AF Ablasyon Mortalite Çalışmaları

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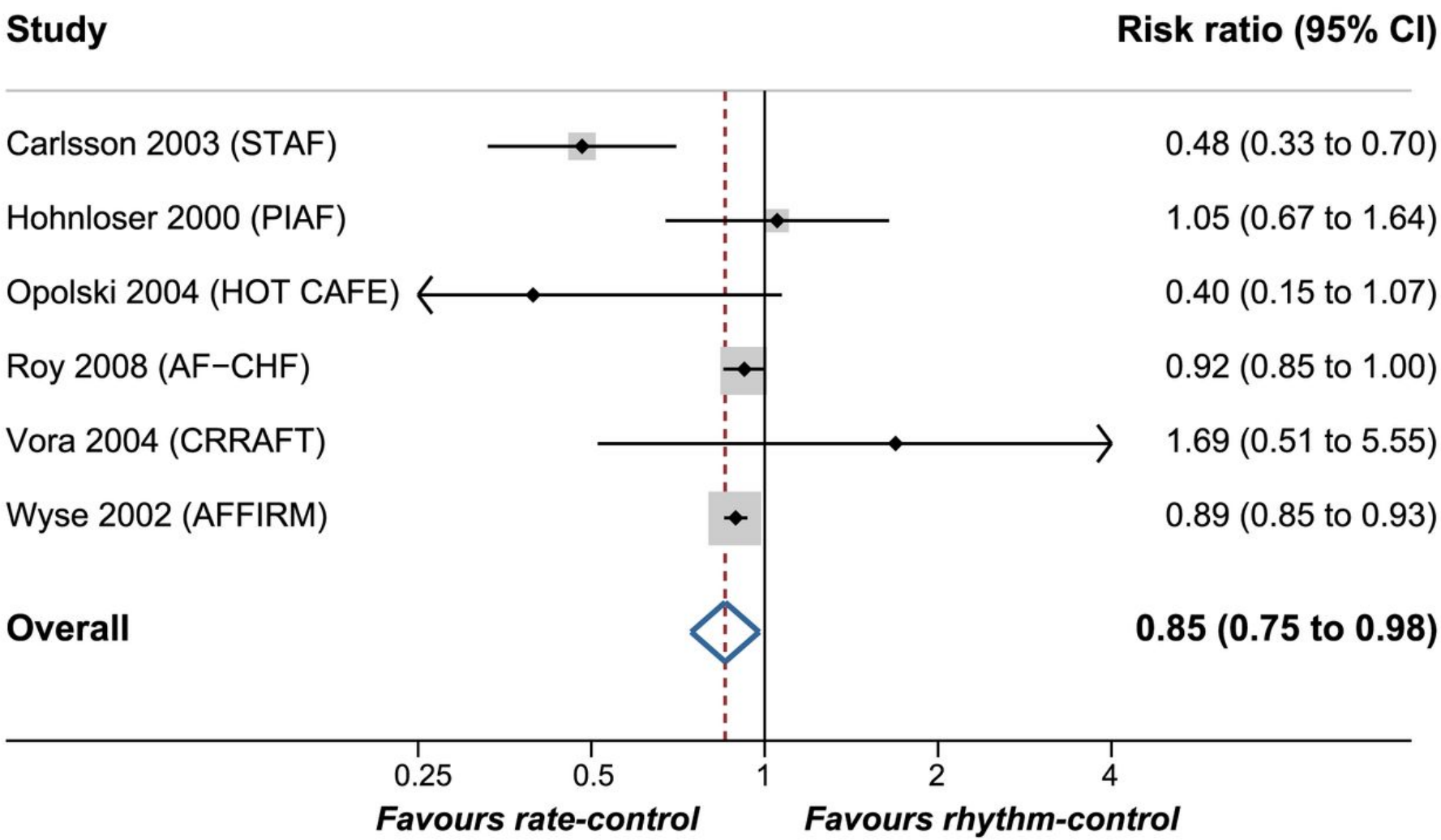
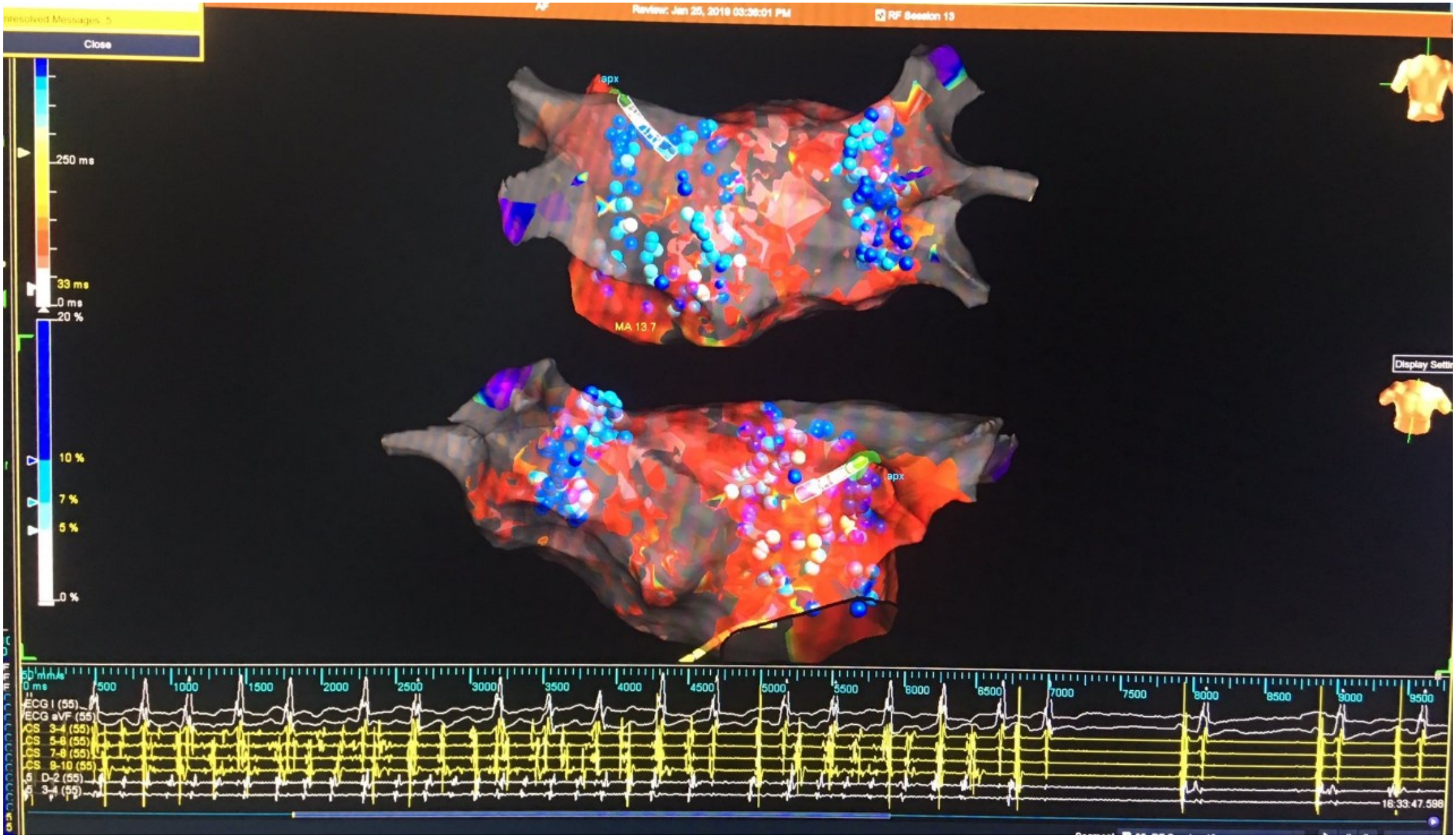
DISTRIBUTION OF INPATIENT & SELECTED OUTPATIENT COSTS FOR TREATING AFIB (Coyne 2006)
Direct Inpatient
$2.93
BILLION
Outpatient
$1.53
BILLION
Drugs
$235
MILLION
Indirect Inpatient
$1.95
BILLION
44%
23%
4%
29%
TOTAL
$6.65
BILLION

