Apixaban vs. Aspirin for the prevention of stroke due to subclinical AF in patients with an implanted cardiac monitor: Analysis from the ARTESiA Trial

Professor Jeff Healey
Yusuf Chair and Director of Cardiology
McMaster University, Canada
Background - 1

Subclinical atrial fibrillation (SCAF) is detected in approximately one-third of patients with implanted pacemakers and defibrillators (ASSERT-I).

Detected at similar rates in patients with implanted cardiac monitors (ICM) in patients without an indication for pacemaker or ICD (ASSERT-II).

The NOAH-AFNET 6 and ARTESiA trials show a reduction in stroke using oral anticoagulation among patients with SCAF and additional stroke risk factors, which is balanced by an increase in bleeding risk.
Background -

ARTESiA included enrolled 200 individuals with SCAF detected by an ICM

This analysis sought to determine if ARTESiA patients with SCAF detected by an ICM:

1. Have similar stroke risk factors as other patients in the trial?
2. Have a similar rate of stroke and systemic embolism?
3. Derive similar benefit from apixaban?
ARTESIA Study Design

Implanted pacemaker, defibrillator or cardiac monitor with SCAF (6 minutes – 24 hours)
AND EITHER
Age ≥ 55 years
CHADS2-VASc score of ≥ 3
OR
Age ≥ 75 years, or History of stroke

Intention-to-treat population N=4012

Apixaban
5 mg BID or 2.5 mg BID
According to label

Primary endpoint:
Stroke or systemic embolism

Safety endpoint:
ISTH major bleeding*

Aspirin
81 mg/day

Double-blind, double-dummy treatment

Mean follow up
3.5 ± 1.8 years


* With sub-classification of presentation and clinical course
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Patients with ICM (n=209)</th>
<th>Patients with PM/ICD (n=3803)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (mean ± SD)</strong></td>
<td>74.9 ± 7.9</td>
<td>76.9 ± 7.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Male sex (%)</strong></td>
<td>49.8</td>
<td>64.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Body mass index</strong></td>
<td>28.1 ± 5.2</td>
<td>28.9 ± 5.8</td>
<td>0.046</td>
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<tr>
<td><strong>Longest SCAF episode (median, IQR)</strong></td>
<td>0.8 hours (0.2 - 3.0 hours)</td>
<td>1.5 hours (0.2 – 5.0 hours)</td>
<td>0.074</td>
</tr>
<tr>
<td><strong>CHADS-VASc score (mean)</strong></td>
<td>3.9 ± 1.2</td>
<td>3.9 ± 1.1</td>
<td>0.92</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>78.9%</td>
<td>81.6%</td>
<td>0.33</td>
</tr>
<tr>
<td><strong>Diabetes Mellitus</strong></td>
<td>20.6%</td>
<td>29.6%</td>
<td>0.005</td>
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<tr>
<td><strong>Congestive Heart Failure</strong></td>
<td>8.6%</td>
<td>29.4%</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Prior stroke or TIA</strong></td>
<td>24.9%</td>
<td>7.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Prior systemic embolism</strong></td>
<td>1.4%</td>
<td>0.3%</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>Coronary artery disease</strong></td>
<td>16.3%</td>
<td>3.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Vascular disease</strong></td>
<td>11.5%</td>
<td>8.2%</td>
<td>0.09</td>
</tr>
</tbody>
</table>
Stroke/SE by Device Type

(a) Stroke/SE: ICM-detected SCAF

- Apixaban: 0.26% per year
- Aspirin: 2.6% per year

HR = 0.11 (0.1-0.88)  
P = 0.04

(b) Stroke/SE: patients with ICD/pacemaker

- Apixaban: 0.8% per year
- Aspirin: 1.2% per year

HR = 0.69 (0.49-0.98)  
P = 0.04

P-Interaction = 0.08
Conclusions

1. Despite an identical CHADS-VASc score, patients with ICM-detected SCAF had a very different risk factor profile
   Younger, with a greater history of stroke/TIA/SE (26%), and CV disease
   Less diabetes and heart failure

2. Aspirin-treated patients with ICM-detected SCAF had a greater risk of stroke/SE than patients with a pacemaker or ICD

3. Patients with SCAF detected by and ICM had a significant reduction in stroke/SE with apixaban
   Which appeared larger in absolute and relative terms than among patients with SCAF detected by a pacemaker or ICD
   First demonstration of reduction in stroke/SE in patients with ICM-detected SCAF using oral anticoagulation