Comparative Efficacy of Dronedarone and Amiodarone for the Maintenance of Sinus Rhythm in Patients With Atrial Fibrillation

Jonathan P. Piccini, MD, MHS, Vic Hasselblad, PhD, Eric D. Peterson, MD, MPH, Jeffrey B. Washam, PharmD, Robert M. Califf, MD, David F. Kong, MD
Durham, North Carolina

Objectives
We sought to compare the efficacy and safety of dronedarone versus amiodarone for the prevention of recurrent atrial fibrillation (AF).

Background
Dronedarone is a noniodinated amiodarone congener developed to maintain sinus rhythm. Few data are available to directly compare the efficacy and safety of dronedarone versus amiodarone.

Methods
We conducted a systematic overview of all randomized controlled trials in which the authors evaluated dronedarone or amiodarone for the prevention of AF. The effect of amiodarone versus dronedarone was summarized by the use of indirect comparison meta-analysis and normal logistic meta-regression models.

Results
We identified 4 placebo-controlled trials of dronedarone, 4 placebo-controlled trials of amiodarone, and 1 trial of dronedarone versus amiodarone. By using random-effects modeling, we found that there was a significant estimated reduction in recurrent AF with amiodarone versus placebo (odds ratio [OR]: 0.12; 95% confidence interval [CI]: 0.08 to 0.19) but not dronedarone versus placebo (OR: 0.79; 95% CI: 0.33 to 1.87). A normal logistic regression model incorporating all trial evidence found amiodarone superior to dronedarone (OR: 0.49; 95% CI: 0.37 to 0.63; p < 0.001) for the prevention of recurrent AF. In contrast, these models also found a trend toward greater all-cause mortality (OR: 1.61; 95% CI: 0.97 to 2.68; p = 0.066) and greater overall adverse events requiring drug discontinuation with amiodarone versus dronedarone (OR: 1.81; 95% CI: 1.33 to 2.46; p < 0.001).

Conclusions
Dronedarone is less effective than amiodarone for the maintenance of sinus rhythm, but has fewer adverse effects. For every 1,000 patients treated with dronedarone instead of amiodarone, we estimate approximately 228 more recurrences of AF in exchange for 9.6 fewer deaths and 62 fewer adverse events requiring discontinuation of drug. (J Am Coll Cardiol 2009;54:1089–95) © 2009 by the American College of Cardiology Foundation

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia. Affecting more than 2.5 million people in the U.S., AF is a major burden to the public health and the health care system (1). Many patients require a rhythm-management strategy designed to maintain sinus rhythm, prevent recurrent AF, and improve quality of life. Rhythm management is hindered by the impotence of current antiarrhythmic drugs and mounting safety concerns, including increased rates of mortality (2–5).

Amiodarone is presently the most effective antiarrhythmic agent for AF, but its use is limited by toxicity (6–8). Dronedarone is a noniodinated benzofuran similar to amiodarone but is not associated with thyroid or pulmonary toxicity. Dronedarone has electrophysiological characteristics spanning all 4 Vaughan-Williams antiarrhythmic classes, with primarily Class III effects. Initial small trials suggested that dronedarone prolonged the time to recurrence of AF and reduced cardiovascular death and hospitalization (9,10). However, the long-term maintenance of sinus rhythm at 12 months was less encouraging (10).

The clinical decision to prescribe drugs for rhythm management hinges on estimates of their net clinical benefit (11). Few direct comparisons of dronedarone and amiodarone exist, although each drug has been evaluated extensively against placebo. Under these circumstances, we conducted a systematic overview using indirect comparison meta-analysis and normal logistic models to summarize the available evidence (12–14).
Study search. We searched MEDLINE (1966 to 2009) and the National Institutes of Health’s ClinicalTrials.gov database for published and unpublished randomized controlled trials of dronedarone versus placebo, amiodarone versus placebo, and dronedarone versus amiodarone for the prevention of recurrent AF. We searched MEDLINE using the following medical subject heading terms: 1) dronedarone, placebo, atrial fibrillation, and randomized controlled trials; and 2) amiodarone, placebo, atrial fibrillation, and randomized controlled trials. A third MEDLINE search string (amiodarone, dronedarone, atrial fibrillation, and randomized controlled trials) revealed no additional citations. MEDLINE queries were limited to studies involving human subjects that were written in English. Finally, the bibliographies of 3 narrative and systematic reviews were manually searched for additional citations (3,8,15).

