
# Effectiveness and Safety of Hybrid Epicardial and Endocardial Ablation Versus Endocardial Ablation in Patients with Persistent and Longstanding Persistent Atrial Fibrillation

## Primary results of the CEASE-AF trial

(Clinicaltrials.gov NCT02695277)

Principal Investigator: Prof. Dr. Nicolas Doll
Schüchtermann-Klinik Bad Rothenfelde
Germany

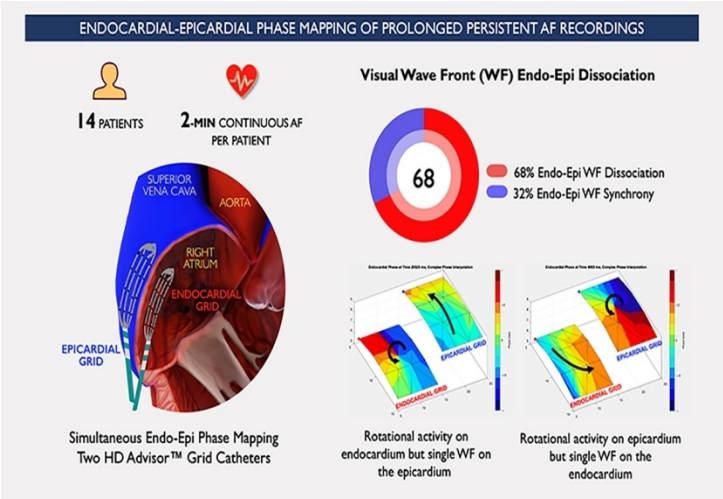
# Declaration of Interest

- Consulting/Royalties/Owner/ Stockholder of a healthcare company : Atricure

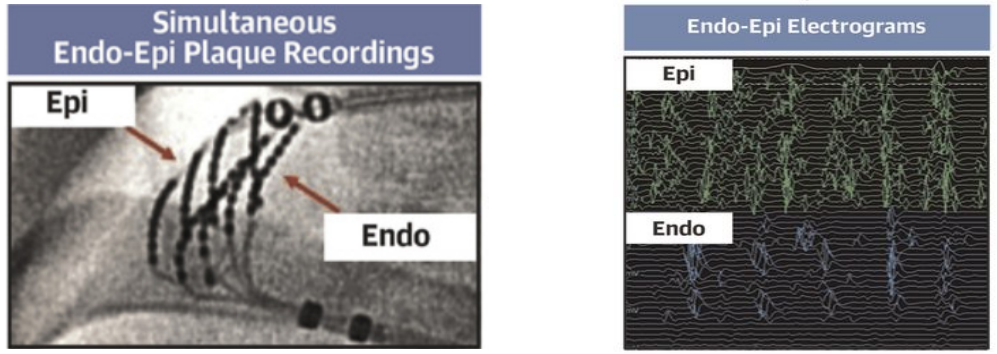
# Background

## Advanced AF – Characterized by high degree of endocardial- epicardial dissociation

Endocardial-Epicardial Phase Mapping of Prolonged Persistent AF Recordings




Site-Specific Epicardium-to-Endocardium Dissocoation of Electrical Activation in a Swine Model of AF




50.3% Endo-Epi dissociation with significant temporal heterogeneity

- Simultaneous endo-epi phase mapping in persistent AF: endocardial-epicardial dissociation and unstable wavefront propagation transitioning between endocardial and epicardial surfaces.
- Due to complex 3D wave propagation phenomenon, endocardial mapping alone cannot fully characterize the AF mechanism and endocardial ablation alone may not be sufficient.


Parameswaran et al. Circ Arrhythm Electrophysiol. 2020;13:e008512
Aronis and Trayanova. Circ Arrhythm Electrophysiol. 2020;13
Nazaroam et a; JACC EP Volume 6, Issue , 2020

# CEASE AF Clinical Study

- **Hypothesis:** Minimally invasive Hybrid Ablation approach that combines endocardial and epicardial ablation would achieve superior effectiveness when compared to endocardial Catheter Ablation alone in persistent AF with enlarged left atrium or longstanding persistent AF.

