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Recurrence of arrhythmia following short-term oral **AMIO**darone after **CAT**heter ablation for atrial fibrillation: a double-blind, randomized, placebo-controlled study

The AMIO-CAT trial

Stine Darkner, Xu Chen, Jim Hansen, Steen Pehrson, Arne Johannessen, Jonas Bille Nielsen, Jesper Hastrup Svendsen.

Rigshospitalet and Gentofte Hospital, Copenhagen University Hospital, Copenhagen, Denmark.

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Disclosures

- No conflicts of interest

Background

- Atrial arrhythmias are common following atrial fibrillation (AF) ablation
- Effect of preventing early arrhythmias with AADs following ablation is not clear
- ”AF begets AF”
- Amiodarone is considered the most effective AAD for rhythm control of AF

Hypothesis

Short-term use of amiodarone to prevent early arrhythmias following ablation for AF can reduce later recurrence

AMIO-CAT trial design

- 2-centre study
- Placebo-controlled
- Double-blind
- Randomized 1:1
- Stratified according to:
  - type of AF (paroxysmal/persistent)
  - history of previous AF ablation
  - ablation centre

Intervention (1)

Ablation procedure

- Radiofrequency ablation
- Ablation endpoint: Pulmonary vein isolation by wide antral circumferential ablation
- Linear or CFAEs ablation was left to the discretion of the operator – conservative strategy
- Each patient underwent one ablation procedure during the study

Intervention (2)

Study medication regimen

- 8 weeks oral **amiodarone** vs. matched **placebo**
  - week 1-2 → 800 mg daily (initiated the night of the ablation)
  - week 3-4 → 400 mg daily
  - week 5-8 → 200 mg daily

Other AADs were discontinued prior to ablation

Follow-up

- Clinical visits: 1, 3, and 6 months (ECG, blood samples etc.)
- 3-day Holter: before ablation, 8 weeks, and 6 months
- Additional symptom driven ECG-monitorings

Endpoints

Primary endpoint

- Any documented atrial tachyarrhythmia (AF, atrial flutter or atrial tachycardia) > 30 seconds from 3 to 6-months follow-up (blanking period of 3 months)

Secondary endpoints

- AF related hospitalizations within the blanking period
- Cardioversions within the blanking period
- Quality of life
- Adverse events/safety

Sample size

- 80 % power, type I error probability of 0.05
- Expected recurrence: 40% after a single ablation procedure
- 50 % reduction in recurrence rate at 6-month follow-up
- => minimum of 182 patients to complete the study