Eligibility and data abstraction. Controlled studies that randomized patients with AF to amiodarone, dronedarone, or placebo were included in the analysis. Additional selection criteria included treatment with follow-up for >6 months and availability of recurrent AF or all-cause mortality as end points. Studies of subjects age <18 years and subjects with acute cardioversion, catheter ablation, and post-operative AF were excluded.

We reviewed citations and abstracted data in a standardized and unblinded fashion. Data were abstracted from each report, including inclusion and exclusion criteria, demographics, baseline characteristics, trial design (including the treatment and control arms), study quality, follow-up, and study outcomes. Pre-specified outcomes included the following: 1) recurrence of AF; 2) all-cause mortality; and 3) adverse events that required study drug cessation. All outcomes were analyzed according to intention to treat. Figure 1 depicts the study selection process (16).

Statistical analysis. Odds ratios (ORs) summarizing the effectiveness of each drug compared with placebo were calculated with the use of FastPro software (17).
combined these ORs by assuming an empirical Bayesian model described by Hedges and Olkin (18). Risk differences between control and treatment arms also were combined by the use of the same model. The empirical Bayesian random-effects model reduces to a fixed-effects model when the studies are homogeneous. The method accommodated heterogeneity by assuming that the true effect differed among studies and therefore must be represented by a distribution of values instead of a single value. The result was a wider range of uncertainty about the point estimate than was calculated with fixed-effects models.

To estimate a comparison between amiodarone and dronedarone from these data, we calculated the following product:

\[
\frac{\text{Odds of event on amiodarone}}{\text{Odds of event on placebo}} = \frac{\text{Odds of event on amiodarone}}{\text{Odds of event on placebo}} \times \frac{\text{Odds of event on dronedarone}}{\text{Odds of event on placebo}}
\]

This fundamental relationship has been previously examined by several investigators (12,14,19). To further examine the relationship between amiodarone and dronedarone, we used the methods of Hasselblad (20) to fit a generalized meta-analysis (meta-regression), using random-effects logistic regression models with terms for each antiarrhythmic drug and for each study.

The multivariate logistic normal models, implemented in EGRET software (Cytel Software Corp., Cambridge, Massachusetts), contained a term for a random-error component that allowed for extra variation in the model. The models assume that the odds ratios between the various treatments remain constant, except for some random variation.

Results

Search results. After searching the MEDLINE and ClinicalTrials.gov databases, we identified 10 reports in the dronedarone search and 88 reports in the amiodarone search that were reviewed for inclusion and exclusion criteria (Fig. 1). Among this group of reports, 5 dronedarone studies and 83 amiodarone studies were excluded. The majority of reports were excluded on the basis of the absence of randomization (observational studies), because they were studies of acute cardioversion, or because they were studies of post-operative AF (Fig. 1). The full papers for the remaining 8 published trials were retrieved for detailed review and abstraction. The results of the DIONYSOS (Efficacy & Safety of Dronedarone Versus Amiodarone for the Maintenance of Sinus Rhythm in Patients With Atrial Fibrillation) study (NCT00489736), which randomized patients to either dronedarone or amiodarone, were publicly released by the sponsor (Sanofi-Aventis, Bridgewater, New Jersey) (21).

Trial characteristics and study quality. Four randomized controlled trials of dronedarone were included in this meta-analysis (Table 1) (9,10,22). These 4 multicenter trials enrolled 5,967 patients who were randomized to long-term dronedarone or placebo. One study was a dose-ranging study; the remaining trials used a common 800-mg daily dose of dronedarone with a mean follow-up of 13 ± 6 months. The 4 randomized, placebo-controlled trials of amiodarone enrolled a total of 669 patients (7,23–25). All of the amiodarone trials used a daily maintenance dose of 200 mg. The mean follow-up duration was 16 ± 5 months.

