A Randomized, Controlled Trial of RSD1235, a Novel Anti-Arrhythmic Agent, in the Treatment of Recent Onset Atrial Fibrillation

Denis Roy, MD, FACC,* Brian H. Rowe, MD, MSc,† Ian G. Stiell, MD, MSc,‡ Benoit Coutu, MD,§ John H. Ip, MD,‖ Denis Phaneuf, MD,¶ Jacques Lee, MD, MSc,# Humberto Vidailliet, MD, FACC,** Garth Dickinson, MD,‡ Sheila Grant, MBA,†† Alan M. Ezrin, PhD,†† Gregory N. Beatch, PhD,††† for the CRAFT Investigators

Montreal, Edmonton, Ottawa, Toronto, and Vancouver, Canada; Lansing, Michigan; and Marshfield, Wisconsin

OBJECTIVES
The purpose of this study was to determine the efficacy and safety of intravenous RSD1235 in terminating recent onset atrial fibrillation (AF).

BACKGROUND
Anti-arrhythmic drugs currently available to terminate AF have limited efficacy and safety. RSD1235 is a novel atrial-selective anti-arrhythmic drug.

METHODS
This was a phase II, multi-centered, randomized, double-blinded, step-dose, placebo-controlled, parallel group study. Fifty-six patients from 15 U.S. and Canadian sites with AF of 3 to 72 h duration were randomized to one of two RSD1235 dose groups or to placebo. The two RSD1235 groups were RSD-1 (0.5 mg/kg followed by 1 mg/kg) or RSD-2 (2 mg/kg followed by 3 mg/kg), by intravenous infusion over 10 min; a second dose was given only if AF was present. The primary end point was termination of AF during infusion or within 30 min after the last infusion. Secondary end points included the number of patients in sinus rhythm at 0.5, 1, and 24 h post-last infusion and time to conversion to sinus rhythm.

RESULTS
The RSD-2 dose showed significant differences over placebo in: 1) termination of AF (61% vs. 5%, p < 0.0005); 2) patients in sinus rhythm at 30 min (56% vs. 5%, p < 0.001); 3) sinus rhythm at 1 h (53% vs. 5%, p = 0.0014); and 4) median time to conversion to SR (14 vs. 162 min, p = 0.016). There were no serious adverse events related to RSD1235.

CONCLUSIONS
RSD1235, a new atrial-selective anti-arrhythmic agent, appears to be efficacious and safe for converting recent onset AF to sinus rhythm. (J Am Coll Cardiol 2004;44:2355–61) © 2004 by the American College of Cardiology Foundation

Atrial fibrillation (AF) is the most common sustained arrhythmia, and its development or exacerbation often prompts emergency department presentations. Conversion of AF to sinus rhythm is often attempted in the acute setting to improve symptoms and to prevent the detrimental hemodynamic effects that AF may have in some patients (e.g., valvular disease or left ventricular dysfunction). Early conversion of AF may also prevent the development of electrical remodeling (1) and the embolic risks associated with intra-atrial thrombus formation (2). Electrical cardioversion is effective in restoring sinus rhythm but requires procedural sedation or anesthesia and is not successful in all cases. Currently available converting agents have highly variable efficacy and several safety limitations associated with their use (3–21). In addition, placebo-controlled trials that establish the efficacy and safety of these pharmacologic therapies for acute conversion are limited. An efficacious, simple, and safe pharmacologic alternative to existing methods of cardioversion would be a welcome development for patients with AF and their treating physicians.

RSD1235, a novel compound, was developed by Cardiome Pharma (Vancouver, British Columbia, Canada) and is a mixed frequency-dependent Na+ and atria-preferential K+ channel blocker. In animal models of AF, RSD1235 is effective in terminating and preventing relapse of AF. In several preclinical studies, RSD1235 has been shown to selectively prolong atrial refractory periods without significant effects on ventricular refractoriness or QT intervals (22,23). The drug has been demonstrated to be safe in a variety of doses in healthy volunteers (24). The present clinical study was designed to examine the efficacy and safety of intravenous RSD1235 using a step-dosing design for rapid termination of AF.

