CASTLE-AF

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

## *The CASTLE-AF trial*

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on behalf the CASTLE AF Investigators

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# Declaration of interest

- Research contracts (Abbott; Boston Scientific; GE Healthcare; Siemens; Biotronik; Vytronus; Biosense Webster)
- Consulting/Royalties/Owner/ Stockholder of a healthcare company (Abbott; Biotronik; Wavelet Health; Cardiac Design; Medtronic; Preventice; Vytronus; Biosense Webster; Marrek Inc; Boston Scientific)

# Background

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- Atrial fibrillation (AF) and heart failure are well intertwined
- Catheter ablation of AF in patients with heart failure has been shown feasible

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# CASTLE-AF
## *Rationale and Objective*

- Study the effectiveness of *catheter ablation* of atrial fibrillation in patients with heart failure in *improving hard primary endpoints of mortality and heart failure progression* when compared to conventional standard treatment

# CASTLE-AF

## Primary Endpoint

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

## Secondary Endpoints

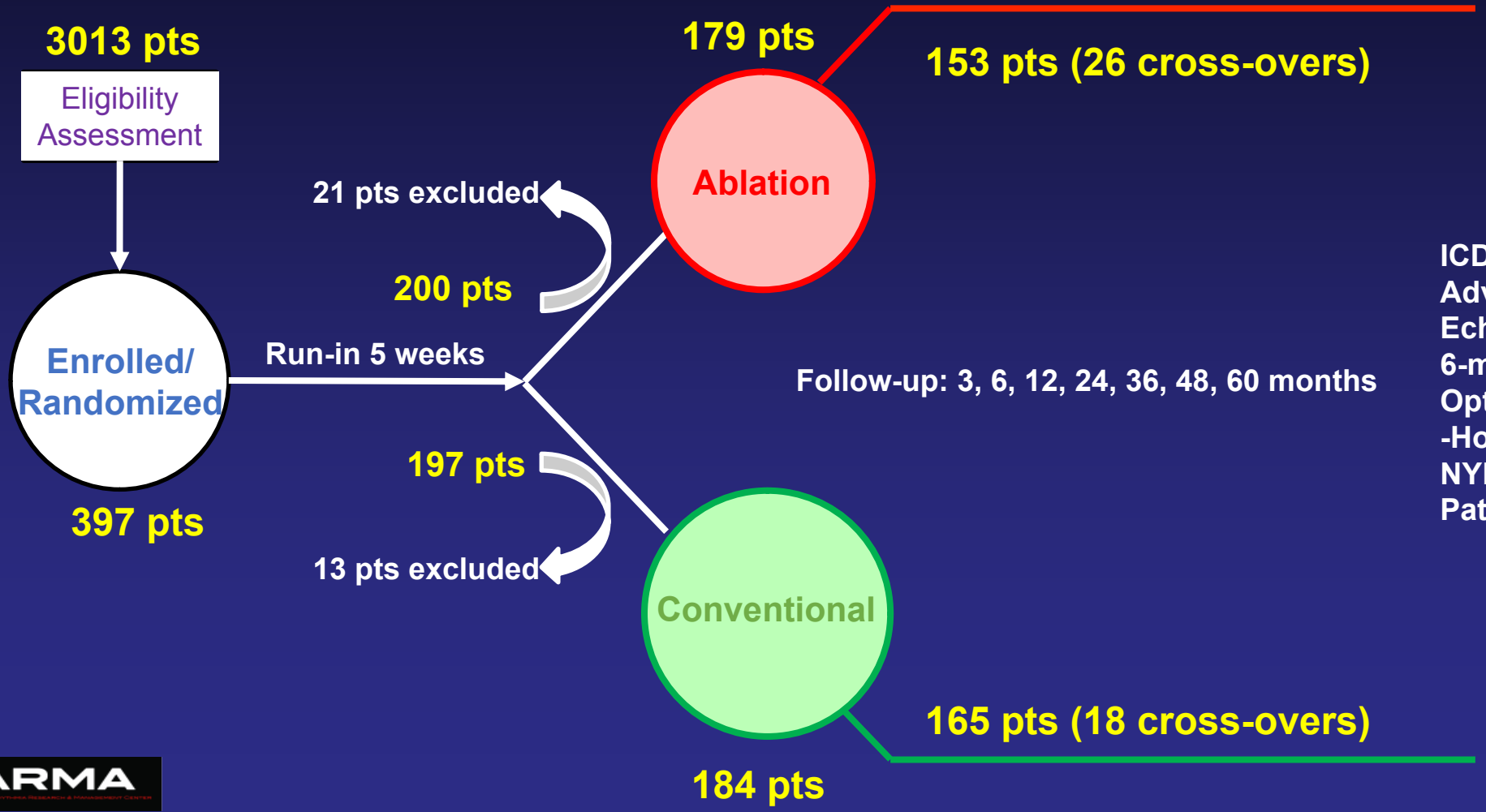
- All-cause mortality
- Worsening of heart failure admissions
- Cerebrovascular accidents
- Cardiovascular mortality
- Unplanned hospitalization due to cardiovascular reason
- All-cause hospitalization
- Quality of Life: Minnesota Living with Heart Failure and EuroQoL EQ-5D
- Exercise tolerance (6 minutes 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