- **Trial Design:** Prospective, multi-center, randomized controlled clinical trial
  170 patients enrolled at 9 sites in 5 countries
  2:1 randomization to Hybrid Ablation vs. Catheter Ablation

- **Patient Population:** Adult patients with Left atrial diameter (LAD >4 cm) and persistent AF; or Longstanding persistent AF (≤10 years)*
  Patients with LAD>6 cm, previous ablation procedure, BMI >35 kg/m$^2$ and LVEF<30% were excluded.

*AF definitions per 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation

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# CEASE AF Clinical Study

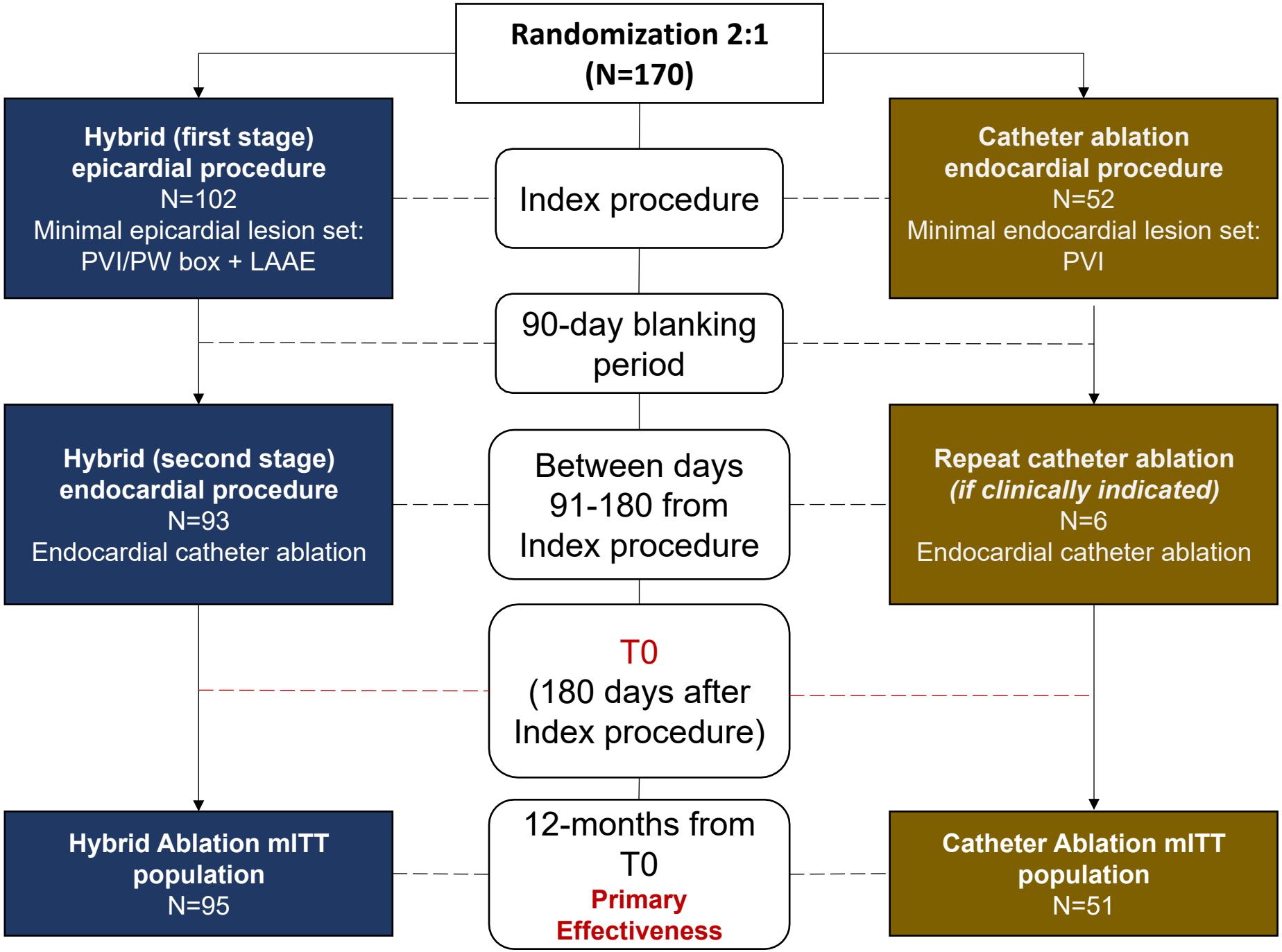
- **Minimal Required Lesion Set:** Hybrid ablation
  - 1st stage epicardial lesions: PVI + posterior box + Left atrial appendage exclusion
  - 2nd stage endocardial lesions: Endocardial mapping / ablation to address gaps

