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

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Although warfarin prevents stroke in patients with nonvalvular AF, the risk for gastrointestinal bleeding, a source of major bleeding in the elderly, was numerically lower in patients treated with apixaban. Interestingly, patients with moderate-to-severe renal impairment were most likely to benefit from the lower risk for bleeding with apixaban.

The ROCKET AF assessed the effect of rivaroxaban in an older population (mean age 73 y vs 70 y) with more comorbid conditions and higher risk for stroke (mean CHADS$_2$ score 3.5 vs 2.1) than ARISTOTLE. Compared with warfarin, rivaroxaban reduced stroke and systemic embolism but without a reduction in major bleeding, although it did decrease intracranial hemorrhage and fatal bleeding.

All 3 new anticoagulants reduced risk for stroke (mostly hemorrhagic, by preservation of tissue factor VIIa complexes in the brain [2]) and systemic embolism as well as serious bleeding compared with warfarin; apixaban also reduced rates of major and gastrointestinal bleeding.

(continued on page 3)
Therapeutics

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†

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of events/100 patient-y</th>
<th>At a median 590 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke or systemic embolism†</td>
<td>Rivaroxaban</td>
<td>Warfarin</td>
</tr>
<tr>
<td>Stroke, systemic embolism, CV death, or MI†</td>
<td>1.7</td>
<td>2.2</td>
</tr>
<tr>
<td>Stroke, systemic embolism, CV death, or MI†</td>
<td>3.9</td>
<td>4.6</td>
</tr>
<tr>
<td>Major or nonmajor clinically relevant bleeding</td>
<td>14.9</td>
<td>14.5</td>
</tr>
</tbody>
</table>

†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