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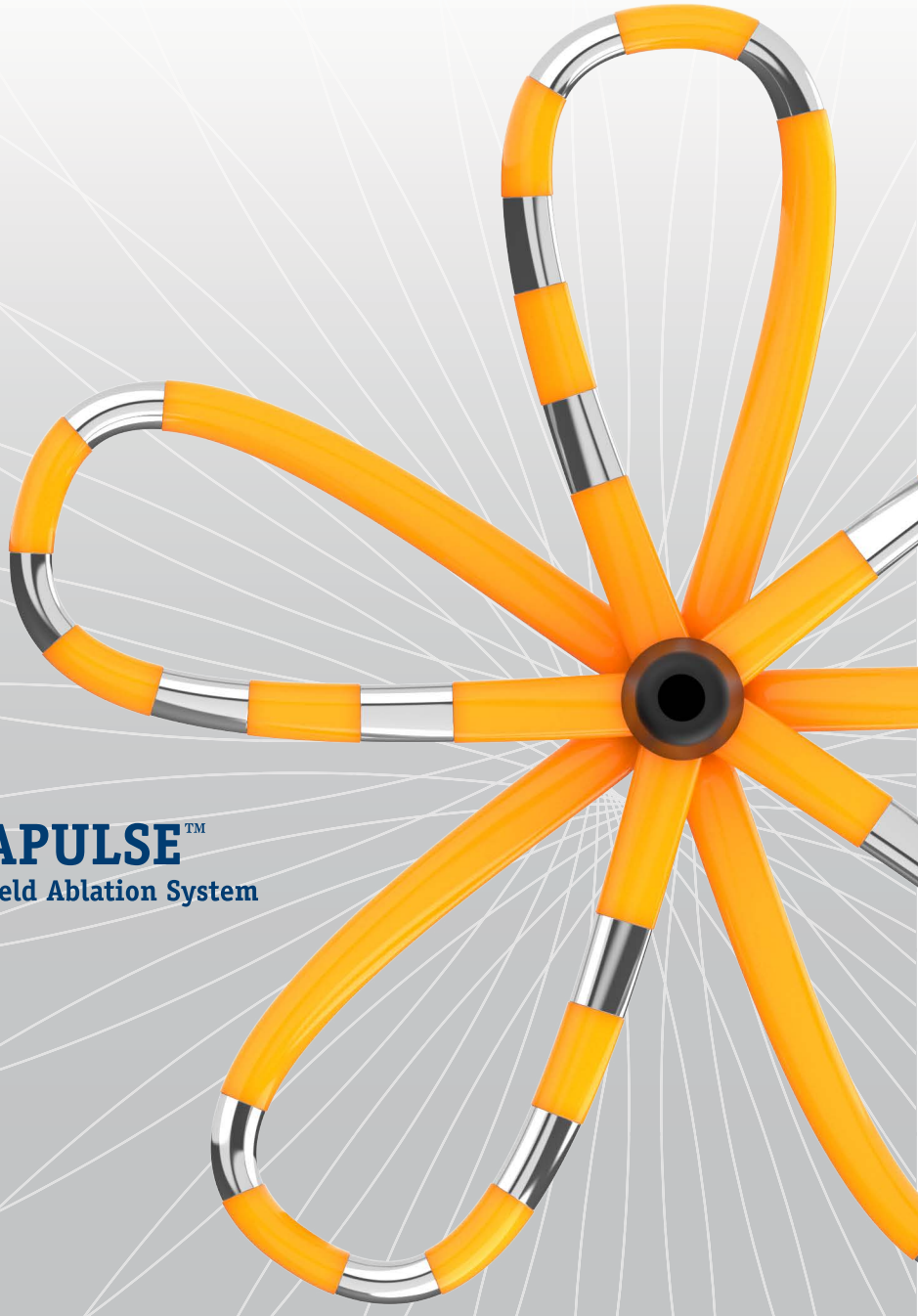
ADVENT
PIVOTAL TRIAL

CLINICAL DATA SUMMARY



FARAPULSE™
Pulsed Field Ablation System

ADVENT US IDE Clinical Trial Results

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OBJECTIVE

- The ADVENT Pivotal Trial is the first randomized clinical trial that directly compares FARAPULSE™ PFA to standard-of-care thermal ablation devices (force-sensing radiofrequency (RFA) or cryoballoon ablation (CBA)), for the treatment of paroxysmal atrial fibrillation (PAF).

