Atrial Fibrillation
2015 Update

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Clinical Cardiac Electrophysiology

AnMed Health Arrhythmia Specialist
Disclosures

Consulting/Research Support

Biosense Webster
Medtronic
St Jude Medical
Biotronik
Why worry about atrial fibrillation?

Outcome parameter

- Death
- Stroke (embolic, hemorrhagic, cerebral bleeds)
- Hospitalization
- Quality of life and exercise
- Left ventricular function

Relative change in AF patients

- ↑ death rate (HR 1.4-2.7)**
- ↑ stroke rate
- Frequent hospitalizations
- Wide variation from no effect to major reduction
- Wide variation from no change to tachycardia mediated cardiomyopathy and heart failure

Outcome parameters for trials in atrial fibrillation: executive summary. Recommendations from a consensus conference organized by the German Atrial Fibrillation Competence NETwork (AFNET) and the European Heart Rhythm Association (EHRA). Eur Heart J 2007;28:2803–2817

Incidence of atrial fibrillation increases with age and...

2.2 million people effected expected to double by 2020

Accounts for 15-20% of all strokes

$6.4 billion annual health care cost
Gender / Ethnic Observations

Graphs showing the adjusted cumulative risk over attained age for different ethnic groups and genders.
Optimizing risk factors decreases atrial fibrillation recurrence

- Blood Pressure
  - <120/80mmHg
- BMI
  - <25kg/m²
- Diabetes
  - Fasting <100mg/dl
- Smoking
  - never
- Family History
  - No CHF or CAD

*Circulation.* 2011; 123: 1501-1508
Natural history of atrial fibrillation

Thromboembolism and atrial fibrillation
## Thromboembolism and atrial fibrillation

### CHADS₂
- Congestive heart failure: 1
- Hypertension: 1
- Age ≥ 75: 1
- Diabetes: 1
- CVA/TIA: 2

### CHA₂DS₂-VASc
- Congestive heart failure: 1
- Hypertension: 1
- Age
  - <65: 0
  - 65-75: 1
  - ≥75: 2
- Diabetes: 1
- CVA/TIA: 2
- Vascular disease: 1
- Female: 1

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BMJ 2011;342:d124
Warfarin
Vit K antagonist
T ½ 36-42 hrs
Reverse with Vit K
∆INR 12-24hrs
Dabigatran
Direct thrombin inhibitor
Onset 2hrs
T ½ 12-17hrs
Dabigatran versus Warfarin in Patients with Atrial Fibrillation (RE-LY)

18,113 pts
w/ non-valvular atrial fibrillation and
at least 1 cardioembolic risk factor
Rivaroxaban
Factor Xa inhibitor
Onset 2.5-4hrs
T ½ 5-9hrs healthy
T ½ 9-13hrs elderly
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)

14,246 patients w/ non-valvular atrial fibrillation ≥2 risk factors

<table>
<thead>
<tr>
<th></th>
<th>dabigatran</th>
<th>rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>72</td>
<td>73</td>
</tr>
<tr>
<td>Median follow up</td>
<td>2.0yrs</td>
<td>1.9yrs</td>
</tr>
<tr>
<td>Mean CHADS₂</td>
<td>2.1</td>
<td>3.5</td>
</tr>
<tr>
<td>CHADS₂ ≥ 2</td>
<td>68%</td>
<td>100%</td>
</tr>
<tr>
<td>Prior CVA</td>
<td>20%</td>
<td>55%</td>
</tr>
</tbody>
</table>

2011 NEJM 365;10
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)

14,246 patients w/ non-valvular atrial fibrillation ≥2 risk factors
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)

14,246 patients w/ non-valvular atrial fibrillation ≥2 risk factors

<table>
<thead>
<tr>
<th></th>
<th>rivaroxaban</th>
<th>warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercranial hemorrhage</td>
<td>0.49%</td>
<td>0.74%</td>
</tr>
<tr>
<td></td>
<td>p=0.019</td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>3.6%</td>
<td>3.45%</td>
</tr>
<tr>
<td></td>
<td>p=0.576</td>
<td></td>
</tr>
<tr>
<td>GI bleeding</td>
<td>3.15%**</td>
<td>2.16%</td>
</tr>
<tr>
<td></td>
<td>p=&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>All cause death</td>
<td>1.87%</td>
<td>2.21%</td>
</tr>
<tr>
<td></td>
<td>p=0.073</td>
<td></td>
</tr>
<tr>
<td>Drug discontinuation</td>
<td>23.9%</td>
<td>22.4%</td>
</tr>
</tbody>
</table>

