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ORIGINAL ARTICLE

Comparative Safety and Effectiveness of Sotalol Versus Dronedarone After Catheter Ablation for Atrial Fibrillation

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BACKGROUND: Atrial tachyarrhythmias are common after atrial fibrillation ablation, so adjunctive antiarrhythmic drug therapy is often used. Data on the effectiveness and safety of dronedarone and sotalol after AF ablation are limited. Here, we compared health outcomes of ablated patients treated with dronedarone versus sotalol.

METHODS AND RESULTS: A comparative analysis of propensity score–matched retrospective cohorts was performed using IBM MarketScan Research Databases. Patients treated with dronedarone after atrial fibrillation ablation were matched 1:1 to patients treated with sotalol between January 1, 2013 and March 31, 2018. Outcomes of interest included cardiovascular hospitalization, proarrhythmia, repeat ablation, and cardioversion. This study was exempt from institutional review board review. Among 30 696 patients who underwent atrial fibrillation ablation, 2086 were treated with dronedarone and 3665 with sotalol after ablation. Propensity-score matching resulted in 1815 patients receiving dronedarone matched 1:1 to patients receiving sotalol. Risk of cardiovascular hospitalization was lower with dronedarone versus sotalol at 3 months (adjusted hazard ratio [aHR], 0.77 [95% CI, 0.61–0.97]), 6 months (aHR, 0.76 [95% CI, 0.63–0.93]), and 12 months after ablation (aHR, 0.70 [95% CI, 0.66–0.93]). Risk of repeat ablation and cardioversion generally did not differ between the 2 groups. A lower risk of proarrhythmia was associated with dronedarone versus sotalol at 3 months (aHR, 0.76 [95% CI, 0.64–0.90]), 6 months (aHR, 0.80 [95% CI, 0.70–0.93]), and 12 months (aHR, 0.83 [95% CI, 0.73–0.94]) after ablation.

CONCLUSIONS: These data suggest that dronedarone may be a more effective and safer alternative after ablation than sotalol.

Key Words: atrial fibrillation ■ catheter ablation ■ treatment

Catheter ablation of atrial fibrillation (AF) is increasingly being used for treatment of medically refractory, symptomatic AF. Despite improvements in the procedural technologies, many patients after ablation continue to have AF, atrial flutter, and atrial tachycardias, collectively referred to as atrial tachyarrhythmias (ATAs). Recurrent ATAs are particularly prevalent in the first 3 months after ablation because of myocardial injury and inflammation,[1] a period known as the recovery or blanking phase. Overall rates of hospitalization during the first 3 months after ablation range from 13% to 20%, driven primarily by admissions for ATAs.[2–5] Even beyond the recovery phase, recurrent ATAs are common. In large-scale clinical trials with different ablation technologies, about 30%–40% of patients continue to have ATAs despite an initial ablation.[6,7] Repeat hospitalizations occur in 29%–43% at 1 year.[2,5] Thus, treatment with antiarrhythmic drugs (AADs) is frequently needed during and even beyond the recovery phase after ablation. Recurrent ATAs after ablation also result in the need for recurrent hospitalizations, cardioversions, and repeat AF ablations. The long-term cardiovascular benefits with comprehensive rhythm control with AADs and AF ablation, however, are still to be established.[8]

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CLINICAL PERSPECTIVE

What Is New?

- Catheter ablation of atrial fibrillation is increasingly being used for treatment of medical refractory symptomatic atrial fibrillation.
- Little is known about the optimal antiarrhythmic drug strategy acutely or chronically after atrial fibrillation ablation.
- From our data, dronedarone appears to be a more effective and safer alternative after ablation than sotalol.

What Are the Clinical Implications?

- Further research is warranted on the treatment effects between dronedarone and sotalol adjunctive to ablation, including results on mortality.

Nonstandard Abbreviations and Acronyms

AAD	antiarrhythmic drug
ATA	atrial tachyarrhythmia

Little is known about the optimal AAD strategy acutely or chronically after AF ablation. Studies comparing the use of a class I or III AAD during the recovery phase after AF ablation have demonstrated a reduced risk of ATAs and ATA-related hospitalizations compared with no AAD therapy.[9] There are also multiple studies comparing specific AADs in patients with AF who are not undergoing catheter ablation.[10–13] Despite this, there are limited data on comparative efficacy or safety of AADs in the recovery or later phases after ablation, when alteration in triggers, substrate, and autonomic milieu may alter the efficacy and/or safety profile of AADs.

Both dronedarone and sotalol are commonly used antiarrhythmic drugs with differing pharmacological effects, although both drugs have Vaughan Williams class II and III effects.[14–16] Both drugs are indicated and used in similar patient populations, whereas other antiarrhythmic drugs are often prescribed to patients with different characteristics compared with dronedarone and sotalol.[17] In particular, both dronedarone and sotalol have been shown to be effective and are recommended in AF guidelines for patients with structural and ischemic heart disease in the absence of significant or recently decompensated heart failure,[18–21] although both may be used in patients without structural heart disease. In comparable patient groups, the European Society of Cardiology's 2020 guidelines recently maintained treatment with dronedarone as a class IA recommendation, but downgraded treatment with sotalol to a IIbA recommendation.[21] A randomized prospective trial comparing dronedarone to sotalol has not been performed in patients either before or after ablation. The present study aimed to compare effectiveness and safety end points of dronedarone and sotalol in patients after AF ablation using a real-world cohort of patients.

METHODS

Qualified researchers may request access to patient level data and related study documents including the clinical study report, study protocol with any amendments, statistical analysis plan, and data set specifications. Patient-level data will be anonymized and study documents will be redacted to protect the privacy of our trial participants. Further details on Sanofi's data-sharing criteria, eligible studies, and process for requesting access can be found at https://www.clinicalstudydatarequest.com/. Analytical methods and study materials are available in Data S1 and S2.

Patient Selection

The study design was an observational study of retrospectively identified, propensity score–matched cohorts using data obtained from the IBM MarketScan Research Databases. MarketScan is commonly used in epidemiological research, including the study of AF, and comprises the Commercial Claims and Encounters Database and Medicare Supplemental and Coordination of Benefits Database.[22–24] These US-based data on over 181 million patients contain adjudicated administrative health information that includes enrollment, inpatient, outpatient, and prescription data. This study used preexisting deidentified data sets, and in compliance with the Health Insurance Portability and Accountability Act of 1996, this study was exempt from institutional review board review and no informed consent was required by participants. Patients with a diagnosis of AF were identified within the study period between January 1, 2013 and March 31, 2018 using *International Classification of Diseases*, *Ninth Revision* and *Tenth Revision* (*ICD-9* and *ICD-10*) codes. Patients aged >18 years who were undergoing an initial index ablation for AF during this period were identified. All patients had to have at least 12 months of continuous enrollment during the baseline period before the index ablation and at least 1 follow-up encounter within the 12-month period after the index ablation. The date of index ablation was used as the start of follow-up.

Patients meeting these inclusion criteria who were prescribed either dronedarone or sotalol as their first antiarrhythmic drug after the index ablation were selected for 1:1 propensity-score matching. Patients

were matched in terms of demographics, baseline comorbidities, medical history, and concomitant medications to ensure comparability. Standard mean differences were calculated for each covariate. Based upon greedy matching with a caliper of 0.1, patients were matched on the covariates including age at index ablation, sex, chronic heart disease, chronic obstructive pulmonary disease, diabetes, heart failure, hypertension, stroke, myocardial infarction, peripheral arterial disease, venous thromboembolism, vascular disease, Charlson Comorbidity Index, and CHA_2DS_2-VASc score. Other matching covariates were baseline procedures including ECG, cardioversion, and implantable cardioverter defibrillator or pacemaker implantation; and baseline drug use including direct-acting oral anticoagulants, warfarin, digoxin, antiplatelet therapy, β-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and loop diuretics. Because MarketScan is an administrative database, information was not available about AF symptom frequency, duration, or severity. Data on the type of AF (paroxysmal versus persistent forms) were not included because *ICD-10* codes were not available throughout the entire study period. In addition, information on the type (eg, radiofrequency, cryoablation) or acute success of the ablation procedure performed was not available in refer the data set and could not be propensity score–matched across cohorts.

Clinical Outcomes

Effectiveness and safety outcomes were evaluated in the matched cohorts within the first 12 months after the index ablation. Prespecified effectiveness outcomes of interest included cardiovascular hospitalization, electrical cardioversion, and repeat AF ablation. Cardiovascular hospitalization included hospitalization for ATA, heart failure, myocardial infarction, and ischemic stroke or transient ischemic attack. Atrial tachyarrhythmia burden after ablation could not be assessed from the database. Prespecified safety outcomes assessed included a proarrhythmia composite end point and implantation of a permanent pacemaker end point.

