Pulmonary vein isolation With vs. without continued antiarrhythmic Drug treatment in subjects with Recurrent Atrial Fibrillation (POWDER AF): results from a multicentre randomized trial

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Aims
Catheter ablation is indicated in patients with symptomatic paroxysmal atrial fibrillation (AF) resistant to antiarrhythmic drug therapy (ADT). We investigated whether continued use of previously ineffective ADT beyond the post-ablation blanking period reduces recurrence of atrial tachyarrhythmia within the 1st year after ablation.

Methods and results
This was a multicentre, randomized controlled study in patients undergoing contact force-guided pulmonary vein isolation (PVI) for paroxysmal AF in whom previously ineffective ADT was continued during a blanking period of 3 months. If free of AF at the end of the blanking period, patients were randomly assigned in the ratio of 1:1 to continue ADT (ADT ON group, n = 77) or discontinue ADT (ADT OFF group, n = 76). Patients were followed up until 1 year after PVI, with clinical visits, Holter monitoring, and quality-of-life (QOL) questionnaires at 6 and 12 months post-procedure. Analysis of the primary endpoint (any documented atrial tachyarrhythmia lasting >30 s) was performed according to the modified intention-to-treat principle. Secondary endpoints included repeat ablation, unscheduled visits, and QOL score. Baseline clinical characteristics and initial ablation procedure characteristics were comparable between both groups. Three patients were lost to follow-up in each arm. The primary endpoint was observed in 2 of 74 (2.7%) patients in the ADT ON group vs. 16 of 73 (21.9%) patients in the ADT OFF group (P < 0.001). The ADT ON group had a lower rate of repeat ablation [1.4% vs. 19.2%, hazard ratio (HR) = 0.053; 95% confidence interval (CI) 0.007–0.399; P < 0.01) and less unscheduled arrhythmia-related health care visits (2.7% vs. 20.5%, HR = 0.055, 95% CI 0.007–0.410; P < 0.01). Quality-of-life scores were similar in both groups.

Conclusion
In patients free of AF at the end of 3 months of post-ablation blanking period, continued use of previously ineffective ADT significantly reduces the recurrence of atrial tachyarrhythmia in the 1st year after PVI.

Keywords
Atrial fibrillation • Ablation • Antiarrhythmic drugs
Introduction

Pulmonary vein isolation (PVI) is a recommended therapy in patients with symptomatic paroxysmal atrial fibrillation (AF) resistant to anti-arrhythmic drug therapy (ADT). In trials reporting on arrhythmia-free survival after PVI, ADT is stopped after an initial 3 months of blanking period. In real-life practice, ADT is continued beyond the blanking period in up to 50% of patients. No randomized trial investigated whether ADT, continued beyond the blanking period, reduces recurrence of atrial tachyarrhythmia (ATA) after PVI. In this multicentre randomized trial, we investigated whether continued use of previously ineffective ADT beyond the blanking period reduces ATA [AF, atrial tachycardia (AT), or atrial flutter] recurrence in the 1st year after PVI.

Methods

Study design

This was a prospective, randomized, open-label, blinded endpoint (PROBE) trial. The study was investigator initiated and conducted in three centres. The investigators had full and exclusive control over study design, data analysis, and writing of the article. Patients who underwent AF ablation at St Jan Hospital Bruges, University Hospital Antwerp, or OLV Aalst Hospital were screened for inclusion. Patients were eligible if still on ADT 3 months after a 1st contact force (CF)-guided PVI for symptomatic, ADT-resistant paroxysmal AF and free from ATA at the end of the blanking period. Exclusion criteria were advanced structural heart disease, left atrial diameter >55 mm, ejection fraction <35%, coronary artery bypass grafting or myocardial infarction within the last 3 months, unstable angina, uncontrolled heart failure, awaiting cardiac transplantation or other cardiac surgery, patients with life expectancy <12 months, acute illness, enrolment in another study evaluating another device or drug, substrate ablation during the initial procedure (except for cavotricuspid ablation), and women with childbearing potential.

The trial was conducted in accordance with the Helsinki Declaration and was approved by the ethics committee of the St Jan Hospital Bruges. The trial was registered at ClinicalTrials.gov (NCT02475642) and was monitored by the regional Good Clinical Practice unit. Written informed consent was obtained from all participants prior to inclusion. Data and safety monitoring was performed by the local principal investigator without predefined data looks or stopping rules. Enrolment was terminated on 26 August 2015. Follow-up was finalized in August 2016.