Primary endpoint of stroke or systemic embolism

<p>| | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Intention-to-treat population</td>
<td>7081</td>
<td>269</td>
<td>2.1</td>
<td>7090</td>
<td>306</td>
<td>2.4</td>
</tr>
<tr>
<td>During treatment</td>
<td>188</td>
<td>1.7</td>
<td>240</td>
<td>2.2</td>
<td>0.79 (0.66–0.96)</td>
<td>0.02</td>
</tr>
<tr>
<td>After discontinuation</td>
<td>81</td>
<td>4.7</td>
<td>66</td>
<td>4.3</td>
<td>1.10 (0.79–1.52)</td>
<td>0.58</td>
</tr>
</tbody>
</table>
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)

14,246 patients w/ non-valvular atrial fibrillation ≥2 risk factors
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)

“After the end of study transition to warfarin, an increased risk of stroke and systemic embolism was observed for patients being treated with rivaroxaban compared with those treated with warfarin, underscoring the importance of expeditious anticoagulation coverage during the transition from one antithrombotic therapy to another.”

| Table 3 |
| Stroke or Non-Central Nervous System Embolism Rates and Stroke, Non-Central Nervous System Embolism, Myocardial Infarction, or Vascular Death During Post-Study-Drug Discontinuation Risk Period* |

<table>
<thead>
<tr>
<th>Events per 100 Patient-Yrs (Total Events)</th>
<th>Rivaroxaban: Warfarin HR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke or non-CNS embolism rates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All discontinuations and interruptions (before end of study)</td>
<td>16.49 (51)</td>
<td>14.05 (44)</td>
</tr>
<tr>
<td>Temporary interruptions</td>
<td>6.20 (9)</td>
<td>5.05 (8)</td>
</tr>
<tr>
<td>Permanent discontinuations</td>
<td>25.60 (42)</td>
<td>23.28 (36)</td>
</tr>
<tr>
<td>After end of study</td>
<td>6.42 (22)</td>
<td>1.73 (6)</td>
</tr>
<tr>
<td>All discontinuations and interruptions (before end of study) + after end of study events</td>
<td>11.20 (73)</td>
<td>7.57 (50)</td>
</tr>
<tr>
<td>Stroke, non-CNS embolism, MI, or vascular death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All discontinuations and interruptions (before end of study)</td>
<td>46.97 (145)</td>
<td>52.50 (164)</td>
</tr>
<tr>
<td>Temporary interruptions</td>
<td>9.66 (14)</td>
<td>10.75 (17)</td>
</tr>
<tr>
<td>Permanent discontinuations</td>
<td>80.01 (131)</td>
<td>95.28 (147)</td>
</tr>
<tr>
<td>After end of study</td>
<td>9.06 (31)</td>
<td>4.03 (14)</td>
</tr>
<tr>
<td>All discontinuations and interruptions (before end of study) + after end of study events</td>
<td>27.02 (176)</td>
<td>26.97 (178)</td>
</tr>
</tbody>
</table>

*J Am Coll Cardiol 2013;61:651–8
Apixaban
Factor Xa inhibitor
Onset 1-3hrs
T ½ 8-15hrs
Apixaban versus Warfarin in Patients with Atrial Fibrillation (ARISTOTLE)