# CASTLE-AF
## *Inclusion Criteria*

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

# Study Design— CASTLE-AF

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



# CASTLE-AF

## *Treatment Protocol - Conventional Arm*

- According to the ACC/AHA/ESC 2006 guidelines for treatment of AF in Heart Failure patients
- Efforts to maintain sinus rhythm in this study arm were recommended
- In case of rate control strategy:
  - 60 and 80 beats per minute at rest
  - 90 and 115 beats per minute during moderate exercise
- Anticoagulation was initiated, if not already started, and maintained throughout the study. The INR was maintained between 2.0 and 3.0

# CASTLE AF
## *Ablation Protocol*

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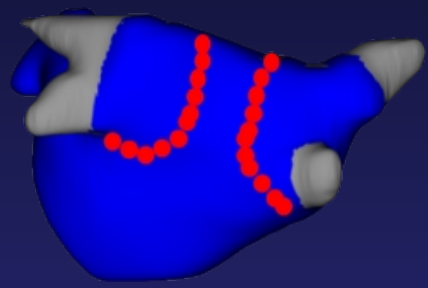

- Pulmonary Vein Isolation
- Additional lesions
  - at discretion of operator
- Repeat ablation after blanking period

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# Baseline Characteristics-CASTLE AF

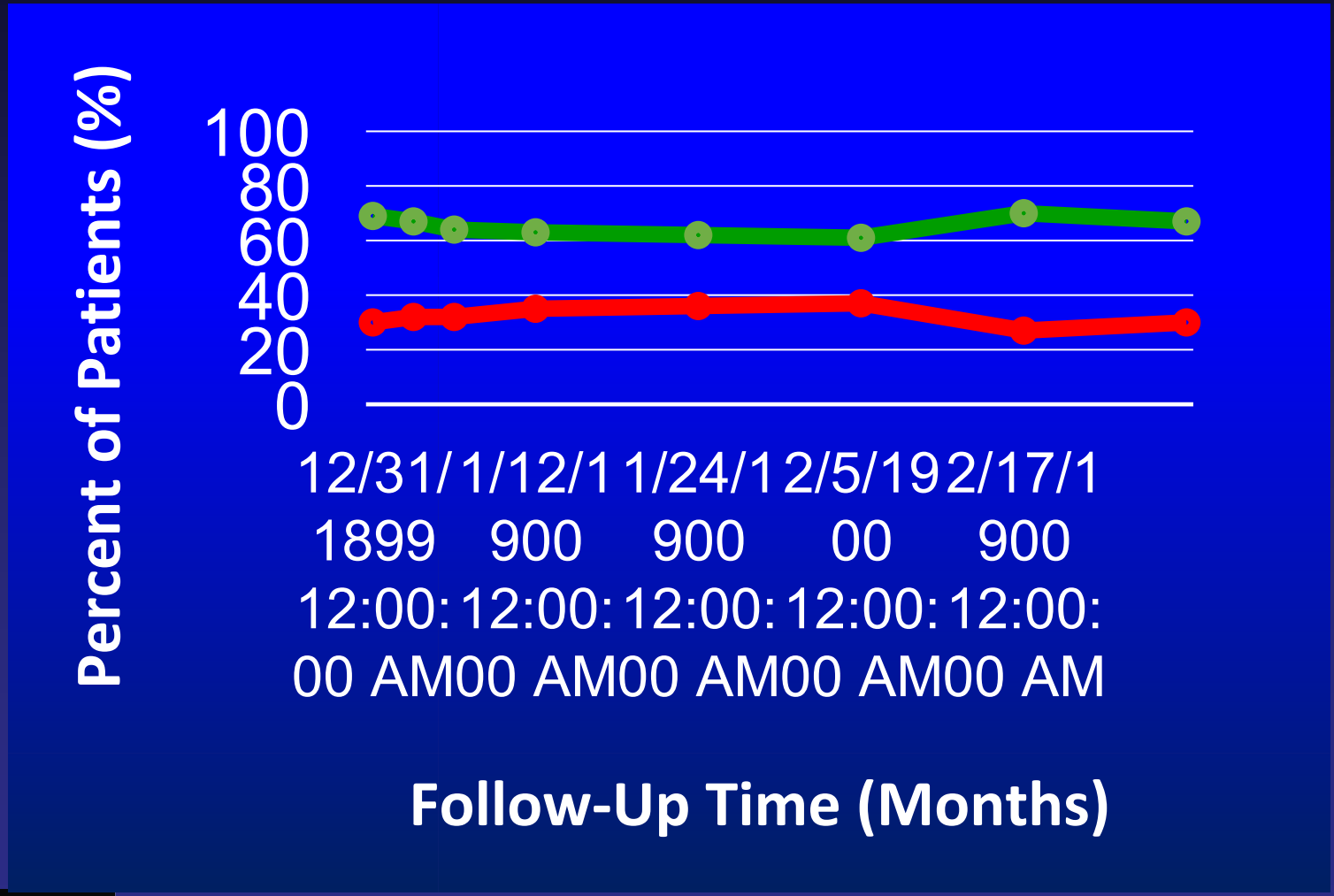
| | Ablation group (179 patients) | Conventional group (184 patients) |
|---|---|---|
| Age – years | 64 (56-71) | 64 (56-73.5) |
| New York Heart Association class | | |
| I (%) | 11 | 11 |
| II (%) | 58 | 61 |
| III (%) | 29 | 27 |
| IV (%) | 2 | 1 |
| Left ventricular ejection fraction – % | 32.5 (25.0-38.0) | 31.5 (27.0-37.0) |
| Current type of atrial fibrillation | | |
| Paroxysmal (%) | 30 | 35 |
| Persistent (%) | 70 | 65 |
| CRT-D implanted (%) | 27 | 28 |
| ICD implanted (%) | 73 | 72 |