Similar to the methods previously described,[10,18,25] we defined the composite proarrhythmia end point, including both ventricular and bradyarrhythmias, as follows. Ventricular proarrhythmia included QT interval prolongation requiring discontinuation of therapy, ventricular fibrillation or flutter, ventricular tachycardia, torsades de pointes, reentry ventricular arrhythmia, cardiac arrest, and implantable cardioverter defibrillator implantation (excluding coincident diagnosis of heart failure). The bradyarrhythmia end point included bradycardia, sinus node dysfunction, second- or third-degree arterioventricular block, and pacemaker implantation. All codes for the baseline characteristics, procedural identification, and outcomes are shown in Data S1 and S2. All effectiveness and safety outcomes were assessed and compared between matched cohorts at 3, 6, and 12 months after ablation (eg, an event that occurred 10 months after the index ablation would contribute toward the 12-month event rate statistics).

Statistical Analysis

Analyses included patients assigned to the treatment groups who were propensity-score matched. Patients were censored when lost to follow-up (eg, because of unenrollment from their health insurance plan) or at the time of their first event. Longitudinal models were based on initial study-group assignment (ie, dronedarone or sotalol). Changes in adherence, persistence, or treatment were not reasons for censoring. Unadjusted incidence rates of the study end points (estimated per 100 person-years) were assessed at time of first event for the given analysis.

Time-to-event analyses were assessed by Kaplan-Meier methods estimated for outcomes of interest among the propensity score–matched patients, and are presented as cumulative incidence curves. Log-rank testing compared the dronedarone group's cumulative incidence curve to the sotalol group's cumulative incidence curve for each outcome of interest. We also compared the relative risk of the study outcomes by estimating the hazards of events in adjusted settings. Cox proportional hazard modeling was used for the comparison of dronedarone-treated to sotalol-treated propensity score–matched patients. As part of the modeling execution, the proportional hazards assumption was confirmed. Adjustment factors for the models were selected from the baseline patient characteristics via forward selection. Specifically, among all baseline characteristics, the variable with the lowest *P* value was added to the model, and then this was repeated until no remaining variables had a *P* value below 0.1 when added.

A sensitivity analysis was performed to assess the impact of events that occurred during the recovery/blanking period, namely, the first 3 months after the index ablation. In this analysis, events that occurred during the first 3 months after the index ablation were not counted toward 6-month and 1-year rates, and patients were not censored because of an event during the 3-month period.

A second sensitivity analysis was performed that censored pacemaker insertion events for proarrhythmia composite and bradycardia outcomes.

Analyses were performed using Python software in the Sanofi analytical platform DARWIN. An α level of 0.05 was used to determine statistical significance.

RESULTS

Cohort Formation

The cohort formation flow diagram is shown in Figure 1. Of the 1 347 147 patients with a diagnosis of AF between January 1, 2013 and March 31, 2018, there were 40 370 (3.0%) who underwent an index AF ablation. Of those patients undergoing ablation, 9674 (24.0%) were excluded from this analysis; 9267 lacked 12 months of continuous enrollment during the baseline period, 406 had no follow-up information after ablation, and 1 patient was under the age of 18 years. Thus, 30 696 patients (76.0%) met enrollment criteria. Of these, 2086 (6.8%) were treated with dronedarone after ablation and 3665 (11.9%) were treated with sotalol after ablation. After propensity-score matching, there were 1815 patients in each treatment group (Figure 1).

Patient Characteristics

Among the propensity score–matched groups, patients were older (dronedarone median age: 63 years, sotalol median age: 62 years) and predominantly men (dronedarone: 67%, sotalol: 67%), with a high prevalence of comorbid illness, including hypertension (dronedarone: 71%, sotalol: 73%), chronic heart disease (dronedarone: 42%, sotalol: 39%), heart failure (dronedarone: 15%, sotalol: 16%), and diabetes (dronedarone: 20%, sotalol: 21%). The prevalence of comorbid disease resulted in a mean CHA_2DS_2-VASc score of 2.26±1.50 for dronedarone and 2.24±1.52 for sotalol, and a Charlson Comorbidity Index of 0.94±1.44 for both dronedarone and sotalol. Most patients had had at least 1 ECG (97%) during the preablation year. In both groups, about 45% had had at least 1 cardioversion for AF within the preablation year and 36% within 6 months before ablation. Overall, 29% of dronedarone-treated patients and 33% of sotalol-treated patients had had at least 1 AF-related hospitalization during the year before ablation. A pacemaker was present in 2.4% and 3.5% of patients treated with dronedarone or sotalol after ablation and an implantable cardioverter defibrillator in 0.1% and 0.4%, respectively. Concomitant medication use was generally similar between the groups (Table 1). After ablation, the median time to dronedarone treatment was 20 days, and the median time to sotalol treatment was 25 days.

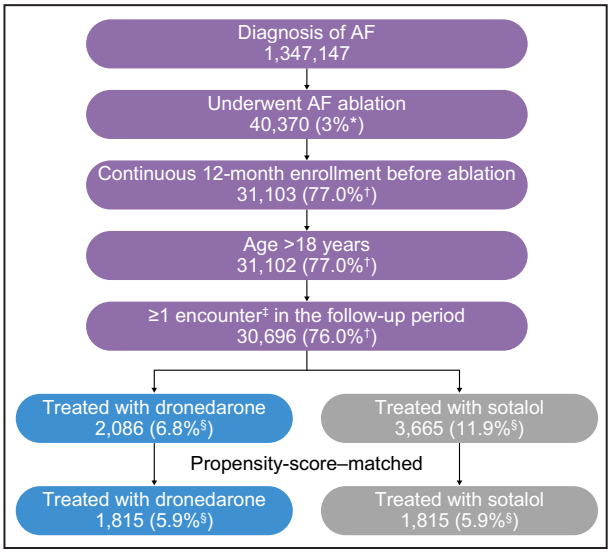

Figure 1. Attrition chart.
*Percentage of patients with AF. †Percentage of patients with index AF ablation. ‡An encounter could be an office visit, an outpatient visit, or hospitalization. §Percentage of patients undergoing ablation meeting inclusion criteria. AF indicates atrial fibrillation.

Cardiovascular Hospitalization

Patients treated with dronedarone after AF ablation had lower rates of cardiovascular hospitalizations throughout the 1 year of follow-up. Unadjusted incidence rates per 100 patient-years for cardiovascular hospitalization for dronedarone and sotalol were 31.6% and 40.9% at 3 months (P=0.03), 22.9% and 29.8% at 6 months (P=0.009), and 17.6% and 22.3% at 12 months (P=0.005), respectively (Table S1). The lower incidence rates at longer follow-up periods indicate a higher frequency of events within the first 3 months after ablation. Although the greatest divergence of the curves occurred in the first month after ablation, unadjusted incidence rates remained significantly different at 6 and 12 months (Figure 2, Table S1). Adjusted hazard ratios (aHRs) and 95% CIs for dronedarone versus sotalol at 3-, 6-, and 12-months follow-up were 0.77 (95% CI, 0.61–0.97), 0.76 (95% CI, 0.63–0.93), and 0.79 (95% CI, 0.66–0.93), respectively (Table 2).

Rates of cardiovascular hospitalization for ATAs were significantly lower among dronedarone-treated patients compared with sotalol-treated patients (Figure 3). Unadjusted incidence rates for dronedarone and sotalol were 27.0% and 38.3% at 3 months (P=0.005), 19.4% and 27.3% at 6 months (P=0.001), and 14.8% and 19.9% at 12 months (P=0.001), respectively (Table S1). These differences remained significant after adjustment through Cox proportional hazard modeling (Table 2). The aHRs for ATA-related hospitalization for dronedarone and sotalol were 0.70 (95% CI, 0.55–0.90), 0.71 (95% CI, 0.58–0.88), and 0.75 (95% CI, 0.63–0.90) at 3, 6, and 12 months, respectively (Table 2). There were no statistically significant differences in rates of hospitalization for myocardial infarction, heart failure, or ischemic stroke or transient ischemic attack (Tables 2 and Table S1, Figures S1 through S3). Despite the significantly lower rates for

Table 1. Baseline Characteristics From the Time Period 1 Year Before Index Ablation Among the Unmatched and Matched Dronedarone- and Sotalol-Treated Patients