18,201 patients with NVAF and 1 risk factor
### Table 3. Bleeding Outcomes and Net Clinical Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Apixaban Group (N=9088)</th>
<th>Warfarin Group (N=9052)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary safety outcome: ISTH major bleeding†</td>
<td>327/2.13</td>
<td>462/3.09</td>
<td>0.69 (0.60–0.80)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intracranial</td>
<td>52/0.33</td>
<td>122/0.80</td>
<td>0.42 (0.30–0.58)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other location</td>
<td>275/1.79</td>
<td>340/2.27</td>
<td>0.79 (0.68–0.93)</td>
<td>0.004</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>105/0.76</td>
<td>119/0.86</td>
<td>0.89 (0.70–1.15)</td>
<td>0.37</td>
</tr>
<tr>
<td>Major or clinically relevant nonmajor bleeding</td>
<td>613/4.07</td>
<td>877/6.01</td>
<td>0.68 (0.61–0.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GUSTO severe bleeding</td>
<td>80/0.52</td>
<td>172/1.13</td>
<td>0.46 (0.35–0.60)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GUSTO moderate or severe bleeding</td>
<td>199/1.29</td>
<td>328/2.18</td>
<td>0.60 (0.50–0.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TIMI major bleeding</td>
<td>148/0.96</td>
<td>256/1.69</td>
<td>0.57 (0.46–0.70)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TIMI major or minor bleeding</td>
<td>239/1.55</td>
<td>370/2.46</td>
<td>0.63 (0.54–0.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any bleeding</td>
<td>2356/18.1</td>
<td>3060/25.8</td>
<td>0.71 (0.68–0.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke, systemic embolism, or major bleeding</td>
<td>521/3.17</td>
<td>666/4.11</td>
<td>0.77 (0.69–0.86)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke, systemic embolism, major bleeding, or death from any cause</td>
<td>1009/6.13</td>
<td>1168/7.20</td>
<td>0.85 (0.78–0.92)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Higher rate of adverse events following discontinuation of study drug

Table 1. Stroke or Systemic Embolism and Major Bleeding Events After Completion of Study Drug

<table>
<thead>
<tr>
<th>Days After Last Dose</th>
<th>Apixaban</th>
<th>Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>%/year</td>
</tr>
<tr>
<td>Stroke or systemic embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-30</td>
<td>21/6791</td>
<td>4.02</td>
</tr>
<tr>
<td>1-2</td>
<td>1/6791</td>
<td>2.69</td>
</tr>
<tr>
<td>3-7</td>
<td>4/6787</td>
<td>4.31</td>
</tr>
<tr>
<td>8-14</td>
<td>5/6780</td>
<td>3.85</td>
</tr>
<tr>
<td>15-30</td>
<td>11/6671</td>
<td>4.18</td>
</tr>
<tr>
<td>Major bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-30</td>
<td>26/6791</td>
<td>3.97</td>
</tr>
<tr>
<td>1-2</td>
<td>0/6791</td>
<td>-</td>
</tr>
<tr>
<td>3-7</td>
<td>1/6787</td>
<td>1.08</td>
</tr>
<tr>
<td>8-14</td>
<td>7/6780</td>
<td>5.39</td>
</tr>
<tr>
<td>15-30</td>
<td>18/6771</td>
<td>6.84</td>
</tr>
</tbody>
</table>
### Table 2. Rates of Stroke or Systemic Embolism During the Initiation of Warfarin²

<table>
<thead>
<tr>
<th>At Start of Trial</th>
<th>At End of Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1-30 After Completing Double-Blind Study Drug*</td>
</tr>
<tr>
<td></td>
<td>%/year</td>
</tr>
<tr>
<td>Warfarin experienced-&gt;warfarin</td>
<td>1.42</td>
</tr>
<tr>
<td>Warfarin naive-&gt;warfarin</td>
<td>5.41</td>
</tr>
</tbody>
</table>

*Patients who completed treatment

### Table 3. Stroke or Systemic Embolism in Patients Who Prematurely Discontinued Study Drug²

<table>
<thead>
<tr>
<th>Days After Last Dose</th>
<th>Apixaban</th>
<th>Warfarin</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>%/year</td>
<td>n/N</td>
</tr>
<tr>
<td>Stroke or systemic embolism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-30</td>
<td>52/1841</td>
<td>39.86</td>
<td>67/2028</td>
</tr>
<tr>
<td>1-2</td>
<td>29/1839</td>
<td>299.47</td>
<td>56/2028</td>
</tr>
<tr>
<td>3-7</td>
<td>4/1700</td>
<td>17.49</td>
<td>11/1868</td>
</tr>
<tr>
<td>8-14</td>
<td>8/1636</td>
<td>25.82</td>
<td>8/1798</td>
</tr>
<tr>
<td>15-30</td>
<td>11/1604</td>
<td>16.03</td>
<td>9/1759</td>
</tr>
</tbody>
</table>
but it cost too much