In all 4 dronedarone trials, patients with permanent AF were excluded. Additional exclusion criteria included advanced symptomatic heart failure, a corrected QT interval >500 ms, and bradycardia with a heart rate <50 beats/min (Table 1). In contrast to the dronedarone trials, the amiodarone trials predominantly included patients with persistent and permanent AF. Two amiodarone trials (GEFACA [Grupo de Estudio de Fibrilacion A Auricular Con Amiodarone] and SAFE-T [Sotalol Amiodarone Atrial Fibrillation Efficacy Trial]) excluded patients with paroxysmal AF (7,24). Using the Delphi criteria (26), we determined that 7 of the 8 trials were of high quality, with a score of 6 or greater (Table 1). One trial was single-blind and had a score of 5 (25). Among the 8 trials, 2 did not report power calculations (24,25).

Baseline patient characteristics. Baseline patient characteristics for each trial are shown in Table 2. The mean age across all 8 trials was 65 ± 3 years. Seventy percent of those enrolled were men. The SAFE-T trial, the largest published randomized trial of amiodarone, conducted in the Veterans Administration, enrolled an almost entirely male population (7). The mean left atrial diameter overall was 44 ± 2 mm, and the mean left ventricular ejection fraction in all trials exceeded 50%. All trials followed patients at least 6 months (range 6 to 22 months). In the 3 dronedarone trials that reported concomitant pharmacotherapy, beta-blocker use ranged from 52% to 71% (9,10,24,25).

Efficacy of dronedarone versus placebo. For prevention of AF ≥6 months (Fig. 2A), the effect of dronedarone had an OR of 0.79 (95% confidence interval [CI]: 0.53 to 1.87), with a risk difference of −0.040 (95% CI: −0.19 to 0.11) equivalent to 40 fewer events per 1,000 patients treated. For mortality, the OR was 0.85 (95% CI: 0.66 to 1.11), with a risk difference of −0.003 (95% CI: −0.011 to 0.006). For adverse events requiring discontinuation, there was a significant increase over placebo with OR: 1.166 (95% CI: 1.36 to 2.02) and risk difference 0.045 (95% CI: 0.028 to 0.062).

Efficacy of amiodarone versus placebo. Compared with placebo, amiodarone significantly prevented AF in follow-up (Fig. 2A), with an OR of 0.12 (95% CI: 0.08 to 0.19) and a risk difference of −0.401 (95% CI: −0.46 to −0.34) equivalent to 401 fewer events per 1,000 patients treated. For mortality, the OR was 1.88 (95% CI: 0.54 to 6.56), with a risk difference of 0.005 (95% CI: −0.016 to 0.026). For adverse events requiring discontinuation, there was a significant increase over placebo with an OR of 11.04
Baseline Patient Characteristics in Randomized Trials of Dronedarone and Amiodarone Versus Placebo for the Maintenance of Sinus Rhythm

Table 1

<table>
<thead>
<tr>
<th>Trial (Ref. #)</th>
<th>Year</th>
<th>No. of Patients</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
<th>Blind</th>
<th>Mean Follow-Up (Months)</th>
<th>Delphi Criteria*</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAFNE (22)</td>
<td>2003</td>
<td>142†</td>
<td>Persistent AF Ages 21–85 yrs</td>
<td>Permanent AF NYHA functional class III to IV QT &gt; 500 ms LVEF &lt; 35%</td>
<td>Double-blind</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>EURIDIS (10)</td>
<td>2007</td>
<td>612</td>
<td>AF episode within previous 3 months Age ≥21 yrs</td>
<td>Permanent AF HR &lt; 50 beats/min NYHA functional class III to IV Cr ≥1.7 mg/dl</td>
<td>Double-blind</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>ADONIS (10)</td>
<td>2007</td>
<td>625</td>
<td>AF episode within previous 3 months Age ≥21 yrs</td>
<td>Permanent AF HR &lt; 50 beats/min NYHA functional class III to IV Cr ≥1.7 mg/dl</td>
<td>Double-blind</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>ATHENA (9)</td>
<td>2009</td>
<td>4,628</td>
<td>Paroxysmal or persistent AF Age ≥70 or &lt; 70 yrs with additional risk factor for stroke</td>
<td>Permanent AF NYHA functional class IV HR &lt; 50 beats/min GFR &lt; 10 ml/min</td>
<td>Double-blind</td>
<td>21</td>
<td>8</td>
</tr>
</tbody>
</table>