Ablation, randomization, and study treatment

All patients underwent PVI by CF-guided point-by-point radiofrequency ablation (SmartTouch, Biosense Inc.). Procedural endpoint was ipsilateral PVI assessed by a circular mapping catheter and challenged by adenosine. Ablation at the cavotricuspid isthmus was performed in patients with documented typical atrial flutter. Patients were discharged the day after the ablation procedure, and oral anticoagulation was continued for at least 3 months. It was the standard of care in all centres to continue or restart previously ineffective Class 1C or 3 ADT throughout the initial blanking period of 3 months. Only in case of pre-procedural use of amiodarone, ADT was switched to conventional Class 1C or sotalol.

If the patient was free of ATA at 3 months, as evidenced by symptom evaluation and 24 h of Holter recording, patients were randomly assigned (block randomization technique with centre stratification) to discontinue ADT (ADT OFF group) or continue ADT (ADT ON group) during the 1st year after ablation. In the ADT OFF group, all Class 1C or 3 ADT was discontinued. If beta-blocking agents were given for other indications (hypertension and ischaemic heart disease), they were continued. In the ADT ON group, ADT was continued after verifying for correct dosage according to the European Society of Cardiology (ESC) guidelines on treatment of AF. If not already the case, beta-blocking agents were added to Class 1C ADT.

Patient follow-up

Study visits were performed at randomization (3 months after ablation) and at 6 and 12 months after ablation. Each visit comprised detailed history, physical examination with blood pressure measurement, and a 12-lead electrocardiogram (ECG). Holter monitoring was performed at randomization (24 h), at 6 months (24 h) and at 12 months visits (7 days). At each visit, the patients completed questionnaires regarding quality of life [QOL: Short Form 36 Health Survey (SF-36), v2] and symptoms (AF Symptom Checklist, v3). Patients were encouraged to register arrhythmia-related symptoms and to have an ECG taken during symptoms. In case of long-lasting arrhythmia symptoms, patients were instructed not to change drug treatment and to contact their cardiologist or their local hospital. If a patient experienced arrhythmia symptoms and could not be monitored during an acute episode, additional monitoring (e.g. extra Holter or event monitoring) was performed. All ECGs and Holter monitorings (both scheduled and unscheduled) were reviewed by the treating physician and a blinded study investigator (A.D.). In case of documented ATA, a repeat ablation was recommended.

Primary and secondary outcomes

The prespecified primary endpoint of the trial was any documented ATA (AF, AT, or atrial flutter) lasting >30 s from 3 to 12 months of follow-up (cumulative occurrence). Secondary endpoints included number of repeat ablations and number of unscheduled arrhythmia-related health care provider visits. Other secondary endpoints included ADT-related adverse events and QOL as well as symptom frequency and severity throughout the study.

Statistics

A power calculation was performed prior to the start of the study. To reveal an absolute 20% reduction in an expected recurrence of ATA of 35% after a single PVI procedure OFF ADT, we calculated the need for a minimum of 144 patients (power of 80% and type I error probability of 0.05) to be randomized in the study. Continuous data are reported as means (±SD) or medians [interquartile range (IQR)]. Shapiro–Wilks test was used to test for normality. Comparisons between groups were performed using the Student’s t-test or Mann–Whitney U test where appropriate. Categorical data were reported as proportions or percentages and comparisons between groups were performed using the χ² test or the Fisher’s exact test where appropriate. Comparisons over time were performed using the Wilcoxon matched-pairs signed-rank test.

Analyses were performed according to the modified intention-to-treat principle. The Kaplan–Meier survival curves with log-rank statistic test were used to compare time to first documented recurrence (there were no competing events). Censored values were used in the Kaplan–Meier survival curve, taking into account patients who were lost to follow-up or died.

Binary logistic regression model was used to assess possible predictors for recurrence during the 1st year. Prespecified relevant clinical characteristics were tested first in a univariate and then in a multivariable-adjusted model.
Comparison of QOL was performed using the Mann–Whitney U test. The physical component score (PCS) and mental component score (MCS) based on SF-36v2 were calculated using factor scoring coefficients from Farivar et al. The symptom frequency score (SFS) and symptom severity score (SSS) based on the AF Symptom Checklist were scored according to the guideline provided by Bubien et al.

