Supplementary Material

Catheter Ablation or Medical Therapy to Delay Progression of Atrial Fibrillation: The Randomised Controlled Atrial Fibrillation Progression Trial (ATTEST)

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2. Definitions

Symptomatic AF	Symptom(s) exhibited by the patient, which made him/her seek medical attention, and was concurrent with a documented episode (ie, by implantable loop recorder, electrocardiogram, transtelephonic monitoring, Holter monitor, or telemetry recording). Symptoms could include, but were not limited to, the following: palpitations, irregular pulse (eg, rapid, racing, pounding, fluttering, bradycardia), dizziness, weakness, chest discomfort, and breathlessness.
Paroxysmal AF	Recurrent AF that terminated spontaneously within 7 days.
Persistent AF/AT	AF/AT that was sustained beyond 7 days or lasted more than 48 hours and less than 7 days but necessitating pharmacological or electrical cardioversion.
Persistent AF/AT	Continuous AF/AT that was sustained beyond 7 days (HRS 2017 consensus statement)
Long-standing persistent AF/AT	Continuous AF of greater than 1-year duration
AF episode	An episode of AF lasting >30 s. AF and atrial flutter (including atypical flutter) were considered episodes of AF. Atrial flutter alone was not considered an episode of AF.
Complete pulmonary vein isolation	Entrance block confirmed with or without the use of a focal catheter
Procedure time	Time from introduction of first catheter to withdrawal of last catheter (minutes)

AF, atrial fibrillation; AT, atrial tachycardia

3. Supplementary Methods

Interventions

Planned follow-up included visits to study sites at 3 and 6 months and 1, 2, and 3 years; standard-of-care electrocardiograms occurred at 3 and 6 months and at 1-, 2-, and 3-year visits. Weekly monitoring using transtelephonic monitoring (TTM) was initiated at 3 months, and monthly TTM monitoring was used after 9 months until the 3-year visit. In addition, TTM was used whenever subjects experienced arrhythmic symptoms. Once AF/AT was identified, daily TTM was initiated for 7 consecutive days.

Telephone follow-up was conducted at 9, 18, and 30 months. All patients were followed for 3 years for adverse event (AE) reporting. Patients who crossed over from the AAD group to receive RF ablation were followed according to their original schedule. Due to budget constraints following slow enrolment, the trial was terminated prematurely by the sponsor in early February 2018 after the second planned interim analysis; termination was independent of study outcomes.

Outcomes measured

Safety endpoints included reports of any catheter-related or drug-related AEs. Primary AEs were defined as the following events that occurred within 7 days of the ablation procedure: death, myocardial infarction, pulmonary vein stenosis, diaphragmatic paralysis, atrio-oesophageal fistula, transient ischaemic attack, stroke/cerebrovascular accident, thromboembolism, bleeding/haematoma requiring blood transfusion, pericarditis, cardiac tamponade, pericardial effusion, pneumothorax, cardiac perforation, vascular access complications, pulmonary oedema, hospitalisation, and heart block.

Statistical analysis

Sensitivity analyses of the primary endpoint were performed on the per-protocol (PP) population (all patients who underwent treatment according to randomisation and had no major protocol violations) as well as on the as-treated population (patients without major protocol violations grouped according to the actual treatment received; patients randomised to AAD who crossed over to ablation were counted as ablation-group patients). A further sensitivity analysis was performed on the ITT population using the 2017 expert consensus definition of persistent AF.[30]

We assumed the rates of disease progression at the end of follow-up to be 25% and 5% in the AAD and ablation groups, respectively. A total sample size of 161 patients per treatment group was required to ensure 85% power to detect the effect size, assuming a 50% crossover rate, a 10% dropout rate in each group over the 3-year follow-up period, and a 1.5-year accrual time. The trial was designed with interim analyses of the primary endpoint at multiple

time intervals during the course of the study to determine whether the study would be stopped for effectiveness or futility. The "α-spending function" approach was used, which accommodated unequally sized groups without having to determine time points and the number of interim analyses in advance.[31]

The number and percentage of patients with new AAD were tabulated, with no statistical testing. Baseline conditions that could potentially impact the time to AF/AT progression were analysed using Cox proportional hazards models. Safety data are presented as numbers and percentages of AEs. Procedure-related complications for crossover subjects were analysed and presented separately. All analyses were performed using SAS® software version 9.4.