Eligibility

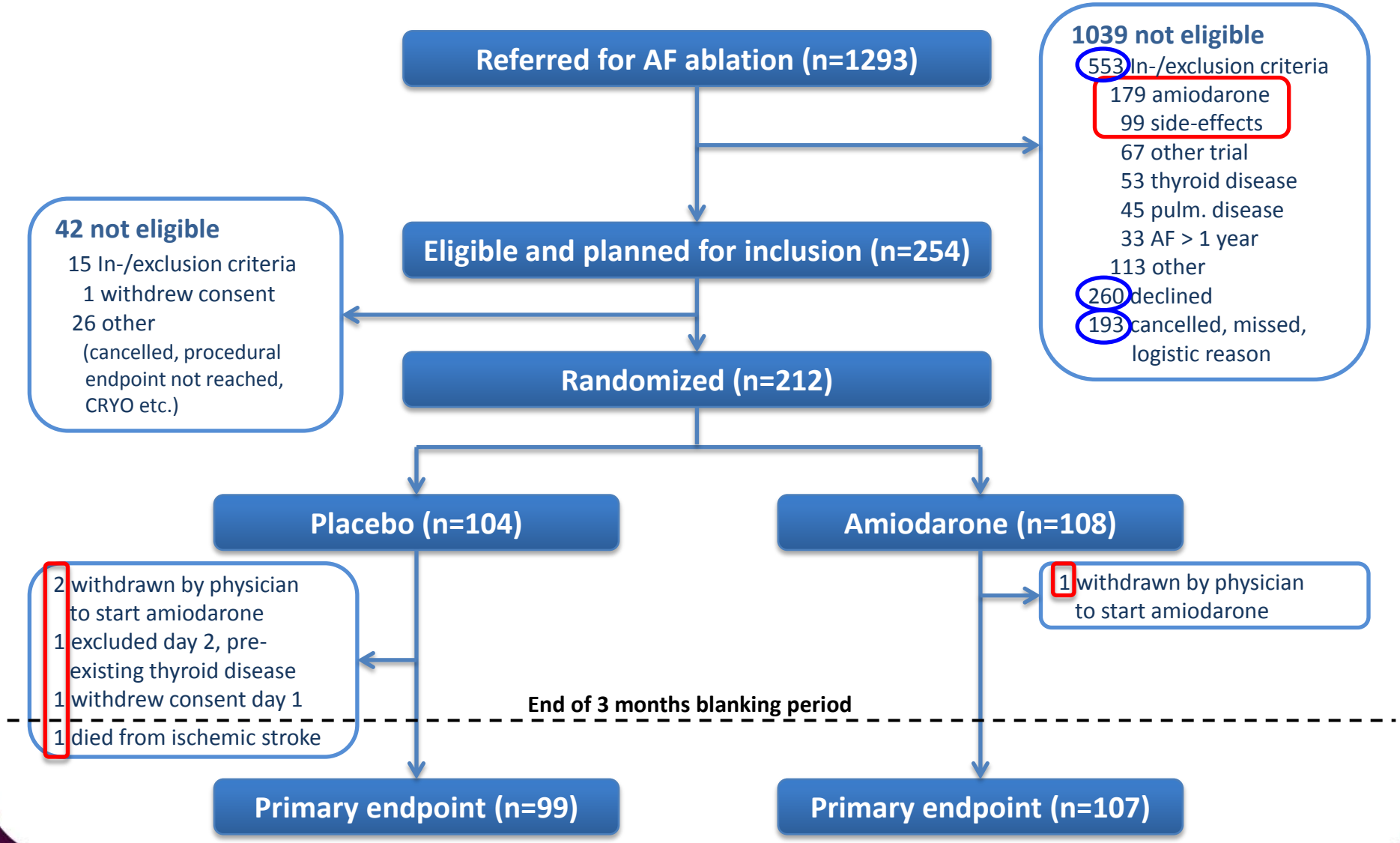
Inclusion criteria

- Planned ablation for paroxysmal or persistent AF

Exclusion criteria

- Age < 18
- Contraindications to or previous side-effects to amiodarone
- Amiodarone within 3 months prior to ablation
- Sustained AF > 1 year
- Severe heart failure (LVEF > 35% or NYHA III-VI)
- Thyroid disease or severe pulmonary disease