Patients who were lost to follow-up or died before completing the 12 months of follow-up visit were excluded from the analysis of the primary endpoint.

Statistical tests were two tailed, and P-value < 0.05 was considered statistically significant. Analyses were conducted using SPSS version 24.0 (IBM Corp., Armonk, NY, USA).

Results

Population

A total of 170 consecutive patients underwent CF-guided PVI for ADT-resistant paroxysmal AF at the participating hospitals and were screened for enrolment at 3 months after ablation (Figure 1); 7 had discontinued ADT at hospital discharge and 3 patients experienced ATA at 3 months. The remaining patients (n = 160) were approached, of which 7 were not eligible for other reasons. A total of 153 were randomized; 76 patients to the ADT OFF group and 77 to the ADT ON group. There were no significant differences in clinical characteristics (Table 1) or procedural characteristics (Table 2).

Patients were followed up for a median of 376 (IQR 362–391) days after the ablation procedure. In each group, three patients were lost to follow-up (1 in the ADT OFF group died due to skull fracture, while the remaining 5 patients did not attend their scheduled visits) (Figure 1).

Therapy after randomization and at follow-up

Figure 2 outlines the type of ADT in the two study groups before ablation (previously ineffective ADT), during the blanking period (standard of care), and at 6 and 12 months after catheter ablation. The proportion of patients taking Class 1C and 3 ADT was similar when comparing the ADT OFF and ON groups. Except for the use of amiodarone (n = 10 in the ADT off group and n = 9 in the ADT on group vs. n = 0 after ablation), the use of Class 1C and 3 ADT was also similar when comparing ADT before ablation vs. ADT throughout the blanking period in both groups.

During the course of the study, 6 patients assigned to the ADT ON group, all free of ATA, abandoned ADT due to ADT-related adverse events. At 12 months, 89.2% of patients were taking ADT (61% Class 1C, 28% sotalol). Median daily dosage of flecainide, propafenone, and sotalol were 200 mg (125–200), 600 mg (525–600), and 160 mg (160–160 mg), respectively. ADT dosage was similar to the dosage used before ablation (previously ineffective ADT) and blanking period.
Throughout the study, four patients assigned to the ADT OFF group (5%) restarted taking previously ineffective ADT. Symptoms with subsequent documentation of AF were the reason for restarting ADT in two of these patients. Beta-blocking drugs were used in nearly one-third of the patients.

**Primary efficacy endpoint**

In total, 147 patients completed the last patient visit and were available for analysis of the primary endpoint (Figure 3). In eight patients, additional monitoring was performed: four patients received 7 days of continuous Holter monitor, and two patients received a patient-activated event recorder. At 12 months of follow-up, 2 of 74 (2.7%) patients in the ADT ON group and 16 of 73 (21.9%) patients in the ADT OFF group had a documented ATA recurrence (P < 0.001). Time to first documented incidence of ATA was plotted using the Kaplan–Meier method (Figure 4). Of the 18 patients with ATA, 15 had AF as their documented event (13/16, 81% in the ADT OFF group and 2/2, 100% in the ADT ON group).

Of interest, analysis treating lost to follow-up and death as competing events (Table 4) showed that at 12 months of follow-up, 5 of 77 (6.5%) patients in the ADT ON group and 19 of 76 (25.0%) patients in the OFF group had a documented ATA recurrence (P = 0.002).

**Primary safety endpoint: antiarrhythmic drug therapy-related adverse events and drug discontinuation**

In the ADT ON group, 13 patients experienced one of the following ADT-related adverse events: fatigue (n = 6), exercise intolerance (n = 6), and impotence (n = 1). In 6 of 13 patients, all free of ATA, adverse events led to discontinuation of ADT.

**Repeat ablation and number of unscheduled arrhythmia-related health care visits**

Continued ADT was associated with a significantly lower rate of repeat ablation (1.4% vs. 19.2%, hazard ratio (HR) = 0.053, 95% confidence interval (CI) 0.007–0.399; P < 0.01) and unscheduled arrhythmia-related health care visits (2.7% vs. 20.5%, HR = 0.055, 95% CI 0.007–0.410; P < 0.01).

**Quality of life and symptoms**

There were no statistically significant differences in PHS (Figure 5A), MHS (Figure 5B), SFS (Figure 5C), or SSS (Figure 5D) between the ADT OFF and ADT ON group, not at 3 months, 6 months, or 12 months. In both groups, QOL and symptom scores were stable over time.