METHODS
Design. The study protocol was approved by the institutional or ethics review boards at each of the participating sites. This was a prospective double-blinded, placebo-controlled, randomized, dose–response trial. Multiple levels
of blinding were employed, including the treating physician, patient, treating nurse, research nurse, family physician, follow-up assessment, and outcome adjudicators.

**Inclusion criteria.** To be eligible, patients with recent onset AF (recurrent or new onset) had to have AF with a continuous duration of 3 to 72 h at the time of randomization. Patients were managed in accordance with American College of Cardiology/American Heart Association/European Society of Cardiology anticoagulation practice guidelines (25). Patients >21 years of age were eligible. All patients had to be hemodynamically stable (systolic blood pressure 90 to 160 mm Hg; diastolic blood pressure <95 mm Hg) and provide written, informed consent.

**Exclusion criteria.** Exclusion criteria included female patients of child-bearing potential; weight >136 kg; history of long QT syndrome, torsade de pointes, or an uncorrected QT’ interval of >450 ms; QRS >120 ms; myocardial infarction; symptoms of angina; congestive heart failure; stroke within the previous three months; cardiac surgery in the previous six months; bradycardia (<50 beats/min) or sick sinus syndrome, unless controlled by a pacemaker; digoxin toxicity; reversible cause of AF (such as hyperthyroidism, pulmonary embolism, alcohol intoxication, acute pericarditis); Wolff-Parkinson-White syndrome; chronic obstructive pulmonary disease requiring daily bronchodilator therapy; cyanotic or other significant congenital heart disease; concurrent treatment with known QT-prolonging drugs or class I or III anti-arrhythmic agents (unless the medication was discontinued more than five half-lives before enrollment); oral amiodarone in the prior six months or intravenous amiodarone in the previous month; end-stage disease; and the following laboratory abnormalities: serum potassium <3.5 mEq/l, magnesium <1.5 mEq/l, serum creatinine ≥1.8 mg/dl, hemoglobin <9 g/dl in women or <11 g/dl in men, and liver enzymes 1.5 times the maximal normal values. No alcohol, caffeine, herbal remedies, or smoking was permitted during the study. Pre-enrollment treatment with beta-adrenergic blocking agents, calcium antagonists, and digoxin for control of ventricular rate was permitted.

**Treatments.** Patients were randomized to one of three groups and in each group received up to two 10-min intravenous infusions, separated by 30 min. Infusions were placebo followed by placebo, 0.5 mg/kg followed by 1.0 mg/kg RSD1235 if required, or 2.0 mg/kg followed by 3.0 mg/kg RSD1235 if required. The second dose in each group was administered only if AF was present 30 min after completion of the first dose. Doses for patients weighing >113 kg were capped as if the patient’s weight was 113 kg.

**Outcomes.** Efficacy outcomes were adjudicated by Drs. Dickinson, Rowe, and Ezrin before unblinding of treatment allocation; disagreements were resolved following a second review and consensus. The primary efficacy end point of this study was the termination of AF (which could include conversion of AF to sinus rhythm or another atrial rhythm, such as atrial flutter) for any length of time during infusion or within 30 min after the end of the last infusion. As such, patients whose AF terminated during or within 30 min after the end of the first infusion met the primary end point, as well as those patients requiring a second infusion, whose AF terminated during or within 30 min after the end of their second infusion. Secondary end points included the number of patients in sinus rhythm at 0.5, 1, and 24 h after the end of their last infusion, as well as the time to conversion to sinus rhythm from first exposure to study drug.