Patient flowchart



Baseline characteristics

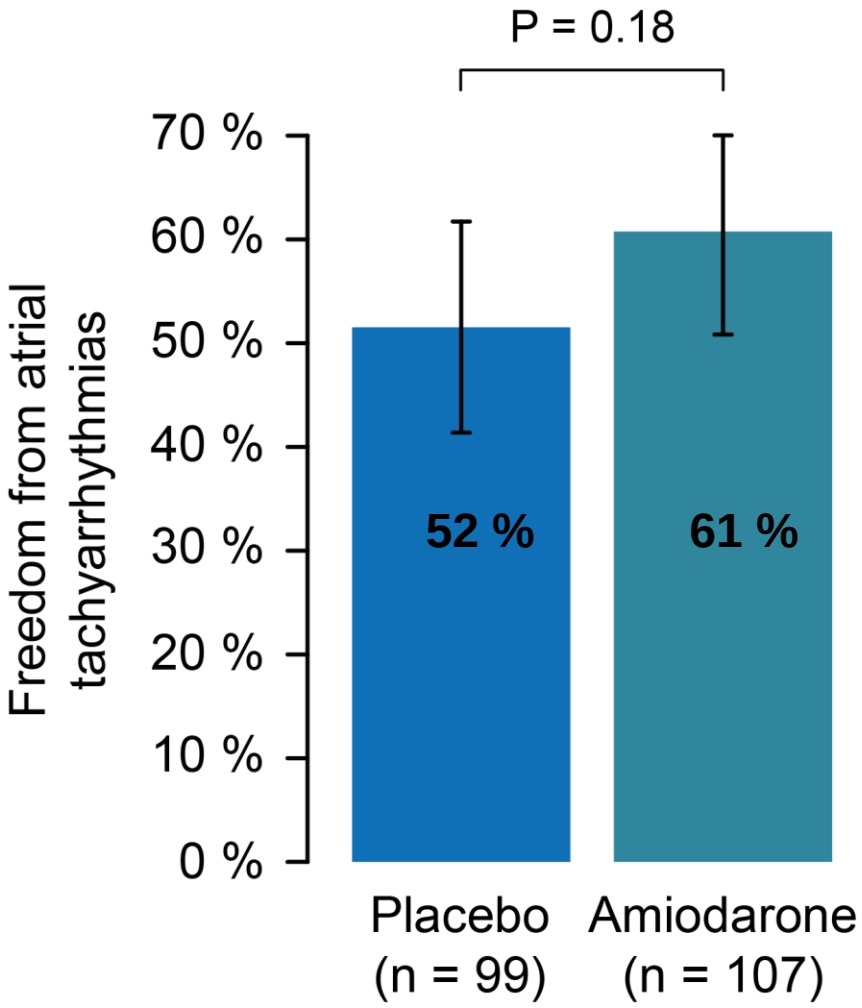
Characteristic	Placebo (n= 104)	Amiodarone (n= 108)	P-value
Age (years)	61 [53;66]	62 [55;66]	0.57
Female gender	15 (14)	21 (19)	0.33
Body-mass index (kg/m2)	26.8 ± 4.3	26.6 ± 4.5	0.99
AF duration, months	76 ± 65	78 ± 78	0.85
Previous AADs (class IC or III)	1.1 ± 0.8	1.2 ± 0.8	0.86
History of previous AF ablation	29 (28)	32 (30)	0.78
History of persistent AF	51 (49)	54 (50)	0.89
Centre 1	60 (58)	64 (59)	0.82
Echocardiographic parameters:			
Left ventricular ejection fraction (%)	50 ± 8	51 ± 9	0.87
Left atrial volume index (ml/m2)	35 ± 10	35 ± 11	0.68
Comorbidities:			
Hypertension	44 (42)	40 (37)	0.43
Coronary artery disease	8 (8)	6 (6)	0.53
Previous TIA/Stroke	7 (7)	6 (6)	0.72
Diabetes	8 (8)	10 (9)	0.68
History of typical atrial flutter	16 (15)	13 (12)	0.48
Sleep apnoea	2 (2)	2 (2)	1.00

Ablation procedural characteristics

Characteristic	Placebo (n= 104)	Amiodarone (n= 108)	P-value
Procedural time (min)	159 ± 56	166 ± 65	0.45
Fluoroscopy time (min)	7 [4;16]	8 [4;20]	0.64
Radiofrequency time (min)	36 ± 18	35 ± 16	0.75
Pulmonary vein isolation, only	72 (69)	81 (75)	0.35
Roof line	19 (18)	13 (12)	0.21
Mitral isthmus linear ablation	1 (1)	2 (2)	0.58
CFAEs ablation	23 (22)	18 (17)	0.32
Superior vena cava isolation	1 (1)	0 (0)	0.31
Cavotricuspid isthmus conduction block	7 (7)	8 (7)	0.85
Cardioversion (electrical or medical)	42 (40)	43 (40)	0.93

Primary endpoint

Freedom from AF/AT at 6-month follow-up



Completed final Holter

Off AADs

- except 1 patient (amiodarone group) unwilling to stop amiodarone initiated during Blanking period

