ACP Journal Club. Review: new oral anticoagulants reduced stroke and systemic embolism compared with warfarin in AF.

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Annals of internal medicine, 157(6)

0003-4819

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2012-09-01

10.7326/0003-4819-157-6-201209180-02002

Peer reviewed
Therapeutics

Apixaban reduced stroke and systemic embolism compared with warfarin in atrial fibrillation

Clinical impact ratings: ★★★★★☆ ★★★★★★★★ ★★★★★★★★★ ★★★★★★

Question
In patients with atrial fibrillation (AF), how does apixaban compare with warfarin for prevention of stroke or systemic embolism?

Methods


Allocation: [Concealed]†

Blinding: Blinded (patients, clinicians, outcome assessors, and {data collectors and analysts})*.

Follow-up period: Median 1.8 years.

Setting: 1034 centers in 39 countries.

Patients: 18 201 patients (median age 70 y, 65% men, mean CHADS2 score 2.1) with AF or atrial flutter at enrollment or ≥ 2 episodes of AF or atrial flutter ≥ 2 weeks apart in the 12 months before enrollment, and ≥ 1 of age ≥ 75 years; previous stroke, transient ischemic attack, or systemic embolism; systolic heart failure within 3 months or left ventricular ejection fraction ≤ 40%; diabetes mellitus; and hypertension requiring pharmacologic treatment. Exclusion criteria included AF due to a reversible cause, moderate or severe mitral stenosis, need for anticoagulation other than for AF, stroke within 7 days, need for aspirin at a dose > 165 mg/d or for both aspirin and clopidogrel, and severe renal insufficiency.

Intervention: Apixaban, 5 mg twice daily, plus warfarin placebo (n = 9120), or warfarin, adjusted to achieve a target international normalized ratio (INR) of 2.0 to 3.0, plus apixaban placebo (n = 9081). Apixaban patients received 2.5 mg twice daily if they had ≥ 2 of age ≥ 80 years, body weight ≤ 60 kg, and serum creatinine level ≥ 133 µmol/L (1.5 mg/dL).

Outcomes: Primary efficacy outcome was a composite of stroke or systemic embolism. Primary safety outcome was major bleeding. Secondary outcomes included all-cause mortality and a composite of major bleeding and clinically relevant nonmajor bleeding.

Patient follow-up: 97.9% for vital status (intention-to-treat analysis).

Main results

The main results are in the Table.

Conclusion

In patients with atrial fibrillation, apixaban reduced stroke and systemic embolism compared with warfarin.

*Information provided by author.
†See Glossary.

Sources of funding: Bristol-Myers Squibb and Pfizer.

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(continued on page 3)
Rivaroxaban reduced stroke and systemic embolism compared with warfarin in nonvalvular AF

Clinical impact ratings: ★★★★★★★ ★★★★★★★ ★★★★★★★ ★★★★★★★☆

Question
In patients with nonvalvular atrial fibrillation (AF) at moderate-to-high risk for stroke, how does rivaroxaban compare with warfarin for prevention of stroke or systemic embolism?

Methods
Design: Randomized controlled trial (Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation [ROCKET AF]). ClinicalTrials.gov NCT00403767.

Allocation: Concealed. *

Blinding: Blinded (patients, clinicians, and outcome assessors).*

Follow-up period: Median 590 days.

Setting: 1178 centers in 45 countries.

| Rivaroxaban vs warfarin in nonvalvular atrial fibrillation† |
|-------------------------|---------|-----------------|-----------------|
| Outcomes                | Number of events/100 patient-y | At a median 590 d |
| Stroke or systemic embolism‡ | Rivaroxaban | Warfarin | RRR (95% CI) | NNT (CI) |
| Stroke, systemic embolism, CV death, or MI† | 3.9 | 4.6 | 15% (4 to 25) | 94 (54 to 354) |
| Major or nonmajor clinically relevant bleeding | 14.9 | 14.5 | 2.7% (−4 to 10) | Not significant |

†CV = cardiovascular; MI = myocardial infarction; other abbreviations defined in Glossary. RRR, RRI, NNT, NNH, and CI calculated from hazard ratios and control event proportions in article.

‡Stroke (RRR 15%, CI −3 to 30), systemic embolism (RRR 77%, CI 39 to 91), CV death (RRR 11%, CI −10 to 27), MI (RRR 19%, CI −6 to 37).

Commentary (continued from page 2)

In addition, apixaban reduced mortality compared with warfarin, a trend that was observed with dabigatran (1) and rivaroxaban. Despite their similarities, there are important differences among the trials of these anticoagulants. Whereas patients and clinicians were not blinded to treatment in the RE-LY trial (1), the ROCKET AF and ARISTOTLE trials were double-blind. Dabigatran and apixaban were given twice daily, whereas rivaroxaban was given only once daily. Patients in the ROCKET AF were older and had more comorbid conditions and higher risk for stroke than those in the RE-LY and ARISTOTLE trials. Finally, the average amount of time in which the INR was in the therapeutic range (assessing the quality of warfarin dosing) was 64% in the RE-LY trial (1) and 62% in the ARISTOTLE trial but only 55% in the ROCKET AF.

Although direct thrombin and factor Xa inhibitors overcome the need for routine blood monitoring and are more effective and safer than warfarin, switching to a newer agent may not be necessary for individual patients in whom INR has been well-controlled with warfarin for years. As well, agents to reverse the effect of the newer anticoagulants are still under development and not routinely available (3). Finally, future data on cost-effectiveness will further influence clinical decision-making. Thus, although newer anticoagulants are attractive alternatives, warfarin may continue to be used worldwide in many patients with AF.

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References