

CABANA and Castle-AF: What are the Consequences for AF Ablation?

→ NewYork-¬ Presbyterian Queens

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Disclosure

Speaker name: Seth Goldbarg

I have the following potential conflict of interest to report:

Shareholder in a healthcare company (VOLTA Medical)

AF and Heart Failure



- In Framingham Heart Study, 41% of pts with new HF had AF.
- In HF patients, AF appears independently associated with allcause mortality with an OR of 1.4 regardless of systolic function
- **CAMTAF** 2014: Ablation improved LVEF, oxygen consumption and QOL in systolic heart failure pts
- AATAC 2016: Ablation superior to amiodarone in achieving freedom from AF in systolic heart failure/persistent AF. Lower mortality seen in ablation group (not primary endpoint)

Mamas MA et al. Eur J Heart Fail 2009;11:676-83 Hunter RJ et al. Circ Arrhythm Electrophysiol 2014;7:31-8 DiBiase L et al. Circulation 2016;133:1637-44

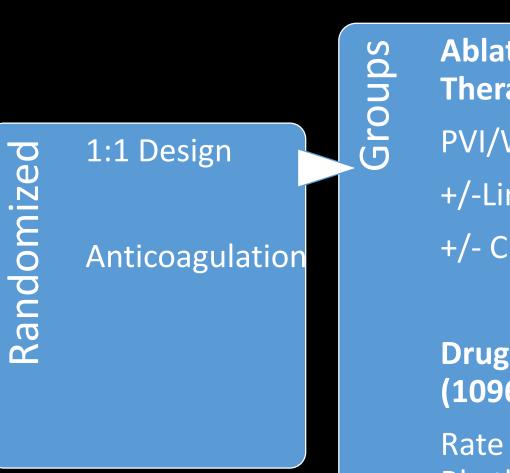


Stated Goal: Compare drug therapy with ablation for patients with new onset or undertreated AF

Primary Endpoint: All-cause mortality, disabling stroke, serious bleeding, or cardiac arrest

126 centers in 10 countries; pts enrolled 2009-2016

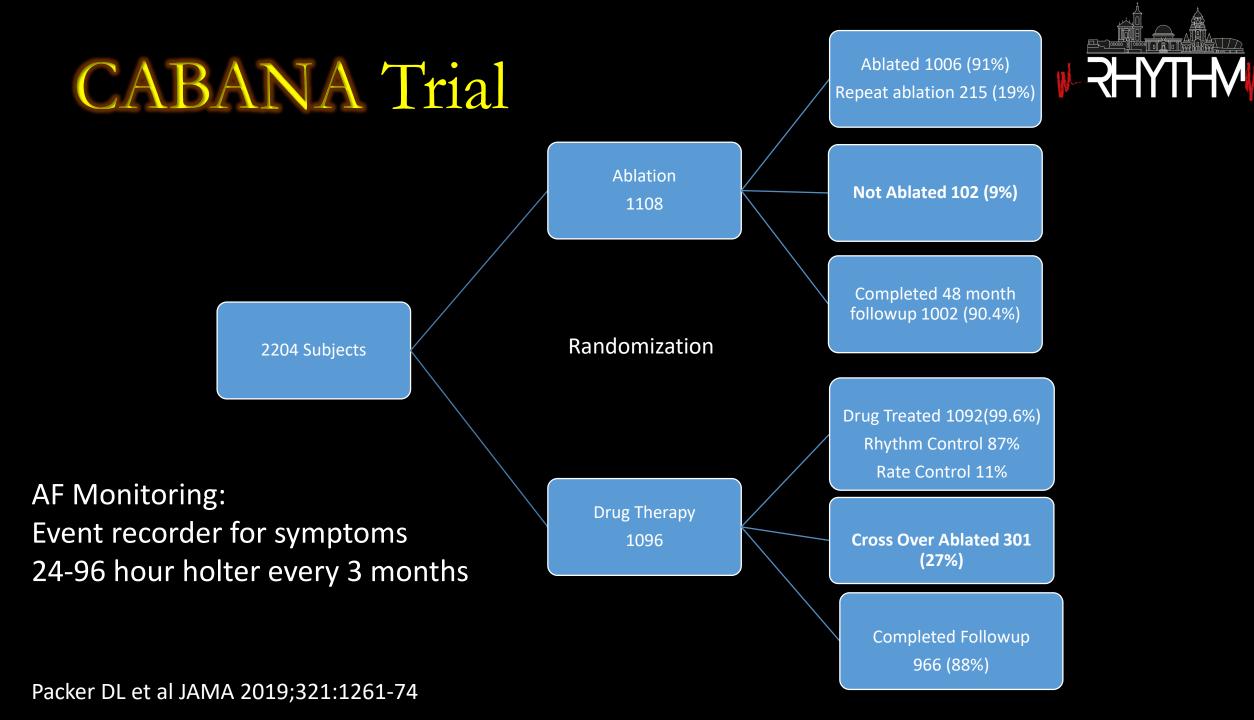
≥65 years of age
 <65 years with ≥1
 CVA/CV risk factor
 Eligible for ablation
 and ≥2 rhythm or
 rate control drugs