**Protocol.** A Holter rhythm strip continuously monitored the electrocardiogram (ECG); vital signs (blood pressure and heart rate) and oxygen saturation were recorded every 2 min from the start of infusion to 5 min after, as well as at 15, 30, 60, 120, 240, 360, and 480 min and at discharge and one-week follow-up. Twelve-lead ECGs were obtained before dosing and every minute during infusion to 5 min after, as well as at 15, 30, 60, 120, 240, 360, and 480 min, discharge, 24-h and 1-week follow-up, and the time of arrhythmia termination or significant rhythm changes. The ECGs were interpreted by individual investigators and independently verified by a core laboratory cardiologist blinded to study treatment. Venous blood samples were drawn for RSD1235 plasma concentrations at 0, 15, 30, 60, 120, 240, and 480 min, discharge, and AF termination or significant adverse events. The infusion was discontinued if the arrhythmia terminated after 1 min of verification, systolic blood pressure decreased to <85 mm Hg or increased to >190 mm Hg, HR was <50 beats/min, intolerable side effects or any change in rhythm or atrioventricular conduction occurred that in the investigator’s opinion was a threat to patient safety, a new bundle-branch block developed, the QRS complex increased >50%, the uncorrected QT’ interval increased to 550 ms or >25% of baseline, or any polymorphic ventricular tachycardia was noted. If AF persisted past 1 h after the end of the last infusion received, electrical cardioversion was permitted. The use of other anti-arrhythmic agents was discouraged until 12 h after the RSD1235 infusion, unless the investigator considered it necessary to restore sinus rhythm earlier.

**Statistical considerations.** The sample size was based on estimates of a placebo conversion rate of 35%, RSD1235 conversion rate of 60%, an alpha value of 0.05, and a beta value of 0.9.

All patients who received any amount of study medication (n = 56) were included in the safety and efficacy analysis. Subjects who where randomized but did not receive study medication were not included in the analysis. Under the principles of randomization and double-blinded treatments, and given that the decision to exclude...
these patients was not based on knowledge of the treatment to be received, the remaining patients conformed to the intention-to-treat philosophy and provide an unbiased comparison of the true effect of RSD1235 in the termination of AF. Furthermore, as no study medication was administered to the excluded patients, it would have been impossible to determine efficacy according to the primary or secondary end points (AF termination relative to infusion time). Data are presented as the mean value ± SD or median value with interquartile range. All tests were performed as two-sided, and the 95% confidence interval was produced; p < 0.05 was considered statistically significant, unless stated otherwise. Analysis of the relationship between termination of AF and treatment was performed using chi-square analysis. In cases of small cell frequencies, the Fisher exact test was used. A Cochran-Armitage test statistic with table scores was used to test the ascending dose evaluation of efficacy.

Patients who were electrically cardioverted were not evaluated for secondary end points. The time to conversion from the start of the first infusion was analyzed by the Cox regression method of event time analysis and one-way analysis of variance. Assessment of the significance of time point values and the mean change from baseline to each follow-up reading of ECG intervals (QRS, QT, corrected QT), blood pressures, and heart rates were made within dose groups using the paired t test, and comparisons among dose groups were made using one-way analysis of variance.

RESULTS

Patient recruitment. Sixty-five eligible patients provided consent to enter the study and were randomized from 15 participating centers between January 16, 2002, and July 5, 2002. Nine patients were randomized but did not receive the study drug (seven not remaining in AF at the time of intended study drug administration; one with screening failure; and one who withdrew consent), and they were withdrawn from further participation in the study. One patient received the study drug (placebo) and was included in the efficacy analysis per the intention-to-treat principle, although he failed to meet the AF duration entry criteria. The treatment allocation was as follows: placebo/placebo (n = 20); 0.5 mg/kg + 1.0 mg/kg RSD1235 (n = 18); and 2.0 mg/kg + 3.0 mg RSD1235 (n = 18).

Patient characteristics (Table 1). There were no statistical differences in the baseline characteristics of the three patient groups. Patients in the placebo group tended to report AF more frequently in the past than did those in the RSD1235-dosed groups.

Primary end point. The cumulative AF termination within 30 min after the last infusion was 61% (11 of 18 patients) after 2 + 3 mg/kg RSD1235 infusion, 11% (2 of 18 patients) after 0.5 + 1 mg/kg RSD1235, and 5% (1 of 20 patients) after placebo + placebo (Fig. 1). Paired comparisons indicated a statistically significant difference (p < 0.0005) between placebo and the RSD-2 groups. There was no significant difference in the success rates between the RSD-1 and placebo groups. Of the 11 AF terminations in the RSD-2 group, 10 converted to sinus rhythm and 1 converted into atrial flutter.

