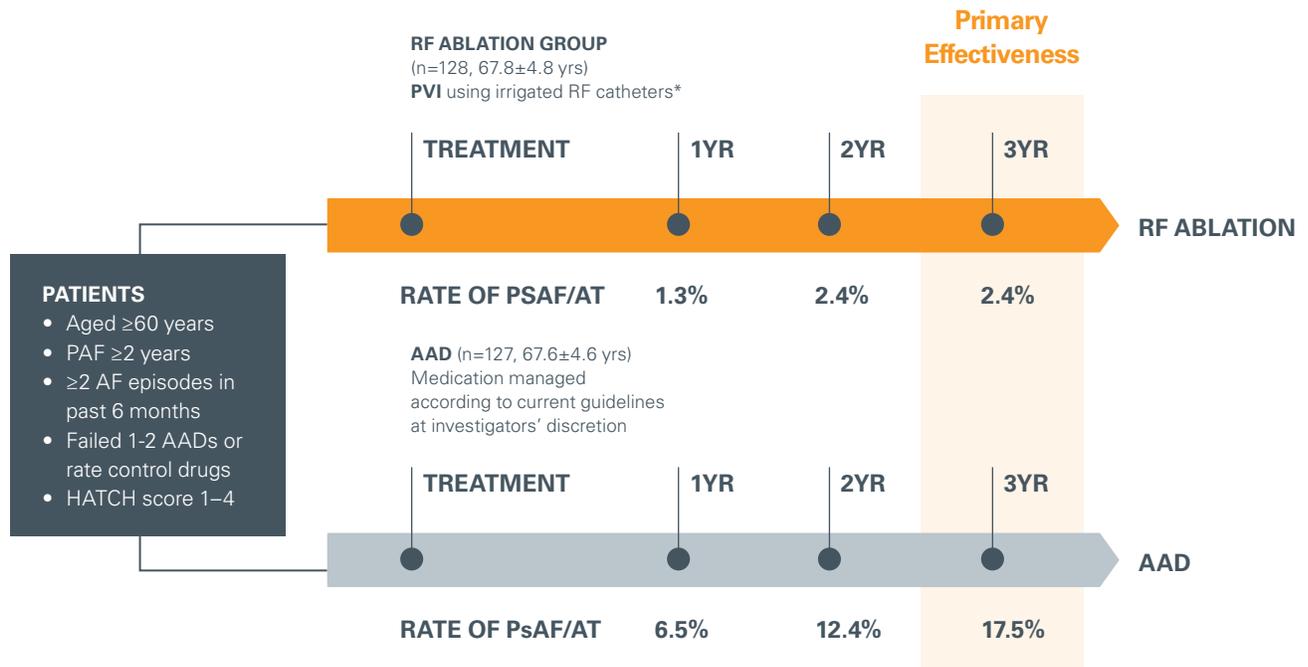


ATTEST Trial Results¹

Results of the Atrial Fibrillation Progression Trial (ATTEST), sponsored by Biosense Webster, Inc. were presented on August 31st at the 2019 ESC Congress (Paris, France). The ESC Congress is one of the largest cardiology meetings globally, and the study was presented by a global key opinion leader in the field of cardiology, Dr. Karl-Heinz Kuck. The study design and key results are summarized in the figure below. This is the first study to show that paroxysmal atrial fibrillation (PAF) patients treated with radiofrequency (RF) catheter ablation were almost 10-times less likely to develop persistent AF (PsAF) than patients on antiarrhythmic drugs (AAD) alone at 3 years follow-up. This is also the first randomized, AF study to introduce progression from PAF to PsAF as a clinical endpoint.



* NAVISTAR THERMOCOOL®, THERMOCOOL® SMARTTOUCH or THERMOCOOL® SF catheters) in conjunction with 3D electroanatomic mapping (CARTO® 3, CARTO® XP, CARTO® RMT)

Key takeaway 1: RF catheter ablation was superior to AAD in delaying the progression to PsAF

At 3 years, more patients from AAD group developed PsAF (ablation: 2.4%, AAD: 17.5%), and treatment with RF ablation reduced the likelihood of developing PsAF by almost 10 times.