Sample Size and Power Considerations

A total sample size of 322 patients (161 in each group) was required to ensure 85% power to detect the effect size measured by negative log of the hazard ratio equal to 1.1541 (catheter ablation group vs AAD group).

$$-\log_e\left(\frac{\bar{\lambda}_t}{\bar{\lambda}_c}\right) = -\log_e\left(\left(-\frac{\log_e(0.95)}{3}\right)/\left(-\frac{\log_e(0.85)}{3}\right)\right) = 1.1541$$

This calculation assumed a 50% crossover rate from the AAD group to the catheter ablation group, a 10% dropout rate in each group over the 3-year follow-up period, and a 1.5-year accrual time.

With a crossover rate of 50%, the estimated proportion of patients without persistent AF/AT was changed from 0.75 to 0.85 in the control group (0.85=0.5*0.75+0.5*0.95; the first part for subjects without crossover, the second part for subjects with crossover). This calculation was based upon 1-sided superiority testing with α=0.025. Using meta-analysis, the rates of disease progression at the end of follow-up were estimated to be 25% and 5% in the AAD and catheter ablation groups, respectively. The sample size calculation was based upon the method developed by Rubinstein et al.[32] and also incorporated group sequential design with multiple interim looks.

<u>Adaptive Sample Size Re-estimation</u>

Due to the uncertainties associated with the crossover rate and the effect size, the sample size was re-estimated at the time of the first interim analysis. Conditional power (CP) was calculated at that time to determine how promising the interim results were. The CP was defined as the conditional probability that the final result would exceed a critical value given the data observed thus far. The assumption was that the trend to be observed in the remainder of the study would follow the expectation used in the original sample size calculation.[33] If the CP was <0.3, then the study was considered not promising, and the sample size was not to be increased. If the CP was >0.9, then the study was deemed fully powered, and the sample size

was not to be increased. If the CP fell in the promising zone (0.3-0.9), the sample size was to be re-estimated based upon the observed effect size.

In detail, the following formula was applied to re-estimate the sample size:

$$M = N\left(\frac{\delta}{\Delta}\right)^2$$

where M is the updated sample size per group, N is the initially planned sample size per group, δ is the expected effect size (1.1541), and Δ is the effect size observed at the time of interim analysis:

$$\Delta = -log_e\left(\frac{D_t/T_t}{D_c/T_c}\right)$$

where D_t and D_c are the number of deaths observed in the test and control group, respectively, and T_t and T_c are the total times observed (up to the time of censoring) in the respective groups.

In case the re-estimated sample size was unrealistically high, the sponsor was to select one of the following 3 options:

1. Determine the maximum realistic sample size and continue the study to enrol the maximum number of subjects.
2. Continue study as planned to enrol original planned sample size.
3. Stop the study for futility.

In case the sample size increased, the Cui, Hung, and Wang (CHW) adaptive method was to be used for statistical testing.[34] The CHW weighting was to be applied according to the following formula:

$$Z = \sqrt{t_{adj}}Z_{0;adj} + \sqrt{(1 - t_{adj})}Z_{adj;max}$$

where Z is the final test statistic, t_{adj} is the (planned) information fraction at the time of sample size adjustment, $Z_{0;adj}$ is the test statistic derived from the data available at the time of sample size adjustment, and $Z_{adj;max}$ is the test statistic derived from data collected after the time of sample size adjustment, including a possibly increased sample.

4. Interim Analyses

The trial was designed with interim examinations of the primary endpoint at multiple time intervals during the course of the study to determine whether the study would be stopped for effectiveness or futility. A group sequential method similar to that proposed by O'Brien and Fleming was applied.[35] This method used the "α-spending function" approach developed by Lan and DeMets,[36] which is flexible to accommodate unequal sized groups and without having the time points and number of interim analyses fixed in advance. At the time point of each interim analysis, the operating characteristics were recalculated based upon the actual information fractions for the interim analyses already conducted and proportionally adjusted information fractions for all future interim analyses following methods described by Proschan, Lan, and Wittes.[37] Calendar time scales were used for the spending function. Number of events was used to estimate covariance. At the time point of each interim analysis, boundaries were re-estimated based on updated current calendar time estimate and actual number of events for all interim analyses up to the corresponding time point. The current calendar time estimate was updated based on the actual time point of current interim analysis but using the maximum duration estimated at the time point of first interim analysis; thus, previous estimates of calendar time would not change.

A first interim analysis was performed in 2016 and included 11 primary endpoints reported in the study. A second interim analysis was done in 2017, at time 15 primary endpoints were reported. For both interim analyses, stopping boundaries for effectiveness were not reached. The study was terminated early due to a business decision on February 2018, the last patient was included in the study on February 14, 2018. Remainder of α (what is left from the α spent by the 2 interim analyses=0.0231) was used for the final primary effectiveness analysis. The type-I error control of the study at 2.5% remains valid since the total α spent on the first 2 interim analyses and the final analysis was 2.5%. The final study database includes 17 subjects who reached their primary endpoint. The final analysis for primary effectiveness showed a significant 1-sided *P* value of 0.0009, substantially lower than the remaining α of 0.0231. The final Z-statistic of 3.12 is larger than the stopping bound of the first and second interim analysis. This suggests that, in the scenario of a third interim analysis, the study would have exceeded the threshold for success, and the study would have been terminated for early detection of primary effectiveness success.