The median time to termination of AF was 11 min after the start of the first infusion (range 3 to 58 min) in the RSD-2 group. In fact, all the responders in this group reached the primary end point during drug infusion or within 10 min of the last infusion. The patient in the RSD-2 group who converted from AF into atrial flutter subsequently converted to sinus rhythm 14.5 h later.

Secondary end points. The percentage of patients in sinus rhythm (excluding those electrically cardioverted) at 30 min after infusion was 56% (10 of 18 patients) in the RSD-2 group, 11% (2 of 18 patients) in the RSD-1 group, and 5%
(1 of 20 patients) in the placebo group. The percentage of patients in sinus rhythm at 1 h after infusion was 53% (9 of 17 patients) in the RSD-2 group, 11% (2 of 18 patients) in the RSD-1 group, and 5% (1 of 20 patients) in the placebo group. The percentage of patients in sinus rhythm at 24 h after infusion was 79% (11 of 14 patients) in the RSD-2 group, 56% (5 of 9 patients) in the RSD-1 group, and 45% (5 of 11 patients) in the placebo group. Only the difference between RSD-2 and placebo was statistically significant at 30 min ($p < 0.01$) and a $t$1h($p < 0.005$).

The median time to conversion to sinus rhythm during the 24-h observation period (excluding those electrically cardioverted) from the start of the first infusion in the RSD-2 group ($n = 11$) was 14 min (range 3 to 87 min, $p = 0.016$), compared with the placebo group ($n = 5$), with a median time of 162 min (range 58 to 1,119 min). The median time to conversion to sinus rhythm in the RSD-1 group ($n = 5$) was 166 min (range 1 to 332 min, $p = 0.886$ vs. placebo).

**Electrocardiographic effects of RSD1235.** The RSD1235 infusion did not significantly prolong the QTc or QRS intervals, as compared with placebo (Table 2). There was no difference in the QT and QTc intervals between placebo ($389 \pm 31$ ms vs. $414 \pm 16$ ms) and RSD-2 treatment ($366 \pm 28$ ms vs. $427 \pm 19$ ms) using the first available ECG records after conversion to sinus rhythm.

**Hemodynamic effects.** There were no clinically significant changes from baseline in systolic blood pressure, and there were no changes in blood pressure that were substantially different from those seen in the placebo group. There were two significant cases of hypotension reported in the placebo group and one mild case of transient hypotension in the RSD-2 group. Clinically significant treatment-related decreases in mean heart rate from baseline (mean 106 beats/min) occurred in patients administered the RSD-2 dose, starting at $T_1 = 15$ min (mean 90 beats/min). This likely reflected the conversion of several patients to normal sinus rhythm.

**Adverse events.** A total of 39 patients experienced 122 adverse events over the course of the study, with a similar incidence of events among the three treatment groups. The majority of adverse events were of mild or moderate intensity. There were four mild adverse events that occurred in two patients considered either definitely or probably related to study drug. Both patients were in the RSD-2 dose group: one patient reported paresthesia, and one patient reported paresthesia, nausea, and hypotension.

The most common adverse events experienced in this study were cardiac disorders, reported by seven patients (35.0%) in the placebo group, four patients (22.2%) in the RSD-1 group, and three patients (16.7%) in the RSD-2 group. In addition to the serious adverse events discussed subsequently, the cardiac disorders in the placebo group included two patients with nonsustained ventricular tachycardia and a patient with ventricular premature beats. Ventricular premature beats were also seen in two patients, and sinus bradycardia was found in one patient in the low-dose group. Ventricular premature beats were seen in two patients, and sinus bradycardia in another patient in the RSD-2 group. Other adverse events occurring with a similar frequency among treatment groups were nervous system disorders, general disorders, and infections.

**Serious adverse events.** Serious adverse events were reported in five patients (four in the placebo group and one in the RSD-1 group). A transient cerebral ischemic attack occurred one day after conversion in a placebo-treated patient with a therapeutic international normalized ratio at
the time of conversion. Severe bradycardia and hypotension immediately after conversion occurred in one patient, pulmonary edema in another patient, and recurrent AF in the fourth placebo patient. One patient in the RSD-1 group experienced ventricular fibrillation, which was attributed to an asynchronous discharge during an electrical cardioversion attempt performed 1 h after receiving the second infusion.