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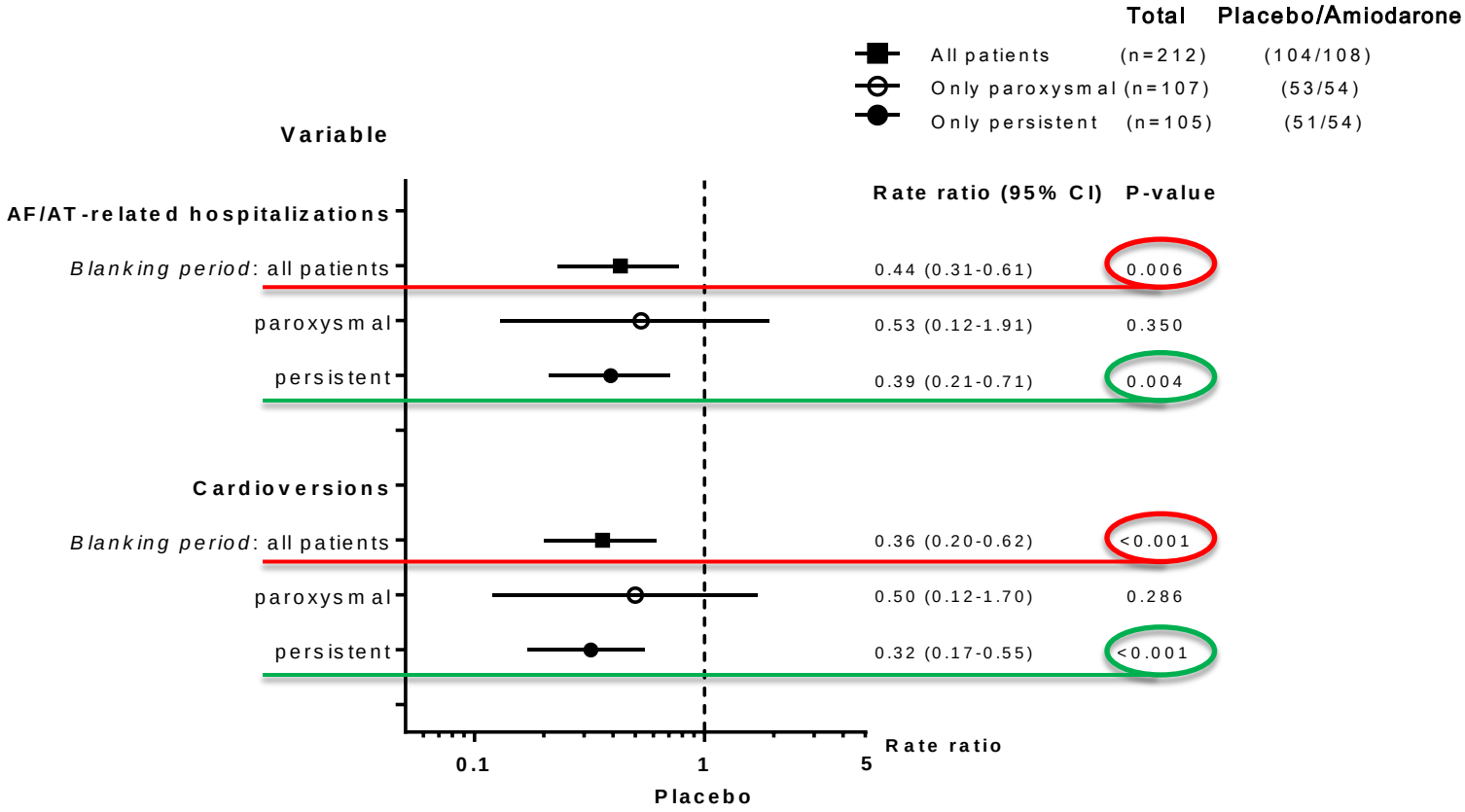
Secondary endpoints

