# Supplemental Material

**Table S1. Unadjusted clinical outcomes by antiarrhythic group**

| Outcomes | Amiodarone Events/ 100 pt-yrs (Total Events) | Other AAD Events/ 100 pt-yrs (Total Events) | No AAD Events/ 100 pt-yrs (Total Events) |
|---|---|---|---|
| Efficacy outcomes | | | |
| Stroke or non-CNS embolism | 1.95 (34) | 0.95 (8) | 2.35 (516) |
| Stroke, non-CNS embolism, MI, or vascular death | 4.85 (84) | 3.13 (26) | 5.45 (1186) |
| Stroke | 1.77 (31) | 0.83 (7) | 2.18 (480) |
| Non-CNS embolism | 0.17 (3) | 0.12 (1) | 0.19 (42) |
| MI | 1.59 (28) | 1.32 (11) | 0.99 (220) |
| All-cause death | 4.01 (71) | 2.25 (19) | 4.68 (1043) |
| Vascular death | 2.20 (39) | 1.18 (10) | 3.01 (671) |
| Non-vascular death | 1.81 (32) | 1.07 (9) | 1.67 (372) |
| Cardiac failure | 8.55 (142) | 3.16 (26) | 6.32 (1331) |
| Hospitalization | 11.05 (207) | 11.96 (106) | 10.83 (2548) |
| ED visit | 22.42 (420) | 24.72 (219) | 23.25 (5468) |
| Safety outcomes | | | |
| Major or NMCR bleeding | 14.87 (200) | 13.41 (89) | 14.76 (2545) |
| Major bleeding | 2.87 (43) | 2.59 (19) | 3.59 (690) |
| NMCR bleeding | 12.16 (166) | 11.01 (74) | 11.60 (2028) |

AAD=antiarrhythmic drug; CNS=central nervous system; ED=emergency department; MI=myocardial infarction; NMCR=non-major clinically relevant.

## Appendix: Statistical methods

**Weighting in Cox models.** Because either new start or cessation of AAD therapy can be influenced by patient characteristics or intervening events that can also be related to the outcomes, patients were weighted by the inverse probability of continuing in their therapy group. Weights were calculated as follows. First, the probability of being on, or not being on, an AAD at baseline was found for each patient with a logistic regression model. Baseline predictors were age, sex, race, BMI, systolic and diastolic BP, creatinine clearance, type of AF, time since AF diagnosis, atrial rhythm on baseline electrocardiogram, New York Heart Association class, ejection fraction, CHF, coronary artery disease (CAD), PAD, hypertension, diabetes, prior stroke or TIA, valvular disease, liver disease, COPD, sleep apnea, prior VKA use, prior cardioversion or ablation, and presence of a biventricular pacemaker or implantable cardioverter defibrillator. Missing values were imputed as described in the main paper, within AAD and no-AAD groups. Continuous variables were assessed for the linearity of their relationship with the outcome, and restricted cubic splines used where necessary. Second, the probability of continuing in their baseline group (amiodarone, other AAD, or none) at any given time during follow-up for each patient was derived from a Cox model (one per therapy group) with therapy change as the outcome. Candidate baseline variables were similar to above. Imputed values from the first model were used, and continuous variables assessed again for linearity. In addition, the following 5 candidate time-dependent covariates were included (first incidence of each): hospitalization or ED visit; CAD (coronary artery bypass graft surgery (CABG), percutaneous coronary interventionI, MI, or angina); cardiac procedure (procedure for AF, intracardiac device, or CABG); major or NMCR bleeding, and stroke or TIA. A reduced model for each therapy group was generated using forward stepwise selection. Third, the weights were calculated for each patient at each time point in the study. These derived weights were then applied to the endpoint Cox models with a robust sandwich variance estimator (method of Zhang et al.) (1).

## Appendix references

1. Zhang M, Tsiatis AA, Davidian M, Pieper KS, Mahaffey KW. Inference on treatment effects from a randomized clinical trial in the presence of premature treatment discontinuation: the SYNERGY trial. Biostatistics 2011;12:258-69.