Follow-up through 24 h. Within the study period (24 h), electrical cardioversion was attempted in 9 (45%) of 20 placebo-treated, 9 (50%) of 18 RSD-1-treated, and 4 (22%) of 18 RSD-2–treated patients, and it was successful in 8 (89%), 9 (100%), and 4 (100%) patients, respectively.

Pharmacokinetic analysis. Mean peak RSD1235 plasma levels were 5.8 μg/ml (range 4.0 to 8.6 μg/ml) in the

Table 2. Corrected QT and QRS Intervals and Heart Rate Values for Patients in Each Study Group

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Placebo</th>
<th>RSD1235 (0.5 and 1.0 mg/kg)</th>
<th>RSD1235 (2.0 and 3.0 mg/kg)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QTc (ms)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predrug baseline</td>
<td>20</td>
<td>16</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>424 ± 6</td>
<td>417 ± 6</td>
<td>434 ± 7</td>
<td>0.233</td>
</tr>
<tr>
<td>End infusion no. 1</td>
<td>19</td>
<td>17</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>430 ± 5</td>
<td>419 ± 6</td>
<td>449 ± 9</td>
<td>0.066</td>
</tr>
<tr>
<td>End infusion no. 2</td>
<td>16</td>
<td>17</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>436 ± 8</td>
<td>414 ± 11</td>
<td>447 ± 17</td>
<td>0.691</td>
</tr>
<tr>
<td>QRS (ms)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predrug baseline</td>
<td>20</td>
<td>17</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>87 ± 2</td>
<td>83 ± 3</td>
<td>86 ± 3</td>
<td>0.823</td>
</tr>
<tr>
<td>End infusion no. 1</td>
<td>19</td>
<td>17</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>89 ± 2</td>
<td>86 ± 3</td>
<td>95 ± 3</td>
<td>0.150</td>
</tr>
<tr>
<td>End infusion no. 2</td>
<td>16</td>
<td>17</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>88 ± 2</td>
<td>90 ± 6</td>
<td>99 ± 5</td>
<td>0.120</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predrug baseline</td>
<td>20</td>
<td>16</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>112 ± 6</td>
<td>101 ± 6</td>
<td>108 ± 6</td>
<td>0.585</td>
</tr>
<tr>
<td>End infusion no. 1</td>
<td>19</td>
<td>17</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>115 ± 6</td>
<td>104 ± 7</td>
<td>98 ± 5</td>
<td>0.045</td>
</tr>
<tr>
<td>End infusion no. 2</td>
<td>16</td>
<td>17</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>109 ± 6</td>
<td>107 ± 6</td>
<td>104 ± 6</td>
<td>0.601</td>
</tr>
</tbody>
</table>

This table shows the baseline values and effects of infusion on QTc and QRS intervals as well as heart rate in the treatment groups. There were no statistically significant differences in electrocardiographic intervals after infusion between groups. Heart rate was decreased after 2 mg/kg RSD1235 (p < 0.05), reflecting the number of patients who converted to sinus rhythm in this group. Data are presented as the mean value ± SD.

Figure 2. Plasma concentrations of RSD1235 after infusion in patients dosed at 2 mg/kg intravenously (inverted triangles) and those additionally dosed at 3 mg/kg intravenously (circles). The RSD1235 doses were infused over 10 min, as indicated in the text. Initially, a 2-mg/kg infusion was given, and, if required, an additional 3 mg/kg was infused 30 min later in the RSD-2 group. Time is shown relative to the end of the first infusion (T1).
patients who received both the 2.0- and 3.0-mg/kg infusions of RSD1235 (Fig. 2) and 1.9 μg/ml (range 0.1 to 3.4 μg/ml) in those who received both the 0.5- and 1.0-mg/kg RSD1235 infusions. Maximum plasma levels were seen at the end of the second infusion. The lower limit of detection/ quantification of RSD1235 in plasma was 5 ng/ml. Plasma levels of RSD1235 at 24 h were below this lower limit of quantification in most patients who received RSD-1. Similarly, negligible plasma levels were seen at 24 h in the RSD-2 group; mean plasma levels were 0.017 μg/ml (range <0.005 to 0.028 μg/ml). In those patients who received only the 2-mg/kg infusion, the mean peak plasma levels at the end of infusion were 2.6 μg/ml (range 1.4 to 4.5 μg/ml). The median plasma level at the time of AF conversion in these patients was 1.3 μg/ml (range 1.1 to 3.5 μg/ml). The mean terminal elimination half-life in these patients was 3.1 h (range 1.7 to 5.4 h).