  Endocardial catheter ablation (including repeat ablation)
  - Index procedure: PVI
  - Repeat ablation: Endocardial ablation as clinically indicated

  *In both arms, additional ablation techniques / lesions were permitted per institutional practice for non-paroxysmal AF*

- **Primary Effectiveness Endpoint:** Freedom from AF/AFL/AT >30 sec through 12-months in absence of Class I/III AADs except previously failed AADs at doses not exceeding those previously failed

- **Safety Endpoint:** Composite major complication rate during the course of the study


Randomization 2:1
(N=170)
Hybrid (first stage) epicardial procedure
N=102
Minimal epicardial lesion set:
PVI/PW box + LAAE
Index procedure
Catheter ablation endocardial procedure
N=52
Minimal endocardial lesion set:
PVI
90-day blanking period
Hybrid (second stage) endocardial procedure
N=93
Endocardial catheter ablation
Between days 91-180 from Index procedure
Repeat catheter ablation
(if clinically indicated)
N=6
Endocardial catheter ablation
T0
(180 days after Index procedure)
Hybrid Ablation mITT population
N=95
12-months from T0
Primary Effectiveness
Catheter Ablation mITT population
N=51

# Baseline characteristics

| | Hybrid Ablation Arm (ITT), n=102 | Catheter Ablation Arm (ITT), n=52 |
|---|---|---|
| Age (years), Mean ± SD | 60.8±8.1 | 60.6±7.4 |
| Male, n (%) | 77 (75.5) | 38 (73.1) |
| BMI (kg/m$^2$), Mean ± SD | 29.7±3.5 | 29.8±3.1 |
| AF classification, n (%) | | |
| Persistent | 81 (79.4) | 43 (82.7) |
| Longstanding persistent AF | 21 (20.6) | 9 (17.3) |
| Left atrial size (cm) | | |
| Mean ± SD | 4.7±0.5 | 4.7±0.4 |
| Median (Q1–Q3) | 4.70 (4.3, 4.9) | 4.65 (4.3, 5.0) |
| Min–Max | 4.0–6.0 | 4.0–5.6 |
| Number of years in AF | 2.94±3.29 | 3.34±3.52 |