	Before matching				After matching				Standardized mean difference
	Dronedarone		Sotalol		Dronedarone		Sotalol		
	N	%	N	%	N	%	N	%	
N	2086		3665		1815		1815		…
Demographics									
Age, y									
Mean (SD)	62.94	(9.67)	62.69	(9.84)	63.08	(9.63)	62.48	(9.92)	0.0063
Median (range)	63	(20–95)	62	(19–95)	63	(20–95)	62	(19–92)	…
Sex									
Women	671	32.2	1166	31.8	599	33.0	597	32.9	0.0023
Men	1415	67.8	2499	68.2	1216	67.0	1218	67.1	0.0023
Baseline patient comorbidities									
Chronic heart disease	839	40.2	1547	42.2	757	41.7	708	39.0	0.0550
Diabetes	406	19.5	890	24.3	362	19.9	389	21.4	0.0367
Heart failure	289	13.9	690	18.8	272	15.0	283	15.6	0.0168
Hypertension	1471	70.5	2803	76.5	1292	71.2	1329	73.2	0.0455
Ischemic stroke	66	3.2	124	3.4	64	3.5	62	3.4	0.0060
Myocardial infarction	121	5.8	266	7.3	110	6.1	101	5.6	0.0212
Chronic kidney disease	223	10.7	414	11.3	199	11.0	172	9.5	0.0491
CHA_2DS_2-VASc score, mean (SD)	2.20	(1.50)	2.34	(1.53)	2.26	(1.50)	2.24	(1.52)	0.0088
Charlson Comorbidity Index, mean (SD)	0.90	(1.41)	1.08	(1.51)	0.94	(1.44)	0.94	(1.44)	0.0000
Baseline procedures and health care use									
At least 1 ECG	2036	97.6	3584	97.8	1776	97.9	1768	97.4	0.0031
At least 1 cardioversion	897	43.0	1765	48.2	809	44.6	829	45.7	0.0221
At least 1 cardioversion in 6 mo before index	729	34.9	1408	38.4	652	35.9	671	37.0	0.0218
At least 1 AF-related hospitalization	590	28.3	1,299	35.4	533	29.4	608	33.5	0.0891
Pacemaker	48	2.3	127	3.5	44	2.4	63	3.5	0.0619
Implanted cardioverter defibrillator	2	0.1	11	0.3	2	0.1	7	0.4	0.0554
Baseline concomitant medications									
Direct-acting oral anticoagulants	1340	64.2	2211	60.3	1203	66.3	1142	62.9	0.0703
Warfarin	605	29.0	1204	32.9	544	30.0	562	31.0	0.0215
Digoxin	277	13.3	539	14.7	249	13.7	257	14.2	0.0127
β-Blockers	1513	72.5	3302	90.1	1512	83.3	1512	83.3	0.0000
Calcium channel blockers	804	38.5	1373	37.5	685	37.7	690	38.0	0.0057
Any AAD	1634	78.3	3128	85.3	1442	79.4	1547	85.2	0.1522

AAD indicates antiarrhythmic drug; AF, atrial fibrillation.

ATA-related hospitalizations, rates of cardioversion were not significantly different between treatment arms (Table 2, Table S1, Figure 3, Figure S4). There was a trend toward lower rates of repeat AF ablation with dronedarone compared with sotalol at the 12-month follow-up only (Table S1, Figure 4). Unadjusted incidence rates of repeat AF ablation at 12 months for dronedarone and sotalol were 21.8% and 25.5% (P=0.04), respectively (Table S1). The aHR at 12 months was 0.86 (95% CI, 0.74–1.01; Table 2).

In regard to the sensitivity analysis that incorporated a 3-month recovery/blanking phase (Table S2), the aHR for cardiovascular hospitalization was statistically significant at 12 months (aHR, 0.79 [95% CI, 0.63–0.99]) but not at 6 months (aHR, 0.79 [95% CI, 0.56–1.11]). The aHR for the component ATA hospitalization at 6 months was 0.75 (95% CI, 0.52–1.08) and at 12 months was 0.76 (95% CI, 0.60–0.98). The aHRs for the remaining end points were not statistically significant in this sensitivity analysis.

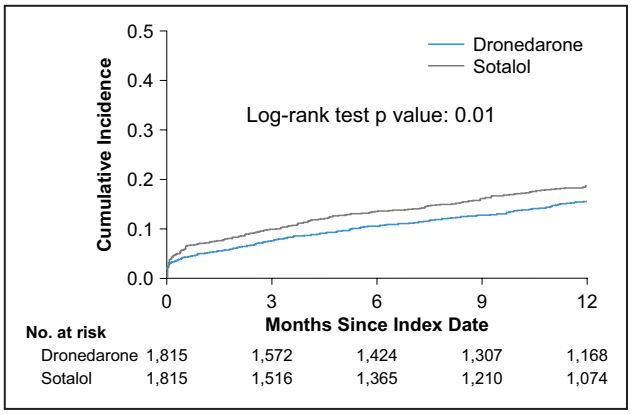

Figure 2. Cumulative incidence of cardiovascular hospitalization after index ablation procedure.

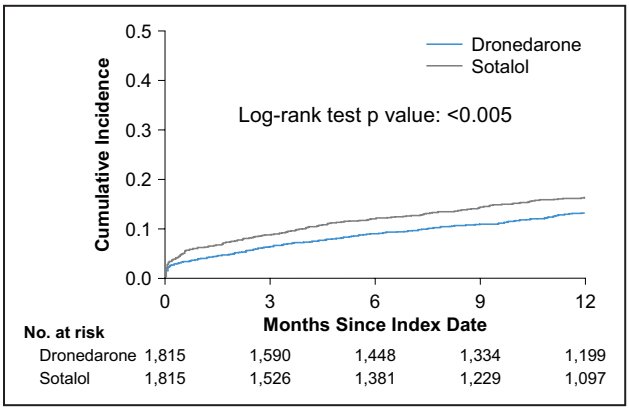

Figure 3. Cumulative incidence of atrial tachyarrhythmia hospitalization after index ablation procedure.

Proarrhythmia

There was a significantly lower risk of the proarrhythmia composite end point, which included both ventricular tachyarrhythmias and bradyarrhythmias, in patients treated with dronedarone compared with sotalol (Table 2 and Figure 5). The unadjusted rates of the proarrhythmia composite end point with dronedarone and sotalol were 63.2% and 83.0% at 3 months (*P*=0.001), 47.0% and 57.9% at 6 months (*P*=0.004), and 32.5% and 39.4% at 12 months (*P*=0.004), respectively. The aHRs were 0.76 (95% CI, 0.64–0.90), 0.80 (95% CI, 0.70–0.93), and 0.83 (95% CI, 0.73–0.94) at 3, 6, and 12 months, respectively. The aHRs from the

Table 2. Adjusted Cox Proportional Hazard Modeling Results for the Comparison of Propensity Score–Matched Patients Prescribed Dronedarone After AF Ablation Relative to Patients Prescribed Sotalol After AF Ablation

	3 months		6 months		12 months	
	aHR (95% CI)	*P* Value	aHR (95% CI)	*P* Value	aHR (95% CI)	*P* Value
Any cardiovascular hospitalization*	0.77 (0.61–0.97)	0.03	0.76 (0.63–0.93)	0.01	0.79 (0.66–0.93)	0.01
MI hospitalization†	0.32 (0.03–3.10)	0.33	0.48 (0.09–2.61)	0.4	1.09 (0.37–3.25)	0.87
Heart failure hospitalization‡	1.46 (0.79–2.72)	0.23	1.25 (0.74–2.10)	0.41	1.00 (0.66–1.52)	1
Stroke hospitalization§	0.61 (0.10–3.63)	0.58	0.71 (0.16–3.19)	0.65	1.38 (0.39–4.90)	0.62
AF hospitalization‖	0.70 (0.55–0.90)	0.01	0.71 (0.58–0.88)	<0.005	0.75 (0.63–0.90)	<0.005
Repeat catheter ablation¶	0.82 (0.63–1.06)	0.14	0.89 (0.73–1.08)	0.24	0.86 (0.74–1.01)	0.06
Cardioversion#	1.13 (0.96–1.32)	0.15	1.03 (0.90–1.19)	0.67	1.05 (0.93–1.19)	0.42
Pacemaker insertion**	0.63 (0.31–1.27)	0.19	0.54 (0.31–0.91)	0.02	0.64 (0.41–0.99)	0.04
Proarrhythmia††	0.76 (0.64–0.90)	<0.005	0.80 (0.70–0.93)	<0.005	0.83 (0.73–0.94)	<0.005
Ventricular proarrhythmia‡‡	0.74 (0.55–0.99)	0.04	0.84 (0.66–1.06)	0.15	0.91 (0.74–1.13)	0.41
Bradycardia§§	0.84 (0.73–0.99)	0.03	0.82 (0.67–0.99)	0.04	0.84 (0.73–0.99)	0.03

AF indicates atrial fibrillation; aHR, adjusted hazard ratio; CCI, Charlson Comorbidity Index; and MI, myocardial infarction.

*Adjusted for CHA_2DS_2-VASc score, CCI score, ECG during baseline before ablation, digoxin use, rivaroxaban use, and calcium channel blocker use.

†Adjusted for age and history of MI.

‡Adjusted for heart failure status, loop diuretic use, and history of MI.

§Adjusted for rivaroxaban use.

‖Adjusted for sex, ECG during baseline before ablation, digoxin use, rivaroxaban use, and calcium channel blocker use.

¶Adjusted for age at index, cardioversion during baseline before ablation, diabetes status, and ECG during baseline before ablation.

#Adjusted for ECG during baseline before ablation, cardioversion during baseline before ablation, β-blocker use, and heart failure status.