# Baseline Characteristics-CASTLE AF

| | Ablation group (179 patients) | Conventional group (184 patients) |
|---|---|---|
| ACE-inhibitor or ARB – no. (%) | 94 | 91 |
| Beta-blocker – 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 |

# Results-CASTLE AF

## *Rate Versus Rhythm Control in Conventional Arm*




**Rate control:**

- Beta-blocker
- Digitalis
- Calcium antagonist
- Atrioventricular node ablation (in 5 patients)

**Rhythm control:**

- Antiarrhythmic drug
- Atrial fibrillation ablation (18 crossover cases)

# Results-CASTLE AF

## *AF Burden Derived from Memory of Implanted Devices*

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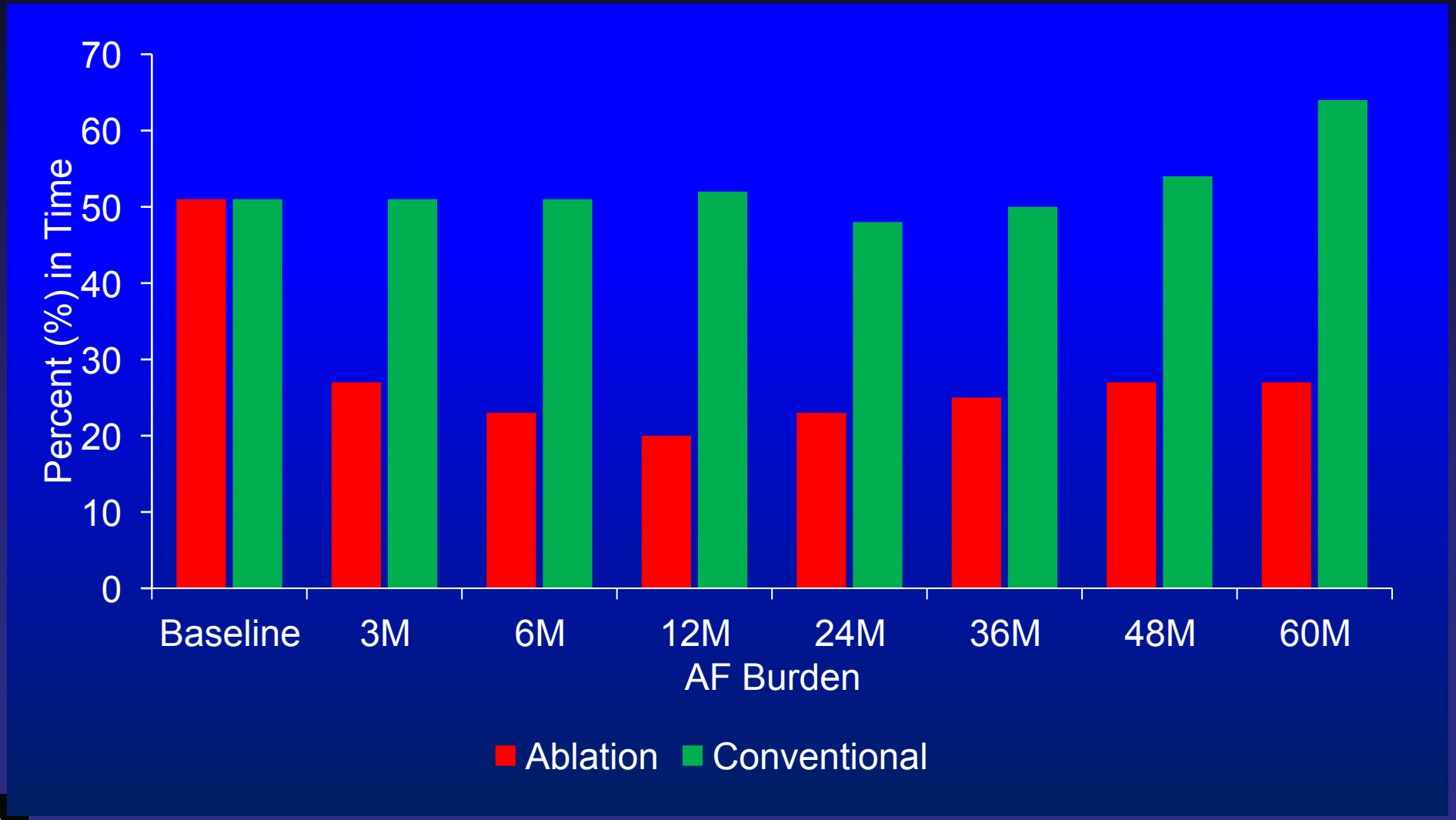