AF/AT related hospitalizations and cardioversions within the blanking period



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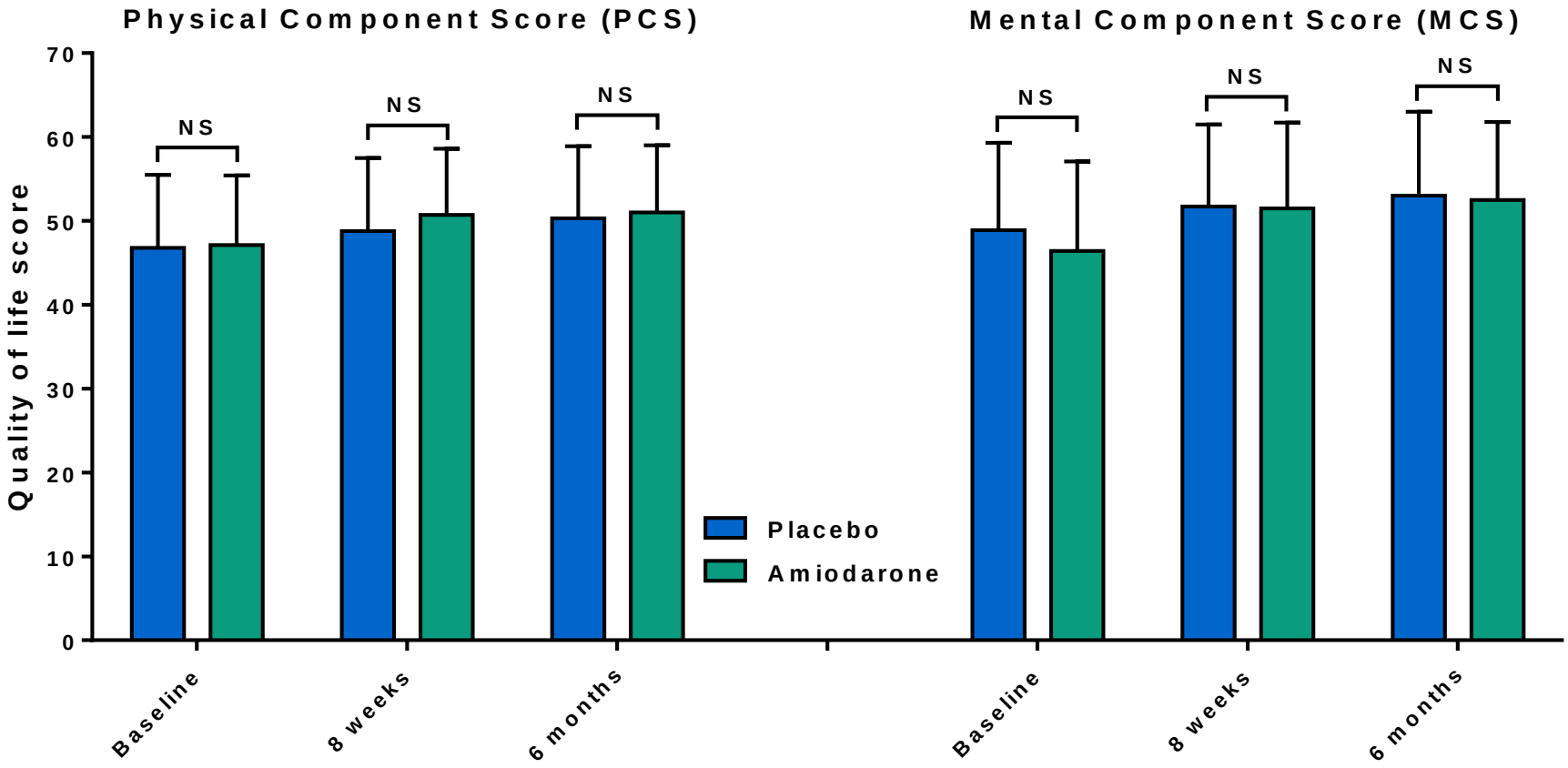
Adverse events