5. Cross-over guidelines

Patients randomised to AAD could cross over to the RF ablation group if the patient had severe symptoms of AF in the absence of evidence that the patient was not taking the prescribed medication and consensus that further medication would be unsuccessful. In addition, patients could cross over if the patient experienced severe side effects or AF symptoms, there was evidence of adherence to the prescribed AAD regimen, and there were no other drug options to which to switch the patient. Cross over to the RF ablation group was avoided if there was evidence that the patient did not take the medications as prescribed and/or took concurrent incompatible medications for other chronic diseases. In this instance, the patient was provided with medication management and then returned to the hospital 3 weeks later for re-evaluation. If the patient still complained of the initial problem, a blood sample may have be drawn to measure for long-term drug metabolite as a good indicator of how well the patient was taking the prescribed medication. Cross over was also avoided if no blood tests were done for medication adherence but the evidence was not sufficiently strong to merit cross over in the minds of the Cross-over Committee members.

6. Supplementary Table S1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Age ≥60 years • Paroxysmal atrial fibrillation for at least 2 years with ≥2 episodes over the last 6 months • Failure of treatment with 1-2 antiarrhythmic or rate control drugs • HATCH score (Hypertension=1 point; Age >75 years=1 point; Transient ischaemic attack or stroke=2 points; Chronic obstructive pulmonary disease=1 point; Heart failure=2 points) of between 1 and 4 • Eligible for radiofrequency ablation or antiarrhythmic drugs • Left atrium diameter of ≤55 mm by transthoracic echocardiography • Left ventricular ejection fraction of ≥50% when in sinus rhythm or ≥35% when in atrial fibrillation	• Awaiting cardiac transplantation or other cardiac surgery • Acute ongoing illness, active systemic infection or sepsis • Reversible causes of atrial fibrillation, e.g., due to thyroid disorders, acute alcohol intoxication or recent major surgical procedures or trauma • Previous diagnosis of persistent/permanent atrial fibrillation or atrial tachycardia • Previous requirement for cardioversion >48 hours after the onset of atrial fibrillation/atrial tachycardia • Previous left atrial ablation or surgical procedures for atrial fibrillation • Prior atrioventricular nodal ablation • Recent cardiac events, e.g., myocardial infarction, percutaneous coronary intervention, or valve or coronary artery bypass surgery within the preceding 3 months • Decompensated heart failure • Class IV angina or class IV congestive heart failure • Hypertrophic obstructive cardiomyopathy • Mandated antiarrhythmic drug therapy for conditions other than atrial fibrillation • Heritable arrhythmias • Transient ischaemic attack or stroke within the year preceding trial enrolment • History of embolism or thrombosis • Contraindications to the study catheter(s) • Contraindications to warfarin or other anticoagulants, or antiplatelet agents

7. Supplementary Table S2. Previously Failed Cardiovascular Medication and Dose (ITT Population)

Previously Failed Therapeutic Strategies, n (%)	**RF ablation (n=128)**	**AAD (n=127)**	**Total (N=255)**
Any previously failed therapeutic strategy	128 (100%)	126 (99.2%)	254 (99.6%)
Propafenone*	38 (29.7%)	34 (26.8%)	72 (28.2%)
Dose, mean ± SD	438.2 ± 117.7	420.6 ± 94.4	429.9 ± 107.0
Flecainide*	16 (12.5%)	12 (9.4%)	28 (11.0%)
Dose, mean ± SD	178.3 ± 83.2	150.0 ± 52.2	166.2 ± 71.8
Cibenzoline*	0	0	0
Dose, mean ± SD			
Amiodarone†	22 (17.2%)	23 (18.1%)	45 (17.6%)
Dose, mean ± SD	354.7 ± 213.0	315.2 ± 170.2	334.5 ± 191.1
Sotalol†	31 (24.2%)	30 (23.6%)	61 (23.9%)
Dose, mean ± SD	141.9 ± 55.5	182.8 ± 84.5	162.0 ± 73.8
Dronedarone†	3 (2.3%)	3 (2.4%)	6 (2.4%)
Dose, mean ± SD	466.7 ± 305.5	666.7 ± 230.9	566.7 ± 265.8
Dofetilide†	0	0	0
Dose, mean ± SD			
Betablocking agents	67 (52.3%)	66 (52.0%)	133 (52.2%)
Other	5 (3.9%)	10 (7.9%)	15 (5.9%)
Dose, mean ± SD	302.0 ± 274.2	82.1 ± 41.8	155.4 ± 184.7