Medical costs in the US of clinical events associated with oral anticoagulant (OAC) use compared to warfarin among non-valvular atrial fibrillation patients ≥75 and <75 years of age, based on the ARISTOTLE, RE-LY, and ROCKET-AF trials, 2013 J Med Econ

Evaluated medical costs per year for clinical events occurring in approval trials

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran RE-LY</th>
<th>Rivaroxaban ROCKET-AF</th>
<th>Apixaban ARISTOTLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;75y/o</td>
<td>$180</td>
<td>-$23</td>
<td>-$825</td>
</tr>
<tr>
<td>Warfarin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;75y/o</td>
<td>-$367</td>
<td>-$88</td>
<td>-$254</td>
</tr>
</tbody>
</table>
....but there is no reversal agent

Drug T 1/2

Clinically significant change of INR

Coagulation Protein Synthesis

Vit K administration

Warfarin

Rivaroxaban

Dabigatran

Apixaban

Hours
….but there is no reversal agent

- **Dabigatran**: activated charcoal, hemodialysis (overdose), PCC (prothrombin complex concentrates), or recombinant Factor VII
- **Rivaroxaban**: activated charcoal, FFP, PCC, activated Factor VII
- **Apixaban**: activated charcoal, FFP, PCC, activated Factor VII
....but I’m on a blood thinner, aspirin

### Table 5. Trials Comparing Antithrombotics Vs Aspirin in Patients With Nonvalvular Atrial Fibrillation

<table>
<thead>
<tr>
<th></th>
<th>ACTIVE A³⁵</th>
<th>AVERROES³⁶</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Clopidogrel 75 mg/day + aspirin 75–100 mg</td>
<td>Apixaban 5 mg b.i.d.³¹</td>
</tr>
<tr>
<td>No. of patients</td>
<td>7554</td>
<td>5599</td>
</tr>
<tr>
<td>Pertinent exclusion criteria</td>
<td>History of peptic ulcer disease in past 6 mo, intracerebral hemorrhage, platelet count &lt; 50 x 10⁷/mm³</td>
<td>Serious bleeding event in previous 6 mo or high risk of bleeding, SCr &gt; 2.5 mg/dl, CrCl &lt; 25 ml/min, significant liver disease 1.1</td>
</tr>
<tr>
<td>Follow-up period (yrs, median)</td>
<td>3.6</td>
<td>1.1</td>
</tr>
<tr>
<td>Primary outcome</td>
<td>Stroke, systemic embolism, myocardial infarction, vascular death</td>
<td>Stroke or systemic embolism</td>
</tr>
<tr>
<td>Baseline characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yrs, median)</td>
<td>71</td>
<td>70</td>
</tr>
<tr>
<td>CHADS² score (mean)</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Efficacy results (event rate [%]/yr; intervention vs aspirin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary outcome</td>
<td>6.8 vs 7.6 (p=0.01)</td>
<td>1.6 vs 3.7 (p&lt;0.001)</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>1.9 vs 2.8 (p&lt;0.001)</td>
<td>1.1 vs 3.0 (p&lt;0.001)</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>0.23 vs 0.17 (p=NS)</td>
<td>0.2 vs 0.3 (p=0.45)</td>
</tr>
<tr>
<td>Safety results (event rate [%]/yr; intervention vs aspirin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>2.0 vs 1.3 (p&lt;0.001)</td>
<td>1.4 vs 1.2 (p=0.57)</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>0.4 vs 0.2 (p=0.006)</td>
<td>0.4 vs 0.4 (p=0.69)</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>1.1 vs 0.5 (p&lt;0.001)</td>
<td>0.4 vs 0.4 (p=0.71)</td>
</tr>
</tbody>
</table>
….but my Coumadin clinic will not have anything to do

- “Anticoagulation Clinic”
- Drug monitoring
  - Coumadin “holdouts”
  - Physiologic monitoring
    - Dabigatran
      - 80% renal - 20% hepatic
      - Multiple drug interactions
    - Rivaroxaban
      - 33% renal - 67% hepatic
      - Multiple drug interactions
    - Apixaban
      - 25% renal - 75% hepatic
      - Multiple drug interactions
- Antiarrhythmic monitoring
  - Renal, hepatic, QTc, thyroid, PFT’s
Rhythm Control