Amiodarone versus placebo

- Kochiadakis et al. (25) 2000 125‡ Symptomatic paroxysmal or chronic AF Age >18 yrs Refractory heart failure LVEF < 40% Recent CV surgery Single-blind 21 5
- GEFACA (24) 2001 50§ Chronic AF Paroxysmal AF Age >75 yrs HR < 50 beats/min LA diameter >60 mm Double-blind 16 7
- Channer et al. (23) 2004 99§ AF >72 h Age >18 yrs LVEF <20% PA pressure >40 mm Hg Significant valvular disease Double-blind 12 9
- SAFE-T (7) 2005 390§ AF >72 h Paroxysmal AF NYHA functional class III/IV GFR < 60 ml/min Intolerance to beta-blockers Double-blind 12 (minimum) 8

*Number of Delphi criteria met of a total of 9. †DAFNE (Dronedarone Atrial Fibrillation study after Elective cardioversion) was a dose-ranging study. Only the placebo and dronedarone 800 mg daily arms were included in this analysis. ‡Excluded 61 patients randomized to sotalol. §Only long-term treatment patients included. *Number of Delphi criteria met of a total of 9. †DAFNE (Dronedarone Atrial Fibrillation study after Elective cardioversion) was a dose-ranging study. Only the placebo and dronedarone 800 mg daily arms were included in this analysis. ‡Excluded 61 patients randomized to sotalol. §Only long-term treatment patients included.

Comparative efficacy of dronedarone and amiodarone.

The indirect meta-analysis estimates indicated that amiodarone significantly reduced recurrent AF compared with dronedarone (OR: 0.16; 95% CI: 0.06 to 0.42), with a risk difference of −0.36 (95% CI: −0.52 to −0.19), which is equivalent to 360 fewer events per 1,000 patients treated (Fig. 2A). This finding was consistent with the direct results from DIONYSOS (OR: 0.44; 95% CI: 0.30 to 0.64), with a risk difference of −0.186 (95% CI: −0.266 to −0.1028). The normal logistic model also indicated greater efficacy for

Table 2

Baseline Patient Characteristics in Randomized Trials of Dronedarone and Amiodarone Versus Placebo for the Maintenance of Sinus Rhythm

<table>
<thead>
<tr>
<th>Trial (Ref. #)</th>
<th>Mean Age (yrs)</th>
<th>Male (%)</th>
<th>Paroxysmal AF (%)</th>
<th>Persistent AF (%)</th>
<th>Permanent AF (%)</th>
<th>Mean LA Diameter (mm)</th>
<th>Mean EF (%)</th>
<th>Heart Failure (%)</th>
<th>Warfarin (%)</th>
<th>Beta-Blockers (%)</th>
<th>ACE Inhibitors (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAFNE (22)</td>
<td>65</td>
<td>68</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>45</td>
<td>56</td>
<td>19</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>EURIDIS (10)</td>
<td>62</td>
<td>69</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>42</td>
<td>60</td>
<td>17</td>
<td>68</td>
<td>60</td>
<td>42</td>
</tr>
<tr>
<td>ADONIS (10)</td>
<td>64</td>
<td>69</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>43</td>
<td>58</td>
<td>18</td>
<td>72</td>
<td>52</td>
<td>37</td>
</tr>
<tr>
<td>ATHENA (9)</td>
<td>72</td>
<td>53</td>
<td>NR</td>
<td>NR</td>
<td>0</td>
<td>NR</td>
<td>21</td>
<td>60</td>
<td>71</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Kochiadakis et al. (25)</td>
<td>63</td>
<td>52</td>
<td>66</td>
<td>0</td>
<td>34</td>
<td>44</td>
<td>55</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>GEFACA (24)</td>
<td>63</td>
<td>73</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>48</td>
<td>58</td>
<td>NR</td>
<td>NR</td>
<td>100</td>
<td>NR</td>
</tr>
<tr>
<td>Channer et al. (23)</td>
<td>67</td>
<td>78</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>44</td>
<td>58</td>
<td>NR</td>
<td>NR</td>
<td>100</td>
<td>NR</td>
</tr>
<tr>
<td>SAFE-T (7)</td>
<td>67</td>
<td>79</td>
<td>0</td>
<td>79</td>
<td>21</td>
<td>48</td>
<td>50</td>
<td>25</td>
<td>100</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

ACE = angiotensin-converting enzyme; EF = ejection fraction; NR = not reported; other abbreviations as in Table 1.
the prevention of AF with amiodarone over dronedarone (OR: 0.49; 95% CI: 0.37 to 0.63; p < 0.001).