**Adjusted for age at index, β-blocker use, and CCI score.

††Adjusted for age at index, CCI score, preexisting implanted cardioverter defibrillator, preexisting pacemaker, chronic heart disease status, heart failure status, hypertension status, CHA_2DS_2-VASc score, rivaroxaban use, and antiplatelet therapy (P2Y12i) use.

‡‡Adjusted for ECG during baseline before ablation, heart failure status, hypertension status, chronic heart disease status, history of MI, antiplatelet therapy (P2Y12i) use, and apixaban use.

§§Adjusted for age at index, rivaroxaban use, CHA_2DS_2-VASc score, preexisting pacemaker, CCI, and chronic heart disease status.

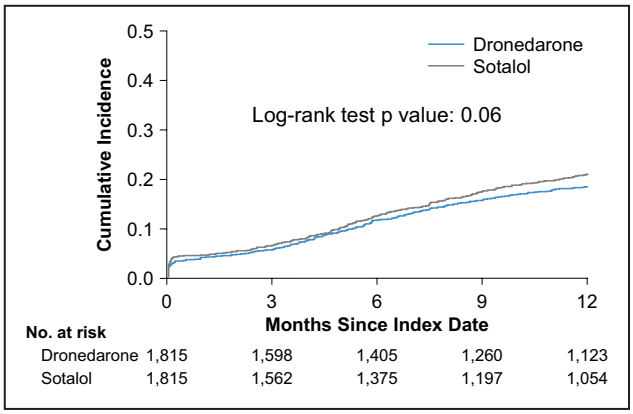

Figure 4. Cumulative incidence of repeat ablation after index ablation procedure.

recovery period sensitivity analysis were 0.89 (95% CI, 0.73–1.07) at 6 months and 0.90 (95% CI, 0.77–1.04) at 12 months (Table S2).

Rates of ventricular proarrhythmia were significantly lower with dronedarone at 3 months of follow-up only (Figure S5). Unadjusted ventricular proarrhythmia rates were 18.9% and 25.7% (*P*=0.037) for dronedarone and sotalol at 3 months of follow-up, respectively (Table S1). The aHR for 3 months of follow-up was 0.74 (95% CI, 0.55–0.99). Differences in ventricular proarrhythmia between patients treated with dronedarone and sotalol were not significant at 6 and 12 months of follow-up (Table 2; Figure S5).

Bradyarrhythmic proarrhythmia was the dominant determinant of the increase in the proarrhythmia composite at 3, 6, and 12 months (Figure S6). Unadjusted incidence rates of bradyarrhythmic proarrhythmia with dronedarone and sotalol were 46.8% and 57.0% at 3 months (*P*=0.045), 33.9% and 39.8% at 6 months (*P*=0.06), and 22.6% and 27.0% at 12 months (*P*=0.02), respectively (Table S1). The aHRs were 0.84 (95% CI, 0.73–0.99), 0.82 (95% CI, 0.67–0.99), and 0.84 (95% CI, 0.73–0.99) at 3, 6, and 12 months of follow-up (Table 2; Figure S6).

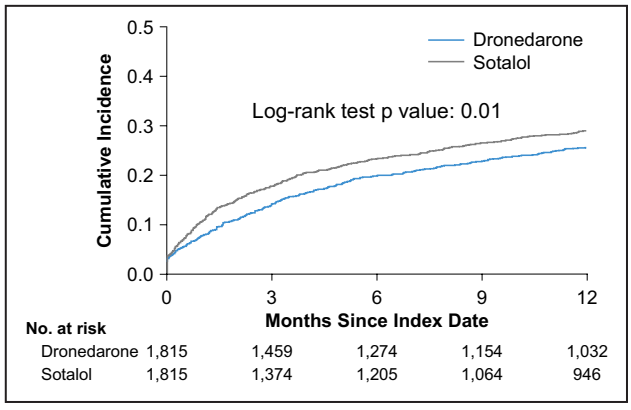

Figure 5. Cumulative incidence of proarrhythmia after index ablation procedure.

There were significantly higher rates of pacemaker implantation (a component of the bradyarrhythmic proarrhythmia composite end point) in patients treated with sotalol compared with dronedarone at 6 and 12 months of follow-up, but not at 3 months (Table S1, Figure S7). Unadjusted rates of pacemaker implantation for dronedarone and sotalol were 3.0% and 5.0% at 3 months (*P*=0.15), 2.5% and 5.0% at 6 months (*P*=0.009), and 2.2% and 3.7% at 12 months (*P*=0.019), respectively. The aHRs for pacemaker insertion at 3, 6, and 12 months were 0.63 (95% CI, 0.31–1.27), 0.54 (95% CI, 0.31–0.91), and 0.64 (95% CI, 0.41–0.99) (Table 2, Figure S7). A sensitivity analysis was performed censoring pacemaker insertion events for proarrhythmia outcomes. Results were similar to those without censoring (Table S3).

DISCUSSION

This comparison of propensity score–matched patients from nationwide US clinical practice suggests several major differences in safety- and effectiveness-related health outcomes among ablated patients with AF who were treated with dronedarone versus sotalol. First, compared with sotalol-treated patients, those treated with dronedarone had lower risk of cardiovascular hospitalization, including hospitalization for ATA. Second, dronedarone exhibited fewer safety events, with less proarrhythmia and pacemaker implantation after AF ablation when compared with sotalol. Finally, there was also a trend toward lower risk of repeat AF ablation at 1 year of follow-up in patients treated with dronedarone. This is the first study to demonstrate a difference in the effectiveness and safety of specific antiarrhythmic therapy other than amiodarone in the postablation setting.

Effectiveness

Patients treated with dronedarone had lower cumulative rates of cardiovascular hospitalizations throughout the 1 year of follow-up after ablation compared with patients treated with sotalol. This was driven primarily by lower rates of hospitalization for treatment of ATA. There was no difference in the rates of hospitalization for myocardial infarction, heart failure, or ischemic stroke or transient ischemic attack. The difference in ATA-related hospitalizations was greatest in the first 3 months after ablation, when there is typically a high burden of ATA because of ablation-induced myocardial injury, inflammation, and autonomic changes. Several studies have demonstrated that the use of an AAD in the recovery phase results in decreased ATA

recurrence and, in 2 studies, cardiovascular hospitalizations for ATA management.[3,26–29] Most of these studies included sotalol but not dronedarone. In the study by Noseworthy et al,[3] amiodarone was significantly better in reducing ATA-related hospitalization compared with other AADs, including dronedarone and sotalol, in the recovery phase. However, the study was underpowered to specifically compare dronedarone and sotalol.

This is the first specific comparative evaluation of dronedarone and sotalol in any US patient population. Both dronedarone and sotalol are more effective than placebo/control in patients with AF who have not undergone ablation, and their efficacies appear similar by indirect comparisons.[13,30] However, a randomized prospective trial comparing the 2 drugs has not been performed in nonablated patients with AF. Overall, dronedarone reduced cardiovascular hospitalizations, predominantly because of a reduction in ATA-related hospitalization, compared with placebo in the A Placebo-controlled, Double-Blind, Parallel Arm Trial to Assess the Efficacy of Dronedarone 400 mg Bid for the Prevention of Cardiovascular Hospitalization or Death from Any Cause in Patients with Atrial Fibrillation/Atrial Flutter (ATHENA) trial in older patients with risk factors.[18] In a post hoc analysis of patients with prior AF ablation in the ATHENA trial, dronedarone reduced the frequency of ATAs, but not cardiovascular hospitalizations, compared with placebo.[31] However, the time between drug randomization and prior ablation was not stated, and the number of patients in each group was relatively small. Our study extends the observation of lower rates of cardiovascular hospitalization with dronedarone compared with placebo in the ATHENA trial to the postablation setting compared with sotalol. Although the impact on total ATA burden of dronedarone compared with sotalol given after ablation cannot be assessed in our study, the decrease in hospitalization for ATA is consistent with this and with the post hoc analysis of the ATHENA patients with prior ablation. The greater relative efficacy with dronedarone compared with sotalol may explain the difference in ATA-related hospitalizations after ablation; however, other factors may be contributing. These include potentially better rate control and lesser symptoms during AF because of stronger antidromotropic effects and/or greater concomitant use of arterioventricular nodal blocking agents because of lesser concern about drug-induced bradycardia with dronedarone. Other factors include potentially more consistent dosing with dronedarone, and perhaps better conversion of persistent to paroxysmal episodes of ATA with dronedarone compared with sotalol in the postablation setting. The lack of difference in cardioversions between groups in our study is, however, contrary to this latter possibility.

