FIRE AND ICE℠

AF Ablation Clinical Trial

STUDY DESIGN[1,2]

Randomized non-inferiority study design with the Cryoballoon meeting the primary endpoints

The FIRE AND ICE Trial included 762 patients randomized 1:1 at 16 sites in 8 countries

SECONDARY ANALYSES[3]

Secondary analyses from the FIRE AND ICE trial demonstrated significant improvements that favor the Cryoballoon group over the RFC group for clinically meaningful outcomes.

Relative to RFC, Cryoballoon Demonstrated:

21% Fewer All-cause Hospitalizations

33% Fewer Repeat Ablations*

34% Fewer Cardiovascular Hospitalizations* (including AF hospitalization†)

50% Fewer Direct Current Cardioversions

*Predefined secondary analyses
†Not predefined but included in analyses

Arctic Front Advance™ Cryoballoon

Medtronic

Study Design/ Objectives[1]	Multicenter, prospective, 1:1 randomized, non-inferiority, parallel group, open, blinded-endpoint study comparing the efficacy and safety of pulmonary vein isolation using Arctic Front™ catheters versus THERMOCOOL® point-by-point radiofrequency catheters with CARTO® 3D mapping system in patients with paroxysmal atrial fibrillation.
Enrollment Criteria	Key Inclusion Criteria: ▪ Symptomatic paroxysmal atrial fibrillation (PAF) ▪ Prior failure of ≥ 1 antiarrhythmic drug (class I or III AAD) ▪ ≥ 18 and ≤ 75 years of age
Primary Endpoints	**Primary Efficacy Endpoint:** Time to first documented recurrence of atrial fibrillation (AF) > 30 sec/atrial tachycardia (AT)/ atrial flutter (AFL), prescription of AAD, or repeat ablation (a blanking period of 3 months was maintained after the index procedure) **Primary Safety Endpoint:** Time to first all-cause death, all-cause stroke/TIA or treatment-related serious AEs
Primary Outcomes	The Cryoballoon met the primary safety and efficacy endpoints of non-inferiority.
Secondary Analyses[2]	Sites reported time to first and number of all-cause hospitalizations, including: ▪ Cardiovascular-related hospitalizations* (including AF hospitalization†) (e.g., repeat ablations*, and direct current cardioversions) ▪ Hospitalizations defined as a prolonged stay of ≥ 2 nights post index ablation (or) ▪ In-patient stay not concurrent with index procedure of ≥ 1 calendar day Quality of life* was assessed every 6 months using the SF-12 and EQ-5D-3L
Secondary Outcomes	**All-cause hospitalizations: RFC:** 267 events in 156 patients (156/376; 41.5%) **Cryo:** 210 events in 122 patients (122/374; 32.6%) Kaplan Meier Log-Rank p-value = 0.01 **Cardiovascular hospitalizations: RFC:** 203 events in 135 patients (135/376; 35.9%) **Cryo:** 139 events in 89 patients (89/374; 23.8%) Kaplan Meier Log-Rank p-value < 0.01 **Repeat ablation: RFC:** 70 events in 66 patients (66/376; 17.6%) **Cryo:** 49 events in 44 patients (44/374; 11.8%) Kaplan Meier Log-Rank p-value = 0.03 **Direct Current Cardioversion: RFC:** 28 DCCVs in 24 patients (24/376; 6.4%) **Cryo:** 13 DCCVs in 12 patients (12/374; 3.2%) Kaplan Meier Log-Rank p-value = 0.04

*Predefined secondary analyses

†Not predefined but included in analyses

References

[1] Kuck KH, Brugada J, Fürnkranz A, et al. Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation. *New Engl J Med*. Published online April 4, 2016.

[2] Fürnkranz A, Brugada J, Albenque JP, et al. Rationale and Design of FIRE AND ICE: A multicenter randomized trial comparing efficacy and safety of pulmonary vein isolation using a cryoballoon versus radio frequency ablation with 3D-reconstruction. *J Cardiovasc Electrophysiol*. December 2014;25(12):1314-1320.

[3] Kuck KH, Brugada J, Fürnkranz A, et al. The FIRE and ICE Trial: looking beyond the primary efficacy and safety endpoints. Late-breaking clinical trial. Presented at Cardiostim 2016 (Abstract).

Brief Statement
Arctic Front™ and Arctic Front Advance™ Cardiac CryoAblation Catheter Systems
Indications: The Arctic Front Advance™ Cardiac CryoAblation Catheter catheter is indicated for the treatment of patients with atrial fibrillation (AF).

Contraindications: Use of either Arctic Front or Arctic Front Advance cryoballoons is contraindicated:

1. In the ventricle because of the danger of catheter entrapment in the chordae tendinae,
2. In patients with one or more pulmonary vein stents,
3. In patients with cryoglobulinemia,
4. In patients with active systemic infections,
5. In conditions where the manipulation of the catheter within the heart would be unsafe (e.g., intracardiac mural thrombus).

Brief Statement: Refer to the device technical manual for detailed information regarding the procedure, indications, contraindications, warnings, precautions, and potential complications/adverse events. For further information, please contact your Medtronic Sales Representative and/or consult Medtronic's website at www.medtronic.eu

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