	Placebo (n= 104)	Amiodarone (n= 108)	P-value
Sleep disturbance	1 (1)	16 (15)	<0.001
Gastrointestinal complaints	7 (7)	26 (24)	<0.001
Abnormal thyroid parameters (asymptomatic)	5 (5)	27 (25)	<0.001
- stopped study medication due to abnormality	1	3	NS
Photosensitivity	0 (0)	6 (6)	0.03
Headache	4 (4)	10 (9)	0.13
Tremor of the extremities	1 (0)	4 (4)	0.37
High blood pressure (>150/100 mmHg)	5 (5)	7 (6)	0.60
Chest pains	7 (7)	5 (5)	0.51
Contacted emergency ward due to palpitations	20 (19)	14 (13)	0.21
Dizziness	4 (4)	8 (7)	0.26
Fatigue	3 (3)	2 (2)	0.68

Quality of Life – SF-36



Limitations

- No continuous ECG-monitoring
- Ablation technique between the two ablation centres not entirely uniform, but stratified
- Detection of a smaller reduction in recurrence is limited by our sample size and power calculation
- Relatively selected population
- Relatively short follow-up time

Conclusion

- Short-term amiodarone treatment following ablation did not significantly reduce recurrence of atrial tachyarrhythmias at 6-month follow-up
- Amiodarone significantly reduced arrhythmia related hospitalizations and cardioversions within the blanking period, especially in persistent AF patients
- No difference in serious adverse events, but more transient adverse events in the amiodarone group
- No difference in quality of life

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Recurrence of arrhythmia following short-term oral AMIOdarone after CATheter ablation for atrial fibrillation: a double-blind, randomized, placebo-controlled study (AMIO-CAT trial)

Stine Darkner[1]*, Xu Chen[1], Jim Hansen[2], Steen Pehrson[1], Arne Johannessen[2], Jonas Bille Nielsen[1], and Jesper Hastrup Svendsen[1,3,4]

[1]Department of Cardiology, Rigshospitalet, Copenhagen University Hospital, Section 2013, Blegdamsvej 9, Copenhagen DK-2100, Denmark; [2]Department of Cardiology, Gentofte Hospital, Copenhagen University Hospital, Gentofte, Denmark; [3]The Danish National Research Foundation Centre for Cardiac Arrhythmia, Copenhagen, Denmark; and [4]Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

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Aims Patients undergoing catheter ablation for atrial fibrillation (AF) often experience recurrent arrhythmias within the first few months post-ablation. We aimed to investigate whether short-term use of amiodarone to prevent early arrhythmias following radiofrequency ablation for AF could reduce later recurrence.

Methods and results In a two-centre, randomized, double-blind, placebo-controlled study, we randomized a total of 212 patients undergoing AF ablation. Patients were stratified according to type of AF (paroxysmal/persistent) and history of previous AF ablation and randomly assigned to 8 weeks of oral amiodarone therapy or matched placebo following catheter ablation. Patients were followed for 6 months. Analyses were performed according to the intention-to-treat principle. Of 212 enrolled patients [median age 61 (inter-quartile range 54–66), 83% male, 50% paroxysmal, 29% with history of previous ablation], 206 patients were available for analysis of the primary end-point which was any documented atrial tachyarrhythmia lasting >30 s following a blanking period of 3 months. This was observed in 42/107 (39%) in the amiodarone group vs. 48/99 (48%) in the placebo group ($P = 0.18$). Among the secondary end-points, the amiodarone group showed significantly lower rate of atrial tachyarrhythmia-related hospitalizations [rate ratio = 0.43; 95% confidence interval (CI) = 0.23–0.77, $P = 0.006$] and cardioversions (rate ratio = 0.36; 95% CI = 0.20–0.62, $P = 0.0004$) within the blanking period.

Conclusion Short-term oral amiodarone treatment following ablation for paroxysmal or persistent AF did not significantly reduce recurrence of atrial tachyarrhythmias at the 6-month follow-up, but it more than halved atrial arrhythmia related hospitalization and cardioversion rates during the blanking period.

Keywords Atrial fibrillation • Ablation • Antiarrhythmic drugs