Ablation
- Catheter/Surgical/Both

Drugs
- Antihypertensive/Antiarrhythmic
Vaughan-Williams Classification

★ Class I: sodium channel
★ Class IA
★ Quinidine Procainamide Disopyramide
★ Class IB
★ Lidocaine Mexiletine Tocainide Phenytoin
★ Class IC
★ Flecainide Encainide Propafenone Moricizine

★ Class II: beta receptor

★ Class III: potassium channel
★ Amiodarone Bretylium Sotalol Ibutilide Dronedarone Dofetilide
★ Minimal conduction velocity effect, significant increase action potential duration

★ Class IV: calcium channel

★ Class V: other
★ Digoxin Adenosine Magnesium

★ Moderate slowing of conduction velocity (widens QRS), prolongs action potential duration (↑Torsades risk)
★ Minimal slows conduction, shortens action potential (↓Torsades risk)
★ Marked slowing of conduction (wide QRS), minimal action potential effect
Left panel demonstrates atrial flutter with QRS prolongation in a patient taking flecainide.

Zimetbaum P. Circulation 2012;125:381-389
# New antiarrhythmics

## Class I: sodium channel
- Class IA
  - Quinidine
  - Procainamide
  - Disopyramide
- Class IB
  - Lidocaine
  - Mexiletine
  - Tocainide
  - Phenytoin
- Class IC
  - Flecainide
  - Encainide
  - Propafenone
  - Moricizine

## Class II: beta receptor

## Class III: potassium channel
- Amiodarone
- Bretylium
- Sotalol
- Ibutilide
- Dronedarone
- Dofetilide

## Class IV: calcium channel

## Class V: other
- Digoxin
- Adenosine
- Magnesium

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**Vernakalant**

Acute conversion of atrial fibrillation

IV formulation only (oral form dropped)

Hybrid Class I and Class III properties

Atrial selective (little/no ventricular effect on action potential)

Not available in US

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*Circ Arrhythm Electrophysiol 2009;2:652–9.*
*Am J Cardiol 2010;106:1277–83.*
*Am Coll Cardiol 2011;57:313–21.*
Ranolazine: novel antianginal and antiarrhythmic

Class I: sodium channel
  - Class IA
    - Quinidine
    - Procainamide
    - Disopyramide
  - Class IB
    - Lidocaine
    - Mexiletine
    - Tocainide
    - Phenytoin
  - Class IC
    - Flecainide
    - Encainide
    - Propafenone
    - Moricizine

Class II: beta receptor

Class III: potassium channel
  - Amiodarone
  - Beryllium
  - Sotalol
  - Butilide
  - Dronedarone
  - Dofetilide

Class IV: calcium channel

Class V: other
  - Digoxin
  - Adenosine
  - Magnesium

• Decreases atrial fibrillation following ACS


• Decreases atrial fibrillation following coronary artery bypass surgery


• Augments pharmacologic conversion of atrial fibrillation


• Suppresses non-sustained ventricular tachycardia in ACS

Relationship between nonsustained ventricular tachycardia after non-ST-elevation acute coronary syndrome and sudden cardiac death: Observations from the metabolic efficiency with ranolazine for less ischemia in non-ST-elevation acute coronary syndrome-thrombolysis in myocardial infarction 36 (MERLIN-TIMI 36) randomized controlled trial Circulation 2010;122:455–62.

• Ranolazine to reduce ICD shocks

Clinical trial ongoing
Effect of increasing action potential duration

Potassium channel activity

Amiodarone
Bretylium
Sotalol
Ibutilide
Dronedarone
Dofetilide
Ranolazine as adjunctive therapy

Effect on control

Effect of EAD

Dronedarone: PALLAS

- Dronedarone for “rate control” in chronic AF

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Placebo (n=1577), n (%)</th>
<th>Dronedarone (n=1572), n (%)</th>
<th>Hazard ratio</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death, MI, stroke, systemic embolism</td>
<td>14 (0.9)</td>
<td>32 (2)</td>
<td>2.3</td>
<td>0.009</td>
</tr>
<tr>
<td>Death, unplanned CV hospitalization*</td>
<td>81 (5.1)</td>
<td>118 (7.5)</td>
<td>1.5</td>
<td>0.006</td>
</tr>
<tr>
<td>Death</td>
<td>7 (0.4)</td>
<td>16 (1)</td>
<td>2.3</td>
<td>0.065</td>
</tr>
<tr>
<td>MI</td>
<td>3 (0.2)</td>
<td>3 (0.2)</td>
<td>1.0</td>
<td>1</td>
</tr>
<tr>
<td>Stroke</td>
<td>7 (0.4)</td>
<td>17 (1.1)</td>
<td>2.4</td>
<td>0.047</td>
</tr>
<tr>
<td>HF hospitalization</td>
<td>15 (1)</td>
<td>34 (2.2)</td>
<td>2.3</td>
<td>0.008</td>
</tr>
</tbody>
</table>