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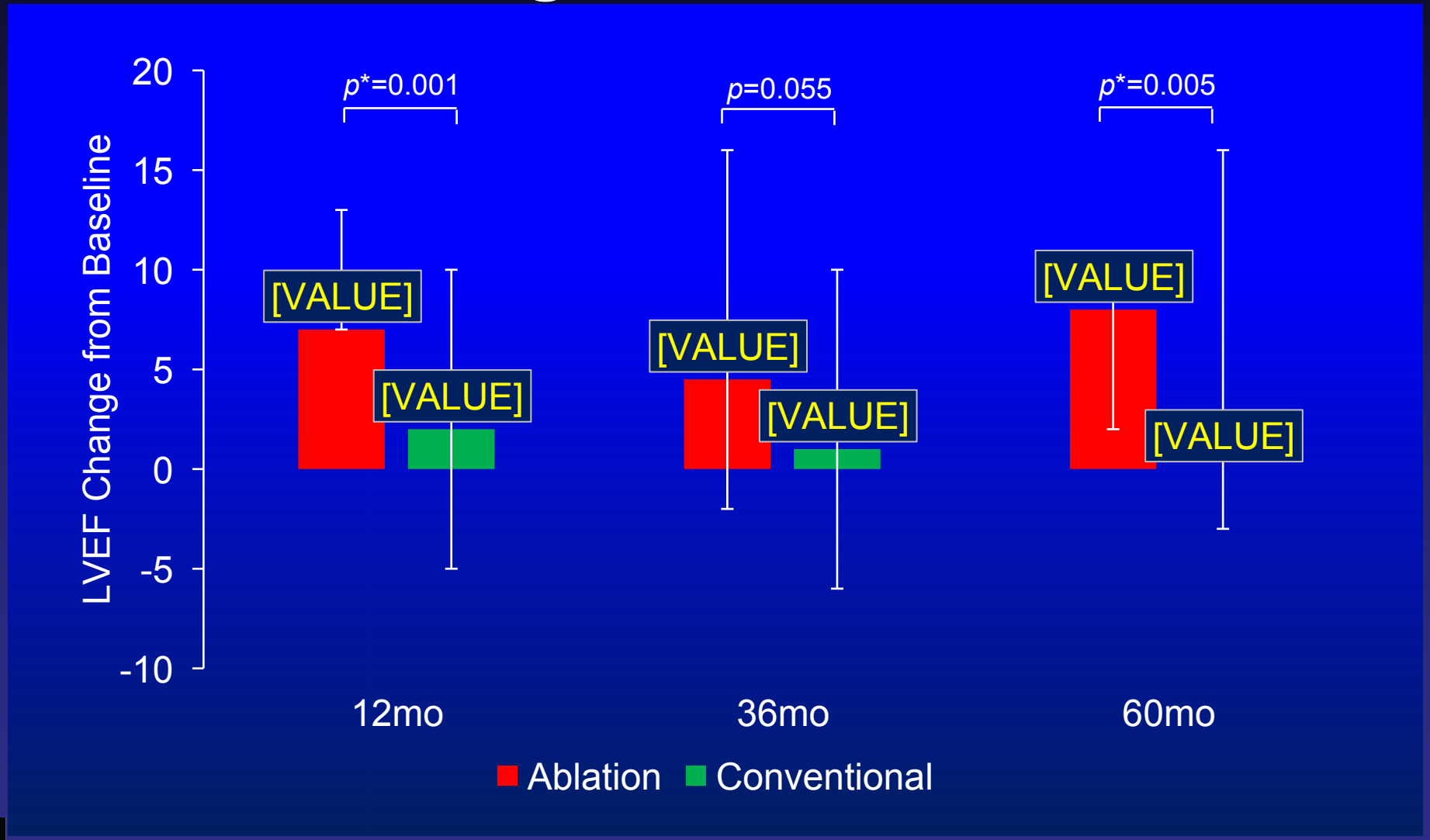
# Results-CASTLE AF