Hospitalisation: Rate vs rhythm-control

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Review: Jan 25, 2019 03:36:01 PM
RF Session 13
250 ms
33 ms
0 ms
20 %
10 %
7 %
5 %
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MA 13.7
apx
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ECG I (55)
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CASTLE-AF

Catheter Ablation versus Standard conventional Treatment in patients with LEft ventricular dysfunction and Atrial Fibrillation

The CASTLE-AF trial

Nassir F. Marrouche MD

on behalf the CASTLE AF Investigators

CARMA

CASTLEAF

CASTLE-AF

Primary Endpoint

- *All-cause mortality*
- *Worsening heart failure admissions*

Secondary Endpoints

- Allcause mortality
- Worsening of heart failure admissions
- Cerebrovascular accidents
- Cardiovascular mortality
- Unplanned hospitalization due to cardiovascular reason
- Allcause hospitalization
- Quality of Life: Minnesota Living with Heart Failure and EuroQoL EQ5D
- Exercise tolerance (6 minutes walk test)
- Number of delivered ICD shocks, and ATPs (appropriate/inappropriate)
- LVEF
- Time to first ICD shock, and time to first ATP
- Number of device detected VT/VF
- AF burden: cumulative duration of AF episodes
- AF free interval: time to first AF recurrence after 3 months blanking period post ablation

CARMA

Inclusion Criteria

CASTLE-AF

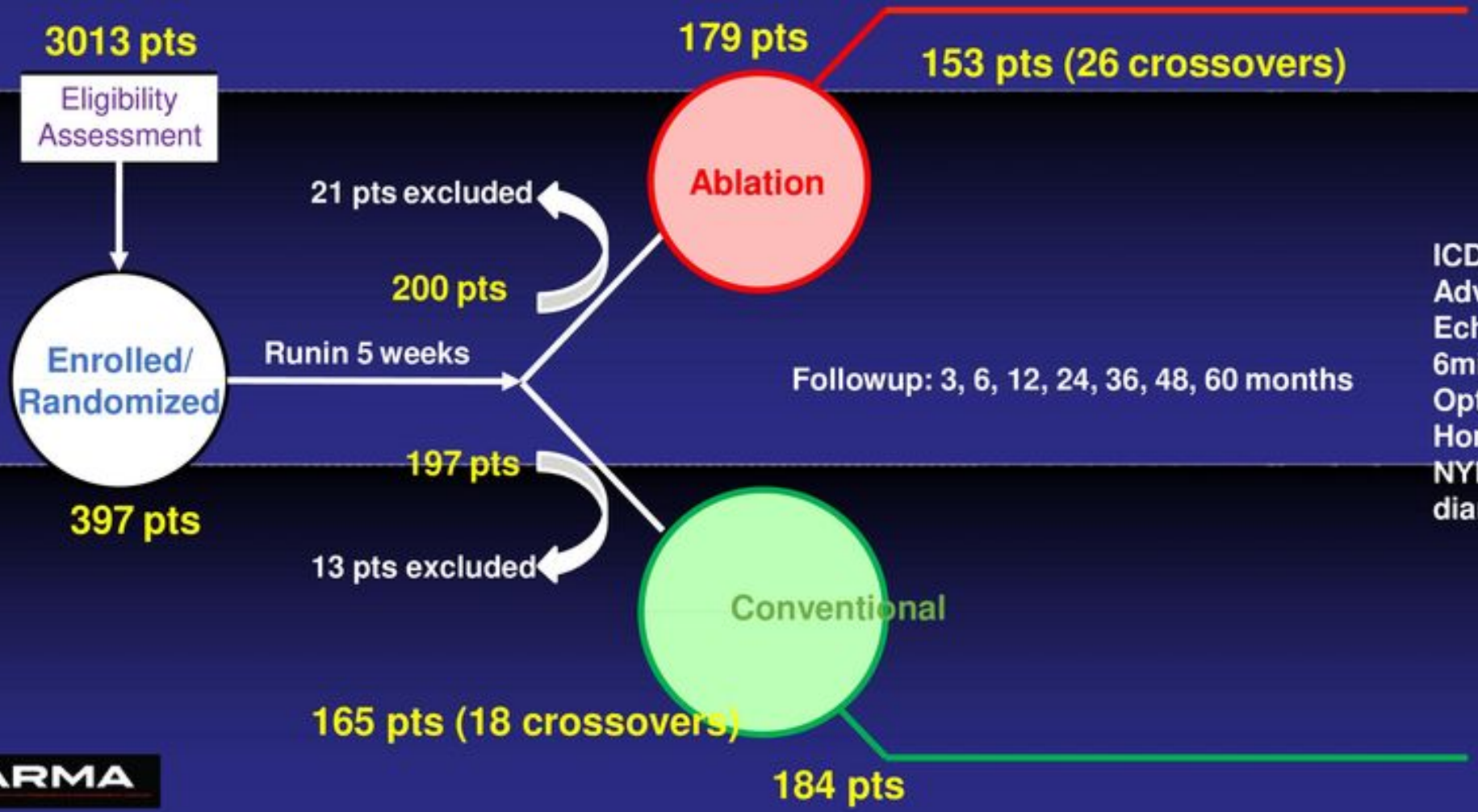
- **Symptomatic paroxysmal or persistent AF**
- **Failure or intolerance to ≥ 1 or unwillingness to take AAD**
- **LVEF ≤ 35%**
- **NYHA class ≥ II**
- **ICD/CRTD with Home Monitoring capabilities already implanted due to primary or secondary prevention**

CARMA

Study Design— CASTLEAF

CASTLE-AF

- Investigator initiated, Prospective, Multicenter (31 sites, 9 countries), Randomized, Controlled



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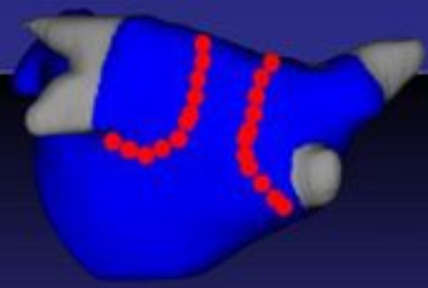
CASTLE AF

Ablation Protocol

CASTLE-AF



- Pulmonary Vein Isolation
- Additional lesions
  - ∅ at discretion of operator
- Repeat ablation after blanking period

