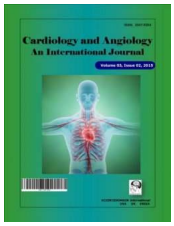

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Dronedarone after Catheter Ablation of Atrial Fibrillation: A New Option in Hybrid Therapy

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Authors' contributions

This work was carried out in collaboration between all authors. Author FG designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors MN and EK managed the analyses of the study. Authors FV and KK participated in the study design, managed the literature searches and proof-read the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background and Aim: Catheter ablation has become the therapy of choice in patients with symptomatic, recurrent, drug-refractory atrial fibrillation (AF). However, frequent AF recurrences often necessitate an adjunctive antiarrhythmic drug (AAD) therapy. Dronedarone is a new class III AAD with modest side effects. We compared a conventional AAD therapy (CAAT) with class I/III AADs to a novel therapy with dronedarone (NAAT)in regard to AF recurrences and improvement of symptoms.
Methodology: One hundred twenty five consecutive patients (84 men; mean age 62.1±12.4 years) with symptomatic paroxysmal (n=70) or persistent (n=55) drug refractory AF were enrolled in an

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open-label randomized study. Following successful pulmonary vein isolation (PVI) patients were randomized to receive CAAT (n=50), NAAT (n=50) or no AAD therapy (=control; n=25). Follow-up visits were scheduled at 3, 6, 9, and 12 months post ablation. Seven-day-Holter monitoring and patients' histories served as indicators of treatment success. Bar signs of AF recurrence AADs were discontinued 6 months post ablation.

Results: The pre-ablation European Heart Rhythm Association (EHRA)-score decreased from 2.8±0.4 to 1.4±0.6 (NAAT) and 1.5±0.7 (CAAT) 6 months after PVI (1.7±0.7 in the control group). Fifty patients experienced an arrhythmia recurrence within 3 months. After 6 months, both hybrid therapy groups showed a significant advantage over the control group favoring sinus rhythm (SR).Whereas CAAT could retain its significant benefit at 9 months NAAT lost its relative advantages with only a positive trend remaining over the control group but a significant disadvantage compared to CAAT patients. At this point AF recurrences were found in 34% of NAAT patients, 26% of CAAT patients, and 40% of control patients. At 12 months, however, no group could preserve a significant lead over either of the others.

Conclusion: Dronedarone after PVI is safe and effective. Compared to a CAAT, NAAT reveals similar improvements of EHRA-scores and non-significantly different AF recurrence rates from 9 months on. Despite this, CAAT keeps significantly more patients in SR 9 months after PVI.

Keywords: Atrial fibrillation; dronedarone; catheter; ablation.

1. INTRODUCTION

Atrial fibrillation (AF) is the most common clinical arrhythmia, affecting more than 2-9% of the population aged 60-89 years. It is a significant cause of morbidity, doubles mortality, and is a cause for a decreased quality of life [1,2]. The current antiarrhythmic drug (AAD) treatment of AF consists of β-adrenergic blockers, *Vaughan-Williams* class I or III AADs such as flecainide, propafenone, and amiodarone [3,4]. Recently, dronedarone has received regulatory approval in the USA and European Union for the treatment of AF. Dronedarone is a relatively novel multichannel blocker that is a non-iodinated benzofuran derivative of amiodarone [3]. Its modifications were intended to eliminate major organ toxicities and prevent tissue accumulation [5]. Despite the available arsenal of AADs to fight AF conservative drug-based treatment is faced witha high percentage of AF recurrences ranging around 42-67% within one year after cardioversion [6]. For those patients with symptomatic, drug-refractory AF catheter ablation has become the first line of therapy [7]. Depending on the type of AF, i.e. paroxysmal vs. persistent, there are different ablation strategies [7]. It is generally accepted that pulmonary vein isolation (PVI) is an integral part of any AF ablation procedure [8]. Common are segmental or circumferential approaches, both of which may be combined with further ablation steps (particularly in persistent AF). Most frequently, such steps consist of linear lesions, electrogram-guided ablation strategies, and ablation of autonomic ganglia. However, the effectiveness of these various ablation strategies is a matter of ongoing discussion [8]. Moreover, the resulting procedures may be very complex and time-consuming. Follow-up strategies vary widely: often a 3 month blanking period is followed by visits at e.g. monthly or quarterly intervals including 1- to 7-day Holter electrocardiograms (ECGs) or implantable loop recorders. For some, the definition of a successful ablation is purely a matter of preventing the recurrence of AF; for others, success means improving symptoms despite occasional bouts of AF.