ADVENT TRIAL DESIGN[1]

- Multicenter, prospective, non-inferiority randomized controlled trial (NCT04612244).
- Study sample size was 706 patients (80 Roll-ins, 626 Randomized). The primary results included the **607 patient modified Intent-to-Treat (mITT) cohort** across 30 centers and 65 operators.
  - Modified Intent-to-Treat (mITT) patients are ITT patients who received any energy delivery for pulmonary vein isolation (PVI) with the randomized endocardial ablation catheter at an Index/Rescheduled Index Procedure.
- *Primary Safety Endpoint:* A composite endpoint defined as serious adverse event related to either the use of an ablation catheter or the ablation procedure with onset within 7 days of the primary procedure and PV stenosis and atrio-esophageal fistula out to 12 months.
- *Secondary Safety Endpoint:* Aggregate pulmonary vein (PV) cross-sectional area changes from baseline to day 90.
- *Primary Effectiveness Endpoint:* Both acute and chronic procedural success through 12 months which included freedom from re-abalation or use of amiodarone. After the 90-day blanking period, chronic success required freedom from AF, AFL, AT, cardioversion and no Class I/III AAD use.

SAFETY[2,3]

- **Primary Safety Endpoint**
  - The ADVENT study met the criterion for **non-inferiority** of PFA to thermal ablation (posterior probability >0.999).
  - The primary composite safety endpoint of serious adverse events occurred in 6 FARAPULSE versus 4 thermal ablation patients (estimated incidence, 2.1% versus 1.5% (posterior means)).
- **Secondary and Additional Safety Analysis**
  - The secondary endpoint of the ADVENT trial met the criterion for **superiority** of PFA compared to thermal ablation (posterior probability >0.999).

✓ **ADVENT met the primary safety endpoint for non-inferiority* vs thermal ablation**

2.1% for PFA vs 1.5% for thermal ablation

✓ **ADVENT met the secondary safety endpoint for superiority* for less PV cross-sectional area narrowing**

0.9% for PFA vs 12% for thermal ablation

* Posterior probability > .999

EFFICACY

- **Primary Efficacy Endpoint**
  - The Bayesian estimated 12-month, single-procedure, off-drug treatment success probabilities were 73.3% for FARAPULSE and 71.3% for thermal ablation meeting the criterion for **non-inferiority** (posterior probability >0.999).
- **Additional Efficacy Endpoints**
  - *12-Month Kaplan Meier Estimate*
    - The 12-month Kaplan Meier single-procedure, off-drug estimates were 73.1% for FARAPULSE, 71.3% for thermal ablation, and more specifically 73.6% for CBA and 69.2% for RFA.
  - *Effectiveness allowing Class I/III AADs*
    - The ADVENT primary efficacy endpoint did not allow Class I/III AAD use post-90 day blanking period. The Bayesian estimated single-procedure success probabilities when Class I/III AAD use was allowed were 78.5% for FARAPULSE and 76.3% for thermal ablation.

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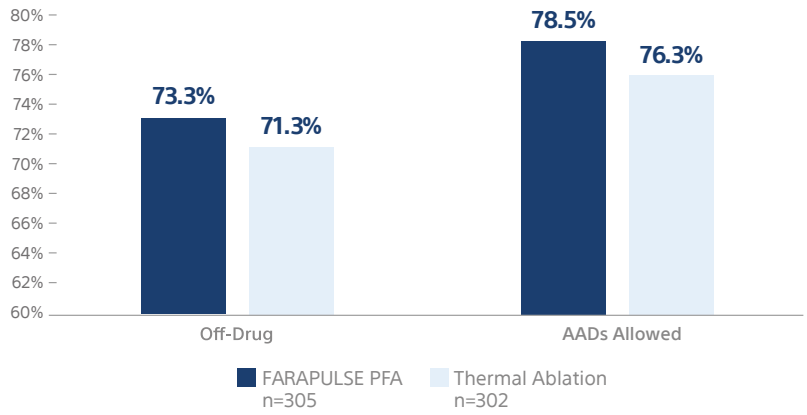
EFFICACY *(cont.)*

- *Acute PVI, Re-Ablation and PV Durability*
  - The acute PV isolation rate was 99.6% (1208/1213 PVs) for FARAPULSE and 99.8% (1182/1184 PVs) for thermal ablation.
  - Repeat ablations were performed in 4.6% of FARAPULSE patients and 6.6% in thermal ablation patients. The PVI durability in re-ablated patients was 64.8% per vein (28.6% per patient) for FARAPULSE and 64.9% per vein (26.3% per patient) for thermal ablation.