CARMA

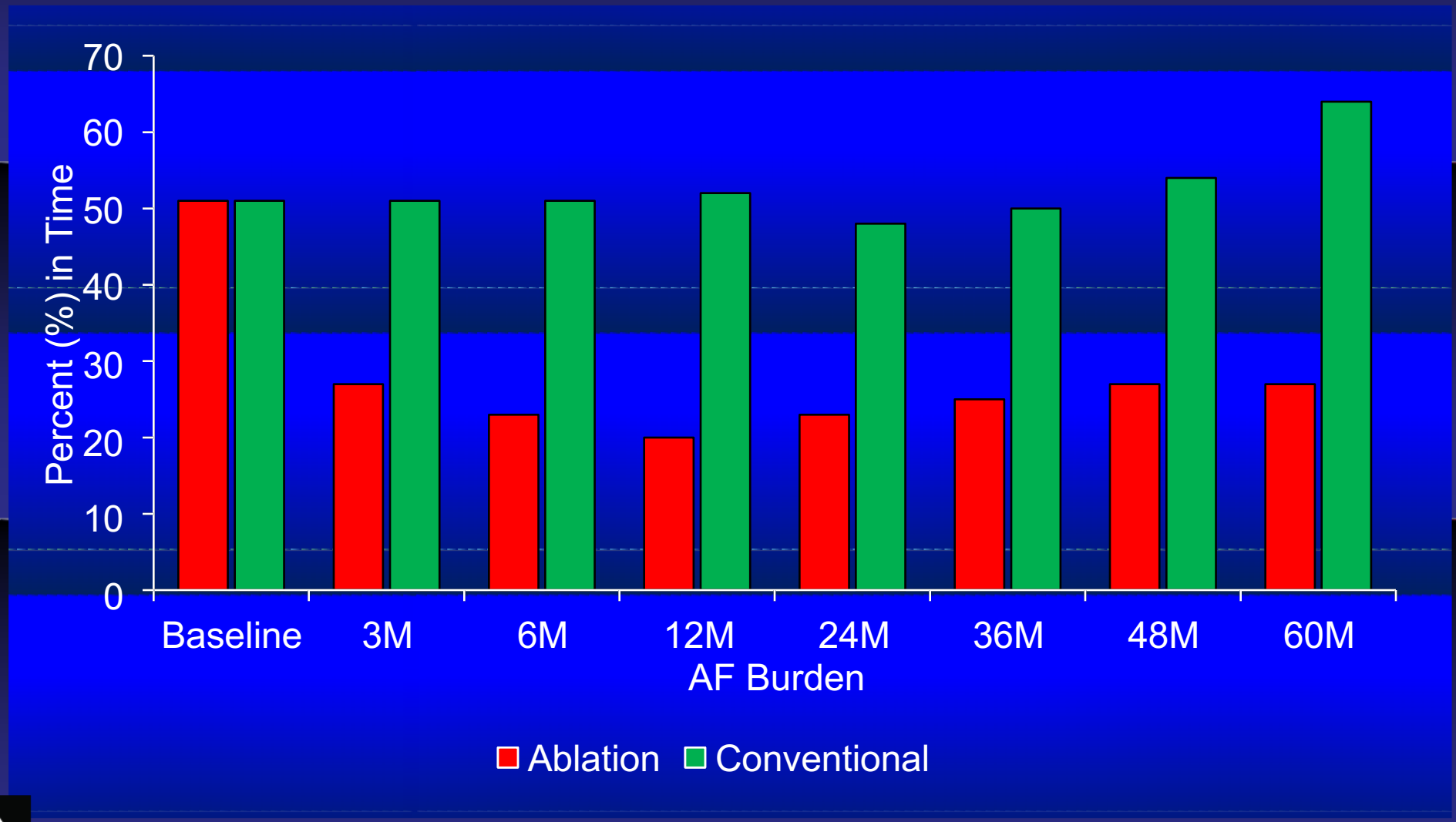
Baseline CharacteristicsCASTLE AF

	Ablation group (179 patients)	Conventional group (184 patients)
Age – years	64 (5671)	64 (5673.5)
New York Heart Association class		
I (%)	11	11
II (%)	58	61
III (%)	29	27
IV (%)	2	1
Left ventricular ejection fraction – %	32.5 (25.038.0)	31.5 (27.037.0)
Current type of atrial fibrillation		
Paroxysmal (%)	30	35
Persistent (%)	70	65
CRTD implanted (%)	27	28
ICD implanted (%)	73	72

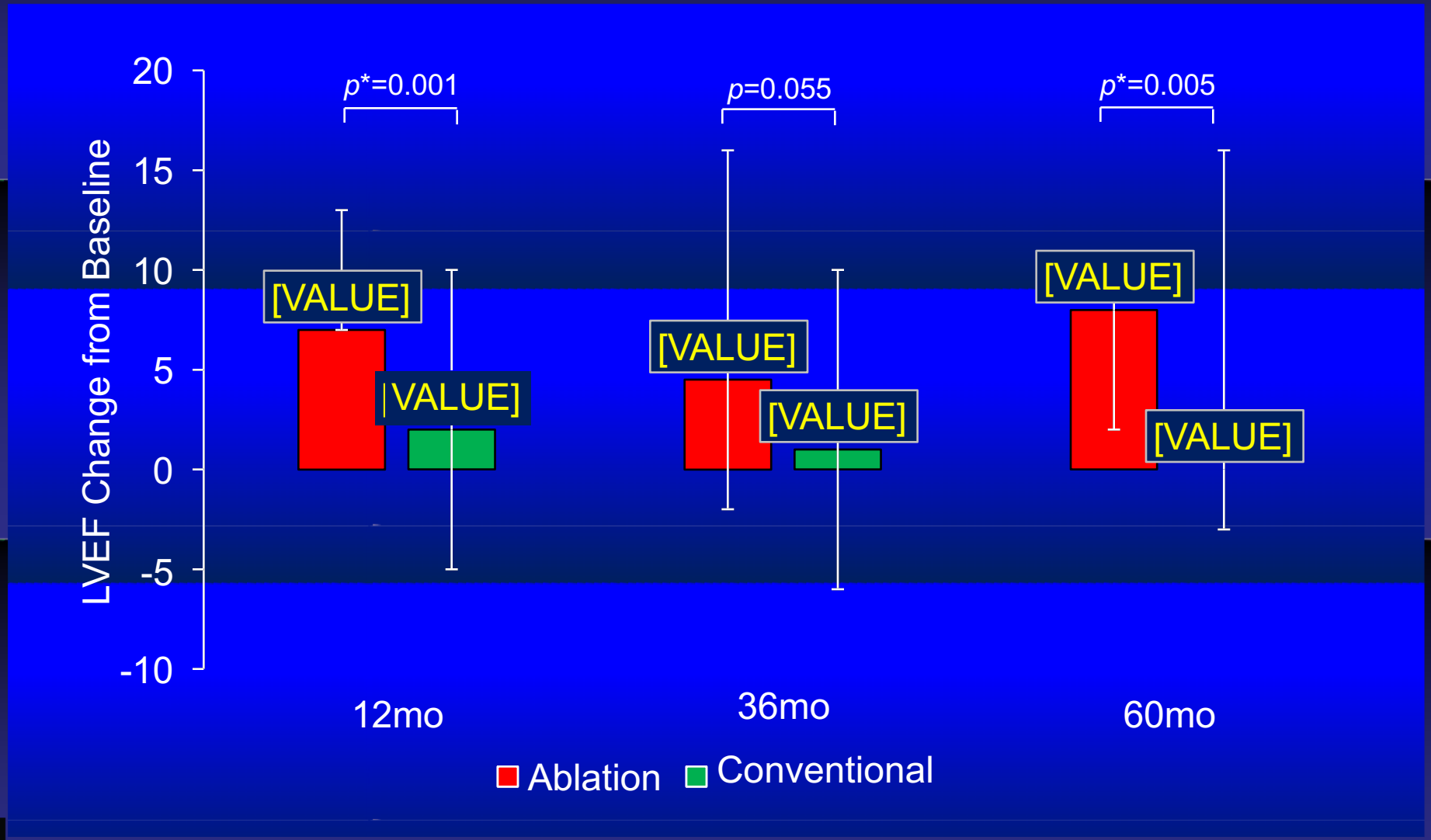
Baseline CharacteristicsCASTLE AF

	Ablation group (179 patients)	Conventional group (184 patients)
ACEinhibitor or ARB – no. (%)	94	91
Betablocker – no. (%)	93	95
Diuretic – no. (%)	93	93
Digitalis – no. (%)	18	31
Oral anticoagulant – no. (%)	93	96
Antiarrhythmic drug – no. (%)	32	30
Amiodarone – no. (%)	97	85