On account of this complex situation and to prevent early recurrences of AF, it may be feasible to combine AF ablation with an adjuvant antiarrhythmic drug treatment following the procedure (hybrid therapy) [2,9]. Consequently, the aim of this study is to evaluate a well-defined reasonable approach to catheter ablation of paroxysmal and persistent AF with an adjuvant antiarrhythmic drug treatment.

2. METHODOLOGY

2.1 Patient Population

A total of 125 patients (84 men, 41 women; mean age 62.1±12.4 years) with symptomatic paroxysmal or persistent atrial fibrillation were enrolled in this study after giving informed consent.

All patients underwent catheter ablation of AF according to protocol. Twelve patients had to undergo a repeat procedure. The redo

procedures were not evaluated in this study. The ablation procedures were performed at our medical center between January 2010 and March 2011.

All patients referred to our center for AF ablation were screened. Inclusion criteria were (1) paroxysmal (defined as lasting more than 30 seconds and spontaneously returning to SR within 7 days) or persistent AF (defined as AF sustained beyond 7 days), (2) severe symptoms despite AAD therapy (excluding beta-blockers) or prior attempts at electrical cardioversion, (3) ability and willingness to give informed consent, and (4) age between 18 and 70 years. Patients were not accepted for catheter ablation and study participation if one of the following conditions was present: severe mitral regurgitation or any other concomitant cardiac disease requiring surgery, severely impaired left venticular function (left ventricular ejection fraction <30 %), recent heart failure,left atrial diameter >65 mm (parasternal long-axis view, left atrial thrombus, hyperthyroidism, severe renal insufficiency (creatinine ≥3 mg/dl), or another severe concomitant illness. In addition, the inability to tolerate any AAD treatment or pretreatment with amiodarone during the 3 months preceeding the ablation procedure prohibited study participation.

Irrespective of the underlying type of AF, patients were randomly assigned to one of three groups in a 2:2:1 fashion. On the first day after completion of the ablation procedure, the first group received open-label dronedarone (novel hybrid therapy or NAAT), the second group was treated with conventional *Vaughan-Williams* class I or III AAD (conventional hybrid therapy or CAAT), and the thirdgroup(control)got neither type of AAD. Dronedarone was dosed at 400 mg BID. Patients in the CAAT-group received flecainide (50 to 100 mg BID), propafenone (225 mg BID or 150 mg TID), or amiodarone (200 mg QD). A preference was given to flecainide (generally in combination with a β-blocker) or propafenone. Amiodarone was used after an initial loading dose only if a structural heart disease such as coronary artery disease (CAD), decreased LV function, LV hypertrophy, or relevant valvular disease was present. Amiodarone loading consisted of a 10-day period with 200 mg TID.

2.2 Ablation Procedure

In all patients, a circumferential pulmonary vein ablation was performed in combination with a potential-guided segmental approach in order to achieve complete pulmonary vein isolation using a standard irrigated-tip ablation catheter (7F; D-type, 3.5-mm-tip; Biosense Webster, Diamond Bar, CA, USA). To aid the ablation procedure a 3D geometry of the LA was createdusing the NAVX-system or the CARTO-system in all patients. Furthermore, in selected cases and at the discretion of the operator a linear lesion was created at the roof of the left atrium and, if indicated, mitral isthmus ablations were performed.

At the end of the ablation procedure inducibility of AF (or atrial flutter) was tested. Finally, the completeness of the pulmonary vein isolation and of all linear lesions was reassessed after a waiting period of at least 20 minutes.