**Subgroup analyses**

Overall, the ADT ON group was associated with a significantly lower rate of ATA recurrence (HR = 0.111, 95% CI 0.026–0.485; P < 0.01) (Figure 6). This trend was present for subgroups of age, gender, left atrial diameter, and CHA2DS2-VASc [cardiac failure, hypertension, age ≥ 75 (doubled), diabetes, stroke (doubled)-vascular disease, age 65–74 and sex category (female)] score. For age, gender, and CHA2DS2-VASc score, no significant interaction was seen with the treatment effect of continuing ADT. The magnitude of reduction in ATA seemed to be greater among patients with smaller atria than among patients with larger atria (P for interaction = 0.023).

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**Table 1** Clinical characteristics

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>ADT OFF (n = 76)</th>
<th>ADT ON (n = 77)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (IQR)</td>
<td>62 (54–70)</td>
<td>63 (56–63)</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>55 (72)</td>
<td>57 (74)</td>
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<tr>
<td>BMI (kg/m²), mean ± SD</td>
<td>27.3 ± 4</td>
<td>27.3 ± 4</td>
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<tr>
<td>Paroxysmal AF, n (%)</td>
<td>76 (100)</td>
<td>77 (100)</td>
</tr>
<tr>
<td>Prior cardioversion, n (%)</td>
<td>18 (24)</td>
<td>14 (18)</td>
</tr>
<tr>
<td>AF history (months), median (IQR)</td>
<td>26 (12–81)</td>
<td>26 (7–84)</td>
</tr>
<tr>
<td>Left atrial diameter (mm), mean ± SD</td>
<td>41 ± 5</td>
<td>41 ± 5</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>33 (43)</td>
<td>23 (30)</td>
</tr>
<tr>
<td>Structural heart disease, n (%)</td>
<td>7 (9)</td>
<td>7 (9)</td>
</tr>
<tr>
<td>Previous TIA/stroke, n (%)</td>
<td>6 (8)</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>3 (4)</td>
<td>6 (8)</td>
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<tr>
<td>History of typical atrial flutter, n (%)</td>
<td>8 (11)</td>
<td>16 (21)</td>
</tr>
<tr>
<td>CHA2DS2-VASc score &gt;2, n (%)</td>
<td>15 (20)</td>
<td>12 (16)</td>
</tr>
<tr>
<td>At least 1 AF episode, n (%)</td>
<td>15 (20)</td>
<td>16 (21)</td>
</tr>
<tr>
<td>Per 3 months</td>
<td>15 (20)</td>
<td>16 (21)</td>
</tr>
<tr>
<td>Per month</td>
<td>18 (24)</td>
<td>17 (22)</td>
</tr>
<tr>
<td>Per week</td>
<td>33 (43)</td>
<td>37 (48)</td>
</tr>
<tr>
<td>Per day</td>
<td>10 (13)</td>
<td>7 (9)</td>
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ADT, antiarrhythmic drug therapy; AF, atrial fibrillation; BMI, body mass index; IQR, interquartile range; SD, standard deviation; TIA, transient ischaemic attack.

**Table 2** Procedural characteristics

<table>
<thead>
<tr>
<th>Procedural characteristics</th>
<th>ADT OFF (n = 76)</th>
<th>ADT ON (n = 77)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Procedural time (min), mean ± SD</td>
<td>151 ± 47</td>
<td>162 ± 59</td>
<td>0.33</td>
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<tr>
<td>General anaesthesia during procedure, n (%)</td>
<td>48 (63)</td>
<td>50 (65)</td>
<td>0.82</td>
</tr>
<tr>
<td>Major complications, n (%)</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0.50</td>
</tr>
<tr>
<td>Minor complications, n (%)</td>
<td>1 (1)</td>
<td>3 (4)</td>
<td>0.62</td>
</tr>
</tbody>
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ADT, antiarrhythmic drug therapy.
Figure 2 Use of antiarrhythmic drug therapy before ablation, during blanking, and at 6 and 12 months after pulmonary vein isolation. See text for explanation.

Figure 3 Bar charts illustrating the difference in any documented atrial tachyarrhythmia lasting >30 s from 3 months to 12 months of follow-up after pulmonary vein isolation between the antiarrhythmic drug therapy OFF and ON groups (cumulative occurrence).