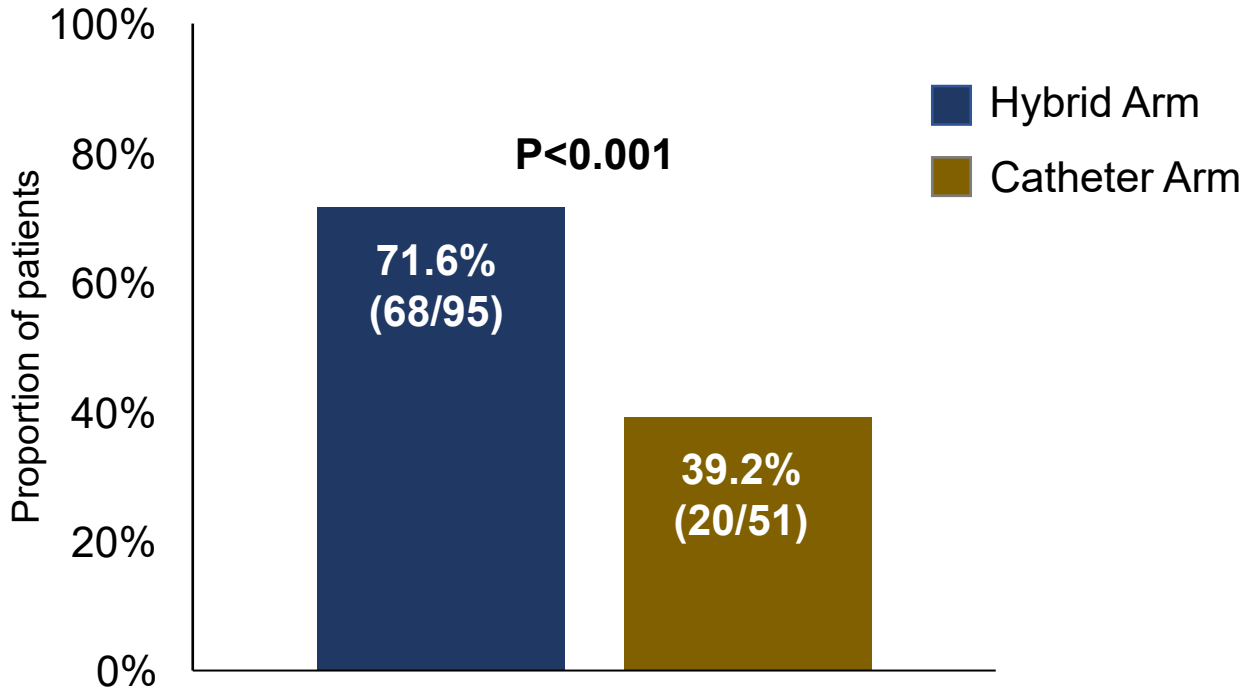
# Procedure & Fluoroscopy Duration

- Total procedure duration was higher in Hybrid arm
- The endocardial ablation time decreased by ~94 minutes in the Hybrid arm
- Fluoroscopy time was ~8 minutes shorter in the Hybrid arm

| | Hybrid Ablation | Catheter Ablation | |
|---|---|---|---|
| Total procedure duration, minutes (n) | 336.4±97 (102) | 251.9±114 (52) | <0.001 |
| Index procedure | 192.4±51 (102) | 232.2±98 (52) | |
| Hybrid arm second stage (endocardial) procedure | 158.0±80 (93) | NA | |
| Repeat catheter ablation pre-T0 | NA | 170.5±75 (6) | |
| Total fluoroscopy duration, minutes (n) | 16.0±13 (93) | 24.3±19 (52) | 0.001 |
| Index procedure | NA | 21.8±15 (52) | |
| Hybrid arm second stage (endocardial) procedure | 16.0±13 (93) | NA | |
| Repeat catheter ablation pre-T0 | NA | 22.2±16 (6) | |

# Primary effectiveness

*Freedom from AF/AFL/AT off AADs (not exceeding previously failed doses) through 12 months*