Ablation Therapy(1108) PVI/WACA +/-Linear lesions +/- CFAE

Drug Therapy (1096)

Rate Control or Rhythm Control





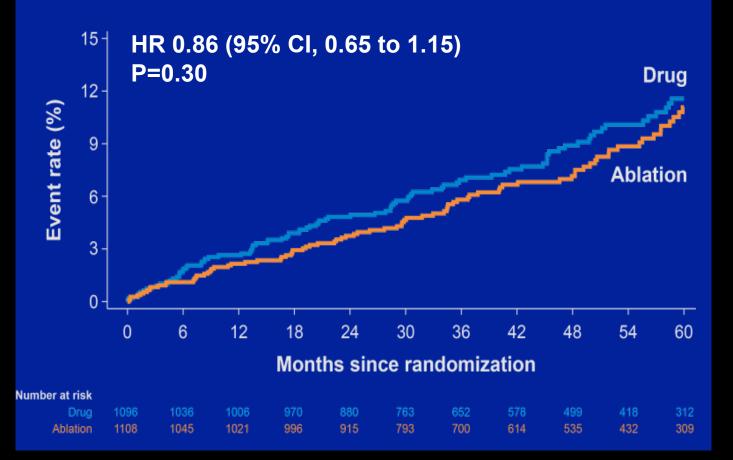
	Ablation (1108)	Drug Therapy (1096)
Age (Median)	68	67
Sex (Female)	37%	37%
Minority	10%	10%
Sleep Apnea	24%	23%
Cardiomyopathy	9%	11%
EF < 35%	5%	4%
CHF Class I Class II/III	48% 14% 34%	49% 12% 37%

	Ablation (1108)	Drug Therapy (1096)
Paroxysmal	43%	44%
Persistent	47%	47%
Longstanding Persistent	10%	9%
Years Since onset of AF	1.1	1.1
BMI	30	30
Prior CVA/TIA	10%	9%
HTN or LVH	83%	85%



CABANA Primary Composite Endpoint

Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest Intention to Treat (ITT)

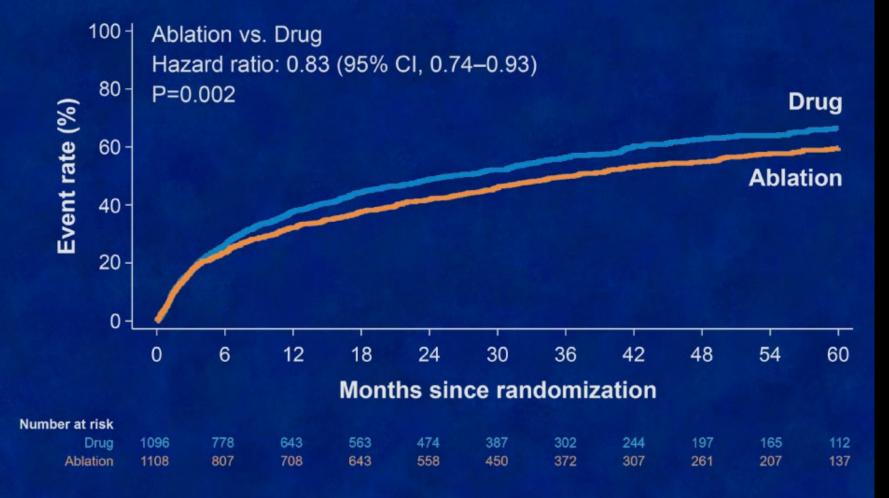


Per Protocol (PP) (Prespecified) HR 0.73 (0.54,0.99)

As Treated (Prespecified) HR 0.67 (0.50,0.89)



All-Cause Mortality or Cardiovascular Hospitalization (ITT)