*Class 1C

†Class III

8. Supplementary Table S3. Catheters Used for the First (Index) Ablation During the ATTEST Trial

Catheters used, n (%)	**RF ablation group (n=102)**
Navistar THERMOCOOL Catheter	56 (54.9)
EZ Steer THERMOCOOL NAV Catheter	0
THERMOCOOL SF NAV Catheter Bi-Directional Navigation Catheter	8 (7.8)
THERMOCOOL SF NAV Catheter Uni-Directional Navigation Catheter	0
THERMOCOOL SmartTouch Bi-Directional Navigation Catheter	10 (9.8)
THERMOCOOL SmartTouch Uni-Directional Navigation Catheter	21 (20.6)
Navistar RMT THERMOCOOL Catheter	4 (3.9)
Lasso Circular Mapping Catheter	32 (31.4)
Lasso 2515 Variable Circular Mapping Catheter	33 (32.4)
Coronary sinus catheter	43 (42.2)
Intracardiac echocardiography catheter	2 (2.0)
Other catheter	12 (11.8)
Other: BW ST F curve	1 (1.0)
Any other except the above	12 (11.8)

RF, radiofrequency.

9. Supplementary Table S4. New AADs Initiated During the Study (ITT Population)

New AAD, n (%)	RF ablation group (n=128)	AAD group (n=127)
Any new AAD	59 (46.1)	68 (53.5)
Beta-blocking agents	39 (30.5)	35 (27.6)
Alpha- and beta-blocking agents	0	4 (3.1)
Nonselective beta-blocking agents	11 (8.6)	13 (10.2)
Selective beta-blocking agents	36 (28.1)	23 (18.1)
Selective beta-blocking agents and thiazides	1 (0.8)	0
Calcium channel blockers	12 (9.4)	13 (10.2)
Benzothiazepine derivatives	0	1 (0.8)
Dihydropyridine derivatives	12 (9.4)	11 (8.7)
Phenylalkylamine derivatives	0	2 (1.6)
Cardiac therapy	30 (23.4)	53 (41.7)
Class I and III antiarrhythmics	0	1 (0.8)
Class IA antiarrhythmics	0	1 (0.8)
Class IC antiarrhythmics	19 (14.8)	35 (27.6)
Class III antiarrhythmics	16 (12.5)	25 (19.7)

AAD, antiarrhythmic drug; RF, radiofrequency.

10. Supplementary Table S5. All AADs Taken During Study Period

AAD Treatment, n (%)	RF ablation (n=128)	AAD (n=127)	Total (N=255)
Baseline			
Any AAD	113 (88.3)	114 (89.8)	227 (89.0)
Beta-blocking agents	78 (60.9)	78 (61.4)	156 (61.2)
Atenolol	2 (1.6)	0	2 (0.8)
Betaxolol	0	2 (1.6)	2 (0.8)
Bisoprolol	31 (24.2)	28 (22.0)	59 (23.1)
Carvedilol	1 (0.8)	1 (0.8)	2 (0.8)
Metoprolol	19 (14.8)	24 (18.9)	43 (16.9)
Nebivolol	5 (3.9)	3 (2.4)	8 (3.1)
Propranolol	0	3 (2.4)	3 (1.2)
Sotalol	21 (16.4)	19 (15.0)	40 (15.7)
Calcium Channel Blockers	24 (18.8)	19 (15.0)	43 (16.9)
Amlodipine	19 (14.8)	18 (14.2)	37 (14.5)
Lacidipine	2 (1.6)	0	2 (0.8)
Lercanidipine	2 (1.6)	1 (0.8)	3 (1.2)
Verapamil	1 (0.8)	0	1 (0.4)
Cardiac Therapy (Class I/III)	61 (47.7)	69 (54.3)	130 (51.0)
Amiodarone	17 (13.3)	21 (16.5)	38 (14.9)
Antiarrhythmic agents	1 (0.8)	0	1 (0.4)
Disopyramide	0	1 (0.8)	1 (0.4)
Dronedarone	0	2 (1.6)	2 (0.8)
Ethacizine	0	1 (0.8)	1 (0.4)
Flecainide	11 (8.6)	15 (11.8)	26 (10.2)
Propafenone	32 (25.0)	29 (22.8)	61 (23.9)
	RF ablation (n=95)	**AAD (n=99)**	**Total (N=194)**
6-month follow-up			
Any AAD	81 (85.3)	96 (97.0)	177 (91.2)
Beta-blocking agents	70 (73.7)	66 (66.7)	136 (70.1)
Atenolol	4 (4.2)	0	4 (2.1)
Bisoprolol	34 (35.8)	25 (25.3)	59 (30.4)
Carvedilol	1 (1.1)	3 (3.0)	4 (2.1)
Metoprolol	19 (20.0)	16 (16.2)	35 (18.0)
Nebivolol	5 (5.3)	4 (4.0)	9 (4.6)
Propranolol	1 (1.1)	2 (2.0)	3 (1.5)
Sotalol	6 (6.3)	17 (17.2)	23 (11.9)
Calcium Channel Blockers	18 (18.9)	16 (16.2)	34 (17.5)
Amlodipine	16 (16.8)	13 (13.1)	29 (14.9)
Diltiazem	0	1 (1.0)	1 (0.5)
Lercanidipine	2 (2.1)	2 (2.0)	4 (2.1)
Nifedipine	0	1 (1.0)	1 (0.5)
Cardiac Therapy (Class I/III)	30 (31.6)	65 (65.7)	95 (49.0)
Amiodarone	9 (9.5)	20 (20.2)	29 (14.9)
Dronedarone	0	2 (2.0)	2 (1.0)
Flecainide	6 (6.3)	17 (17.2)	23 (11.9)