12-Month Effectiveness Outcomes (%)

Bayesian Estimates



ADVENT met the primary efficacy endpoint for non-inferiority* vs thermal ablation

73.3% for PFA vs
71.3% for thermal ablation

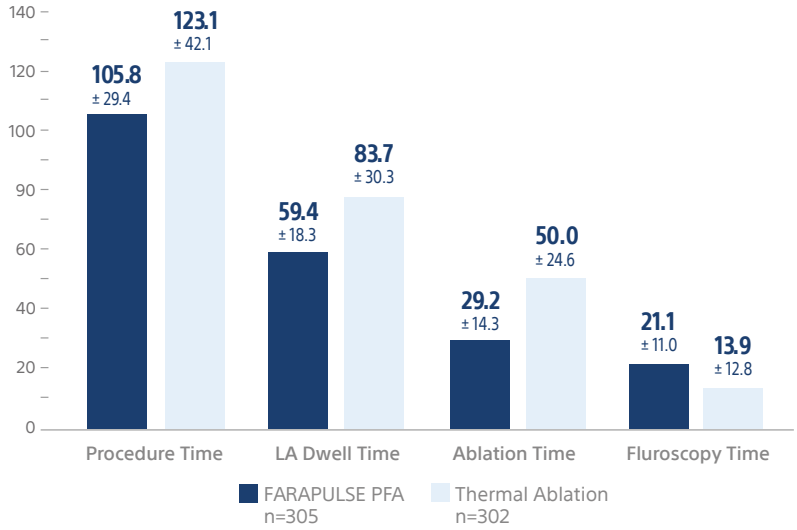
* Posterior probability > .999

PROCEDURAL CHARACTERISTICS

- The FARAPULSE AF ablation procedure time (105.8 ± 29.4 min) and catheter LA dwell time (59.4 ± 18.3 min) were significantly* shorter than thermal ablation (123.1 ± 42.1 min and 83.7 ± 30.3 min, respectively). Both included a protocol mandated 20-min waiting period. *(Bayesian credible interval (BCI) does not contain zero)
- The time from first ablation to last ablation was significantly shorter with FARAWAVE™ PFA Catheter (29.2 ± 14.3 min) versus thermal ablation (50.0 ± 24.6 min).
- Pulsed field ablation required a longer duration of fluoroscopy versus thermal ablation, as expected with operators who are new to the PFA system.

Procedural Characteristics

Procedure and LA Dwell times include a 20 minute protocol-mandated waiting period



FARAPULSE PFA procedure times were significantly* shorter with less variability than thermal ablation.

105.8 ± 29.4 min for PFA vs
123.1 ± 42.1 min for thermal ablation

* BCI does not contain zero

CONCLUSIONS

The ADVENT RCT included an experienced group of thermal ablators with limited clinical experience with the novel FARAPULSE technology. In this RCT, FARAPULSE demonstrated:

- Non-inferiority for both the primary safety and effectiveness outcomes compared to thermal ablation technology.*
- Significantly less pulmonary vein cross-sectional narrowing compared to thermal ablation.*
- Significantly shorter procedure times, reduced LA dwell time and total ablation time versus thermal ablation. Lower standard deviations across these characteristics also indicate less variability within the PFA procedures.

* Posterior probability > .999

1. Reddy, Vivek Y., et al. "A randomized controlled trial of pulsed field ablation versus standard-of-care ablation for paroxysmal atrial fibrillation: The ADVENT trial rationale and design." Heart Rhythm O2 4.5 (2023): 317-328.
2. Reddy et al. Pulsed Field Ablation or Conventional Thermal Ablation for Paroxysmal Atrial Fibrillation. Presented at: ESC 2023; August 27, 2023, Amsterdam, NL.
3. Reddy, et al., Pulsed Field or Conventional Thermal Ablation for Paroxysmal Atrial Fibrillation. *New England Journal of Medicine* (2023). *In press.*

FARAPULSE™ Pulsed Field Ablation
Indications, Safety, and Warnings

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