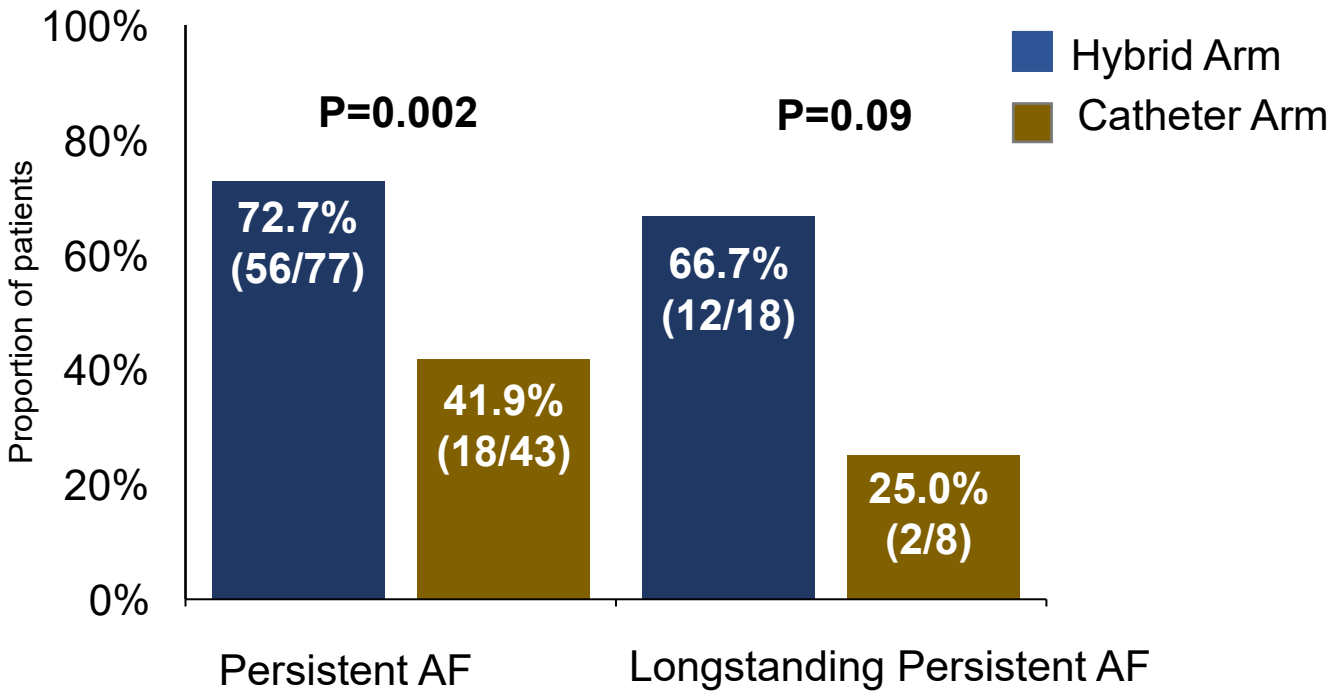

Hybrid ablation resulted in

- **32.4%** absolute
- **82.7%** relative

benefit increase in effectiveness

# Primary effectiveness: subgroup analysis

*Freedom from AF/AFL/AT off AADs (not exceeding previously failed doses) through 12 months*