After the recovery phase, dronedarone treatment was associated with lower 1-year rates of ATA-related hospitalization, relative to sotalol treatment. The rates of ATA-related hospitalization were the same between dronedarone and sotalol treatment groups 6 months after AF ablation. This is consistent with other studies evaluating AADs versus no therapy given during the recovery phase. In those studies, the rates of ATA recurrence were the same after the recovery phase at 6 and/or 12 months of follow-up[26,28,29,32] despite significant suppression of ATAs with AADs during the recovery phase. It has been hypothesized that suppression of ATAs in the recovery phase would suppress atrial remodeling by decreasing ATA burden and subsequently might decrease the risk of ATAs beyond the recovery phase. This consideration was not supported by previous studies or our results with ATA-related hospitalizations. There was a trend toward lower rates of repeat catheter ablation in dronedarone-treated patients at 1 year of follow-up in our study. In the prospective, randomized trial comparing AADs to no therapy in the recovery phase by Kaitani et al,[29] there was no difference in repeat ablation at 1 year of follow-up despite a significant reduction of ATA burden in the AAD-treated patients during the recovery phase. Thus, the trend seen in our study is probably attributable to other uncontrolled factors.

In the prospective, randomized controlled Pulmonary Vein Isolation With Vs. Without Continued Antiarrhythmic Drug Treatment in Subjects with Recurrent Atrial Fibrillation (POWDER AF) Trial,[9] continued use of AADs beyond the recovery phase resulted in less recurrent ATA, fewer unscheduled arrhythmia-related health care visits, and fewer repeat ablations after 1 year of follow-up compared with not using an AAD. Cardiovascular hospitalization rates were not stated. In that trial, 21%–28% of patients were treated with sotalol during the year after ablation, but dronedarone was not used. The relative efficacy of sotalol compared with class IC agents and amiodarone was not stated.

Safety

There was a higher risk of composite proarrhythmia with sotalol compared with dronedarone after AF ablation. This difference was driven predominantly by a higher risk of significant bradyarrhythmias and pacemaker implantation in patients treated with sotalol. This is consistent with the known bradycardic effects of sotalol.[15,21] There was a marginal increase in ventricular proarrhythmia at the 3-month follow-up, but no subsequent differences in ventricular proarrhythmia at 6 and 12 months. This slight trend in increased ventricular proarrhythmia may reflect the risk of long-QT interval development requiring drug discontinuation or

ventricular tachyarrhythmias in patients newly started on sotalol after ablation. Patients treated with sotalol or other QT-prolonging AADs before ablation or who continued on sotalol beyond the recovery phase were preselected for tolerance of the drug's ventricular proarrhythmia risks. A recent study of torsades de pointes risk suggests a higher risk among sotalol users, but a direct comparison to dronedarone was not reported.[33] A recent meta-analysis of AADs suggested an increase in mortality with sotalol compared with other AADs, including dronedarone.[13] Most of the sudden deaths within the trials included in that meta-analysis occurred within the first week of starting sotalol. Although this increase in mortality is presumed to be attributable to proarrhythmia, it cannot be determined if this is because of ventricular and/or bradyarrhythmias with sotalol. An increase in mortality was not seen with dronedarone in our study of postablation patients, in the ATHENA trial of predominantly nonablated patients, or in various meta-analyses.[13,18]

As mentioned, the dominant driving factor for the difference in the proarrhythmia composite at 3, 6, and 12 months was the increased risk of bradyarrhythmias with sotalol. The composite proarrhythmia curve diverged mostly during the recovery phase after ablation, probably attributable to the higher use of AADs within that phase. Of interest, the pacemaker insertion curves for dronedarone and sotalol diverged continuously during the follow-up period out to 1 year, becoming significant only at 6 and 12 months of follow-up. The higher incidence of significant bradycardia and pacemaker implantation in the recovery phase with sotalol compared with dronedarone in our study raises concern that acute changes after ablation may alter the safety profile of a drug. Antral or wide circumferential ablations of the pulmonary veins cause autonomic dysfunction, resulting in higher resting and exercise heart rates in the first few months after ablation.[34] This may provide some protection from the bradycardic effects of sotalol in the recovery phase after ablation. Once this attenuates, the bradycardic effects of sotalol may become more pronounced to necessitate pacemaker implantation. However, other confounding factors such as a higher incidence of sinus node dysfunction after superior vena cava isolation or ablation of foci along the superior crista terminalis cannot be excluded. Direct injury during the ablation procedure, however, would be expected to increase the need for pacemaker implantation shortly after the ablation procedure during the recovery phase.

Several studies have demonstrated an increased risk of significant bradycardia with sotalol compared with placebo or other AADs in the setting of prevention of AF after cardiac surgery. In the meta-analysis by Somberg and Molnar,[35] there was a roughly 2.5-fold increase in significant bradycardia with sotalol compared with amiodarone for prevention of postoperative AF. In a randomized placebo-controlled trial comparing sotalol, amiodarone plus metoprolol, metoprolol, and placebo for prevention of AF after cardiac surgery, sotalol had similar efficacy to amiodarone plus metoprolol (both better than placebo) for suppression of AF, but had a 3-fold higher risk of bradycardia requiring dose reduction and/or withdrawal compared with amiodarone plus metoprolol and placebo, and similar to metoprolol only.[36] Whether this represents a significantly higher bradycardic risk compared with the nonpostoperative setting cannot be determined. Rates of discontinuation for bradycardia were similar between amiodarone and propafenone or sotalol in the Canadian Trial of Atrial Fibrillation,[37] but the difference between propafenone and sotalol was not stated. The increase in patients in need of pacemaker implantation late after AF ablation in our sotalol cohort suggests that patients treated with sotalol after ablation may need to be monitored more closely for development of significant bradyarrhythmias.

Limitations

There are several limitations to our study. The type or duration of AF, the progression pattern of AF, and the type of AF ablation cannot be determined from the database, which possibly affected propensity score–matching balance. Although ATA-related hospitalizations may be a good surrogate marker for AF burden, true burden requires consistent and frequent cardiac rhythm monitoring, which is not available from these real-world data. We cannot exclude the possibility of misclassification bias because of the use of a 1-year baseline period to capture patient medical histories, including full history of AF management. A longer medical history would provide further details about previous procedures, diseases, and disorders, and some patients might have had previous episodes of bradyarrhythmia or conduction disorders years earlier that were not captured, but would have lowered sample size and statistical power. Administrative claims have limited resolution with respect to disease severity among other relevant clinical attributes (eg, degree of renal dysfunction, left atrial size or volume, symptoms). Patients who receive an antiarrhythmic drug are more likely have different characteristics, including being symptomatic, than patients who do not receive an antiarrhythmic drug, which limited our ability to use a referent of patients not treated with an antiarrhythmic drug. The analysis methodology modeled patients longitudinally based on initial study group assignment (ie, initial drug use) preserved the balance between the dronedarone and sotalol groups created by the propensity-score–matching process (minimizing type I error and increasing generalizability) but restricted

the ability to evaluate patients while solely on their assigned treatment (potentially elevating type II error[38]). Emphasis was put on propensity-score matching to mitigate indication/channeling bias.[39]

Dronedarone was compared with sotalol because patients with atrial fibrillation who had similar characteristics received these medications in the United States during the study period. This is likely a reflection of Heart Rhythm Society and European Society of Cardiology guideline recommendations that were operative at the time of the study periods and where dronedarone and sotalol are recommended for similar patient types.

Further research is warranted on the treatment effects between dronedarone and sotalol adjunctive to ablation, including results on mortality. Moreover, further research on ablation type, other antiarrhythmic drugs, and persistence of use may provide more information on treatment choices for a wider array of clinical considerations.

CONCLUSIONS

Patients treated with dronedarone after AF ablation had lower risk of cardiovascular hospitalization compared with patients treated with sotalol, predominantly attributable to lower rates of ATA-related hospitalization. In addition, dronedarone-treated patients had a much better safety profile after ablation compared with sotalol patients because of lower rates of combined proarrhythmia, predominantly driven by lower rates of bradycardic proarrhythmia and need for pacemaker implantation. From our data, dronedarone appears to be a more effective and safer alternative after ablation than sotalol.

ARTICLE INFORMATION

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Supplemental Material

Tables S1–S3
Figures S1–S7
Data S1–S2

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SUPPLEMENTAL MATERIAL

Data S1. Comorbid Codes (see Excel file).

Data S2. HO Codes (see Excel file)

Table S1. Unadjusted Incidence Rates of Events After Index Ablation Procedure Among Patients Prescribed Dronedarone After AF Ablation Propensity-Score–Matched to Patients Prescribed Sotalol Following AF Ablation.