For the ablation procedure, a Bard EP system (LabSystem Pro, EP Recording System; Bard, Electrophysiology Division, Lowell, MA, USA)and a Stockert RF generator (EP-shuttle; Stockert, Freiburg, Germany) were used. A Philips x-ray system (Philips Medical Systems, Best, The Netherlands) was used to provide high-resolution x-ray imaging.

All relevant periprocedural complications were recorded and statistically evaluaded. Such complications were defined as bleeding or hematomas which necessitate blood transfusions, pericardial effusions mandating pericardiocentesis, atrial-esophageal fistulas, relevant pulmonary vein stenosis, cerebrovascular accidents, or any other complication requireingmedical intervention.

2.3 Follow-up

After hospital discharge, patients were seen regularly on an outpatient basis. Three, 6, 9, and 12 months after the procedure, a physical examination, a resting ECG, and a transesophageal echocardiogram (TEE, only at the 3 month follow-ups) were performed. Electrolytes, liver- and kidney-function tests were performed as needed or mandated by antiarrhythmic treatment. Patients' histories were taken to gather evidence for a possible arrhythmia recurrence. In addition, a 7-day Holter ECG recording was performed in connection with each follow-up visit. External event recorders were used as needed to help document short bouts of AF. Any documented AF episode lasting >30 seconds was considered to be a recurrence of AF. In the case of an arrhythmia recurrence or

other problems, the further follow-up and future strategy (e.g. electrical cardioversion, repeat ablation procedure) were planned on an individual basis. In regard to AF recurrences, no blanking period was defined. Oral anticoagulation was continued for at least 3 months after the procedure in all patients. Thereafter the anticoagulation regimen was undertakenaccording to current AF guidelines implementing the CHA_2DS_2-VASc-Score. The hybrid antiarrhythmic treatment (i.e. dronedarone, flecainid, propaphenone, or amiodarone) was discontinued after 6 months inasmuch as no signs of AF recurrence were found.

2.4 Quality of Life

Quality of life (QoL) was assesed 6 and 12 months after the ablation procedure using a self-administered QoL questionnaire [10,11] focusing on AF-related symptoms, daily activities, treatment concerns, and treatment satisfaction. The questionaire was designed to refer to the three months preceeding the follow-up visit. The resulting score ranges from 0 (poorest possible QoL) to 100 (best possible QoL).

2.5 Statistical Analysis

All parameters with a normal distribution are given as a mean (± 1 SD). Categorical data are given as absolute as well as corresponding relative frequencies (in %) and were compared using Fisher's exact test. Continuous variables are summarized by arithmetic mean and corresponding standard deviation. The unpaired t-test was conducted for pair-wise comparison of the calculated arithmetic means where appropriate.

A global significance level of α=5% was chosen for all statistical test procedures. All statistical analyses were conducted in an explorative manner [12]; thus p-values ≤0.05 can be regarded as statistically significant results. SAS Statview for Windows Version 5.0 was used for statistical calculations.

3. RESULTS

3.1 Ablation Procedure and Antiarrhythmic Drug Therapy

It was possible to carry out the ablation procedure as planned in all patients. Parts I and II of Table 1 summarize clinical characteristics of and specific data on the procedures of the patients enrolled in the study. During the follow-up period of 12 months 12 patients had to undergo repeat procedures (10%). Of these 12 patients 5 had left atrial tachycardias. Neither immediately after the procedures nor during any point in time within the follow-up period did any patient experience relevant complications. Minor complications occurred in 28 patients (hematoma at the venous access site without need for blood transfusion in 25 patients, pericardial effusion without need for pericardiocentesis in 2 patients, mild allergic reaction to contrast agent in 1 patient).