## *Absolute change in LVEF from baseline*



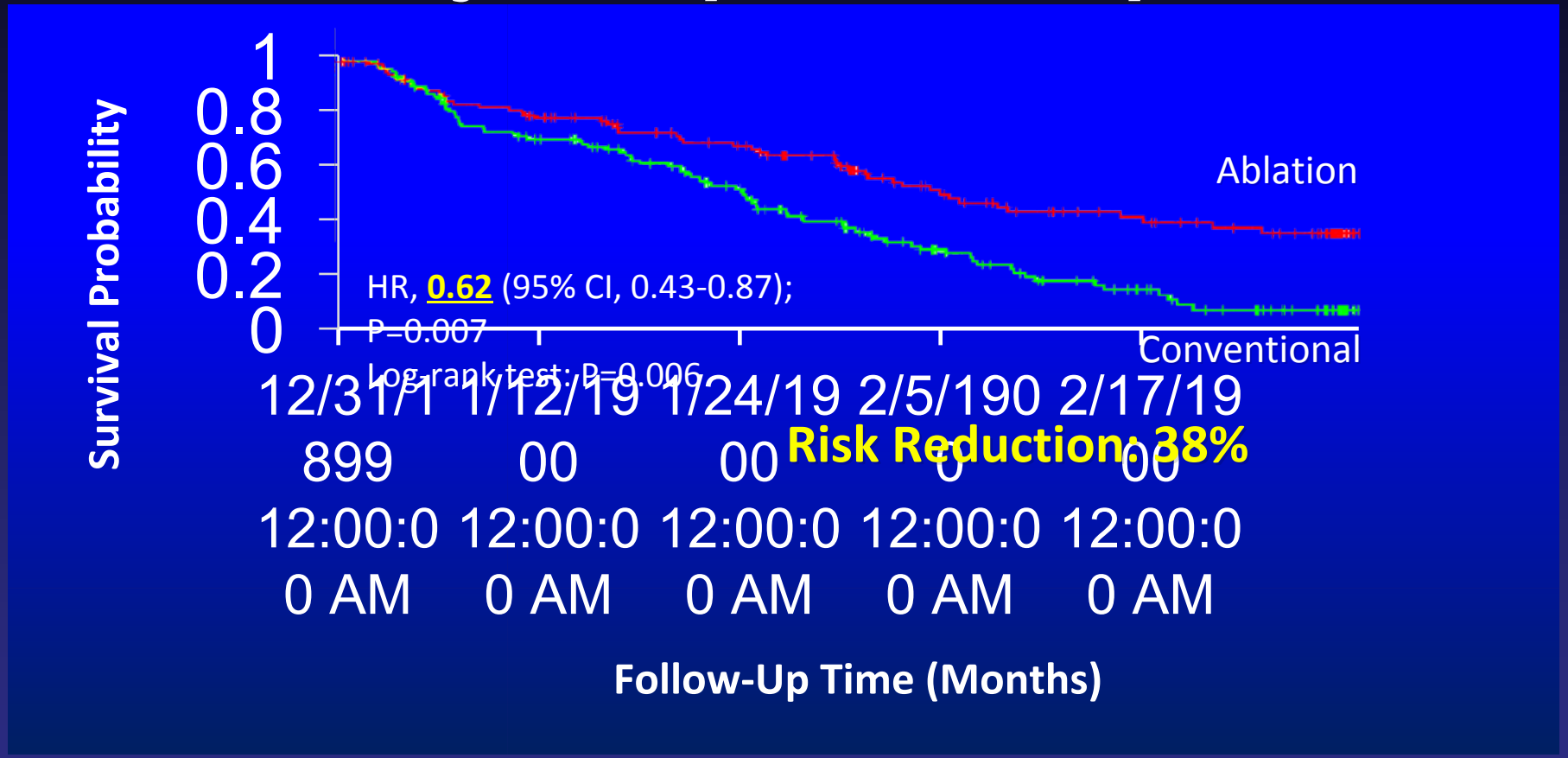
# Results-CASTLE AF

## *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 |

# Results-CASTLE AF

## *Primary Composite Endpoint*

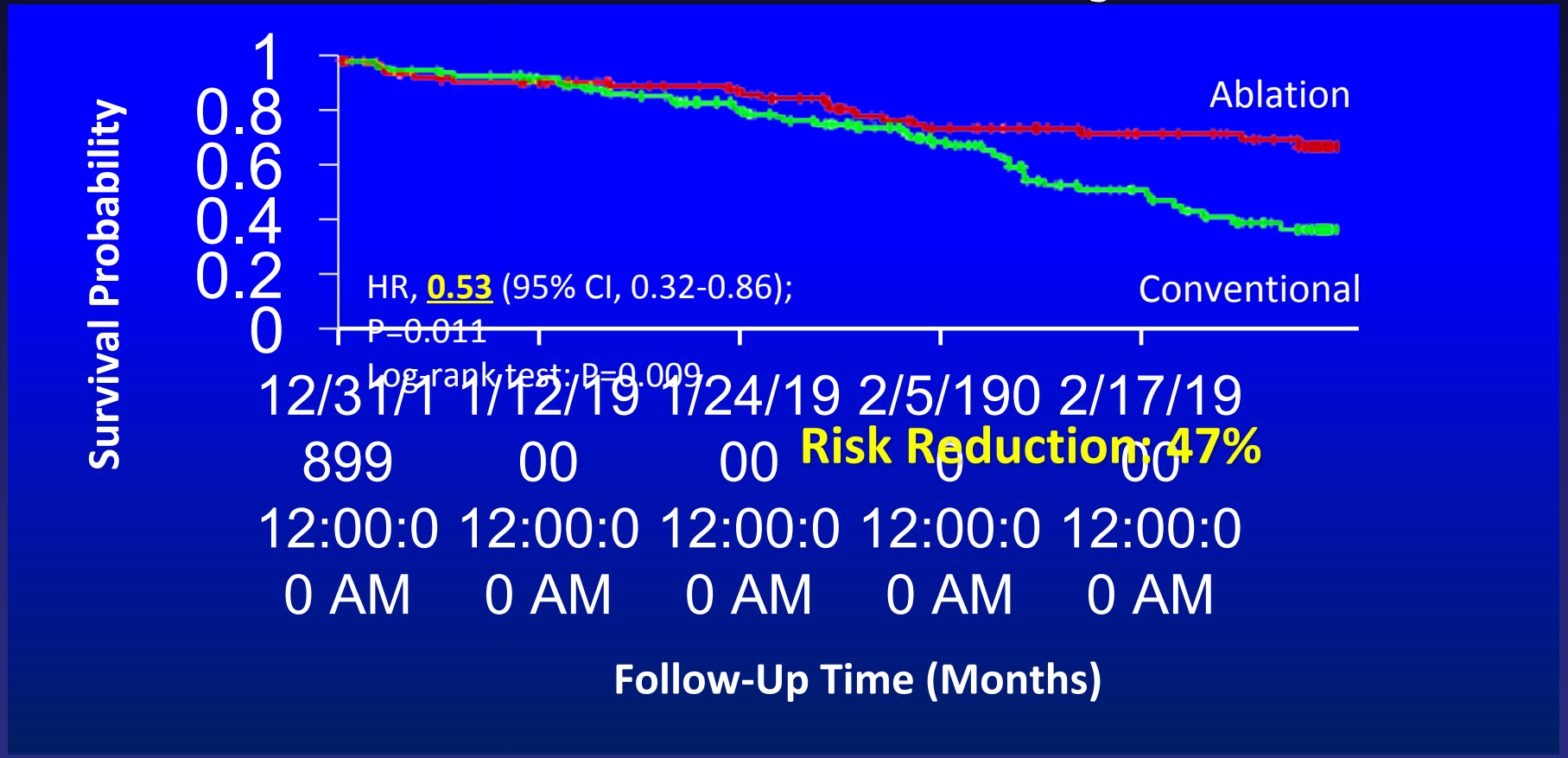



**Patients at Risk**

| | | | | | | |
|---|---|---|---|---|---|---|
| **Ablation** | **179** | **141** | **114** | **76** | **58** | **22** |
| **Conventional** | **184** | **145** | **111** | **70** | **48** | **12** |