AF Burden Derived from Memory of Implanted Devices



Absolute change in LVEF from baseline



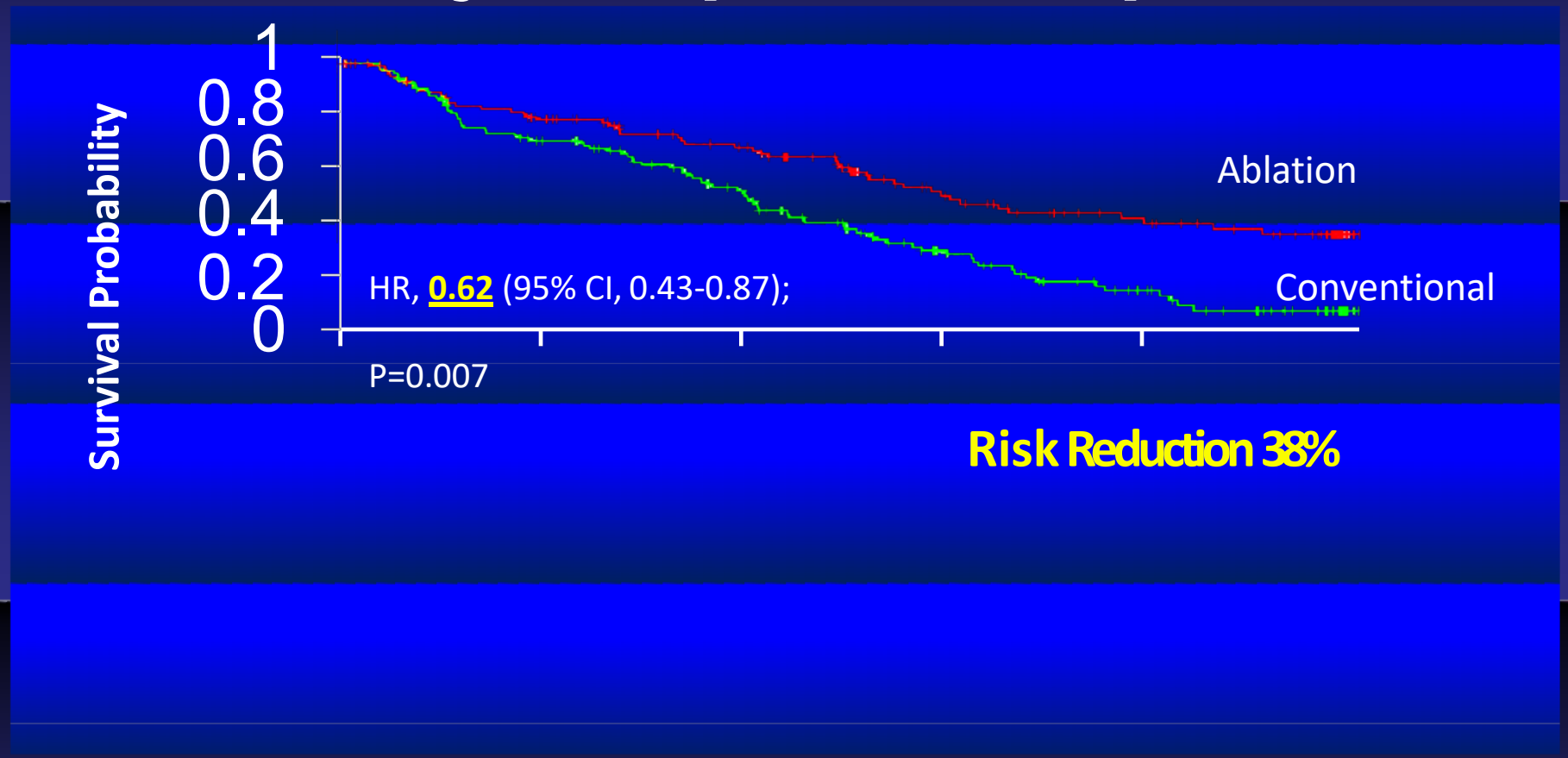
CASTLE-AF

Serious Adverse Events

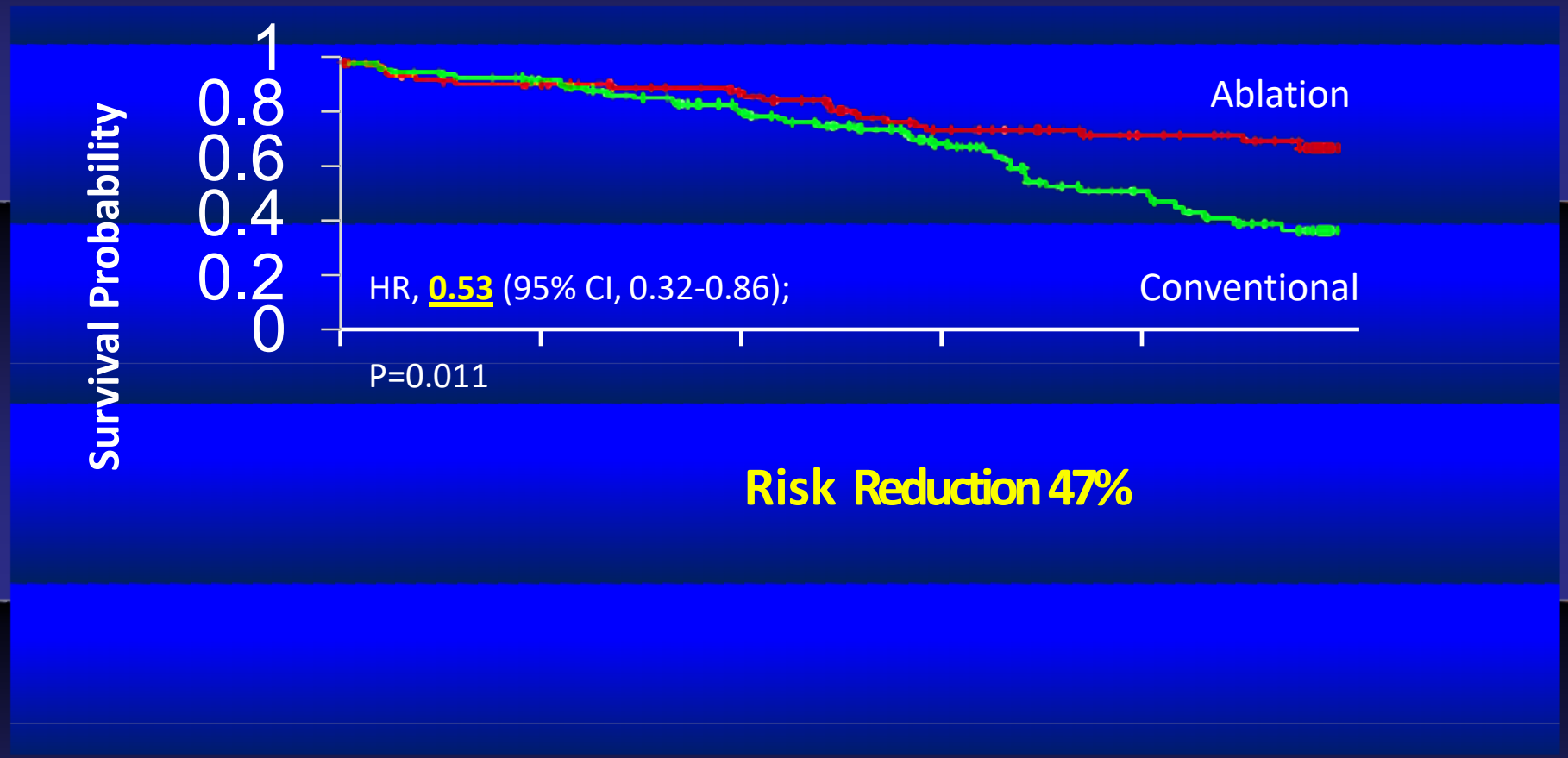
Event	Ablation Group (n=179)	Conventional Group (n=184)
	no. patients with event (%)	no. patients with event (%)
Pericardial effusion (acute)	3 (1.7)	0
Severe bleeding (acute)	3 (1.7)	0
Stroke or TIA	7 (3.9)	12 (6.7)
Pulmonary vein stenosis	1 (0.6)	0
Pneumonia	3 (1.7)	1 (0.5)
Groin infection	1 (0.6)	0
Worsening heart failure	1(0.6)	0