MAYO CLINIC U Duke Clinical Research Institute NIH National Heart, Lung

CABANA

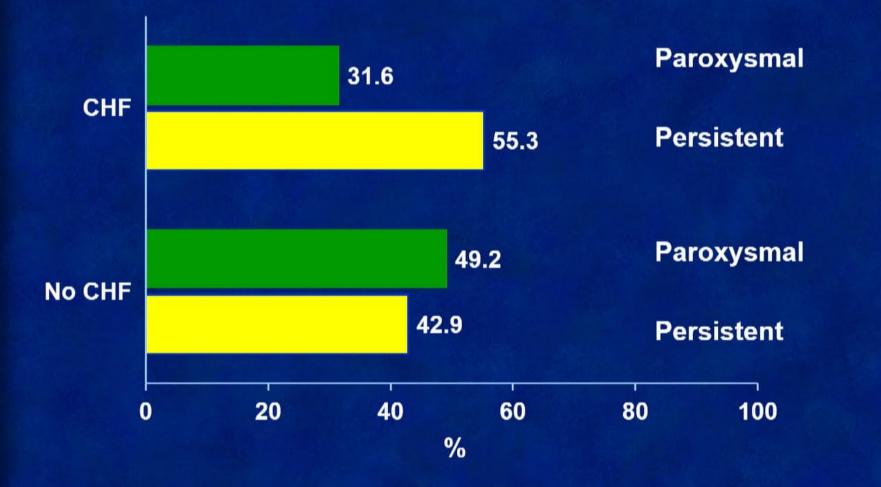


CABANA: Heart Failure Subgroup

- 1422 (65%) No heart failure/class 1 778 (35%) Class 2 or 3
- 571 HF patients with recorded LVEF
 - 451 (79%) EF > 50%
 - 67 (12%) EF 40-49%
 - 53 (9%) EF < 40%
- Class 2 or 3 Heart failure Ablation group: 34%
 Drug Therapy: 37%

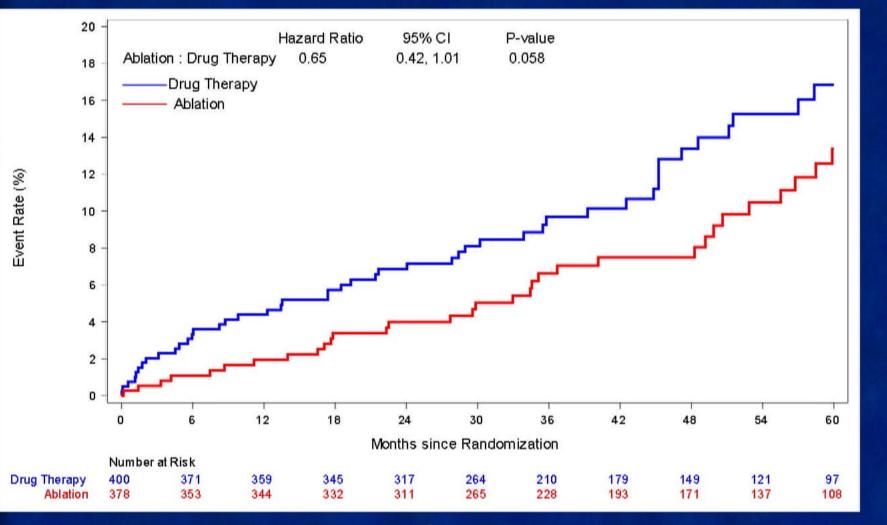
AF Type at Enrollment in CABANA:HF





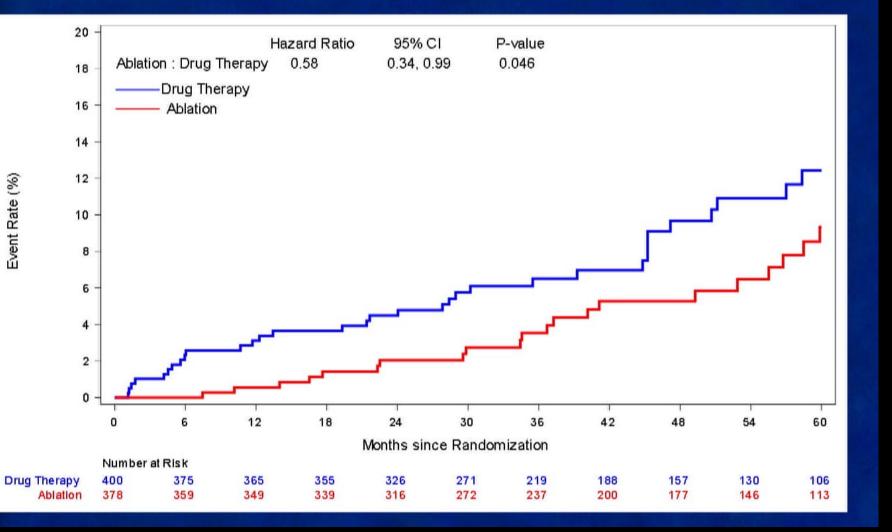
All-Cause Mortality, Disabling Stroke, Serious Bleeding, or Cardiac Arrest (ITT): In HF Patients