DISCUSSION

This phase II dose-finding study demonstrated that the upper dose of RSD1235 (2 + 3 mg/kg) rapidly and effectively terminated AF compared with lower dose RSD1235 and placebo. There were no serious adverse events associated with RSD1235. In contrast to other anti-arrhythmic drugs used for conversion of recent onset AF, there were no instances of drug-related pro-arrhythmia. Although these initial findings will require confirmation in larger scale clinical trials, this safety profile, coupled with an efficacious and rapid onset, confirms that RSD1235 is a promising new agent for the medical conversion of recent onset AF.

Cardioversion of AF may be accomplished using electrical or pharmacologic approaches. Electrical cardioversion is effective in rapidly restoring sinus rhythm; however, it requires procedural sedation and a suitable recovery period and/or may cause pain after treatment. Experimental data suggest that AF itself conditions the substrate for maintenance of AF and supports the need for early arrhythmia termination to prevent electrical remodeling (1). In this regard, rapid intravenous conversion of AF should be preferable to oral anti-arrhythmic agents that may require up to 24 h to act (3). We chose a very short follow-up time after infusion for primary efficacy analysis in order to distinguish drug efficacy from placebo, as the placebo response rate is relatively high in patients with AF of less than three days’ duration. We also thought that responsiveness to drug within 30 min of infusion was a clinically relevant end point, because it allows for rapid conversion of AF within an emergency department setting.

RSD1235 appears to shows a high clinical efficacy (56%) for conversion of recent onset AF to sinus rhythm within 2 h of exposure and compares favorably to other intravenous anti-arrhythmic agents reported in published data. For example, in recent onset AF, placebo-controlled studies of intravenous class IC agents (flecainide and propafenone) have had efficacy rates (corrected for placebo response rate) of 25% to 53% within 2 h of infusion (3). The efficacy of intravenous amiodarone is highly variable; however, it is considered less than that with the class IC agents (15–18). Furthermore, responses that take 24 h to manifest, such as with amiodarone, are of limited usefulness for acute intravenous conversion of AF. Class III anti-arrhythmics, such as ibutilide and dofetilide, show 20% to 30% net efficacy rates for conversion of AF, with slightly higher efficacy in termination of atrial flutter (3,18,20,21). These latter agents are associated, however, with a relatively high incidence of drug-induced pro-arrhythmia (18,20). Intravenous sotalol, another agent with class III activity, has not been shown to be effective in restoring sinus rhythm in patients with atrial arrhythmias (19).

Study limitations. First, this study had a small sample size, and these initial findings will require confirmation in ongoing larger scale clinical trials. Second, the inclusion and exclusion criteria were rigid, and future trials should include post-cardiac surgery patients and those concurrently receiving other anti-arrhythmic agents. Finally, there were no quality-of-life assessments.

Conclusions. Notwithstanding these concerns, this randomized, controlled trial provides evidence for the efficacy of this novel, atrial-selective, Na+/K+ channel blocking agent for the treatment of recent onset AF. Intravenous RSD1235 (2 + 3 mg/kg) was effective in rapidly terminating AF and was not associated with any drug-induced pro-arrhythmia or any serious adverse event. RSD1235 appears to be a potential alternative to existing chemical and electrical cardioversion for rapid termination of AF.

Acknowledgments

The authors thank the nurse coordinators in the participating sites for their cooperation with this study.

Reprint requests and correspondence: Dr. Denis Roy, Montreal Heart Institute, 5000 Belanger Street, Montreal, Quebec, Canada, H1T 1C8. E-mail: d_roy@icm-mhi.com.

REFERENCES


APPENDIX

For a list of the CRAFT Investigators, please see the December 21, 2004, issue of JACC at http://www.onlinejacc.org.