CARMA

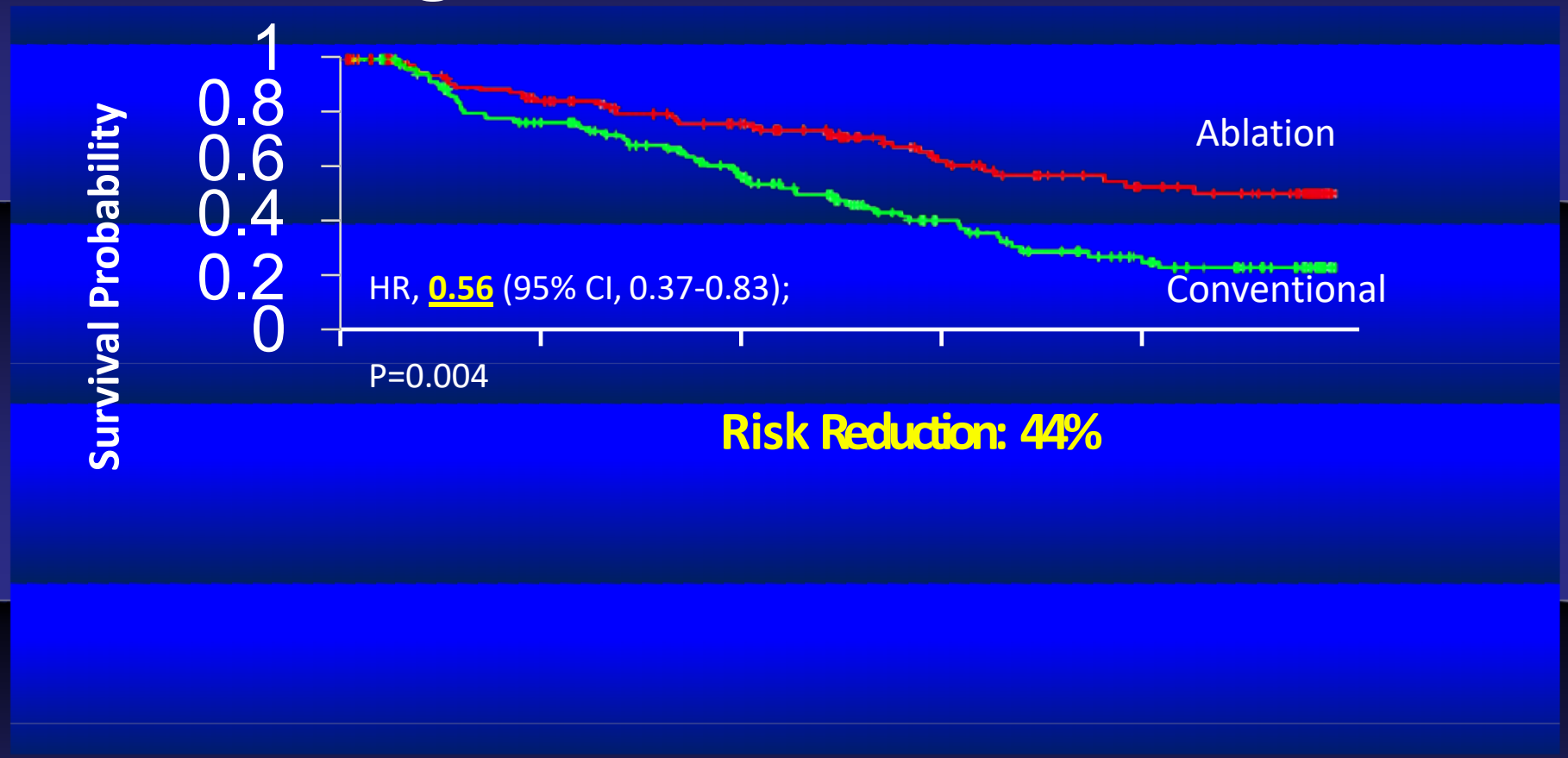
Primary Composite Endpoint



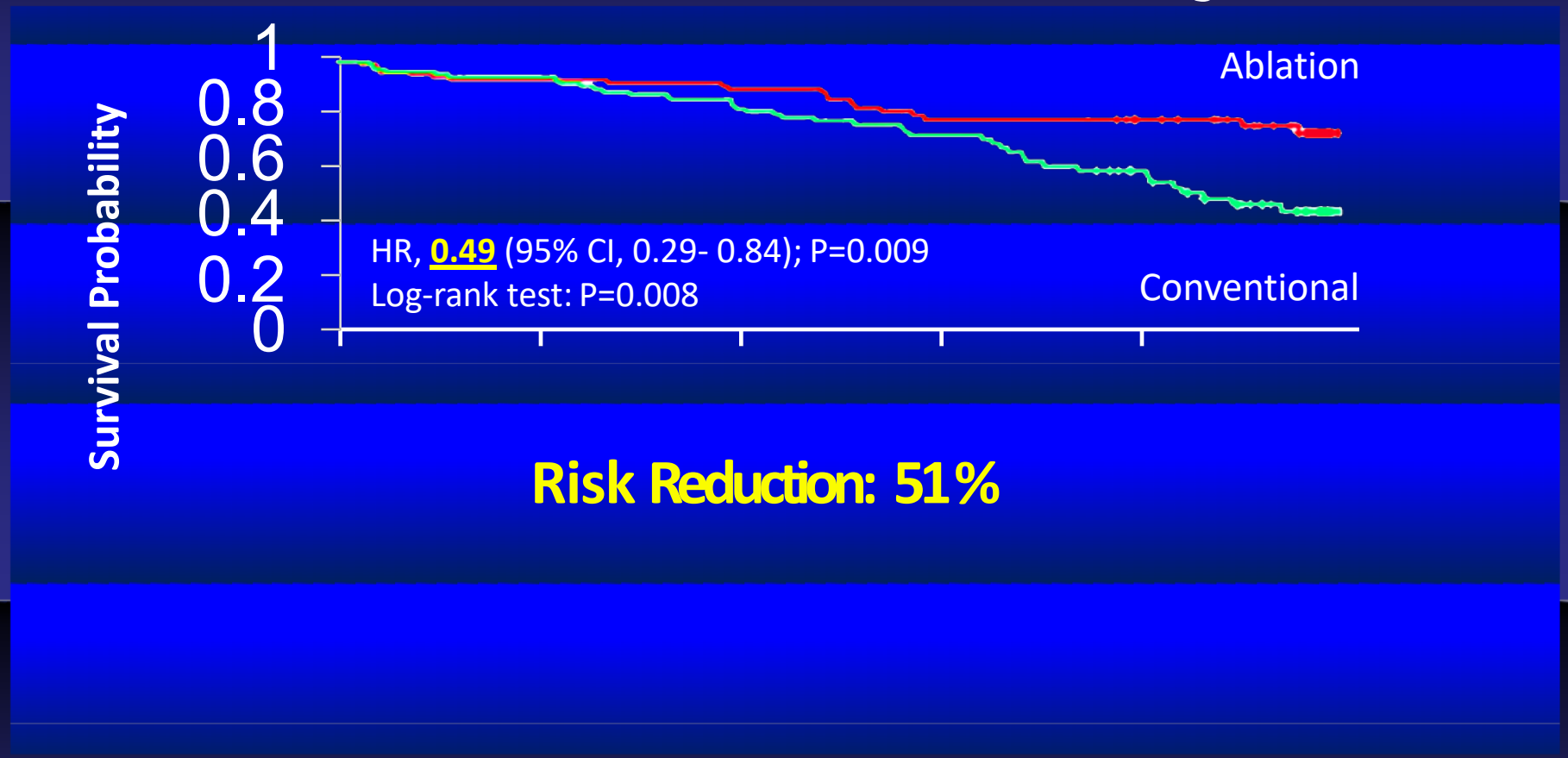
All-cause Mortality



Worsening Heart Failure Admissions

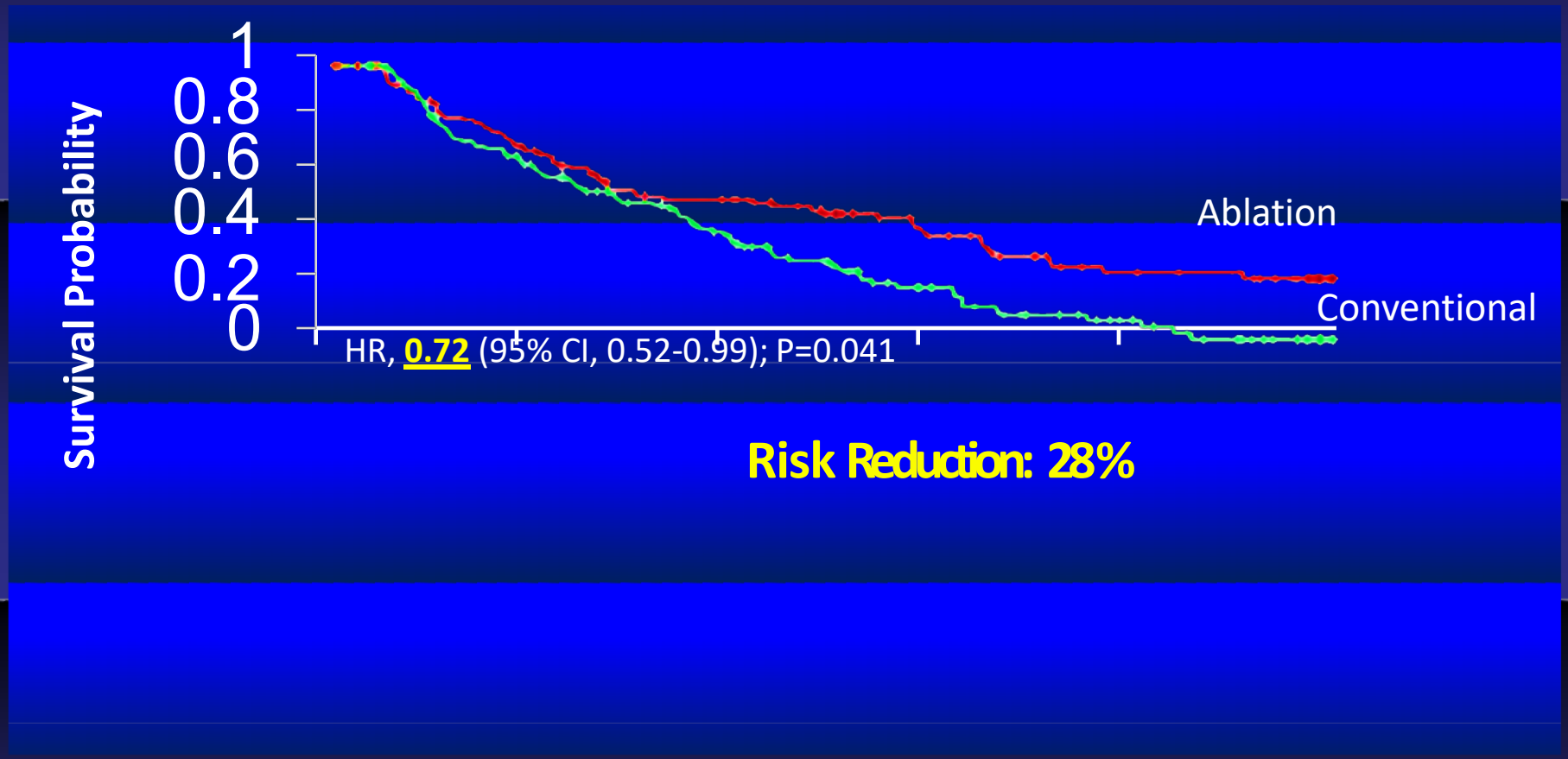


Cardiovascular Mortality



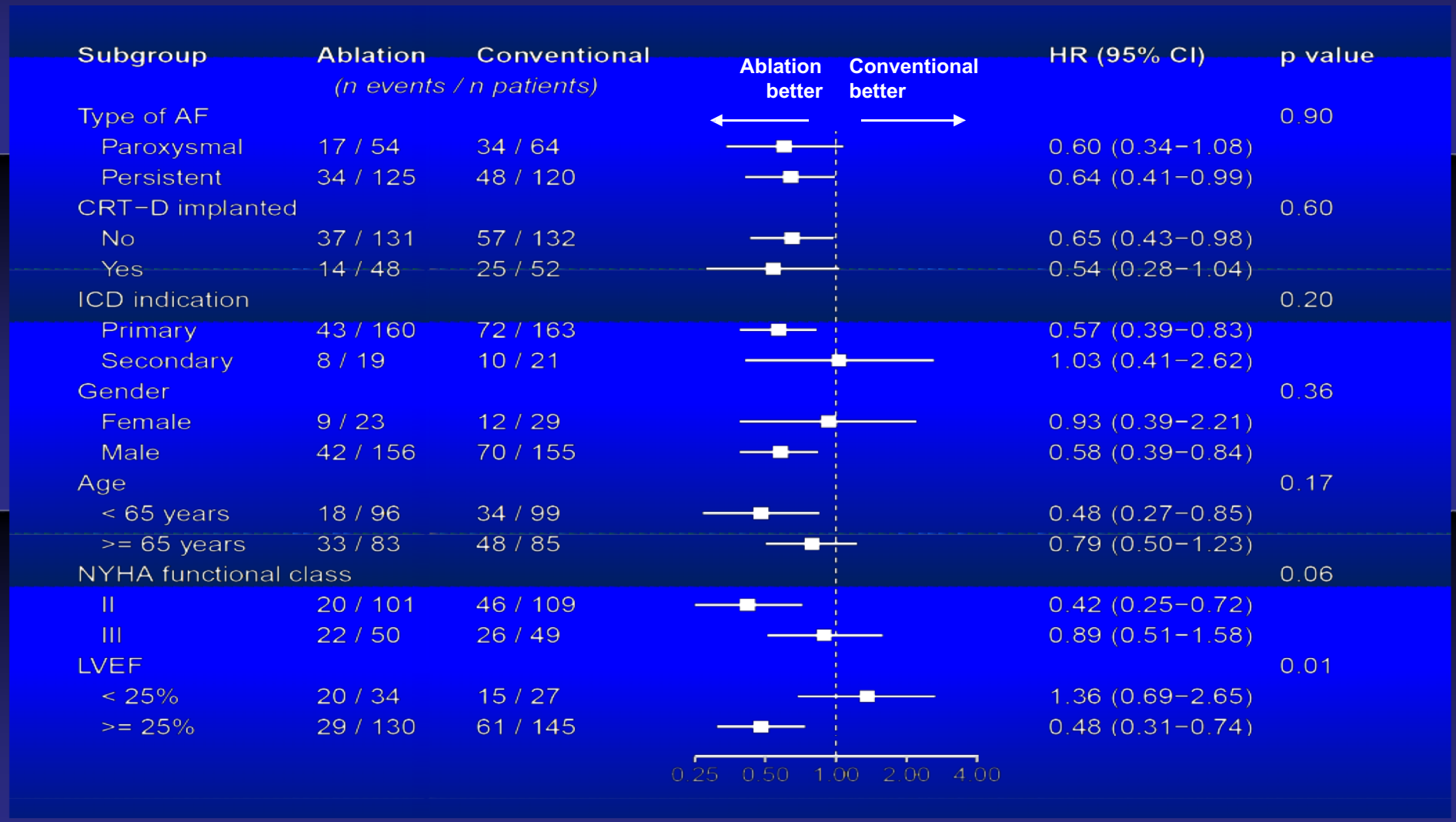
Risk Reduction: 51%

Cardiovascular Hospitalization



Risk Reduction: 28%

Primary Endpoint-Subgroups



Subgroup	Ablation (n events / n patients)	Conventional (n events / n patients)	HR (95% CI)	p value
Type of AF				0.90
Paroxysmal	17 / 54	34 / 64	0.60 (0.34–1.08)	
Persistent	34 / 125	48 / 120	0.64 (0.41–0.99)	
CRT–D implanted				0.60
No	37 / 131	57 / 132	0.65 (0.43–0.98)	
Yes	14 / 48	25 / 52	0.54 (0.28–1.04)	
ICD indication				0.20
Primary	43 / 160	72 / 163	0.57 (0.39–0.83)	
Secondary	8 / 19	10 / 21	1.03 (0.41–2.62)	
Gender				0.36
Female	9 / 23	12 / 29	0.93 (0.39–2.21)	
Male	42 / 156	70 / 155	0.58 (0.39–0.84)	
Age				0.17
< 65 years	18 / 96	34 / 99	0.48 (0.27–0.85)	
>= 65 years	33 / 83	48 / 85	0.79 (0.50–1.23)	
NYHA functional class				0.06
II	20 / 101	46 / 109	0.42 (0.25–0.72)	
III	22 / 50	26 / 49	0.89 (0.51–1.58)	
LVEF				0.01
< 25%	20 / 34	15 / 27	1.36 (0.69–2.65)	
>= 25%	29 / 130	61 / 145	0.48 (0.31–0.74)	


CABANA

FIGURE 1

Design of the CABANA Pivotal Study

Atrial fibrillation
Eligible for ablation and/or drug therapy

65 years of age
<65 years with ≥1 CVA risk factor

R

Drug Rx & AC
- Rate control
- Rhythm Rx

1° ablation & AC
- PV isolation
- Adjunctive

Descriptive analysis
- NSR vs AF impact
- With or w/o heart disease
- AF type (paroxysmal; persistent; long-standing persistent)
- CT/MR image analysis
- ECG/EGM analysis