Propafenone	15 (15.8)	26 (26.3)	41 (21.1)
	RF ablation (n=85)	**AAD (n=84)**	**Total (N=169)**
1-year follow-up			
Any AAD	75 (88.2)	82 (97.6)	157 (92.9)
Beta-blocking agents	63 (74.1)	62 (73.8)	125 (74.0)
Atenolol	5 (5.9)	0	5 (3.0)
Bisoprolol	31 (36.5)	28 (33.3)	59 (34.9)
Carvedilol	1 (1.2)	4 (4.8)	5 (3.0)
Metoprolol	17 (20.0)	15 (17.9)	32 (18.9)
Nebivolol	5 (5.9)	3 (3.6)	8 (4.7)
Propranolol	0	3 (3.6)	3 (1.8)
Sotalol	4 (4.7)	10 (11.9)	14 (8.3)
Calcium Channel Blockers	15 (17.6)	15 (17.9)	30 (17.8)
Amlodipine	13 (15.3)	12 (14.3)	25 (14.8)
Lercanidipine	2 (2.4)	1 (1.2)	3 (1.8)
Nifedipine	0	1 (1.2)	1 (0.6)
Verapamil	0	1 (1.2)	1 (0.6)
Cardiac Therapy (Class I/III)	26 (30.6)	53 (63.1)	79 (46.7)
Amiodarone	6 (7.1)	16 (19.0)	22 (13.0)
Ethacizine	0	1 (1.2)	1 (0.6)
Flecainide	7 (8.2)	15 (17.9)	22 (13.0)
Propafenone	13 (15.3)	23 (27.4)	36 (21.3)
	RF ablation (n=66)	**AAD (n=62)**	**Total (N=128)**
2-year follow-up			
Any AAD	59 (89.4)	59 (95.2)	118 (92.2)
Beta-blocking agents	51 (77.3)	43 (69.4)	94 (73.4)
Atenolol	4 (6.1)	0	4 (3.1)
Bisoprolol	27 (40.9)	19 (30.6)	46 (35.9)
Carvedilol	1 (1.5)	3 (4.8)	4 (3.1)
Metoprolol	11 (16.7)	10 (16.1)	21 (16.4)
Nebivolol	4 (6.1)	3 (4.8)	7 (5.5)
Propranolol	0	2 (3.2)	2 (1.6)
Sotalol	4 (6.1)	6 (9.7)	10 (7.8)
Calcium Channel Blockers	10 (15.2)	10 (16.1)	20 (15.6)
Amlodipine	8 (12.1)	8 (12.9)	16 (12.5)
Lercanidipine	2 (3.0)	1 (1.6)	3 (2.3)
Verapamil	0	1 (1.6)	1 (0.8)
Cardiac Therapy (Class I/III)	18 (27.3)	39 (62.9)	57 (44.5)
Amiodarone	5 (7.6)	8 (12.9)	13 (10.2)
Dronedarone	0	2 (3.2)	2 (1.6)
Ethacizine	0	1 (1.6)	1 (0.8)
Flecainide	3 (4.5)	12 (19.4)	15 (11.7)
Propafenone	10 (15.2)	17 (27.4)	27 (21.1)
	RF ablation (n=46)	**AAD (n=50)**	**Total (N=96)**
3-year follow-up			
Any AAD	38 (82.6)	47 (94.0)	85 (88.5)