*Co-primary end points

- FDA and EMA are reassessing Dronedarone in ongoing reviews

Heartwire.org
Rhythm Control

Ablation
- Catheter/Surgical/Both

Drugs
- Antihypertensive/Antiarrhythmic
Pulmonary vein isolation

45 patients with recurrent atrial fibrillation
Induction of atrial fibrillation from the right inferior vein

Radiofrequency ablation eliminates PV potential
Mapping of Left Atrium
Outcomes following catheter ablation of atrial fibrillation

6167 patients in 19 studies

Single procedure
12 month follow up
“late” follow up (27mths)

Multiple procedures
“late” follow up

J Am Heart Assoc. 2013;2:e004549
Outcomes following catheter ablation of atrial fibrillation

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Multiple procedures  
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Outcomes following catheter ablation of atrial fibrillation

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Multiple procedures
“late” follow up
Invasive monitoring
  “pill in the pocket” anticoagulation
  Cessation of anticoagulation

Combined “hybrid” ablation

Left atrial appendage closure

Atrial fibrillation disease scoring system
“pill in the pocket” anticoagulation

Rhythm Evaluation for AntiCoagulaTion With COntinuous Monitoring (REACT COM)
Paroxysmal and persistent atrial fibrillation
CHADS$_2$ 1-2
Novel OAT

Adapted from R Passman, Northwestern Univ.
Invasive monitoring
  “pill in the pocket” anticoagulation

Combined “hybrid” ablation

Left atrial appendage closure

Atrial fibrillation disease scoring system
Open ablation of Atrial Fibrillation

- Combined effort with Cardiothoracic Surgery and Electrophysiology
- Epicardial Pulmonary Vein Isolation via mini-thoracotomy or laparoscopic approach
- Endocardial confirmation of PVI and creation of line of block in mitral isthmus and tricuspid isthmus

Dual Epicardial Endocardial Persistent Atrial Fibrillation (AF) Study (DEEP)

AtriCure Bipolar Radiofrequency Ablation of Permanent Atrial Fibrillation (ABLATE)

Registry Trial (ABLATE AF)
101 patients
High risk for recurrence
AF detected by ECG, Holter, CIED
**ILR data not reported
- Invasive monitoring
  - “pill in the pocket” anticoagulation
- Combined “hybrid” ablation
- Left atrial appendage closure
- Atrial fibrillation disease scoring system
Watchman®
Watchman®: PROTECT AF

- 707 patients with non-valvular Afib
- 2:1 device verses warfarin

Warfarin
4.9 events per 100 pt years

Occlusion device
3.0 events per 100 pt years

*Lancet 2009; 374: 534–42*
Watchman®: PROTECT AF

Occlusion device

Warfarin

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n=463)</th>
<th>Control (n=244)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious pericardial effusion*</td>
<td>22 (4.8%)</td>
<td>0</td>
</tr>
<tr>
<td>Major bleeding†</td>
<td>16 (3.5%)</td>
<td>10 (4.1%)</td>
</tr>
<tr>
<td>Procedure-related ischaemic stroke</td>
<td>5 (1.1%)</td>
<td>0</td>
</tr>
<tr>
<td>Device embolisation</td>
<td>3 (0.6%)</td>
<td>0</td>
</tr>
<tr>
<td>Haemorrhagic stroke‡</td>
<td>1 (0.2%)</td>
<td>6 (2.5%)</td>
</tr>
<tr>
<td>Other‡</td>
<td>2 (0.4%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Lancet 2009; 374: 534–42
Invasive monitoring
  “pill in the pocket” anticoagulation

Combined “hybrid” ablation

Left atrial appendage closure

Atrial fibrillation disease scoring system
Thank you