# Results-CASTLE AF

## *All-Cause Mortality*

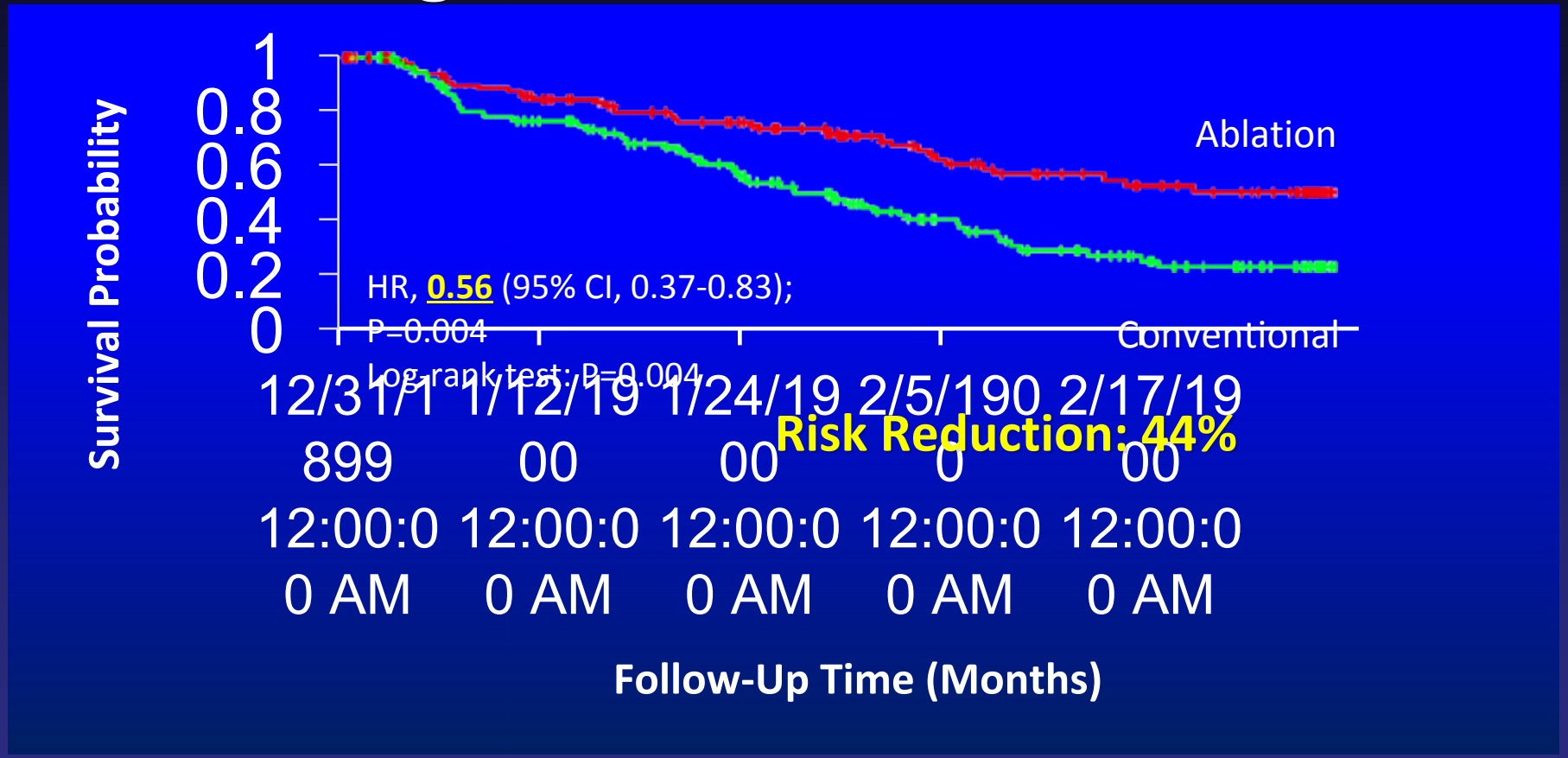



**Patients at Risk**

| | | | | | | |
|---|---|---|---|---|---|---|
| **Ablation** | **179** | **154** | **130** | **94** | **71** | **27** |
| **Conventional** | **184** | **168** | **138** | **97** | **63** | **19** |