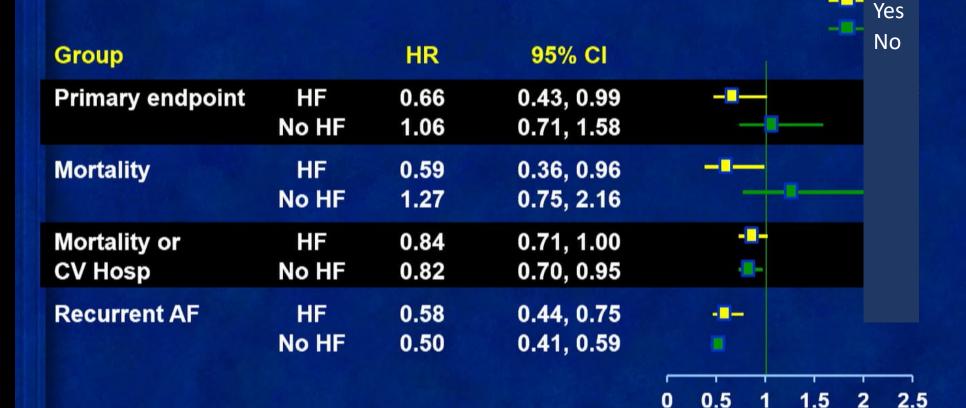


Risk of All-Cause Mortality (ITT): In HF Patients





Clinical Outcomes in CABANA HF by ITT





CHF

Drug better

Ablati

on better

- Adverse event rates were low
- Significant decrease in time to 1st AF recurrence...but 50% had recurrence during the trial
- Future directions
 - Is a sham-control trial feasible/ethical?
 - What about a mortality trial looking at asymptomatic patients?





Stated Goal: Determine if catheter ablation of AF improves outcomes in patients with heart failure

Primary Endpoint: Death or hospitalization from worsening heart failure

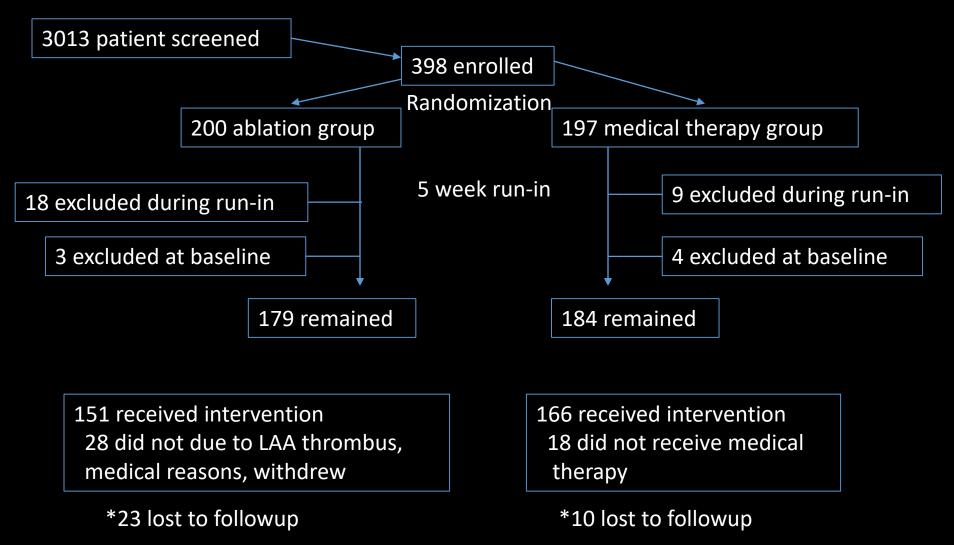
Enrollment January 2008-January 2016



Inclusion Criteria:

- Class II, III, IV heart failure
- LVEF 35% or less
- Symptomatic paroxysmal or persistent AF
- Poor response, side effects, or unwillingness to take antiarrhythmic drugs
- Biotronik ICD with automatic daily remote monitoring
- Ablation: PVI +/- discretionary lesions

