

## New and improved? Oral anticoagulants to reduce stroke in atrial fibrillation

**The clinical issue:** In patients with atrial fibrillation (AF), anticoagulation reduces the risk of stroke by two-thirds, making it a superb preventive strategy. For 50 years, warfarin has been the main drug used for this purpose, but it is notoriously challenging to use, and causes more adverse events than any other medication. Three new oral anticoagulants have recently been compared to warfarin in large randomized trials in AF patients. All three new agents were at least as effective as warfarin at reducing stroke, and did not increase the risk of bleeding.

### The trials:

Trial name Drug Studied Median follow-up time	Patients enrolled	Stroke/emboli rate		Intracranial bleed rate		Major bleed rate	
		new drug	warfarin	new drug	warfarin	new drug	warfarin
“RE-LY” <sup>1</sup> Dabigatrab [Pradaxa] 150 mg b.i.d. 2 years	>18,000 patients ≥1 risk factor for stroke	1.1 % <sup>‡</sup>	1.7%	0.1% <sup>‡</sup>	0.4%	3.1% (NS)	3.4%
“ROCKET-AF” <sup>2</sup> Rivaroxaban [Xarelto] 20 mg q.d. 1 year	>14,000 patients History of stroke or ≥2 risk factor for stroke	1.7% <sup>†</sup>	2.2%	0.5% <sup>‡</sup>	0.7%	15% <sup>§</sup> (NS)	15%
“ARISTOTLE” <sup>3</sup> Apixaban [Eliquis] ¶ 5 mg b.i.d. 1.8 years	>18,000 patients ≥1 risk factor for stroke	1.3% <sup>‡</sup>	1.6%	0.2% <sup>‡</sup>	0.5%	2.1% <sup>*</sup>	3.1%

**Difference compared to warfarin:** \* p<0.001 † p<0.001 for non-inferiority ‡ p<0.05 (NS) p-value not significant  
 § major + minor bleed rate ¶ apixaban is not currently FDA approved for AF-related stroke reduction

**Implications for practice:** Based on the clinical trial data, these three new oral anticoagulants appear to be at least as effective as warfarin in reducing the risk of stroke in AF without increasing the risk of bleeding, and are promising alternatives to warfarin. However, experience with these drugs is still limited, and there is not yet evidence that their performance in actual practice will measure up to the encouraging trial data. They cannot be used in patients with renal insufficiency, cannot be reversed in case of bleeding, and are very expensive (~\$3,000 per year). Among the currently available agents, the once-daily dosing of rivaroxaban may make it easier for patients to use than dabigatran, which requires twice daily dosing for efficacy. Until more evidence becomes available from typical practice settings, the novel oral anticoagulants may not be appropriate for all patients, in particular those whose INRs are stably controlled on warfarin.

**References:** 1. Connolly SJ et al. Dabigatran versus warfarin in patients with atrial fibrillation. *NEJM* 2009;361:1139-2. Patel MR et al. Rivaroxaban versus warfarin in non-valvular atrial fibrillation. *NEJM* 2011;365:883. 3. Granger CB et al. Apixaban versus warfarin in patients with atrial fibrillation. *NEJM* 2011;365:981.

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**These are general recommendations only; specific clinical decisions should be made by the treating physician based on an individual patient’s clinical condition.**