Of all 125 patients, 50 were randomly assigned to each of the NAAT- and the CAAT-groups and 25 to the control group. Drug compliance was good with no patient discontinuing the antiarrhythmic drug treatment. During the follow-up period no patient experienced relevant side effects that could have been attributed to the AAD treatment. Elevated liver function test results, particularly in the NAAT group, were not observed. Five patients experienced minor transient abdominal discomfort in the NAAT group without need for treatment or drug discontinuation. Three patients in the CAAT group developed a prolonged QTc time, which, however, could be tolerated and did not mandate discontinuation of amiodarone. In the CAAT-group 25 patients (50%) received flecainide, 21 patients (42%) received amiodarone and 4 patients (8%) propafenone. Patients who received amiodarone rather than other conventional AAD encompassed e.g. the 20% of patients with CAD as well as patients with LV-hypertrophy and reduced LV function. Six months after the index procedure the AAD therapy was discontinued in a total of 73 patients (73%). However, 12 patients in the NAAT- and 15 patients in the CAAT-group (7 flecainide, 8 amiodarone) continued taking antiarrhythmics. After 9 months a further 3 patients discontinued dronedarone, and 2 patient stopped taking flecainide. This left 9 patients from the NAAT group on dronedarone and 5 patients on flecainide and 8 patients on amiodarone from the CAAT group at 12 months after ablation. On average, patients in the NAAT group received AAD treatment for 7.25 months. In the CAAT group this value lay at 7.72 months. There were no statistically significant differences in mean AAD treatment duration between NAAT and CAAT. Also, the number of patients treated beyond 6 months did not differ between these two groups.

Table 1. Patient characteristics, ablation procedure, and results

	Total *n*=125	**Control *n=25***	**NAAT *n=50***	**CAAT *n=50***	**p-value <0.05 Control vs. NAAT vs. CAAT**
			Part I: Patient characteristics		
Age (years)	62.1±12.4	62.2±11.2	62.3±9.2	61.9±10.9	n.s.
Male Sex (no./%)	84/67	17/67	36/72	31/61	n.s.
Paroxysmal AF (no./%)	70/56	14/56	27/54	29/58	n.s.
CAD (no./%)	25/20	4/16	9/18	12/24	n.s.
BMI (kg/m²)	26.9±4.2	27.3±5.4	26.3±5.4	27.4±4.3	n.s.
NYHA class (1-4)	2±1	2±1	2±1	2±1	n.s.
TR (degree 0-3)	1±1	1±1	1±1	1±1	n.s.
RVSP (mmHg+CVP)	28.0±10.6	27.2±9.9	28.5±8.9	27.9±11.2	n.s.
LV EF (%)	57.9±5.8	59.1±8.2	58.1±6.0	57.1±5.6	n.s.
Left atrium size (mm)	51.0±5.1	50.8±4.2	49.8±4.7	52.3±5.7	n.s.
CHA_2DS_2-VASc-Score	1.2±0.9	1.2±0.8	1.2±0.8	1.2±1.0	n.s.
Hypertension (no./%)	93/74	18/72	36/72	39/78	n.s.
ACE-I (no./%)	71/57	14/56	27/53	30/60	n.s.
β-blocker (no./%)	103/82	21/83	41/81	41/81	n.s.
			Part II: Ablation procedure		
Fluoroscopy (min)	38.8±9.3	38.9±8.3	38.3±9.5	39.5±12.3	n.s.
Procedure time (min)	243±32	242±30	249±29	234±36	n.s.
Number of PVs isolated	3.9	4.0	4.0	3.9	n.s.
Number of procedures	1.1±0.5	1.1±0.5	1.1±0.5	1.1±0.4	n.s.
			Part III: Results		
SR (no./%)					
- immediately after PVI	125/100	25/100	50/100	50/100	n.s.
- @ 3 months	75/60	14/56	32/64	29/58	n.s.
- @ 6 months	89/71	17/67	38/75	37/74	CAAT and NAAT vs. control
- @ 9 months	89/71	15/61	33/66	39/78	CAAT vs. NAAT and control
- @ 12 months	84/67	14/56	32/64	38/75	n.s.
EHRA score (1-4)					
- prior to PVI	2.8±0.6	2.8±0.5	2.8±0.4	2.8±0.8	n.s.
- @ 3 months	1.7±0.4	2.0±0.5	1.5±0.4	1.7±0.4	n.s.
- @ 6 months	1.6±0.5	2.0±0.7	1.4±0.6	1.5±0.7	n.s.
- @ 9 months	1.7±0.9	2.1±0.7	1.6±0.9	1.6±0.7	n.s.
- @ 12 months	1.8±0.7	2.2±0.6	1.7±0.8	1.6±0.4	n.s.

