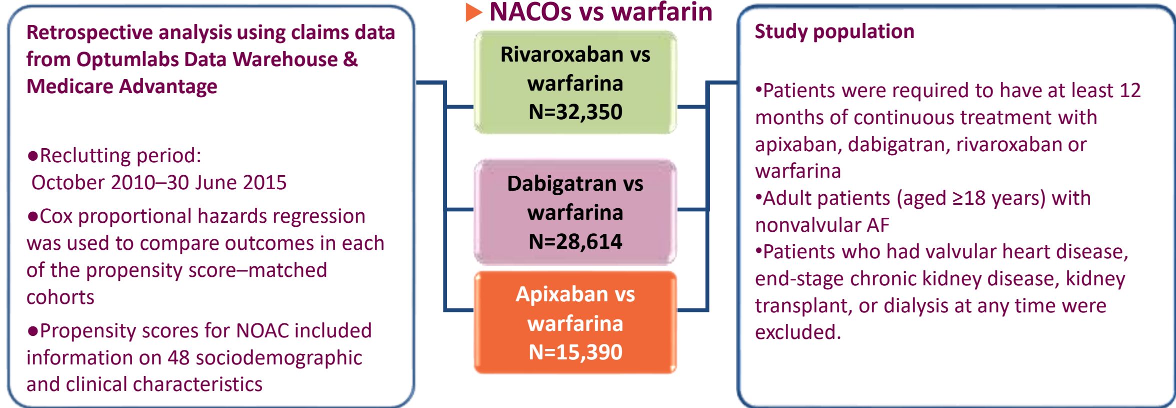
Summary of the main efficacy and safety results



Schulman et al. Thromb Res 2013;131 (Suppl.1):S63–S66

Mayo clinic RWD study design

▶ **3 matched cohorts were created using 1:1 propensity score matching**



Outcomes were assessed using the ICD-9 coding

Yao et al. J Am Heart Assoc. 2016;5:e003725.

Results: effectiveness

	Event Rate per 100 person-year		Hazard Ratio (95% CI)	*P* Value
Apixaban vs Warfarin				
	n=7695	n=7695		
S/SE	1.33	1.66	0.67 (0.46–0.98)	0.04
Ischemic	1.03	1.05	0.83 (0.53–1.29)	0.40
Hemorrhagic	0.19	0.46	0.35 (0.14–0.88)	0.03
Dabigatran vs Warfarin				
	n=14 307	n=14 307		
S/SE	1.18	1.22	0.98 (0.76–1.26)	0.88
Ischemic	0.92	0.88	1.06 (0.79–1.42)	0.70
Hemorrhagic	0.16	0.29	0.56 (0.30–1.04)	0.07
Rivaroxaban vs Warfarin				
	n=16 175	n=16 175		
S/SE	1.26	1.29	0.93 (0.72–1.19)	0.56
Ischemic	0.95	0.88	1.01 (0.75–1.36)	0.95
Hemorrhagic	0.21	0.32	0.61 (0.35–1.07)	0.08

Favors NOAC 1.0 **Favors Warfarin**

Yao et al. J Am Heart Assoc. 2016;5:e003725.

Results: safety

	Event Rate per 100 person-year			Hazard Ratio (95% CI)	*P* Value
	Apixaban vs Warfarin				
	n=7695	n=7695			
Major Bleeding	2.33	4.46		0.45 (0.34–0.59)	<0.001
Intracranial	0.29	1.06		0.24 (0.12–0.50)	<0.001
Gastrointestinal	1.78	3.04		0.51 (0.37–0.70)	<0.001
	Dabigatran vs Warfarin				
	n=14 307	n=14 307			
Major Bleeding	2.37	3.03		0.79 (0.67–0.94)	<0.01
Intracranial	0.28	0.79		0.36 (0.23–0.56)	<0.001
Gastrointestinal	1.97	1.95		1.03 (0.84–1.26)	0.78
	Rivaroxaban vs Warfarin				
	n=16 175	n=16 175			
Major Bleeding	4.04	3.64		1.04 (0.90–1.20)	0.60
Intracranial	0.44	0.79		0.51 (0.35–0.75)	<0.001
Gastrointestinal	3.26	2.53		1.21 (1.02–1.43)	0.03
			Favors NOAC 1.0 **Favors Warfarin**		

Yao et al. J Am Heart Assoc. 2016;5:e003725.

Summary

- **The NOACs should be considered rather than VKA in most patients with NVAF[1]**
- **All NOACs have benefits over warfarin, but the efficacy and safety profiles of the NOACs vs warfarin vary[2]**
  - These are to be considered when selecting the appropriate NOAC for each patient
- **Consistent with RCT results,[3] initial findings of real-world research suggest that apixaban is associated with significantly less major bleeding than warfarin[4]**

1. Camm et al. *Europace* 2012;14:1385–1413; 2. Schulman. *Thromb Haemost*. 2014;111:575-82; 3. Granger et al. *N Engl J Med.* 2011;365:981–992; 4.Yao et al. J Am Heart Assoc. 2016;5:e003725;

RCT: randomised controlled trial