# Results-CASTLE AF

## *Worsening Heart Failure Admissions*

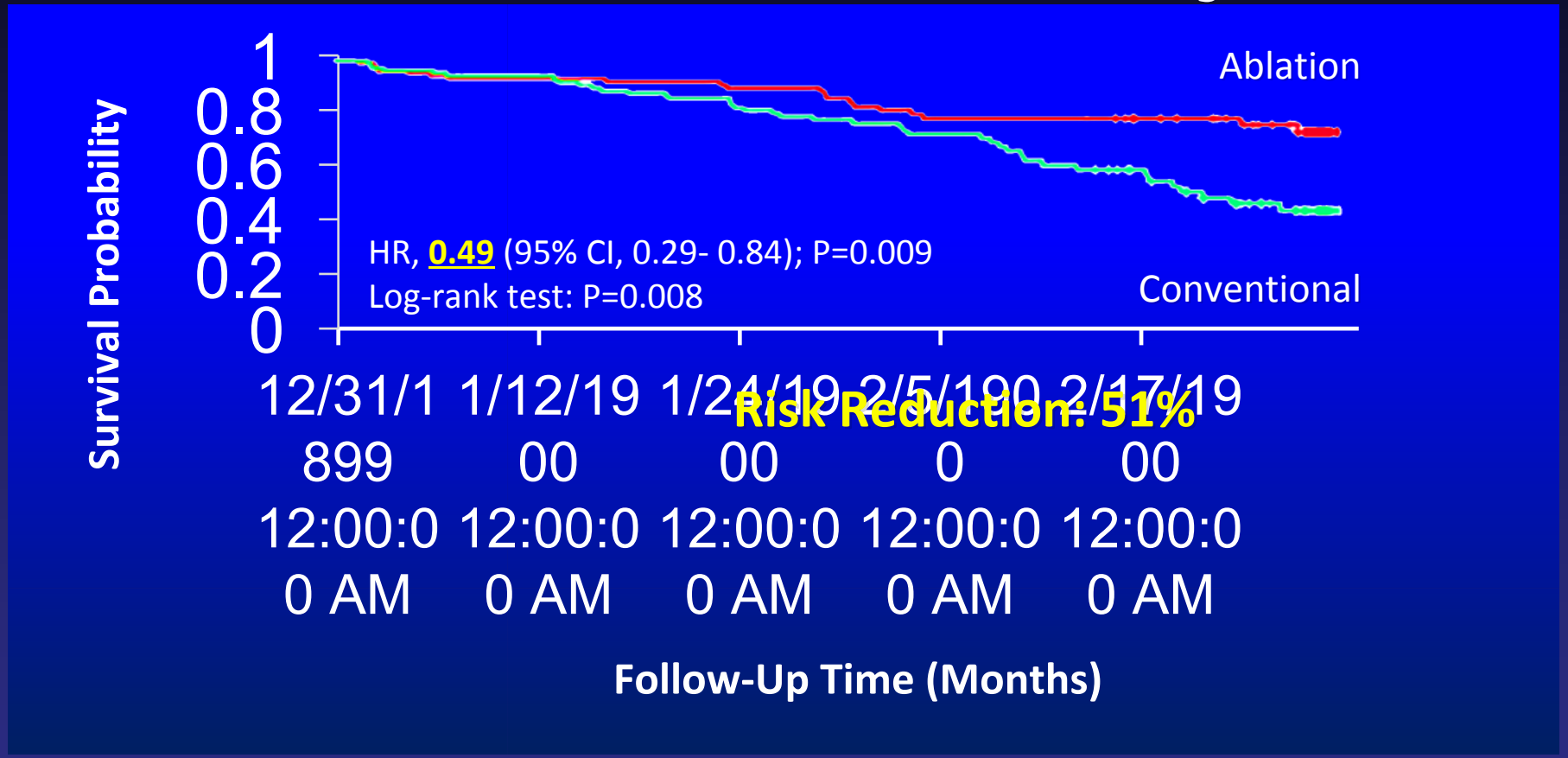



**Patients at Risk**

| | | | | | | |
|---|---|---|---|---|---|---|
| **Ablation** | **179** | **141** | **114** | **76** | **58** | **22** |
| **Conventional** | **184** | **145** | **111** | **70** | **48** | **12** |