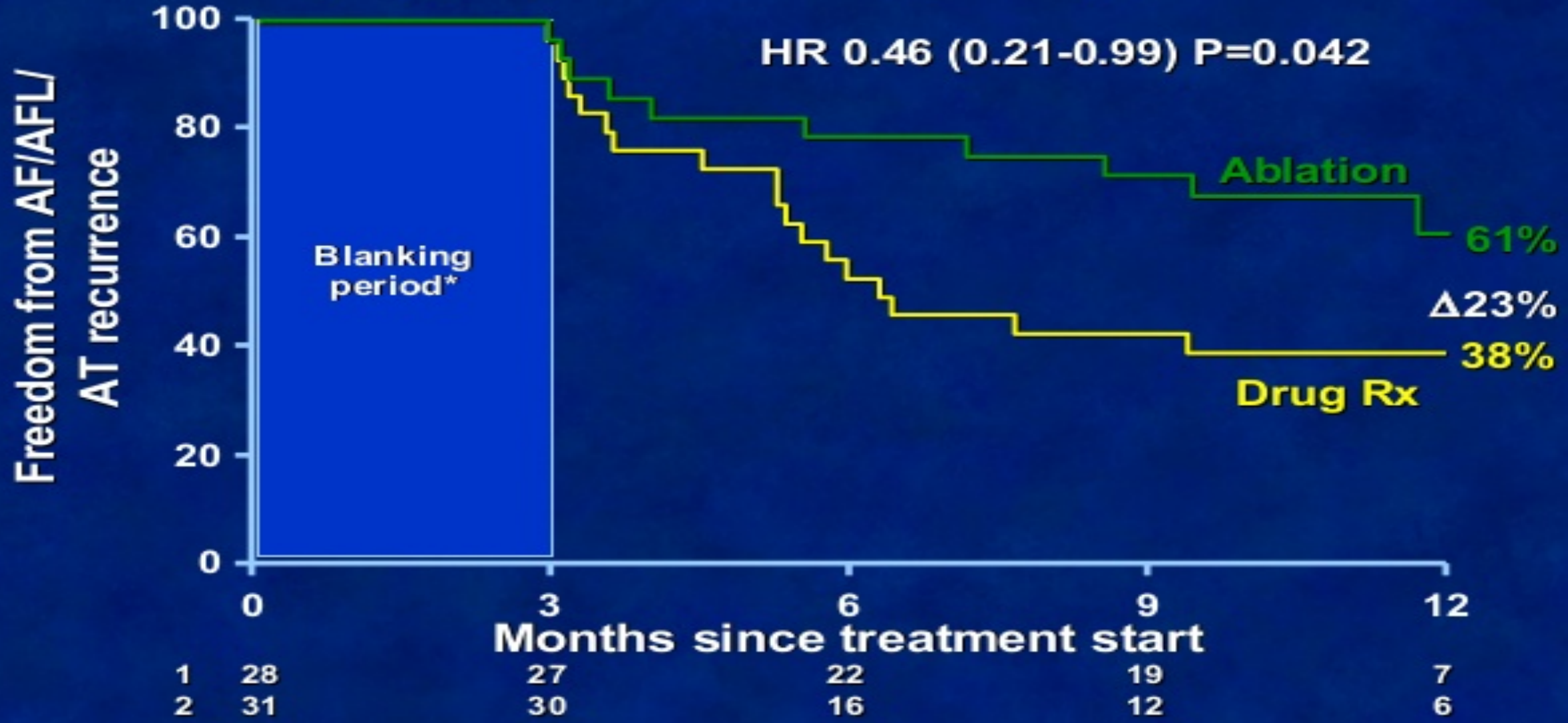
Follow-up
36 months

Packer: CABANA Investigator Meeting, 2009

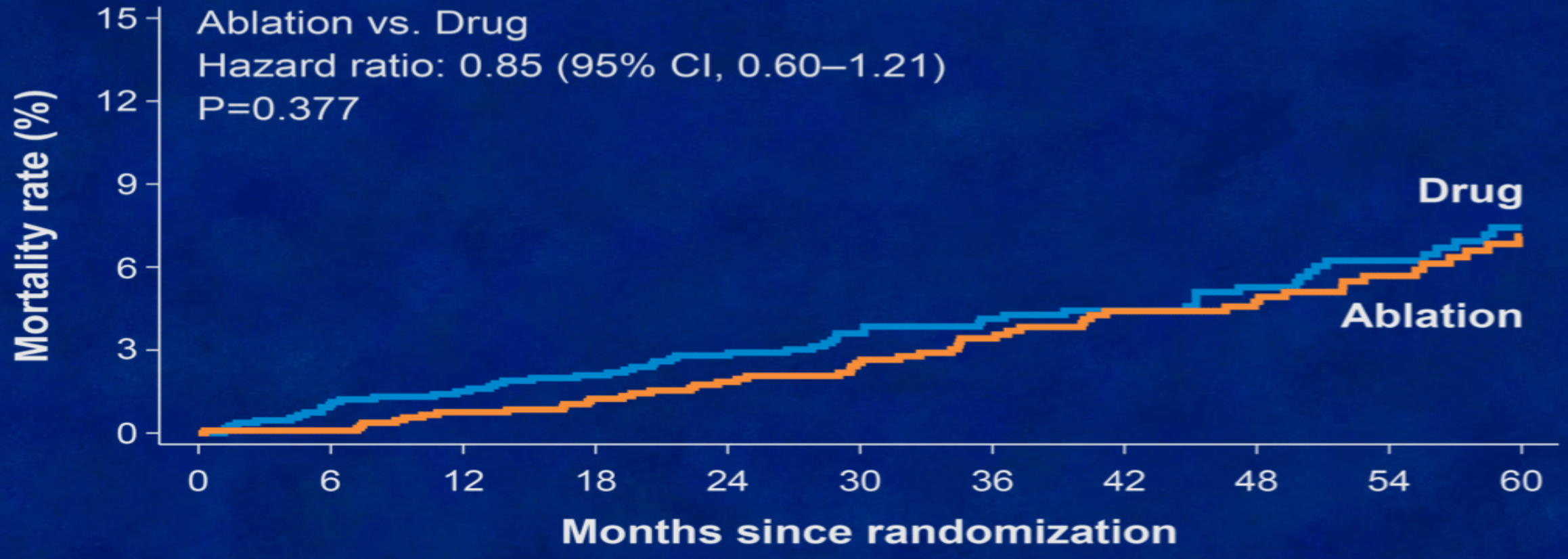
Selected Baseline Characteristics

Selected Baseline Characteristics	Ablation n = 1108	Drug Therapy n = 1096
Age - Median (Q1, Q3)	68 (62, 72)	67 (62, 72)
Female	37%	37%
NYHA Class II/III	34%	37%
History of Stroke or TIA	11%	9%
CHA_2DS_2VASc -- Median (Q1, Q3)	3.0 (2.0, 4.0)	3.0 (2.0, 4.0)
Yrs from onset AF - Median (Q1, Q3)	1.1 (0.3, 4.1)	1.1 (0.3, 3.7)
Type of AF at enrollment		
Paroxysmal	42%	43%
Persistent	47%	47%
Longstanding Persistent	10%	9%

Freedom from Recurrence of Any *Symptomatic* AF, AFL, or AT



Estimates of All-Cause Mortality Risk (ITT)



Number at risk											
Drug	1096	1046	1023	992	903	783	679	606	527	445	334
Ablation	1108	1058	1035	1013	933	814	724	632	555	455	332

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Primary and Secondary Outcomes as Randomized (ITT)

	Ablation N = 1108	Drug N = 1096	Hazard Ratio (95% CI)	P-Value
Primary Outcome				
Composite:	89 (8.0%)	101 (9.2%)	0.86 (0.65, 1.15)	0.30
Death	58 (5.2%)	67 (6.1%)	0.85 (0.60, 1.21)	0.38
Disabling stroke	3 (0.3%)	7 (0.6%)	0.42 (0.11, 1.62)	0.19
Serious bleeding	36 (3.2%)	36 (3.3%)	0.98 (0.62, 1.56)	0.93
Cardiac arrest	7 (0.6%	11 (1.0%)	0.62 (0.24, 1.61)	0.33
Secondary Outcomes				
All-cause mortality	58 (5.2%)	67 (6.1%)	0.85 (0.60, 1.21)	0.38
Death or CV hospitalization	573 (51.7%)	637 (58.1%)	0.83 (0.74, 0.93)	0.001

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Primary Endpoint Sub-group Analysis

All-Cause Mortality, Disabling Stroke, Serious Bleeding, Cardiac Arrest (ITT)

Group	Interaction P-Value	N	Hazard Ratio	95% CI
All Subjects		2204	0.86	0.65, 1.15
Age	0.074			
< 65 years old		766	0.52	0.27, 1.00
≥ 65 and < 75 years old		1130	0.84	0.57, 1.23
≥ 75 years old		308	1.46	0.80, 2.67
Sex	0.161			
Male		1385	0.74	0.52, 1.06
Female		819	1.14	0.70, 1.86
Minority status	0.065			
White		1979	0.96	0.71, 1.31
Minority*		225	0.43	0.20, 0.95
AF type	0.925			
Paroxysmal		946	0.82	0.51, 1.31
Persistent		1042	0.87	0.59, 1.28
Long-standing persistent		215	1.01	0.39, 2.61
Years since onset of AF	0.718			