As shown in Figure 2B, there was a mortality trend favoring dronedarone in the indirect meta-analysis (amiodarone vs. dronedarone OR: 2.20; 95% CI: 0.61 to 7.88; risk difference: 0.008; 95% CI: −0.015 to 0.030). This finding was consistent with the DIONYSOS trial (OR: 2.44; 95% CI: 0.48 to 12.6), risk difference 0.011 (95% CI: −0.010 to 0.033). A similar trend was observed in the normal logistic regression model (OR: 1.61; 95% CI: 0.97 to 2.68; p = 0.066).

Comparative safety of dronedarone and amiodarone. For adverse effects requiring interruption of therapy (Fig. 2C), the indirect meta-analysis estimate favored dronedarone; amiodarone was associated with an increased odds of study drug termination (OR: 6.65; 95% CI: 1.13 to 39.3) with a risk difference of 0.083 (95% CI: −0.022 to 0.1866). The effect was similar in DIONYSOS (OR: 2.24; 95% CI: 1.13 to 4.43) with a risk difference of 0.057 (95% CI: 0.010 to 0.105). In normal logistic models that summarized the totality of the evidence, a similar relationship was observed (OR: 1.81; 95% CI: 1.33 to 2.46; p < 0.001). Organ-specific adverse reactions in the amiodarone versus placebo and the dronedarone versus placebo trials are shown in Table 3. Overall, the incidence of thyroid toxicity (4% vs. 3%), symptomatic bradyarrhythmias (2.8% vs. 1.1%), and hepatotoxicity (3.5% vs. 2.5%) leading to treatment discontinuation were comparable between dronedarone and placebo. Patients receiving dronedarone had a greater incidence of impaired creatinine clearance compared with placebo (4.0% vs. 1.1%). There were no cases of torsades de pointes in any of the patients administered amiodarone or in the DIONYSOS trial (21). There was a single case of torsades de pointes in a patient receiving dronedarone in
ATHENA (A Trial With Dronedarone to Prevent Hospitalization or Death in Patients With Atrial Fibrillation) (9).

**Discussion**

There are 3 major findings in our analysis of randomized controlled trials of dronedarone and amiodarone. First, dronedarone is less effective for the prevention of recurrent AF compared with amiodarone. On the other hand, dronedarone is associated with fewer adverse events requiring discontinuation of treatment. Finally, given the limited power of the available studies and the limitations inherent to meta-analysis, it remains unclear whether treatment with dronedarone confers a survival advantage versus other antiarrhythmic pharmacotherapy, including amiodarone.

Drugs for AF have limited antiarrhythmic efficacy. Even in highly selected clinical trial patient populations, most patients develop recurrent AF within 1 year despite antiarrhythmic therapy (3,7). At the same time, AF pharmacotherapy is limited by toxicities that constantly threaten patient safety and quality of life (2–4,27). Although amiodarone is commonly prescribed for the maintenance of sinus rhythm, its use has been plagued by dose-dependent end-organ toxicities, including thyroid dysfunction and pulmonary fibrosis. Dronedarone offers the potential for less toxicity and a shorter half-life (15). In the ATHENA trial, dronedarone therapy decreased hospitalization due to cardiovascular events or death (9). However, the composite end point was driven principally by hospitalizations, and the ATHENA trial did not capture recurrent AF events. In this systematic overview, dronedarone was associated with significantly fewer adverse effects and treatment discontinuations and a trend toward reduced all-cause mortality compared with amiodarone.