	Total *n*=125	Control *n=25*	NAAT *n=50*	CAAT *n=50*	p-value <0.05 Control vs. NAAT vs. CAAT
QoL score (0-100)					
- prior to PVI	36±4	36±5	36±5	36±4	n.s.
- @ 3 months	46±6	43±6	46±4	47±5	n.s.
- @ 6 months	55±6	50±8	57±6	55±4	n.s.
- @ 9 months	54±7	49±5	56±6	54±4	n.s.
- @ 12 months	51±8	47±6	52±5	51±6	n.s.

(In each group column, a bracket with arrows marks p<0.05 for every follow-up value vs. prior to PVI.)

NAAT/CAAT: novel/conventional anti-arrhythmic drug therapy; AF: atrial fibrillation; CAD: coronary artery disease; BMI: body mass index; NYHA: New York Heart Association; TR: tricuspid regurgitation (0=none, 1=mild, 2=moderate, 3=severe); RVSP: right ventricular systolic pressure; CVP: central venous pressure; LV EF: left ventricular ejection fraction; ACE-I: angiotensin converting enzyme-inhibitor; PV: pulmonary vein; PVI: pulmonary vein isolation; EHRA: European Heart Rhythm Association; QoL: quality of life

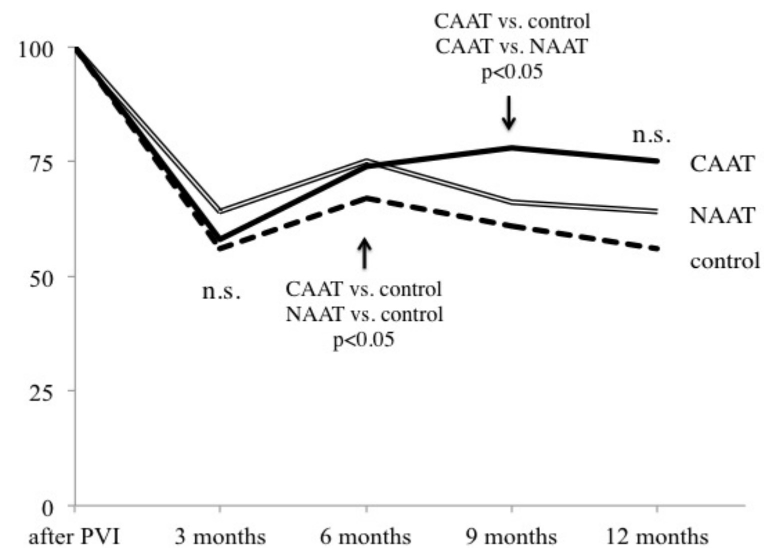

Fig. 1. The line chart depicts the three groups of patients (%) in sinus rhythm. Patients in the control group did not receive any antiarrhythmic medication after the ablation procedure. Patients with a hybrid therapy approach received either dronedarone (NAAT) or conventional antiarrhythmics (CAAT). Immediately after ablation all patients were in sinus rhythm. After 3 months there was a steep drop due to AF recurrences documented during follow-up visits (see *Methodology* for details). A significant difference between patients receiving any hybrid therapy vs. the control group could be noted after 6 months and for CAAT vs. NAAT or the control group after 9 months (both p<0.05)