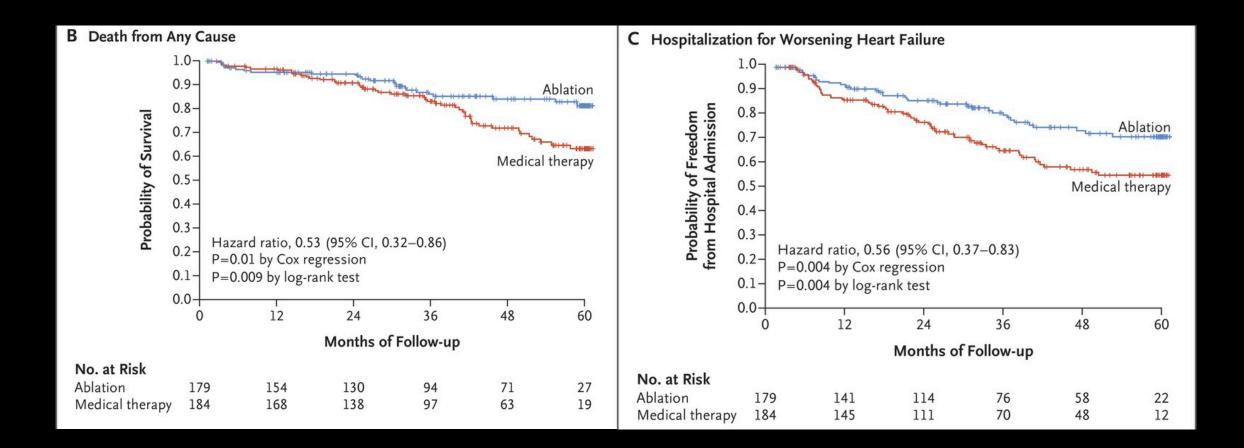






- Mean followup: 38 months
- Average number of procedures in ablation group: 1.3
- 16% did not receive ablation as randomized
- 10% crossover to ablation group
- 30% of medical group pts received antiarrhythmics
- Higher rate of ischemic heart disease and digoxin use in medical therapy group





Marrouche NF et al NEJM 2018; 378:417-427



Age

II III LVEF

> <25% ≥25%

<65 yr ≥65 yr

NYHA functional

Type of atrial Bindlation 17,74 44,04 0.00 0.04(1.01-1.08) 0.00 The of atrial Bindlation 17,74 44,04 0.06 0.06 0.06 0.06 0.06 0.06 0.06 0.07 0.07 0.07 0.07 0.011 0.011 0.011 0.011 0.011 0.011 0.011 0.011 0.011 0.011 0.011 </th <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th>P Value for</th> <th></th> <th></th>								P Value for		
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Conclusions

- The EP community would love to rely on the ontreatment analysis suggesting AF ablation reduces mortality, but the results of CABANA aren't definitive
- AF ablation for HFpEF patients in CABANA was compelling and more data are needed in this population
- Mortality data in HFrEF patients appears strong but the CASTLE-AF had limitations

Ongoing questions:

- Is reducing burden enough?
- How can we improve outcomes through more nuanced patient selection?





Table 2. Primary and Secondary Clinical End Points.*									
End Point	Ablation (N = 179)	Medical Therapy (N=184)	Hazard Ratio (95% Cl)	P Value					
				Cox Regression	Log-Rank Test				
number (percent)									
Primary 'i	51 (28.5)	82 (44.6)	0.62 (0.43-0.87)	0.007	0.006				
Secondary									
Death from any cause	24 (13.4)	46 (25.0)	0.53 (0.32–0.86)	0.01	0.009				
Heart-failure hospitalization	37 (20.7)	66 (35.9)	0.56 (0.37–0.83)	0.004	0.004				
Cardiovascular death	20 (11.2)	41 (22.3)	0.49 (0.29–0.84)	0.009	0.008				
Cardiovascular hospitalization	64 (35.8)	89 (48.4)	0.72 (0.52–0.99)	0.04	0.04				
Hospitalization for any cause	114 (63.7)	122 (66.3)	0.99 (0.77–1.28)	0.96	0.96				
Cerebrovascular accident	5 (2.8)	11 (6.0)	0.46 (0.16–1.33)	0.15	0.14				

* All numbers and percentages represent the total numbers of events and raw event rates after a median follow-up of 37.8 months. Deaths and cerebrovascular accidents were evaluated at baseline and 12 weeks after baseline for hospitalizations in the two groups (the "blanking period"). For Kaplan-Meier estimates at 12, 36, and 60 months, see Table S6 in the Supplementary Appendix.
† The primary end point is a composite of death from any cause or hospitalization for worsening heart failure.