# Results-CASTLE AF

## *Cardiovascular Mortality*

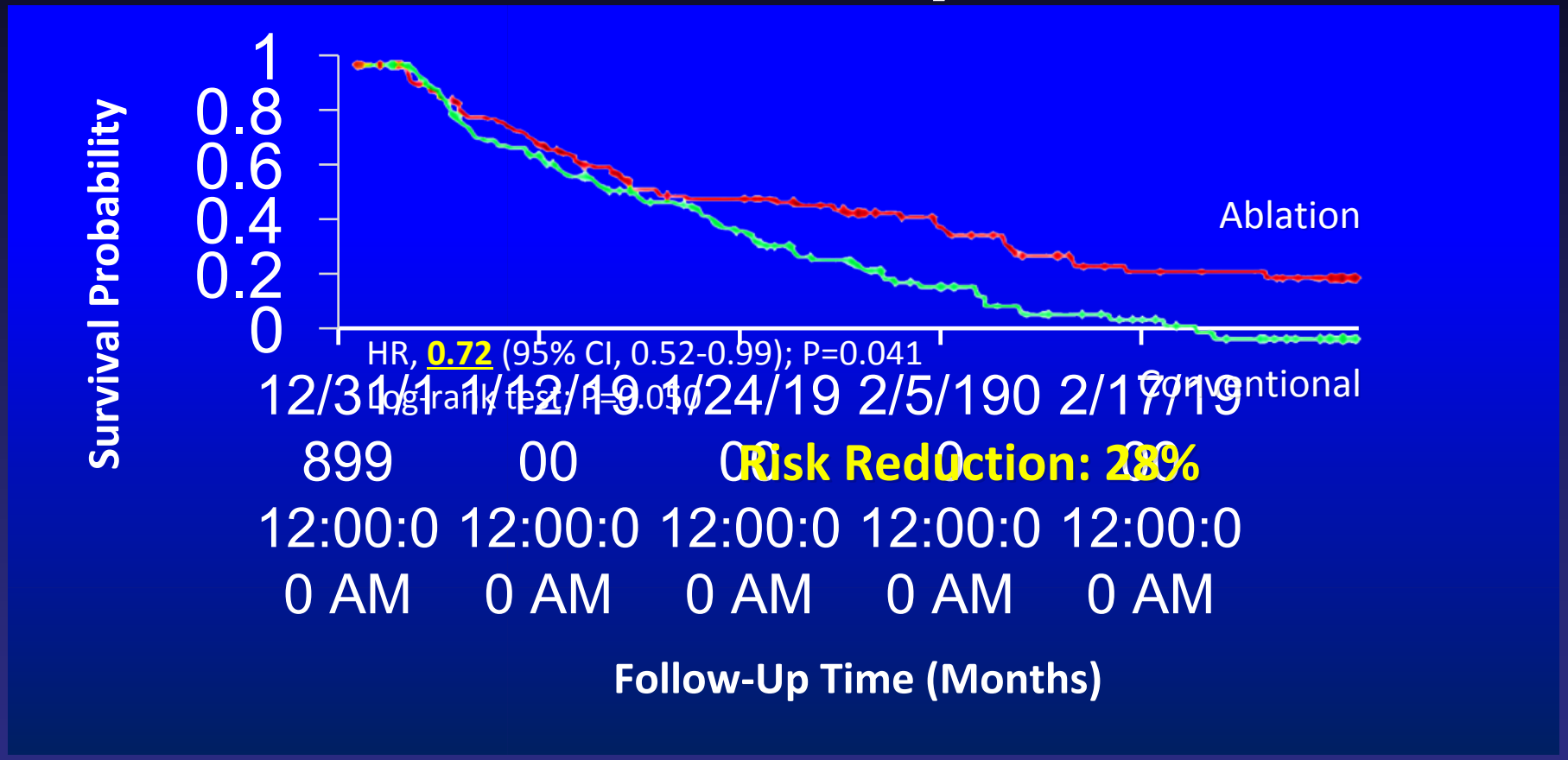



**Patients at Risk**

| | | | | | | |
|---|---|---|---|---|---|---|
| **Ablation** | **179** | **154** | **130** | **94** | **71** | **27** |
| **Conventional** | **184** | **168** | **138** | **97** | **63** | **19** |

# Results-CASTLE AF

## *Cardiovascular Hospitalization*




**Patients at Risk**

| | | | | | | |
|---|---|---|---|---|---|---|
| **Ablation** | **179** | **127** | **95** | **60** | **42** | **17** |
| **Conventional** | **184** | **131** | **91** | **52** | **33** | **8** |

# Results-CASTLE AF

## *Primary Endpoint-Subgroups*

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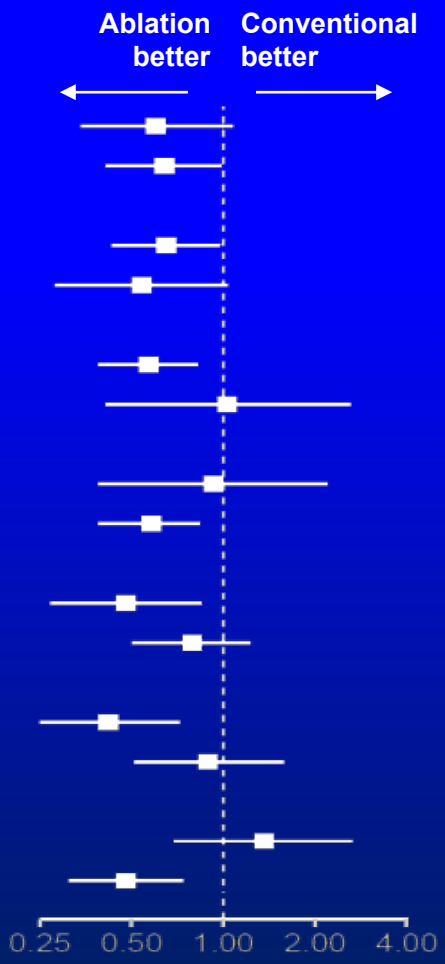
| Subgroup | Ablation (n events / n patients) | Conventional (n events / n patients) | HR (95% CI) | p value |
|---|---|---|---|---|
| Type of AF | | | | 0.90 |
| Paroxysmal | 17 / 54 | 34 / 64 | 0.60 (0.34–1.08) | |
| Persistent | 34 / 125 | 48 / 120 | 0.64 (0.41–0.99) | |
| CRT–D implanted | | | | 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) | |

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# Conclusion-CASTLE AF

- ***Catheter ablation*** of atrial fibrillation in patients with heart failure is associated with ***improved all-cause mortality*** and ***fewer admissions for worsening heart failure*** when compared to conventional standard of care treatment
- ***Catheter ablation*** of atrial fibrillation in patients with heart failure is also associated with ***improved cardiovascular mortality*** and ***hospitalization*** when compared to conventional standard of care treatment

## Steering Committee

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