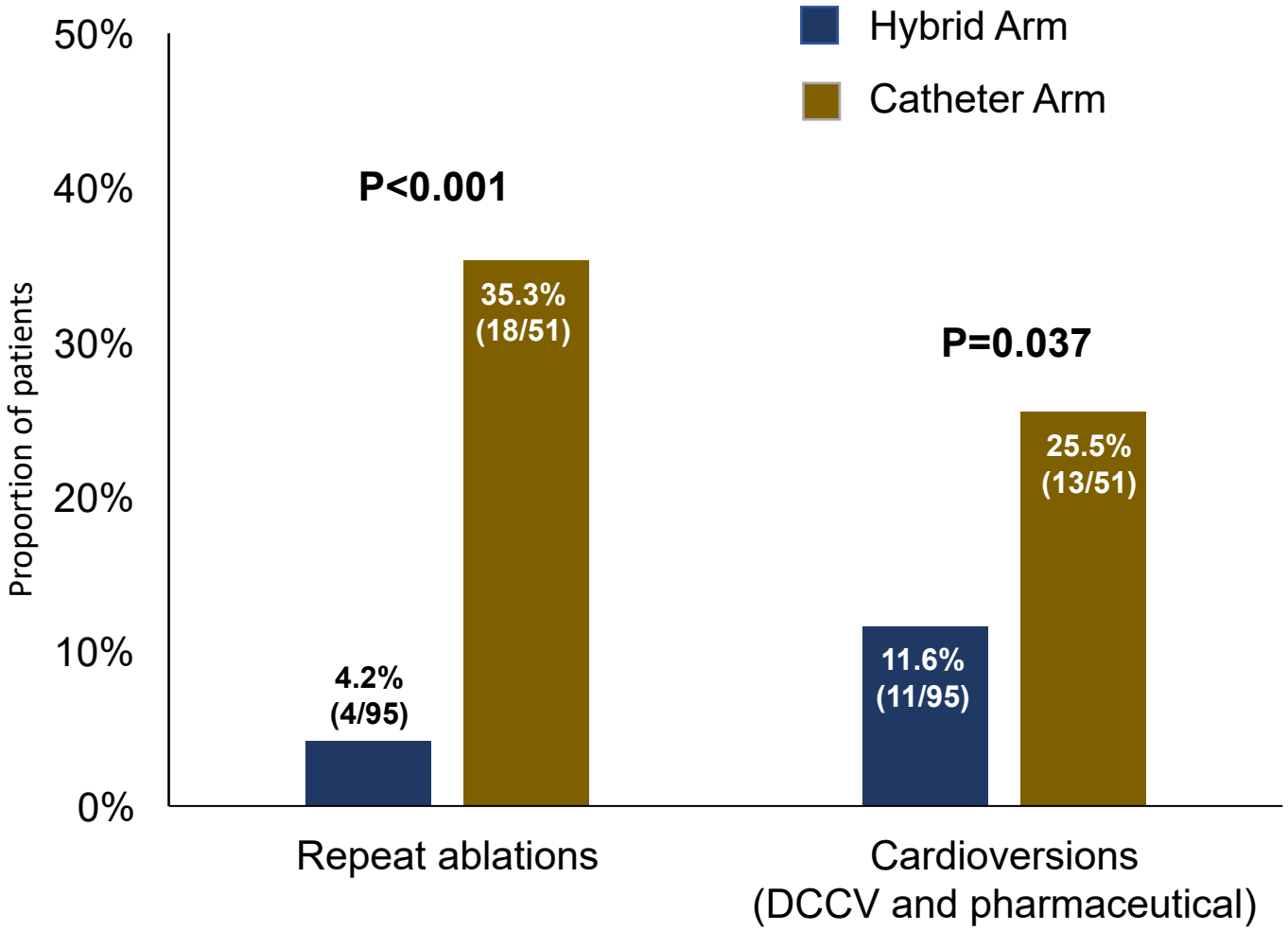



Hybrid ablation resulted in

- **31%** absolute and **74%** relative benefit increase in effectiveness in Persistent AF patients
- **42%** absolute and **167%** relative benefit increase in effectiveness in Longstanding Persistent AF patients

Note: p-values not adjusted for multiplicity

# Repeat ablations and cardioversions from T0 through 12-months follow-up




After Hybrid ablation:

Fewer repeat ablations & cardioversions

# Composite complication rate at 30-days post-index plus 30-days post-2nd stage / repeat ablation

**Hybrid arm: 7.8% (8/102)***

**P=0.751**

**Catheter arm: 5.8% (3/52)****

- *1 stroke (non-disabling)*
- *1 myocardial infarction*
- *1 pericarditis*
- *1 bleeding (at vascular access site)*
- *1 major vascular access complication*
- *1 permanent pacemaker (sick sinus syndrome)*
- *1 pneumothorax requiring intervention*
- *1 pneumonia*
- *1 aspiration after nose bleeding*

- *1 transient ischemic attack*
- *1 pericarditis*
- *1 major vascular access complication*
- *1 cardiac tamponade/perforation*
- *1 mitral valve injury requiring surgical intervention*

**One patient had 3 major complications

*One patient had 2 major complications

During 12-mo follow-up, 1 death occurred 93 days post-index procedure that was unrelated to the device/procedure and due to underlying conditions per Clinical Events Committee adjudication

# Limitations

- Symptom-driven ECG monitoring was performed at unscheduled visits. However, 48-hour Holter monitoring at 6- and 12-month follow-up for primary effectiveness is more intensive than 24-hour Holter monitoring that is currently recommended by the 2017 HRS consensus statement.

- Ablation beyond PVI (Catheter Arm) and PVI/posterior wall box (Hybrid Arm) was not standardized and accommodated institutional standard practices in 5 countries

# CEASE-AF Summary

- CEASE-AF is the largest prospective, multi-center RCT that demonstrated superior freedom from atrial arrhythmias for staged HA compared to endocardial CA including repeat ablation in patients with advanced AF

- Hybrid Ablation with LAAE resulted in a 32.4% absolute and 82.7% relative benefit increase compared to Catheter Ablation through 12-months follow-up

- Adverse safety rates were numerically higher in the Hybrid Arm ( 7.8% Vs 5.8%, p= 0.751) but not statistically different compared to the Catheter Arm

- Success of an epicardial-endocardial approach emphasizes the role of a collaborative heart team approach in the treatment of non-paroxysmal AF