3.2 Clinical Outcome

The mean follow-up was 340±40 days in the NAAT group compared to 344±45 days in the CAAT group and 350±25 days in the control group. Three months after the ablation procedure 75 (60%) of the patients had no signs of recurrent AF or atrial tachycardias (AT). No group differed significantly from the others at this point (part III of Table 1 and Fig. 1). After 6 months both NAAT and CAAT developed a significant benefit ($p<0.05$) over the control group (38 patients or 75% in the NAAT-group and 37 patients or 74% in the CAAT-group had no signs of recurrent AF or AT; control: 67%). While the CAAT group could retain its lead over the control group at 9 months, the NAAT group lost its statistical benefit and was now inferior to the CAAT group though better than the control group (33 patients or 66% in the NAAT-group vs. 39 patients or 78% in the CAAT-group without signs of AF or AT recurrence; control: 61%). However, after 12 months, all significant differences between the three groupswere lost. During the follow-up period 12 patients (6 in the NAAT group, 4 in the CAAT group and 2 in the control group) had to undergo redo procedures because of frequent AF or AT recurrences. There were no statistically significant differences between the three groups in regard to the number of redo procedures. Throughout the follow-up period the rate of ATs was low (3 patients in the NAAT and 2 patients in the CAAT, none in the control group). There was no significant difference between the groups in regard to the occurrence of ATs.

The EHRA score fell significantly ($p<0.05$) from an initial average score of 2.8±0.6 to 1.7±0.4 after 3 months (see part III of Table 1). After this initial drop the average EHRA score fell slightly to 1.6±0.5 at 6 months. After 12 months of follow-up the average EHRA score was 1.8±0.7. At no point in follow-up did the scores differ significantly between the hybrid therapy groups. Similar results were found when looking at the QoL scores. The initial pre-ablation score was 36±4 and improved in to 55±4 (CAAT) and 57±6 (NAAT) at 6 months follow-up (control: 50±8). After 12 months the QoL score lay at 51±6 (CAAT) and 52±5 (NAAT) (control 47±6). There were no statistical differences in regard to QoL score between any of the groups. However, compared to baseline EHRA- and QoL-scores all the scores had improved significantly ($p<0.05$) after 3, 6, 9, and 12 months and there was a trend favouring the hybrid therapy groups compared to the control group.

The study groups were too small to perform a meaningful analysis correlating the time of the AF recurrence and the outcome of treatment. However, there was a trend towards a higher arrhythmia recurrence rate in patients with early AF recurrences.

4. DISCUSSION

The present study demonstrates that both NAAT and CAAT result in a significant early-on reduction in AF burden (compared to a control group) and AF-related symptoms. In regard to symptoms, however, the groups did not differ significantly from one another. When comparing the recurrence of AF, there was a significant difference after 6 months post-PVI favoring the hybrid therapy groups. This statistically significant benefit was only retained by the CAAT group after 9 months post-PVI (three months after discontinuation of most AADs). Finally, one year after the ablation procedure all statistical significant differences were lost in regard to rhythm control. Thus the most important finding of this study is that NAAT which combines AF ablation with dronedarone is a safe and effective treatment option compared to conventional class I and III antiarrhythmics. Furthermore, NAAT showed a significant benefit compared to the control group 6 months post-PVI. However, while a positive trend favoring a NAAT over no AAD remains the statistical significance is lost at 9 monthsand after.

In 1998 Haïssaguerre found ectopic beats originating from the pulmonary veins to be responsible for paroxysmal AF [13]. Since then, pulmonary vein isolation has become central to any AF ablation procedure. Moreover, it has been established that "*AF begets AF*" by electrical remodeling with even minor bouts of rapid atrial pacing leading to increased persistence of AF by reducing, among others, the refractory period [14]. There is also evidence that the duration of AF correlates with the degree of structural atrial remodeling [15] thus further facilitating the persistence of AF. Taken together, in order to achieve stabile sinusrhythm, one has to eliminate the triggering ectopic beats from the pulmonary veins and, if possible, reverse the electrical and structural remodeling processes. This can only happen if patients remain in SR. Hybrid therapy may contribute to suppressing AF episodes and thus help reverse the remodeling process [16]. However, recently the

5A study found that despite the suppression of early AF episodes by AAD treatment (for 6 weeks post-ablation) this did not correlate with the longer term treatment success compared to patients receiving no AAD therapy [9]. One explantation offered is that early atrial arrhythmias within the first weeks after the ablation procedure may be caused more by an inflammatory reaction than a failure of reverse remodeling. Despite the lack of hard evidence it is conceivable that a prolonged hybrid approach after AF ablation could be beneficial.