	Dronedarone				Sotalol				
	Patient-Time (years)	N	Rate (per 100 patient-years)	95% CI	Patient-Time (years)	N	Rate (per 100 patient-years)	95% CI	*P* Value
Total		1815				1815			
Incidence of cardiovascular hospitalizations									
Any cardiovascular hospitalization									
3 months	408	129	31.59	26.58–37.53	396	162	40.91	35.07–47.72	0.028
6 months	778	178	22.87	19.74–26.49	753	224	29.75	26.10–33.92	0.0086
12 months	1429	251	17.57	15.52–19.88	1359	303	22.29	19.92–24.95	0.0052
Myocardial infarction hospitalization									
3 months	430	1	0.23	0.03–1.65	425	3	0.71	0.23–2.19	0.31

	Dronedarone				Sotalol				
	Patient-Time (years)	**N**	**Rate (per 100 patient-years)**	**95% CI**	**Patient-Time (years)**	**N**	**Rate (per 100 patient-years)**	**95% CI**	***P* Value**
6 months	835	2	0.24	0.06–0.96	827	4	0.48	0.18–1.29	0.41
12 months	1575	7	0.44	0.21–0.93	1545	6	0.39	0.17–0.86	0.81
Heart failure hospitalization									
3 months	426	24	5.63	3.78–8.41	422	17	4.02	2.50–6.47	0.29
6 months	825	31	3.76	2.64–5.34	820	26	3.17	2.16–4.66	0.52
12 months	1550	43	2.77	2.06–3.74	1526	45	2.95	2.20–3.95	0.78
Stroke hospitalization									
3 months	430	2	0.47	0.12–1.86	425	3	0.71	0.23–2.19	0.64
6 months	835	3	0.36	0.12–1.11	827	4	0.48	0.18–1.29	0.70
12 months	1575	6	0.38	0.17–0.85	1547	4	0.26	0.10–0.69	0.55

	Dronedarone				Sotalol				
	Patient-Time (years)	**N**	**Rate (per 100 patient-years)**	**95% CI**	**Patient-Time (years)**	**N**	**Rate (per 100 patient-years)**	**95% CI**	***P* Value**
Atrial fibrillation hospitalization									
3 months	412	111	26.95	22.38–32.46	397	152	38.25	32.62–44.84	0.0048
6 months	787	153	19.43	16.59–22.77	758	207	27.31	23.83–31.30	0.0013
12 months	1451	215	14.81	12.96–16.93	1373	273	19.88	17.66–22.38	0.0012
Follow-up procedures									
Incidence of repeat catheter ablation									
3 months	412	101	24.51	20.17–29.79	403	123	30.52	25.58–36.42	0.10
6 months	784	200	25.52	22.22–29.31	767	222	28.94	25.38–33.01	0.20
12 months	1410	307	21.77	19.47–24.35	1364	348	25.52	22.98–28.35	0.042
Incidence of cardioversion									

	Dronedarone				Sotalol				
	Patient-Time (years)	**N**	**Rate (per 100 patient-years)**	**95% CI**	**Patient-Time (years)**	**N**	**Rate (per 100 patient-years)**	**95% CI**	***P* Value**
3 months	372	359	96.57	87.08–107.09	370	340	91.94	82.67–102.25	0.52
6 months	684	452	66.04	60.22–72.41	681	460	67.58	61.68–74.05	0.73
12 months	1206	582	48.26	44.50–52.35	1180	583	49.39	45.54–53.56	0.69
Incidence of pacemaker insertion									
3 months	429	13	3.03	1.76–5.22	422	21	4.98	3.25–7.64	0.15
6 months	831	21	2.53	1.65–3.88	817	41	5.02	3.69–6.81	0.0091
12 months	1562	35	2.24	1.61–3.12	1,516	56	3.69	2.84–4.80	0.019
Proarrhythmia									
Incidence of proarrhythmia									
3 months	391	247	63.2	55.79–71.60	373	309	82.95	74.20–92.73	0.0014

	Dronedarone				Sotalol				
	Patient-Time (years)	**N**	**Rate (per 100 patient-years)**	**95% CI**	**Patient-Time (years)**	**N**	**Rate (per 100 patient-years)**	**95% CI**	***P* Value**
6 months	727	341	46.93	42.20–52.18	691	400	57.93	52.52–63.89	0.0042
12 months	1304	423	32.45	29.50–35.69	1224	482	39.37	36.00–43.04	0.0037
Incidence of ventricular proarrhythmia									
3 months	418	79	18.89	15.15–23.55	408	105	25.73	21.25–31.15	0.037
6 months	801	121	15.11	12.64–18.05	782	141	18.04	15.29–21.27	0.15
12 months	1481	166	11.21	9.63–13.05	1438	176	12.24	10.56–14.19	0.42
Incidence of bradycardia									
3 months	400	187	46.76	40.51–53.96	388	221	57.02	49.98–65.06	0.045
6 months	752	255	33.9	29.99–38.33	729	290	39.76	35.44–44.61	0.063
12 months	1371	310	22.62	20.24–25.28	1310	353	26.95	24.28–29.91	0.0243

	Dronedarone				Sotalol				
	Patient-Time (years)	**N**	**Rate (per 100 patient-years)**	**95% CI**	**Patient-Time (years)**	**N**	**Rate (per 100 patient-years)**	**95% CI**	***P* Value**
CI indicates confidence interval.									

Table S2. Adjusted hazard ratios of sensitivity analysis with inclusion of 3-month recovery/blanking period wherein events during this period did not contribute to 6-month or 12-month results and patients with events during this period were not censored

	6 Months		12 Months	
	HR (95% CI)	***P* Value**	**HR (95% CI)**	***P* Value**
Any CV hospitalization*	0.79 (0.56–1.11)	0.17	0.79 (0.63–0.99)	0.04
MI hospitalization†	N/A	N/A	1.84 (0.45–7.39)	0.39
Heart failure hospitalization‡	1.06 (0.44–2.56)	0.89	0.75 (0.44–1.30)	0.31
Stroke hospitalization§	0.99 (0.06–15.80)	1	3.90 (0.44–35.16)	0.22
AF hospitalization‖	0.75 (0.52–1.08)	0.12	0.76 (0.60–0.98)	0.03
Repeat catheter ablation#	0.91 (0.70–1.19)	0.5	0.88 (0.73–1.05)	0.17
Cardioversion**	1.03 (0.87–1.23)	0.72	1.04 (0.90–1.20)	0.61
Pacemaker insertion††	0.50 (0.23–1.12)	0.09	0.69 (0.40–1.20)	0.19
Proarrhythmia‡‡	0.89 (0.73–1.07)	0.23	0.90 (0.77–1.04)	0.17
Ventricular proarrhythmia§§	0.88 (0.63–1.23)	0.46	0.90 (0.69–1.15)	0.39
Bradycardia‖‖	0.93 (0.74–1.16)	0.52	0.92 (0.77–1.11)	0.38

* Adjusted for loop diuretic use, ECG, CHA_2DS_2-VASc score, and CCI score
† Adjusted for CCI score, antiplatelet therapy, and warfarin use
‡ Adjusted for loop diuretic use, heart failure, and CHA_2DS_2-VASc score
§ No adjustments
‖ Adjusted for ECG, male sex, pacemaker insertion, CCI score, and rivaroxaban use
#Adjusted for age at index, ECG, cardioversion, pacemaker insertion, and ischemic stroke
** Adjusted for ECG, CCI score, age at index, VTE, and beta blocker use
††Adjusted for CHA_2DS_2-VASc score, antiplatelet therapy, and calcium channel blocker use
‡‡Adjusted for CHA_2DS_2-VASc score, hypertension, age at index, CCI score, chronic heart disease, defibrillator, rivaroxaban use, and male sex
Adjusted for heart failure, chronic heart disease, hypertension, male sex, ECG, MI, and beta §§ blocker use
‖‖Adjusted for age at index, CHA_2DS_2-VASc score, rivaroxaban use, chronic heart disease, hypertension, and CCI score

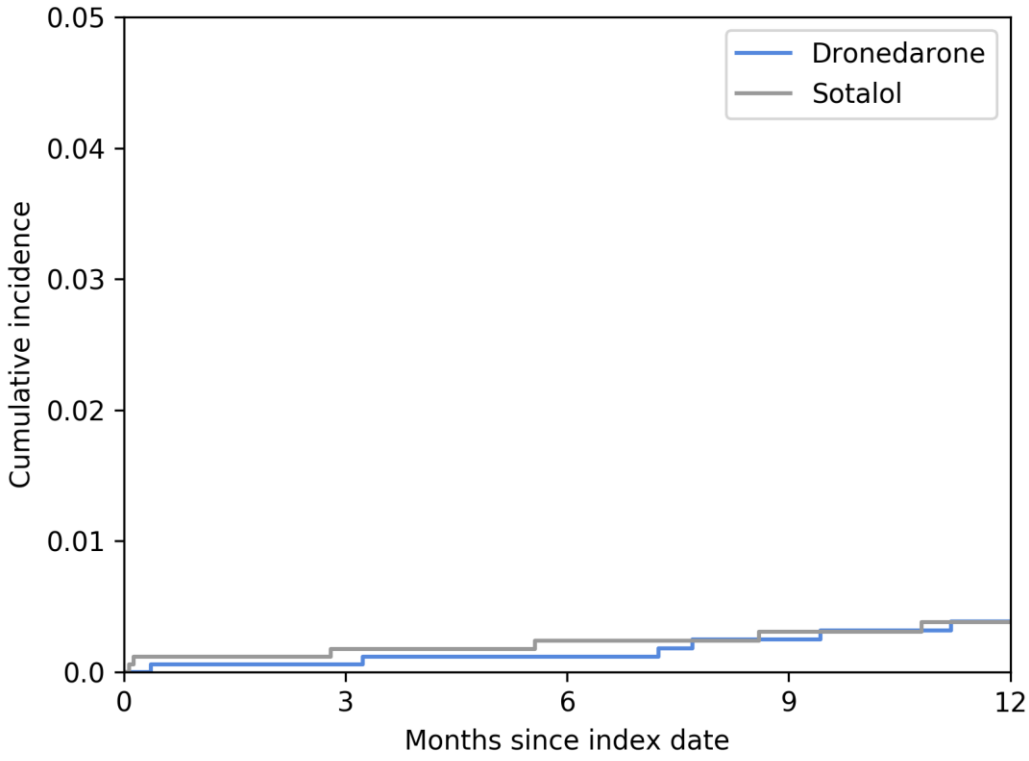
AF indicates atrial fibrillation; CCI, Charlson comorbidity index; CI, confidence interval; CV, cardiovascular; ECG, electrocardiogram; MI, myocardial infarction; N/A, not available due to insufficient number of events; VTE, venous thromboembolism.