Beta-blocking agents	31 (67.4)	33 (66.0)	64 (66.7)
Atenolol	3 (6.5)	0	3 (3.1)
Bisoprolol	20 (43.5)	13 (26.0)	33 (34.4)
Carvedilol	0	2 (4.0)	2 (2.1)
Metoprolol	6 (13.0)	8 (16.0)	14 (14.6)
Nebivolol	2 (4.3)	2 (4.0)	4 (4.2)
Propranolol	0	3 (6.0)	3 (3.1)
Sotalol	1 (2.2)	6 (12.0)	7 (7.3)
Calcium Channel Blockers	8 (17.4)	10 (20.0)	18 (18.8)
Amlodipine	6 (13.0)	7 (14.0)	13 (13.5)
Lercanidipine	2 (4.3)	1 (2.0)	3 (3.1)
Verapamil	0	2 (4.0)	2 (2.1)
Cardiac Therapy (Class I/III)	15 (32.6)	28 (56.0)	43 (44.8)
Amiodarone	5 (10.9)	7 (14.0)	12 (12.5)
Dronedarone	0	1 (2.0)	1 (1.0)
Ethacizine	0	1 (2.0)	1 (1.0)
Flecainide	3 (6.5)	8 (16.0)	11 (11.5)
Propafenone	7 (15.2)	12 (24.0)	19 (19.8)

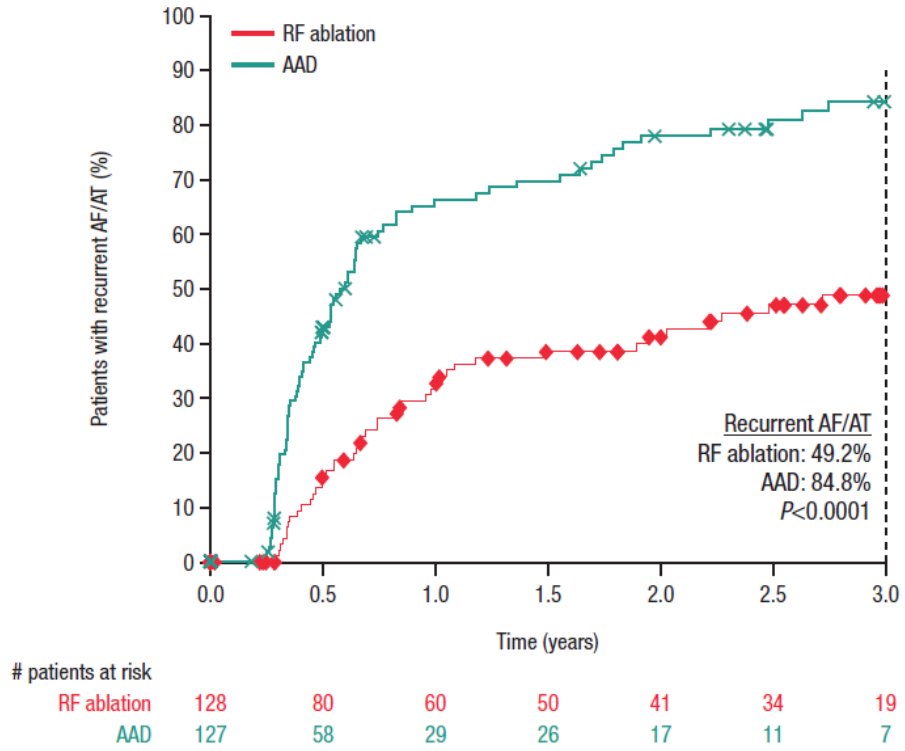
11. Supplementary Table S6. Index Ablation Outcomes for Patients in the Catheter Ablation Group (Safety Population)

Ablation outcome, n (%)	RF ablation group (n=102)
Complete pulmonary vein isolation achieved	
Yes	102 (100)
No	0
Entrance block confirmed	
Yes	100 (98.0)
No	2 (2.0)
Subject in sinus rhythm at the end of the procedure	
Yes	92 (90.2)
No	10 (9.8)
If not in sinus rhythm, ECV done at the end of the procedure	
Yes	9 (8.8)
No	1 (1.0)
If ECV performed, subject in sinus rhythm post ECV	
Yes	8 (7.8)
No	1 (1.0)

ECV, electrical cardioversion; RF, radiofrequency.