≤ 1 year		1063	0.83	0.57, 1.21
> 1 year		1122	0.92	0.59, 1.42
Hypertension	0.734			
Absent		427	0.97	0.47, 2.01
Present		1776	0.85	0.62, 1.15
Hypertension with LVH	0.843			
Absent		1176	0.89	0.61, 1.31
Present		587	0.83	0.47, 1.46
Sleep apnea	0.339			
Absent		1695	0.94	0.67, 1.32
Present		508	0.69	0.41, 1.17
BMI	0.378			
< 30		1064	0.74	0.49, 1.11
≥ 30		1106	0.96	0.64, 1.44
CHADS-VASc score	0.716			
≤ 2		959	0.93	0.54, 1.58
> 2		1245	0.83	0.59, 1.16
History of congestive heart failure	0.196			
No		1865	0.95	0.68, 1.32
Yes		337	0.61	0.35, 1.08
Baseline NYHA class	0.147			
No heart failure or Class I		1408	1.04	0.71, 1.52
≥ Class II		778	0.68	0.44, 1.05

*Minority=Hispanic or Latino or non-white race

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Primary and Secondary Outcomes (Treatment Received)*

	Ablation (N = 1307)	Drug (N = 897)	Hazard Ratio (95% CI)	P-Value
Primary Outcome	92 (7.0%)	98 (10.9%)	0.67 (0.50, 0.89)	0.006
Secondary Outcomes				
All-cause mortality	58 (4.4%)	67 (7.5%)	0.60 (0.42, 0.86)	0.005
Death or CV hospitalization	538 (41.2%)	672 (74.9%)	0.83 (0.74, 0.94)	0.002

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*pre-specified

Background

- Secondary endpoint - All cause mortality:
  - A non-significant 15% reduction with ablation was observed (ITT)

    (HR 0.85; 95% CI 0.60-1.21; p=0.377)
- Analyses by *treatment received and per protocol* showed significant benefits of ablation for both the primary endpoint and for mortality

6.3. AF Catheter Ablation to Maintain Sinus Rhythm

6.3.4. Catheter Ablation in HF

Recommendation for Catheter Ablation in HF Referenced studies that support the new recommendation are summarized in Online Data Supplement 7.		
COR	**LOE**	**Recommendation**
IIb	**B-R**	**1. AF catheter ablation may be reasonable in selected patients with symptomatic AF and HF with reduced left ventricular (LV) ejection fraction (HFrEF) to potentially lower mortality rate and reduce hospitalization for HF (S6.3.4-1, S6.3.4-2).** **NEW**: New evidence, including data on improved mortality rate, has been published for AF catheter ablation compared with medical therapy in patients with HF.