Figure 4 The Kaplan–Meier curves depicting time to first recurrence of documented atrial tachyarrhythmia lasting >30 s in the antiarrhythmic drug therapy ON group and the OFF group. Randomization was performed at 3 months post-pulmonary vein isolation (dotted line).
Discussion

Main findings

In this multicentre randomized Pulmonary vein isolation With vs. without continued antiarrhythmic Drug trEatment in subjects with Recurrent Atrial Fibrillation (POWDER-AF) trial, we observed that in arrhythmia-free patients still on ADT at the end of 3 months of post-ablation blanking period, continued use of previously ineffective ADT significantly reduces the recurrence of ATA (≈20% absolute risk reduction corresponding to a number needed to treat of 6) in the 1st year after PVI. Combining previously ineffective ADT and a single PVI can lead to arrhythmia-free survival of >95% in patients with paroxysmal AF. Of interest, despite a notable difference in the primary endpoint, there were no statistical differences in the QOL or SSS in the two treatment arms. This highlights that recurrent AT/AF after ablation does not eliminate improvement in QOL or symptom relief.

Anti-arrhythmic drug therapy after catheter ablation for atrial fibrillation

In daily practice and in ablation trials, a short regimen of ADT is commonly prescribed to prevent early recurrence during the first 3 months post-ablation.11–14 Also in a large national administrative claims database, Noseworthy et al.15 observed that ADT was associated with fewer readmissions within the first 90 days post-ablation. In dedicated trials reporting on arrhythmia-free survival after ablation, ADT is typically stopped after this blanking period.2–4 In real

<table>
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<th>Table 3</th>
<th>Primary and competing events</th>
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<tr>
<td></td>
<td>ADT OFF (n = 76)</td>
</tr>
<tr>
<td>ATA recurrences, n</td>
<td>16</td>
</tr>
<tr>
<td>Lost to follow-up, n</td>
<td>2</td>
</tr>
<tr>
<td>Death, n</td>
<td>1</td>
</tr>
<tr>
<td>Total, n (%)</td>
<td>19 (25)</td>
</tr>
</tbody>
</table>

ADT, antiarrhythmic drug therapy; ATA, atrial tachyarrhythmia.

Figure 5

Quality of life scores and symptoms scores at 3, 6, and 12 months after ablation in the antiarrhythmic drug therapy OFF and ON groups: physical health score (A), mental health score (B), symptoms frequency score (C), and symptoms severity score (D). See text for further explanation.
life, ADT is often continued beyond the blanking period.\textsuperscript{5–7} In the Belgian KCE report, up to 60% of patients were prescribed ADT throughout a period of 2 years after catheter ablation for AF.\textsuperscript{5} In the ESC–European Heart Rhythm Association (EHRA) AF ablation long-term registry, 46% of patients were taking ADT at their visit at 12 months.\textsuperscript{6} Similarly, in the German ablation registry, 32.1% of patients were taking ADT at 1 year.\textsuperscript{7} It is unclear to what extent patients had restarted ADT (after recurrence) or had simply continued ADT after ablation.

The relatively high proportion of patients continuing ADT after ablation might be due to the fact that in real life, in contrast with studies, there is often no true incentive for stopping ADT. The patient and/or physician might decide to continue well-tolerated ADT, because it is perceived that stopping ADT might lead to complaints of extrasystoles or sinus tachycardia or might end the optimal status of finally being arrhythmia-free after many years.

Explaining the synergy between antiarrhythmic drug therapy and ablation

This POWDER-AF trial provides direct proof that ADT, despite being ineffective before ablation, is effective in reducing recurrence after ablation. As shown by prior studies, this effect is not mediated via a "sinus rhythm begets sinus rhythm" pathophysiology.\textsuperscript{12–14} As paroxysmal AF is mostly trigger initiated, three different mechanisms can be put forward to explain this observation. First, despite recent improvements, long-term durability of PVI remains imperfect and residual conduction gaps might develop over time.\textsuperscript{15} ADT can block residual conduction over ablated linear lesions,\textsuperscript{17} and therefore previously ineffective ADT might prevent AF by blocking residual conduction gaps at the left atrium (LA)–pulmonary vein (PV) junction. A report by Verma et al.\textsuperscript{18}, showing that patients with significant conduction delay between reconnected PVs and LA (residual gap) are likely to maintain sinus rhythm on ADT, is in line with this hypothesis. Second, not all triggers for paroxysmal AF are located within the PVs as evidenced by the status of isolated veins in patients undergoing repeat ablation because of arrhythmia recurrence.\textsuperscript{19} It is conceivable that previously ineffective ADT can suppress residual non-PV triggers. Third, initiation of AF is a stochastic phenomenon relying on the dynamic interplay between the trigger and the underlying atrial substrate.\textsuperscript{20} As such, by influencing the electrophysiological properties of the atrial substrate, ADT might reduce the likelihood of initiation of AF in the presence of a trigger.

