Aortic Stenosis, but not Mitral or Aortic Regurgitation, is Associated with Adverse Outcomes with Atrial Fibrillation: Results from the ARISTOTLE Trial

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Objectives

- To assess the relationship between each subtype of valvular heart disease (VHD) and clinical outcomes in patients with atrial fibrillation (AF) on anticoagulant treatment.
- To assess the efficacy and safety of apixaban vs. warfarin in patients with AF in each of the VHD subtypes.

Background

- VHD is associated with a higher risk of thrombotic events but there is uncertainty about risks for various VHD subtypes.
- The Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) trial found apixaban to be superior to warfarin in efficacy and safety in patients with AF.
- We used the ARISTOTLE trial database to focus on specific VHD subtypes in order to assess the relationship between VHD clinical outcomes, and the treatment effect of apixaban versus warfarin.

Methods

- Patients were considered to have VHD if they had a history or evidence of at least moderate valvular disease. VHD was defined as mitral regurgitation (MR, mitral stenosis), aortic regurgitation (AR, aortic stenosis), or atrial stenosis (AS, mitral valve) (Figure 2).
- Baseline characteristics and efficacy and safety outcomes were compared between each VHD subtype and the no/mild VHD subtype.
- Safety and efficacy of apixaban vs. warfarin in each VHD subtype was assessed using an adjusted Cox proportional hazard model.

Results

- Comparison of baseline characteristics revealed all VHD subtypes had older age, more complex aortic plaques, more persistent AF, and more vascular disease (Table 1).
- Despite these baseline differences, patients with MR or AR did not have higher rates of stroke or MI, sequelae infection, or death (Figure 2), whereas patients with AS did have higher rates of stroke or MI, sequelae infection, or death (Figure 2).

Conclusions

- In chronically anticoagulated patients with AF: valvular regurgitation (MR and AR) was not associated with risk of clinical events, whereas AS was associated with a higher risk of stroke or MI, death, and major bleeding. There were no differences in efficacy or safety of apixaban compared with warfarin in patients with any VHD subtype.

DISCLOSURES

ARISTOTLE was funded by Bristol-Myers Squibb and Pfizer. Author disclosure information: Alice Wang: Nothing to disclose.

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>VHD Subtype</th>
<th>Male/ Female</th>
<th>Age, median (25th, 75th) yrs</th>
<th>CHADS2</th>
<th>HAS-BLED</th>
<th>WPW</th>
<th>Myocardial infarction</th>
<th>Stroke/systemic embolism</th>
<th>Intracranial Bleeding</th>
<th>Mortality</th>
<th>Major Bleeding</th>
<th>Heart Failure</th>
<th>MI</th>
<th>HTN</th>
<th>DM</th>
<th>PAD</th>
<th>AF</th>
<th>Prior MI</th>
<th>Stroke</th>
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<tbody>
<tr>
<td>No VHD</td>
<td>738 (67.9%)</td>
<td>0.53 (103)</td>
<td>0.87</td>
<td>0.55 (319)</td>
<td>2.537</td>
<td>0.873</td>
<td>0.984</td>
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<tr>
<td>MR</td>
<td>3382 (67.8%)</td>
<td>0.52 (103)</td>
<td>0.87</td>
<td>0.52 (319)</td>
<td>2.537</td>
<td>0.873</td>
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<td>AR</td>
<td>324 (68.0%)</td>
<td>0.52 (103)</td>
<td>0.87</td>
<td>0.52 (319)</td>
<td>2.537</td>
<td>0.873</td>
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<tr>
<td>AS</td>
<td>3382 (67.8%)</td>
<td>0.52 (103)</td>
<td>0.87</td>
<td>0.52 (319)</td>
<td>2.537</td>
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Figure 1: Flow diagram illustrating patient population.

Figure 2: Comparison of outcomes of VHD vs. No VHD by subtype.