TABLE S3. Adjusted hazard ratio for proarrhythmia censoring pacemaker insertion events						
	3 Months		6 Months		12 Months	
	aHR (95% CI)	*P* Value	aHR (95% CI)	*P* Value	aHR (95% CI)	*P* Value
Proarrhythmia*	0.76 (0.64–0.90)	<0.005	0.80 (0.70–0.93)	<0.005	0.83 (0.73–0.94)	<0.005
Bradycardia†	0.82 (0.67–0.99)	0.04	0.82 (0.67–0.99)	0.04	0.84 (0.73–0.99)	0.03

*Adjusted for age at index, CCI score, defibrillator procedure, chronic heart disease, rivaroxaban use, hypertension, CHA_2DS_2-VASc score, pacemaker procedure, and antiplatelet therapy (P2Y12i). †Adjusted for age at index, rivaroxaban use, CHA_2DS_2-VASc score, pacemaker procedure, CCI score, chronic heart disease.

aHR indicates adjusted hazard ratio; CCI, Charlson Comorbidity Index; and CI, confidence interval.

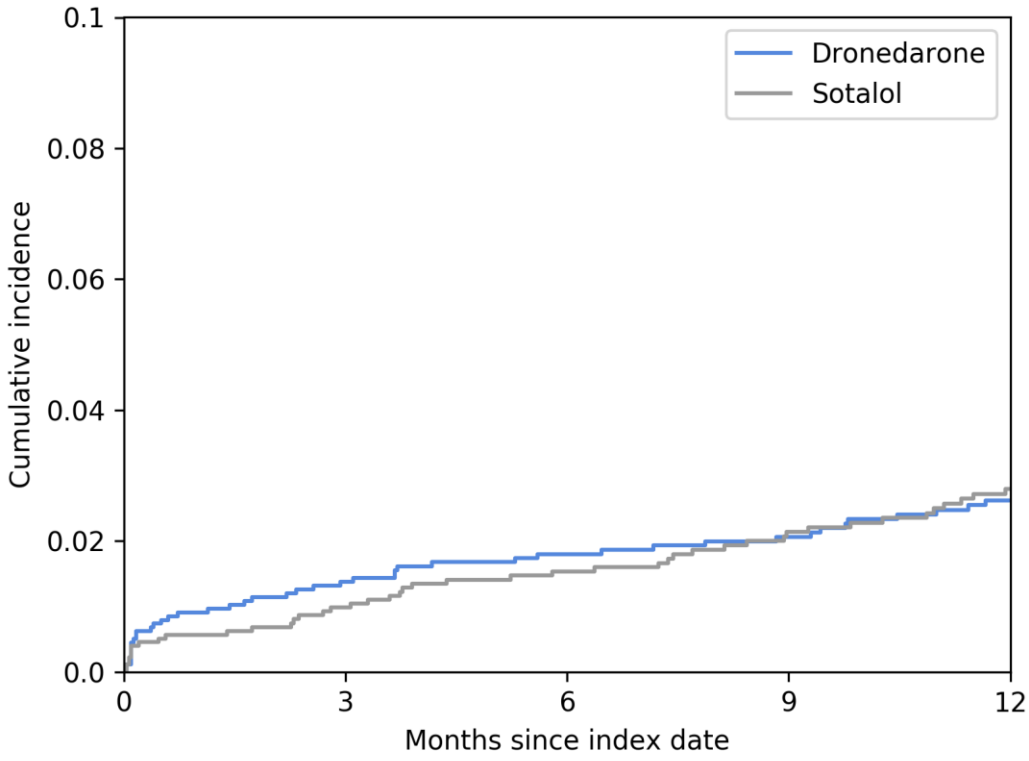
Figure S1. Cumulative incidence of myocardial infarction hospitalization after index ablation procedure.



At risk					
Dronedarone	1815	1691	1581	1486	1364
Sotalol	1815	1669	1563	1438	1316

Log rank test *P* value: 0.81

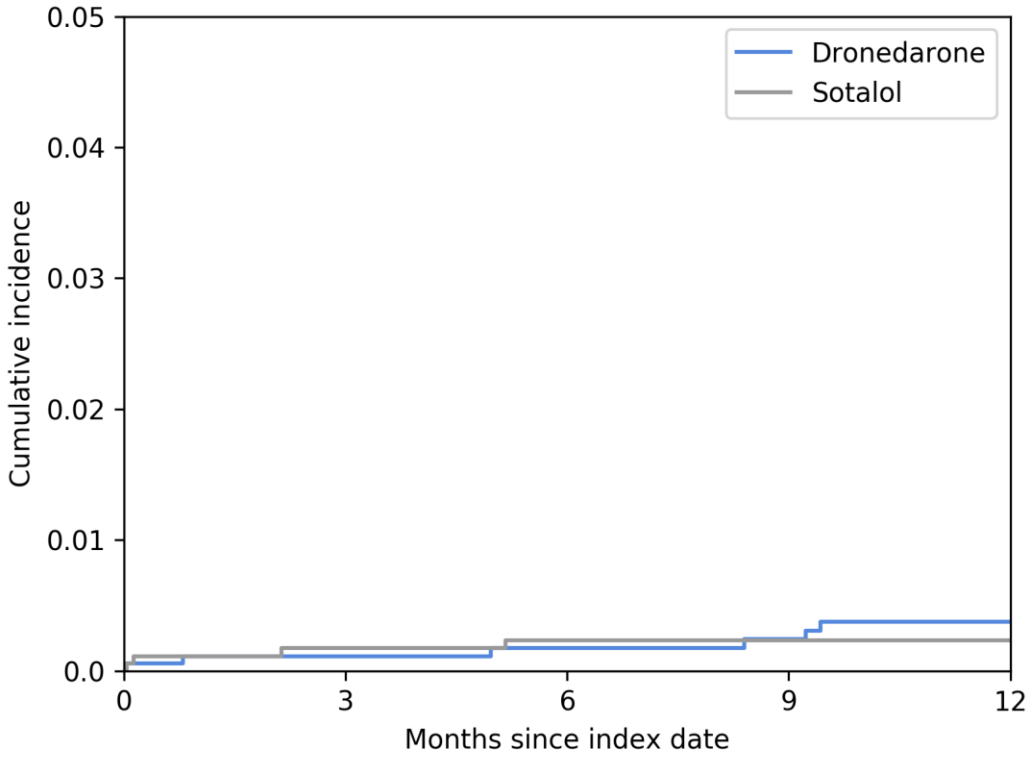
Figure S2. Cumulative incidence of heart failure hospitalization after index ablation procedure.



At risk					
Dronedarone	1815	1668	1553	1458	1332
Sotalol	1815	1656	1544	1412	1283

Log rank test *P* value: 0.78

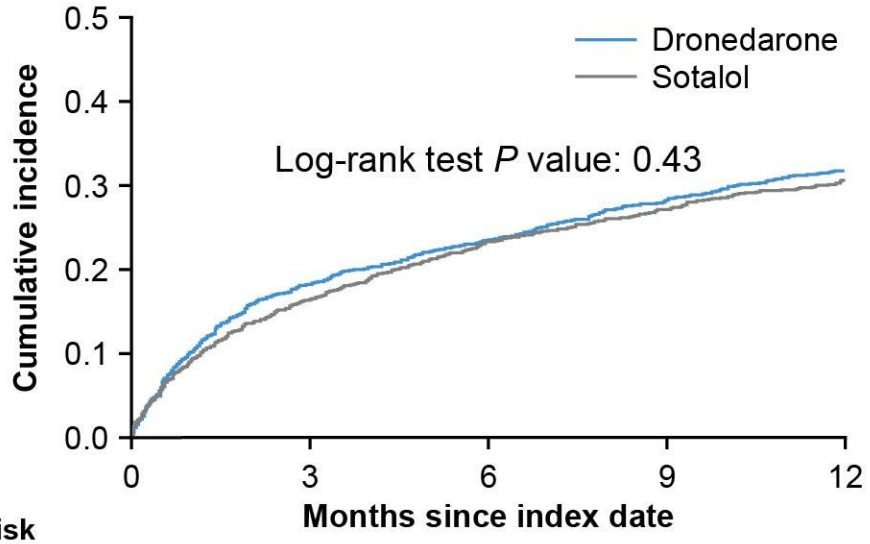
Figure S3. Cumulative incidence of stroke hospitalization after index ablation procedure.