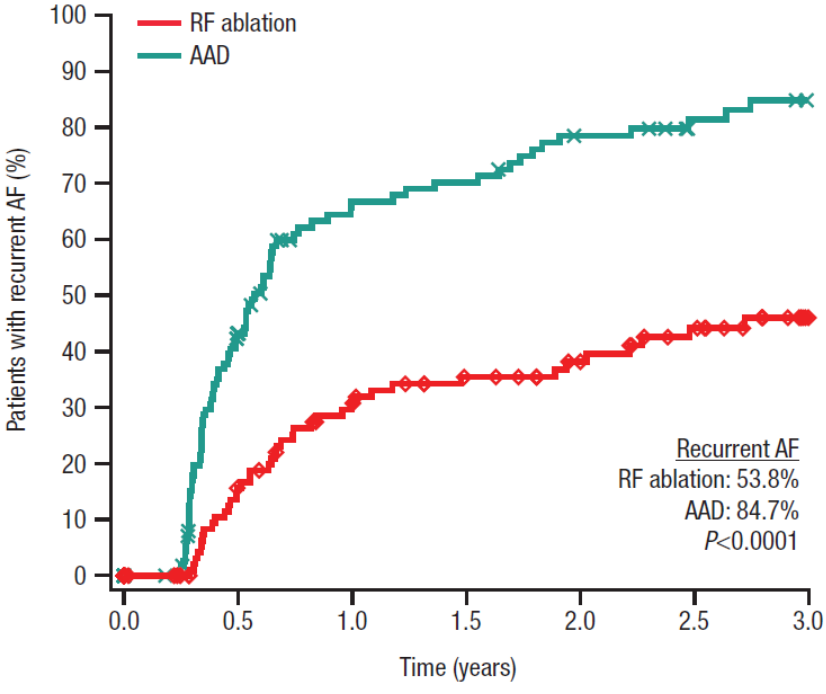
12. Supplementary Figure S1. Time to (A) recurrent AF/AT and (B) recurrent AF in the ITT population

(A)



# patients at risk							
RF ablation	128	80	60	50	41	34	19
AAD	127	58	29	26	17	11	7

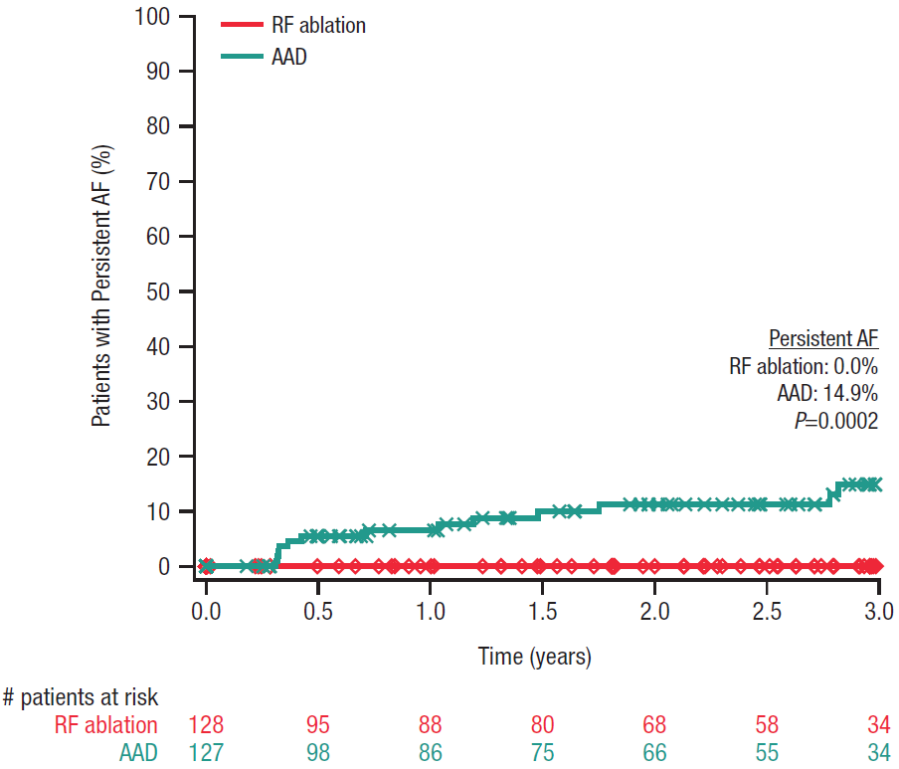
(B)



