New Age Anticoagulants: A Safer and More Effective Alternative to Warfarin?

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Atrial fibrillation is the most common sustained heart rhythm in the United States. This prevalence rate of 8.8/100 (Wolf, Abbott, & Kannel, 1991). The largest risk for patients with atrial fibrillation is that of ischemic stroke from embolization of an atrial clot, thus the long standing treatment for this arrhythmia is aggressive anticoagulation. For decades this has been accomplished with the use of warfarin, however, the increased risk of hemorrhage combined with the inconvenience of weekly blood testing has prompted the development of potentially safer and more effective alternatives. A systematic review of the literature identified studies that examined the safety and efficacy of direct thrombin and factor Xa inhibitors compared with traditional warfarin therapy. It was found that the new anticoagulants reduce the incidence of stroke and thromboembolism without increasing the risk of major hemorrhage when compared to warfarin. This provides health care providers an additional option to safely anti-coagulate patients diagnosed with non-valvular atrial fibrillation without the burden of PT/INR monitoring.

### Research Questions

- In patients with non-valvular atrial fibrillation, are the novel, oral anticoagulants a safer and more effective option for the prevention of stroke and systemic embolism?
- In patients that are anticoagulated with any novel anticoagulant, is there a reversal agent available in the event of major trauma, bleeding, or the need for surgery?
- Are novel anticoagulants a cost effective option compared to warfarin in patients with non-valvular atrial fibrillation?

### Literature Review

**Primary end point of stroke or systemic embolism was lower with novel anticoagulants compared with warfarin**

**Risk factors for any cause was lower with all novel anticoagulants than with warfarin**

**Significant reduction in hemorrhagic stroke with novel anticoagulants compared to warfarin**

### Discussion

- Currently no laboratory test to monitor the effects of any novel anticoagulant.
- In patients with renal insufficiency, half life of drug is lengthened.
- No antidote to counteract the effects of direct thrombin or factor Xa inhibitors.
- All authors indicated the need for an adequately powered head to head study of direct thrombin inhibitors versus factor Xa inhibitors.
- Current literature indicates cost effectiveness but still many more questions than answers.

### Applicability to Clinical Practice

- The issues of cost, safety, and efficacy must be continually investigated by researchers and evaluated by providers in order to optimize outcomes for any patients requiring anticoagulation.
- The use of any novel anticoagulant or warfarin is clearly better than the avoidance of any anticoagulation in patients with atrial fibrillation.
- Consideration should be given to individual patients' stroke and bleeding risk factors, potential financial burden, desired clinical effect, and patient/family concerns prior to initiation or alteration of anticoagulation.

### References


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### Table 1: Main Study Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Drug</th>
<th>No. of Patients</th>
<th>Masking Test</th>
<th>Analysis (Primary Outcome)</th>
<th>Follow-up mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE-LY</td>
<td>Dabigatran</td>
<td>12098</td>
<td>Open label</td>
<td>ITT</td>
<td>30</td>
</tr>
<tr>
<td>ROCKET AF</td>
<td>Rivaroxaban</td>
<td>10544</td>
<td>Double blind</td>
<td>ITT</td>
<td>20</td>
</tr>
<tr>
<td>ARISTOTLE</td>
<td>Apixaban</td>
<td>3031</td>
<td>Double blind</td>
<td>ITT</td>
<td>10</td>
</tr>
</tbody>
</table>

### Table 2: Baseline Characteristics of the Patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>RE-LY Dabigatran</th>
<th>RE-LY Warfarin</th>
<th>ROCKET AF Rivaroxaban</th>
<th>ROCKET AF Warfarin</th>
<th>ARISTOTLE Apixaban</th>
<th>ARISTOTLE Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>63.2</td>
<td>63.2</td>
<td>60.3</td>
<td>60.3</td>
<td>60.5</td>
<td>65</td>
</tr>
<tr>
<td>Age (y)</td>
<td>71.5</td>
<td>71.6</td>
<td>73</td>
<td>73</td>
<td>70</td>
<td>70</td>
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<tr>
<td>Aspirin at entry (%)</td>
<td>38.7</td>
<td>40.6</td>
<td>36.3</td>
<td>36.3</td>
<td>31.3</td>
<td>30.5</td>
</tr>
<tr>
<td>Vitamin K antagonist at entry (%)</td>
<td>62.3</td>
<td>62.3</td>
<td>62.5</td>
<td>62.5</td>
<td>62.3</td>
<td>62.5</td>
</tr>
<tr>
<td>Long-term vitamin K antagonist therapy (%)</td>
<td>50.2</td>
<td>48.6</td>
<td>57.1</td>
<td>57.1</td>
<td>57.1</td>
<td>57.1</td>
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<tr>
<td>Risk factors for stroke (%)</td>
<td>32.6</td>
<td>32.1</td>
<td>87</td>
<td>86.9</td>
<td>30.2</td>
<td>30.2</td>
</tr>
<tr>
<td>Previous stroke, TIA, or both (%)</td>
<td>20.3</td>
<td>19.8</td>
<td>50.4</td>
<td>54.6</td>
<td>44.5</td>
<td>42.9</td>
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<tr>
<td>Previous stroke, TIA, or embolism (%)</td>
<td>78.9</td>
<td>78.9</td>
<td>90.3</td>
<td>90.8</td>
<td>87.3</td>
<td>87.6</td>
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<tr>
<td>Diabetes (%)</td>
<td>21.1</td>
<td>23.4</td>
<td>40.4</td>
<td>39.5</td>
<td>25</td>
<td>24.9</td>
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<tr>
<td>LDL or heart failure (%)</td>
<td>31.8</td>
<td>31.9</td>
<td>62.6</td>
<td>62.6</td>
<td>35.5</td>
<td>35.4</td>
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</tbody>
</table>

### Abbreviations

- ARISTOTLE: Apixaban for the Prevention of Stroke in Subjects With Atrial Fibrillation
- LDL: low density lipoprotein
- RE-LY: Randomized Evaluation of Long-Term Anticoagulant Therapy
- ROCKET AF: An Efficacy and Safety Study of Rivaroxaban With Warfarin for the Prevention of Stroke and Non-Central Nervous System Systemic Embolism in Patients With Non-Valvular Atrial Fibrillation
- TIA: transient ischemic attack

### Special thanks

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