At risk					
Dronedarone	1815	1690	1580	1486	1365
Sotalol	1815	1669	1564	1441	1319

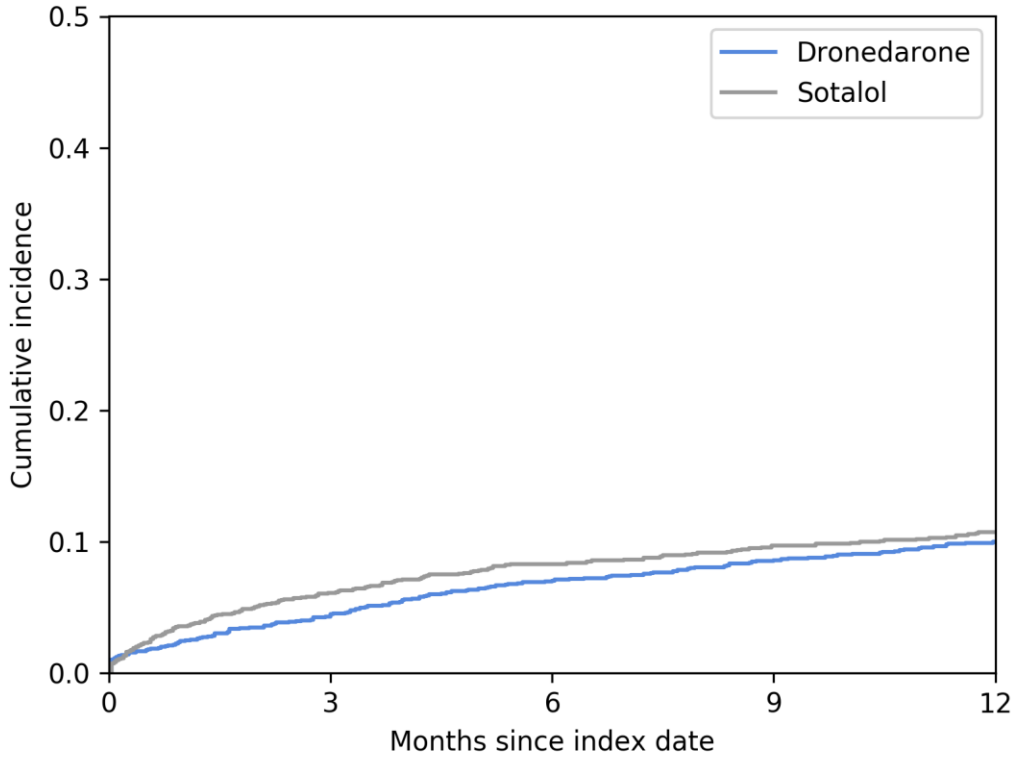
Log rank test *P* value: 0.54

Figure S4. Cumulative incidence of cardioversion after index ablation procedure.



No. at risk					
Dronedarone	1815	1382	1223	1083	953
Sotalol	1815	1395	1207	1054	919

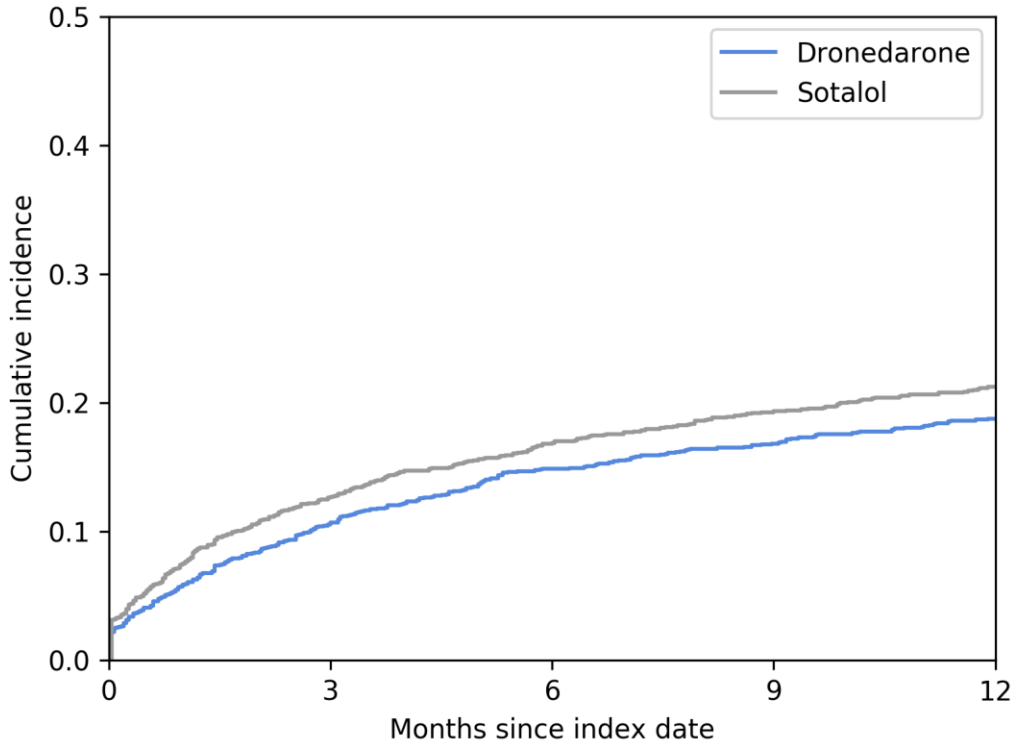
Figure S5. Cumulative incidence of ventricular proarrhythmia after index ablation procedure.



At risk					
Dronedarone	1815	1623	1476	1364	1237
Sotalol	1815	1571	1441	1310	1188

Log rank test *P* value: 0.45

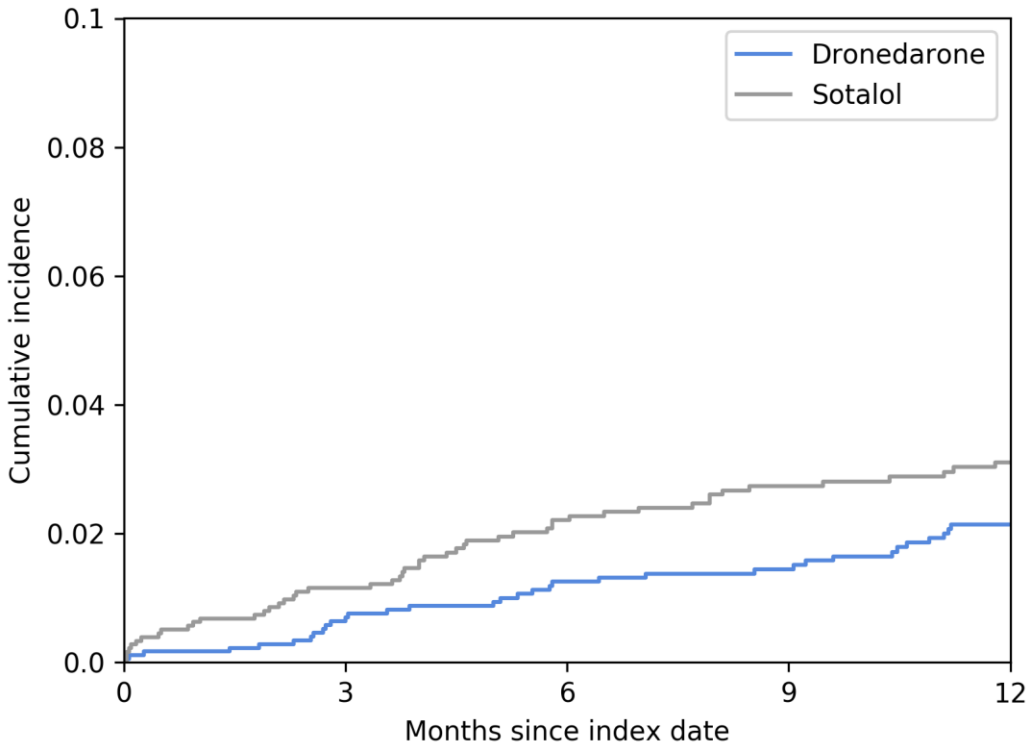
Figure S6. Cumulative incidence of bradycardia after index ablation procedure.



At risk					
Dronedarone	1815	1510	1348	1239	1121
Sotalol	1815	1460	1301	1160	1040

Log rank test *P* value: 0.05

Figure S7. Cumulative incidence of pacemaker insertion after index ablation procedure.



At risk					
Dronedarone	1815	1681	1563	1468	1343
Sotalol	1815	1652	1531	1399	1278

Log rank test *P* value: 0.05