Effectiveness and Safety of The Dual Epicardial & Endocardial Procedure (DEEP) Approach for Treatment of Subjects with Persistent or Long Standing Persistent Atrial Fibrillation (PersAF/LSPerAF) with Radiofrequency Ablation

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Introduction

A collaborative approach between electrophysiologists and cardiothoracic surgeons to effectively target the pulmonary veins (PVs) and substrate beyond PVs may improve outcomes for persistent and long-standing persistent AF (PersAF/LSPerAF). The DEEP trial (NCT02393885) aims to establish the effectiveness and safety of a minimally invasive Hybrid Approach of bilateral thoracoscopic epicardial ablation and left atrial appendage exclusion (LAAE) with endocardial mapping/ablation to treat advanced AF after failed medical therapy.

Methods

DEEP is a prospective, international, single arm trial at 17 sites enrolling adults with drug refractory PersAF or LSPersAF (<10 years duration), left atrial diameter (LAD) ≤ 5.5cm, failed class I/III anti-arrhythmic drugs (AAD), and ≤ 2 previous failed endocardial catheter ablations (CA). Epicardial surgical ablation and LAAE was followed by endocardial CA 91 to 121 days later. Following CA, there were 90-day blanking and 90-day AAD optimization periods. Then, ECG and 24-hour rhythm monitoring was performed at 6- and 12-months post-CA with symptom driven monitoring when necessary.

The primary effectiveness endpoint was defined as freedom from documented AF/atrial flutter (AFL)/atrial tachycardia (AT) episodes >30 seconds through the 12-month follow-up visit, off Class I/III AADs, except previously failed AADs at doses not exceeding those previously failed. The goal of the primary endpoint was to establish that the DEEP procedure significantly increased effectiveness relative to the objective performance criteria of a 60% catheter ablation success rate. The primary safety endpoint was defined as a composite of device/procedure-related serious adverse events (SAE) within 30 days of epicardial ablation and 7 days of endocardial CA (including repeat ablation within the second blanking period). The prespecified safety criteria was an upper confidence limit of <28% with an underlying rate of 19%.

The trial was stopped early, and the primary effectiveness was based on the modified intention to treat (mITT) population (n=85), defined as all subjects who attempted the epicardial procedure (defined as a subject who underwent induction of anesthesia) and had at least one post-procedure follow-up visit after the 2nd blanking period (with the 2nd blanking period defined as the 90-days post endocardial ablation procedure) with non-missing primary effectiveness data. Primary safety was based on the safety population (n=90), which comprised of all enrolled subjects who underwent induction of anesthesia.

Results

Of 90 patients who received anesthesia, 83.3% (75/90) of patients had PersAF and 16.7% (15/90) had LSPersAF, with a median AF duration of 3.8 years and 48% with prior failed CA. Both endpoints met pre-specified safety/performance goals. Primary effectiveness and safety are shown in the Table.

Endpoint	Outcome
Primary effectiveness (Freedom from AF/AFL/AT off AAD (except those previously failed at doses not exceeding those previously failed)	70.6% (60/85; 95% CI: 60.9%, 80.3%; p=0.0232)
Primary safety (SAE within 30 days of epicardial procedure and 7 days of endocardial procedure(s))	6.7% (6/90; 95% CI: 2.5%, 13.9%; p<0.001)
Other effectiveness (Freedom from AF off AAD (except those previously failed at doses not exceeding those previously failed)	78.8% (67/85; 95% CI: 70.1%, 87.5%); p=0.0002

AAD=antiarrhythmic drugs; AF=atrial fibrillation; AFL=atrial flutter; CI=confidence interval; SAE=serious adverse event

Limitations

This study is a single arm design, however comparable effectiveness after Hybrid ablation with LAAE was shown in recent randomized controlled trials and these rates of effectiveness were significantly higher than those achieved with endocardial CA in those studies.2,3 Implantable loop recorders are optimal for continuous rhythm assessment, however this is not typically feasible in a clinical trial setting; DEEP trial monitoring modalities and schedule align with societal guidelines.4 Although the trial was stopped prematurely prior to meeting the predetermined sample size, effectiveness and safety outcomes were still achieved.

Key Takeaways

- DEEP met pre-specified primary effectiveness and safety endpoints, with freedom from AF/AFL/AT off AADs (except those previously failed at doses not exceeding those previously failed) of 70.6% and composite SAE rate of 6.7% within 30 days of epicardial and 7 days of endocardial procedures.
- A collaborative approach between electrophysiologists and cardiothoracic surgeons to Hybrid ablation is effective for treating PersAF/LSPerAF when benefit-risk is deemed favorable, given limited alternative treatments for this population.

Reference:
1. *Ellenbogen K, Khoynezhad A, de Asmundis C et al. Circulation 2023;148: A15606*

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