Progression of paroxysmal to persistent AF involves electrical and structural abnormalities or remodeling. Previous studies showed that continuing AAD in AF patients who have failed prior, albeit different, AAD treatment yields low overall efficacy.²

In the ATTEST study, the superior treatment effect of RF catheter ablation was evident as early as 1-year post-treatment and sustained through 3 years of follow-up.

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Key takeaway 2: Patients receiving RF ablation experienced fewer AF/AT recurrences

At 3 years, the rate of recurrent AF/AT was lower in the RF ablation group compared with the AAD group

In the literature, RF ablation has been shown to be superior to AAD in reducing long-term AF/AT recurrence in patients with drug-refractory paroxysmal AF.^{3,4} In this study, the incidence of recurrent AF/AT was consistently lower with RF ablation than with AAD treatment starting from 1-year through the 3-year follow-up period. Most patients required only 1 ablation within the follow-up period, with a 17.1% repeat ablation rate at 3-years. Note that the study was initiated in 2012 and the majority of ablations were performed with non-CF catheters, hence, the success rates were lower than seen in newer studies performed exclusively with CF catheters.

| AF/AT RECURRENCE* | 1-YEAR | 2-YEAR | 3-YEAR |
|-------------------|--------|--------|--------|
| RF Ablation | 44.1% | 51.2% | 57.1% |
| AAD | 66.9% | 78.4% | 84.7% |

* by Kaplan-Meier analyses; all comparisons are statistically significant (p<0.005)

AAD: Antiarrhythmic drug, AF: Atrial fibrillation AT: Atrial tachycardia, RF: Radiofrequency

Key takeaway 3: Increased clinical benefit with early RF catheter ablation

Patients ≥65 yrs were nearly 4-times more likely to progress to PsAF than patients <65 yrs

Our results support the notion of increased benefit with early catheter ablation. Cox regression analysis yielded a hazard ratio of 3.87 between patients ≥65 yrs and <65 yrs, indicating that patients ≥65 yrs were nearly 4-times more likely to progress to persistent AF/AT, regardless of treatment group. As only RF energy was used in the study, applicability of these catheter ablation results to other ablation technologies (e.g. cryoablation) is unknown.

Bibliography

1. Kuck, K. H. L., D. Mikhaylov, E. Romanov, A. Geller, L. Kalejs, O. Neumann, T. Davtyan, K. On, Y. K. Popov, S. Ouyang, F. Catheter ablation can delay progression from paroxysmal to persistent atrial fibrillation in The European Society of Cardiology Congress (Paris, France, 2019). Pending formal publication.
2. Curtis, A. B. et al. Clinical factors associated with abandonment of a rate-control or a rhythm-control strategy for the management of atrial fibrillation in the AFFIRM study. *Am Heart J* 149, 304-308, doi:10.1016/j.ahj.2004.08.012 (2005).
3. Pappone, C. et al. A randomized trial of circumferential pulmonary vein ablation versus antiarrhythmic drug therapy in paroxysmal atrial fibrillation: the APAF Study. *J Am Coll Cardiol* 48, 2340-2347, doi:10.1016/j.jacc.2006.08.037 (2006).
4. Wilber, D. J. et al. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: a randomized controlled trial. *JAMA* 303, 333-340, doi:10.1001/jama.2009.2029 (2010).



Important information: Prior to use, refer to the instructions for use supplied with the device for indications, contraindications, side effects, warnings and precautions.

Caution: US law restricts this device to sale by or on the order of a physician.

In the US, THERMOCOOL® Navigation Catheters are indicated for the treatment of drug refractory recurrent symptomatic paroxysmal atrial fibrillation, when used with CARTO® 3 Systems (excluding NAVISTAR® RMT THERMOCOOL® Catheter).

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