The HOLIDAY (HOw ALcohol InDuces Atrial TachYarrhythmias) Study

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HOLIDAY Study Statistical Analysis

Normally distributed continuous variables are presented as means ± SD and were compared using t-tests, and continuous variables with skewed distributions are presented as medians and interquartile ranges (IQR) and were compared using Wilcoxon rank sum or signed rank tests as appropriate. Categorical variables were compared using chi squared and Fisher's exact tests. The proportion of atrial effective refractory periods that decreased with the infusion, the proportion of conduction times that decreased with the infusion, and the continuous change in each individual atrial effective refractory period and conduction time were assessed. Linear mixed models (LMMs) to estimate average and site-specific effects on pre- to post-infusion changes in AERP and conduction times were performed, with site and baseline values modeled as fixed effects and participants as random effects; analyses were repeated after adjusting for covariates statistically significantly different between alcohol and placebo groups. Heterogeneous relationships between pulmonary vein and non-pulmonary vein sites were assessed using formal tests for interaction. In addition, given evidence of potential effect modification by biological sex (19), tests for interaction by sex on the relationships between randomization assignment and outcomes were performed. Based on a review of repeat AERP measurements in 30 AF patients at 600 ms drive cycle length prior to the trial (yielding an average ERP of 230 ms ± 20 ms), we estimated that 22 patients in each group would provide 90% power to detect a statistically significant one standard deviation difference in the overall AERP using a single interim analysis for efficacy (assessed by an independent Data Safety Monitoring Board) and an overall two-sided α = 0.05. We based power calculations for the secondary analysis on 25 paroxysmal AF patients in whom AF induction occurred in 20%; we therefore estimated that 50 patients in each group would provide 84% power to detect a 30% increase in AF induction (20% versus 50%) with ethanol, again using a single interim analysis for efficacy and an overall two-sided α = 0.05. Analyses were conducted using Stata version 16 (College Station, Texas). Two-sided p values < 0.05 were considered statistically significant.