Safety and Efficacy of Uninterrupted Anticoagulation with Dabigatran Etexilate versus Warfarin in Patients Undergoing Catheter Ablation of Atrial Fibrillation: The RE-CIRCUIT™ Study

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Background

- Thromboembolic and bleeding events, including cardiac tamponade, are some of the most feared complications of AF ablation.

- Uninterrupted anticoagulation with a vitamin K antagonist (VKA) helps to minimize the risk of these complications, and is now a well-established strategy.

- This approach is cumbersome as many AF patients are anticoagulated with a non-VKA oral anticoagulant (NOAC) prior to AF ablation. Therefore the VKA strategy requires transition to VKA prior to ablation.

- Dabigatran etexilate has established efficacy and safety for stroke prevention in AF.

- Data on the outcomes of AF ablation on uninterrupted NOAC therapy are limited.
OBJECTIVE & DESIGN

- To investigate the safety and efficacy of uninterrupted dabigatran vs. warfarin for peri-procedural anticoagulation in patients undergoing catheter ablation of AF

- Prospective randomized open-label multicenter clinical trial of 704 patients in 104 sites in 11 countries between April 2015 and July 2016

**Primary endpoint:** adjudicated major bleeding events from venous access up to 8 weeks post-ablation†

**Secondary endpoints** adjudicated thromboembolic events from venous access to 8 weeks post-ablation†

*And eligible for dabigatran 150 mg bid according to local prescribing information.
†Primary end point assessed from the start of the ablation procedure and up to 8 weeks post-ablation.
### BASELINE CHARACTERISTICS

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Dabigatran 150 mg bid (n = 317)</th>
<th>Warfarin (n = 318)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (standard deviation), years</td>
<td>59.1 (10.4)</td>
<td>59.3 (10.3)</td>
</tr>
<tr>
<td>Atrial fibrillation, n (%)</td>
<td></td>
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<tr>
<td>Paroxysmal</td>
<td>213 (67.2)</td>
<td>219 (68.9)</td>
</tr>
<tr>
<td>Persistent</td>
<td>86 (27.1)</td>
<td>81 (25.5)</td>
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<tr>
<td>Longstanding persistent</td>
<td>18 (5.7)</td>
<td>18 (5.7)</td>
</tr>
<tr>
<td>CHA&lt;sub&gt;2&lt;/sub&gt;DS&lt;sub&gt;2&lt;/sub&gt;-VASc score, mean</td>
<td>2.0</td>
<td>2.2</td>
</tr>
<tr>
<td>Medical history, n (%)</td>
<td></td>
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<tr>
<td>Congestive heart failure</td>
<td>31 (9.8)</td>
<td>34 (10.7)</td>
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<tr>
<td>Hypertension</td>
<td>166 (52.4)</td>
<td>177 (55.7)</td>
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<tr>
<td>Diabetes mellitus</td>
<td>30 (9.5)</td>
<td>34 (10.7)</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>10 (3.2)</td>
<td>9 (2.8)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>32 (10.1)</td>
<td>48 (15.1)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>10 (3.2)</td>
<td>15 (4.7)</td>
</tr>
<tr>
<td>Prior major bleeding or predisposition</td>
<td>3 (0.9)</td>
<td>4 (1.3)</td>
</tr>
<tr>
<td>TTR during study, mean %*</td>
<td>–</td>
<td>66.4</td>
</tr>
</tbody>
</table>

TTR, time in therapeutic range of INR 2.0-3.0. *Based on treated set, n = 330.
RESULTS

- Significantly fewer major bleeding events with uninterrupted dabigatran compared with warfarin

**Bar Chart**

- **Absolute risk difference**: -5.3% (95% CI: -8.4, -2.2)
- **Relative risk reduction**: 77.2%
- **P = 0.0009**

**Patients with ISTH major bleeding events, %**

- **Dabigatran**: n = 5, 1.6%
- **Warfarin**: n = 22, 6.9%
TIMING OF BLEEDING EVENTS

HR 0.22; 95% CI 0.08, 0.59*

*Cox proportional hazard model and Wald confidence limits.
SECONDARY ENDPOINTS

Low Rate of Thromboembolic Events

• Stroke: no events
• Systemic embolism: no events
• Transient ischemic attack: dabigatran 0 vs warfarin 1

Minor Bleeding Events Similar

• Dabigatran 59 (18.6%) vs warfarin 54 (17.0%)
Summary

- AF ablation on uninterrupted dabigatran results in lower rate of major bleeding compared with uninterrupted warfarin
- Absolute bleeding risk reduction with dabigatran was 5.3% (RR=77% lower)
- No thromboembolic events in either group and one TIA in a patient on warfarin
- Minor bleeding events similar
- No deaths
Conclusion

• AF ablation on uninterrupted dabigatran is a better anticoagulation strategy compared with uninterrupted warfarin

• The reversal agent idarucizumab, while not needed in this trial, also a consideration in adopting uninterrupted dabigatran as the preferred anticoagulation strategy around AF ablation
Uninterrupted Dabigatran versus Warfarin for Ablation in Atrial Fibrillation

Hugh Calkins, M.D., Stephan Willems, M.D., Edward P. Gerstenfeld, M.D., Atul Verma, M.D., Richard Schilling, M.D., Stefan H. Hohnloser, M.D., Ken Okumura, M.D., Ph.D., Harvey Serota, M.D., Matias Nordaby, M.D., Kelly Guiver, M.Sc., Branislav Biss, M.D., Marc A. Brouwer, M.D., Ph.D., and Massimo Grimaldi, M.D., Ph.D., for the RE-CIRCUIT Investigators*