It is well known that the efficacy of dronedarone in maintaining SR is fairly weak compared to other AADs [17]. Thus, contrary to what might have been expected, there was no significant difference between the NAAT and the CAAT at 6 months after ablation, when most patients discontinued their AAD treatment. Apparently, early on after AF ablation the choice of AAD for hybrid therapy does not make a significant difference as any AAD is better than none. Considering the modest toxicicity of dronedarone one can reasonably favor the NAAT. Three months later – 9 months post-PVI – CAAT proved to be superior to either NAAT or the control without AAD treatment (though NAAT patients seemed to benefit non-significantly compared to controls). Thus the initial supression of AF appears to be augmented by a hybrid therapy. This may be due to speedier electrophysiological reverse remodeling in the CAAT and NAAT groups as compared to the control group. Later on at 9 months post-PVI, an early, limited-duration hybrid therapy helps to maintain treatment success primarily in CAAT patients. This difference between CAAT and NAAT needs explanation. Since most patients had discontinued their AAD treatment 6 months after PVI, the difference between the two groups may have been the slightly higher average duaration of amiodarone/flecainide treatment compared to dronedarone treatment. The significantly longer half-life of amiodarone (58 days vs. 24 hours) may have led to residual drug levels at the 9 month follow-up stage, which could have influenced the observed results. At 12 months post-PVI this advantage had disappeared. To improve long-term treatment results beyond 9 months a continued AAD treatment or a re-do procedure may be necessary.

The PALLAS trial has shown adverse effects in treating patients with permanent AF with dronedarone [18]. However, since this study was conducted prior to the publication of PALLAS, the NAAT group included patients with both paroxysmal and persistent AF (all patients treated with the intention of rhythm control). Furthermore, the patient population studied in PALLAS that fared worse with dronedarone was clearly different from the present one with older patients who had higher $CHADS_2$-scores, more coronary artery disease, worse left ventricular functions, and longer-standing AF (69% >2 years) [18]. The PALLAS patient population would not have been ideal for AF ablations and thus cannot be compared to our patients.

The ATHENA study demonstrated, among other things, that dronedarone decreases the risk of hospitalization due to recurrent AF [19]. Furthermore, several studies suggest that the QoL improves if rhythm control can be achieved [20]. Similar findings have been reported after AF-ablation [21]. Thus, the results of this study are in line with the results of others in regard to symptom improvement. Furthermore, to alleviate AF-related symptoms and QoL it does not seem to matter which AAD (conventional or novel) is chosen after AF ablation.Most clinically relevant to patients is not whether one has AF or SR but whether one suffers from AF-related symptoms or not. Our study demonstrates that this is possible in any of the treatment arms.

5. LIMITATIONS

The most important limitation is - as with all AF treatment studies – the monitoring for AF recurrence. Practical issues limit monitoring to AF-related symptoms and repetitive 7-day HolterECGs. However, this may not capture all AF recurrences. The relative importance of short asymptomatic episodes is debatable. Another limitation is the open-label trial design, which always poses a potential threat for bias. Since the discontinuation of AAD treatment was – to a degree - at the discretion of the physician this may have been a confounding factor. By standardizing follow-up procedures we tried to minimize these risks. Finally, a larger study is needed to detect minor differences between the treatment arms.

6. CONCLUSION

In conclusion, a NAAT is a safe and effective treatment option. It is not inferior to a CAAT 6 months post-PVI. However, despite a similar improvement in symptoms compared to a CAAT

with class I or III antiarrhythmics the NAAT appears to be inferior in regard to rhythm control at 9 months after ablation.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this paper and accompanying images.

ETHICAL CONCIDERATION

The local ethics committee was consulted and approved this study.

DISCLAIMER

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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