Given the above mechanisms, one can hypothesize that ADT needs to be continued to maintain its adjunctive benefit and that the magnitude of benefit of ADT will depend on the type of ablation and patient. Although the effect is expected to be similar after balloon-based PVI, most likely, the incremental benefit will be smaller using strategies associated with a higher incidence of durable PVI.\textsuperscript{21} On the other hand, we surmise that the adjuvant effect might increase after longer time of follow-up, because the incidence of gaps is expected to increase over time,\textsuperscript{22} whereas the ADT efficacy is expected to remain constant.\textsuperscript{23} Finally, further studies are needed to determine the incremental benefit of ADT after ablation of patients with...
persistent AF, or more advanced structural heart disease (more non-PV triggers).

Implications for clinical practice
Since the introduction of catheter ablation, the discussion has focused on the choice between ablation on the one hand or ADT on the other hand, with ensuing pro–con debates on ‘outmoded’ ADT. In the meantime, consensus grew to perform catheter ablation after failure of ADT and to report outcome without ADT. A single percutaneous PVI procedure in paroxysmal AF is commonly associated with a 70% arrhythmia-free survival.

Our data, showing that combining ADT and catheter ablation is an effective and safe treatment strategy, might change the way we are discussing outcome among each other as professionals but also towards patients. Combining ADT and ablation—referred to as hybrid rhythm control in the new ESC guidelines for the management of AF—might be more applicable than generally expected. First, in most patients and in line with our study, ADT are well tolerated. Second, in patients without overt structural heart disease, ADT is commonly safe. A 2006 meta-analysis, comparing the clinical efficacy and safety of ADT and radiofrequency ablation in the treatment of AF, showed that adverse events for ADT were common but not severe. Finally, in some patients, the desire to be free of symptoms largely outweighs the desire to stop ADT. In the ESC–EHR A AF ablation long-term registry, the reason for ablation of paroxysmal AF was symptoms in 93% of the procedures, whereas only 30.6% procedures were performed out of a desire for drug-free lifestyle.

This POWDER-AF study does not imply that ADT should be universally continued after ablation, neither does it speak against the use of repeat ablation, an effective and straightforward strategy to treat recurrence of AF after PVI. Rather, it may lead to further optimization of management of paroxysmal AF patients. In those patients free of AF paroxysms after PVI while taking ADT, it is important to communicate that stopping ADT after PVI might be associated with recurrence. Conversely, in patients with post-PVI recurrence while OFF ADT, restarting or starting ADT might be an alternative to repeat ablation. ADT might be preferred by the patient or physician if ADT is well tolerated or if no repeat ablation is desired. Finally, as long as there is no well-defined ablation strategy in patients with recurrent AF despite isolated veins, ADT might be the sole effective strategy for these patients.

Implications for future research
Our data imply that any trial or registry reporting on arrhythmia-free survival after PVI should provide detailed information on the proportion of patients taking ADT to be able to estimate the efficacy of ablation.

On the other hand, our data also imply that arrhythmia-free survival on ADT is a clinically relevant research endpoint. Therefore, we support the new consensus document acknowledging that arrhythmia-free survival on ADT is a valid study endpoint.

Limitations
The amount of monitoring was relatively small, selective, and physician/investigator driven. Because both physician and patients were not blinded to the study arm, this could build bias into the study. No continuous ECG monitoring was performed. Follow-up was relatively short, and the results pertain to a relatively selected population of patients devoid of advanced structural heart disease. By nature of the protocol, only patients with well-tolerated ADT were selected. This recruitment bias might have influenced the results on QOL. Finally, due to the trial design, no data on QOL before ablation were available.

Conclusion
Continuation of previously ineffective ADT beyond the blanking period significantly reduces the recurrence of ATA in the 1st year post-PVI.

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Conflict of interest: none declared.

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