The critical question for clinical practice is whether these potential benefits justify a retreat from the moderate efficacy afforded by amiodarone. Although dronedarone may prolong the time to recurrent AF early on (10), long-term maintenance of sinus rhythm appears disappointing. If the indirect meta-analysis results are given the same approximate weight as the DIONYSOS direct comparison, we estimate that for every 1,000 patients treated with dronedarone instead of amiodarone, there would be 228 more recurrences of AF at 1 year in exchange for 9.6 fewer deaths and 62 fewer adverse events requiring discontinuation of drug.

Despite more limited efficacy for preventing AF, there appears to be a mortality benefit to avoiding toxicity in this select population. As in CAST (Cardiac Arrhythmia Suppression Trial), complete arrhythmia suppression in all patients may not translate into better survival, particularly in the setting of poor ventricular function (2). The ANDROMEDA (Antiarrhythmic Trial with Dronedarone in Moderate-to-Severe Congestive Heart Failure Evaluating Morbidity Decrease) trial was stopped early because of an unfavorable rate of mortality in the dronedarone arm (28).

What would it take to definitively determine whether dronedarone improves survival compared with amiodarone? The overall death rate in the ATHENA trial was 5.5% during the course of 22 months. In a similar population, a trial with 80% power (2-sided alpha 0.05) to detect a 20% mortality decrease would require approximately 14,000 patients. Until direct comparisons with sufficient statistical power for these outcomes are available, indirect estimates (with their inherent limitations) may help quantify the overall clinical benefit. Although indirect comparisons and limited head-to-head data lack precision, definitive trials will be expensive. This dilemma illustrates the challenges facing architects of comparative effectiveness policies.

**Study limitations.** Our analysis was restricted to randomized controlled trials. Although randomized controlled trials minimize bias, they may not reflect patients treated in general clinical practice. Indirect meta-analysis allows estimates of treatment effect that are less biased than pooled event rates. Even so, clinical differences can produce disparity among trials included in meta-analyses (29) and cause discrepancies between meta-analyses and subsequent large, controlled trials. For example, the dronedarone trials included in this meta-analysis excluded patients with permanent AF, which may have biased the results against amiodarone. This analysis included trials with an average follow-up of 1 year and does not address longer-term efficacy or safety. We did not have access to patient-level data and therefore relied on tabular published data. The only available direct treatment comparison (the DIONYSOS trial) has not yet completed the peer-review process.

| Table 3 Organ-Specific Adverse Reactions Requiring Study Drug Termination* |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Adverse Reaction**            | **Dronedarone** | **Placebo**     | **Amiodarone**  | **Placebo**     |
| Pulmonary toxicity              | 12/3,205 (1.0)  | 20/2,802 (0.7)  | 2/419 (0.5)     | 1/245 (0.4)     |
| Thyroid toxicity                | 128/3,205 (4.0)| 83/2,802 (3.0)  | 12/161 (7.5)    | 0/113 (0)       |
| Hepatic toxicity                | 112/3,205 (3.5)| 69/2,802 (2.5)  | 1/161 (0.1)     | 0/113 (0)       |
| Symptomatic bradyarrhythmia     | 89/3,205 (2.8)  | 31/2,802 (1.1)  | 6/161 (3.7)     | 0/113 (0)       |
| Increase in serum creatinine    | 128/3,205 (4.0)| 32/2,802 (1.1)  | NR              | NR              |

Values are n/N (%). *Data are pooled from those studies in which the authors reported organ-specific adverse reactions requiring discontinuation of drug therapy. NR = not reported.
process. Finally, our analysis ignores nonfatal events, such as stroke, which may heavily influence clinical decision-making.

Conclusions

Several phase 3 randomized controlled trials have compared dronedarone with placebo. Indirect meta-analysis and direct randomized data suggest that dronedarone has substantially less efficacy for the maintenance of sinus rhythm. However, dronedarone therapy is associated with less adverse effects and treatment discontinuation and appears to decrease cardiovascular events. More long-term data are needed to refine these estimates and to define the optimum balance of efficacy and toxicity for patients with AF.

Reprint requests and correspondence: Dr. Jonathan P. Piccini, Duke Clinical Research Institute, Duke University Medical Center #31115, Durham, North Carolina 27710. E-mail: jonathan.piccini@duke.edu.

REFERENCES


Key Words: dronedarone • amiodarone • antiarrhythmic drug therapy • atrial fibrillation.

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