# patients at risk							
RF ablation	128	80	62	52	43	35	20
AAD	127	58	29	26	17	11	7

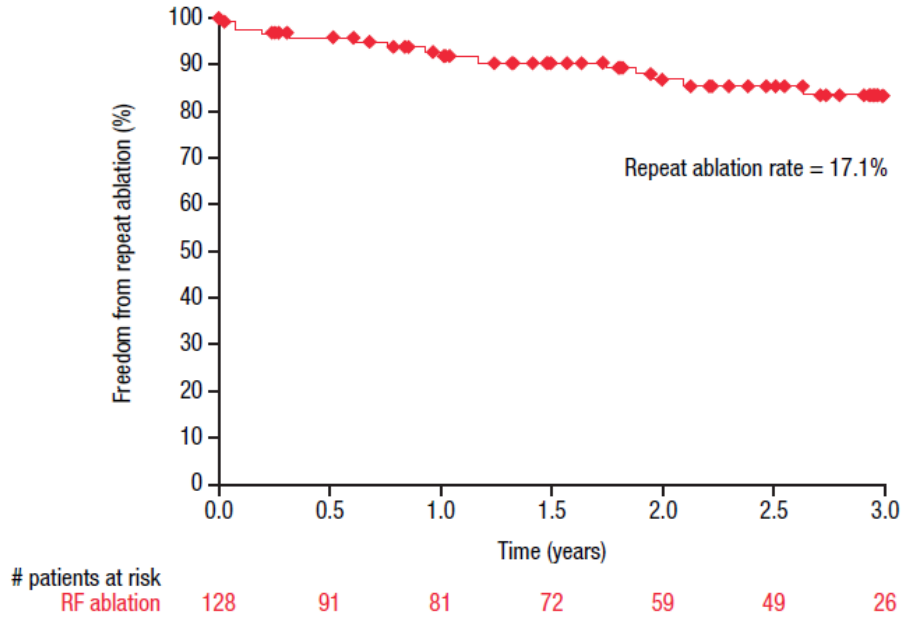
AAD, antiarrhythmic drug; AF, atrial fibrillation; AT, atrial tachycardia; ITT, intention-to-treat; RF, radiofrequency.

13. Supplementary Figure S2. Time to Persistent AF in the ITT population.



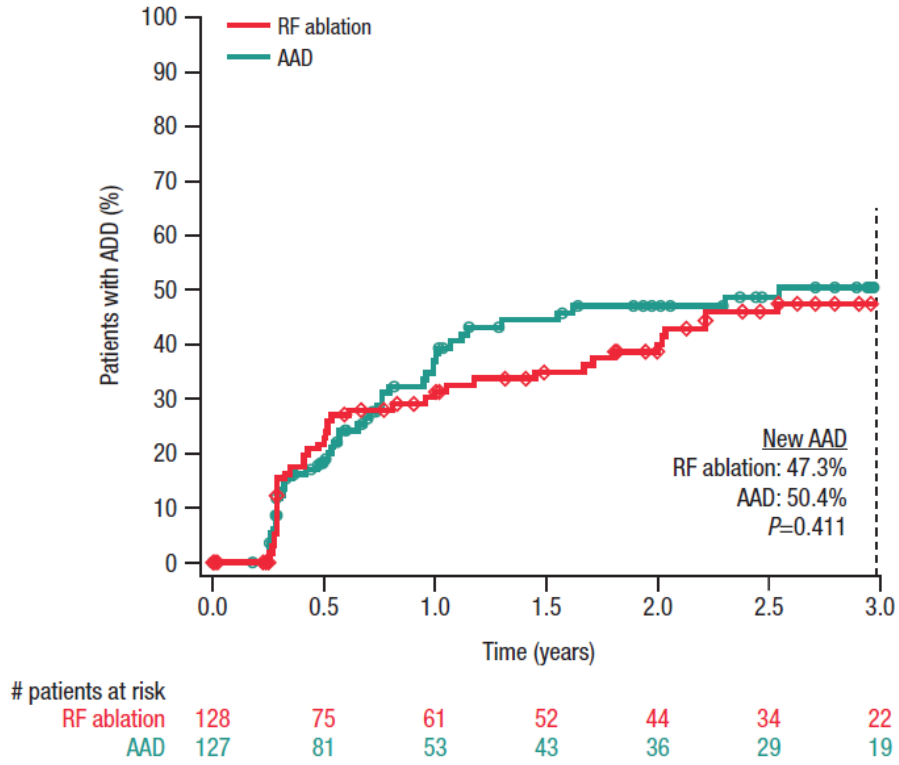
AAD, antiarrhythmic drug; AF. atrial fibrillation; ITT, intention-to-treat; RF, radiofrequency.

14. Supplementary Figure S3. Freedom from repeat ablation in the ITT population.



ITT, intention-to-treat; RF, radiofrequency.

15. Supplementary Figure S4. Time to new AAD in the ITT population.



AAD, antiarrhythmic drug; ITT, intention-to-treat; RF, radiofrequency.