CRYO-FIRST TRIAL RESULTS

Arctic Front Advance™ Cardiac Cryoablation vs. Antiarrhythmic Drugs as a First-Line Therapy for Paroxysmal Atrial Fibrillation

Arctic Front™ cardiac cryoablation catheters hereafter referred to as cryoballoon

CRYOBALLOON ABLATION IS A SAFE AND EFFECTIVE FIRST-LINE TREATMENT[1]

Medtronic
Further, Together

CRYO-FIRST PRIMARY ENDPOINT RESULTS

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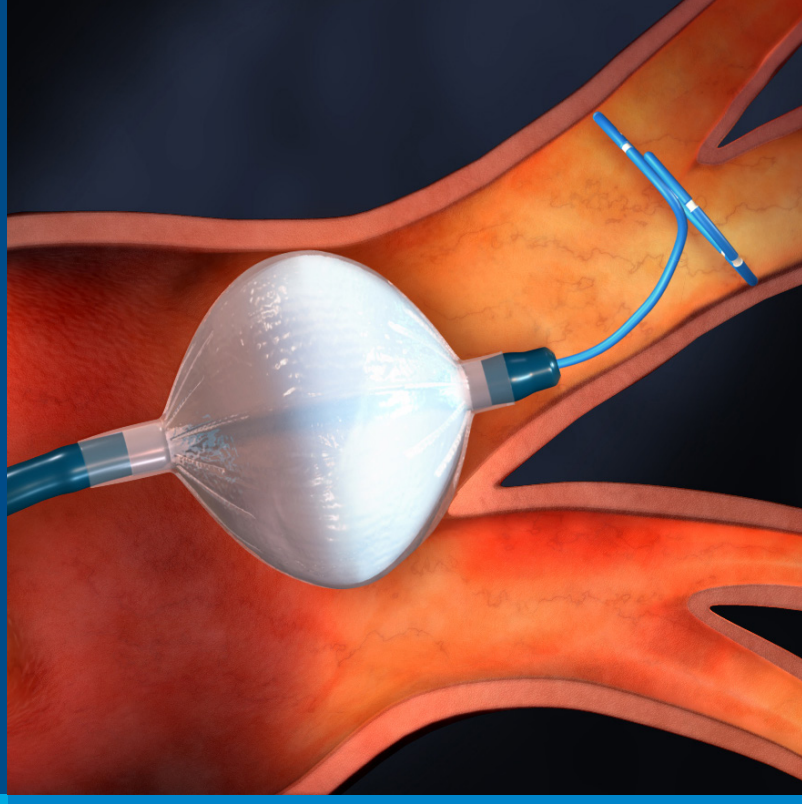


PURPOSE

The Cryo-FIRST trial is designed to compare the clinical safety and efficacy of antiarrhythmic drug (AAD) treatment (Class I or III AAD) with that of pulmonary vein isolation (PVI) using the Arctic Front Advance™ Cardiac Cryoablation Catheter.

TRIAL DESIGN

- Cryo-FIRST is a 1:1 randomized multicenter study with 220 patients enrolled from 18 sites in 9 countries across Europe, Australia, and Latin America
- Patients had symptomatic paroxysmal atrial fibrillation (PAF), were free of underlying heart disease, and had not been administered an AAD
- The blanking period was 90 days, and patients were monitored at 1,3,6,9 and 12 months via 7-day Holter

PRIMARY ANALYSIS

The primary study endpoint was freedom from any atrial arrhythmia recurrence at 12 months defined as at least one episode of AF, atrial flutter or atrial tachycardia with a duration > 30 seconds following a blanking period or a dosing optimizing period of 3 months.

(Holter recordings were classified by an independent core lab)

SECONDARY ANALYSIS

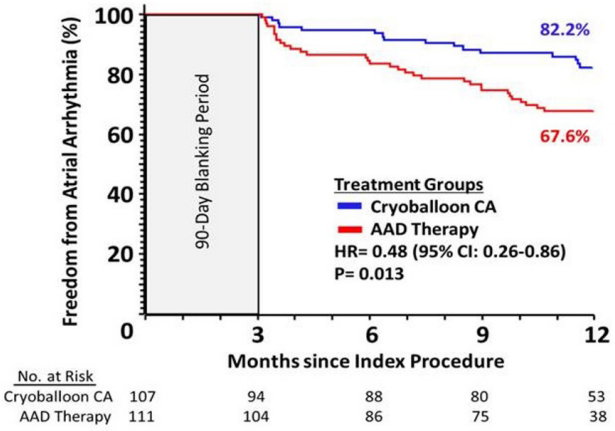
Safety was evaluated by collecting and classifying all adverse events.

(Adverse events were classified by a committee of 3 experienced independent cardiologists)

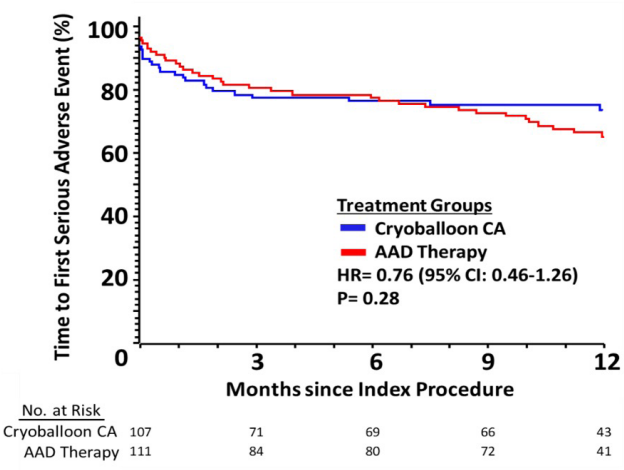
TRIAL RESULTS

- By predefined intention-to-treat analysis, freedom from atrial arrhythmias after blanking was achieved in 82.2% of subjects in the cryoablation arm and 67.6% of subjects in the AAD arm (HR=0.48, P=0.013)
- There was no difference in time-to-first SAE in the cryoablation arm vs AAD arm (HR=0.76, P=0.28)
- There were no deaths, atrio-esophageal fistula, pericardial tamponade, or stroke reported during the study and no phrenic nerve injuries after hospital discharge
- 187 randomized patients completed the 12-month follow-up (85.8% of total randomized patients)
- Crossovers occurred in total in 9% (N=20) of patients, including 1 (1%) patient in the cryoablation arm and 19 (17%) patients in the AAD arm

TIME TO FIRST ATRIAL ARRHYTHMIA RECURRENCE:



TIME TO FIRST SERIOUS ADVERSE EVENT:



BASELINE CHARACTERISTICS OF THE STUDY POPULATION:

	Arctic Front Advance™ Cryoablation (N = 107)	Antiarrhythmic drugs (N = 111)	Total Subjects (N = 218)
Male	76 (71.0%)	72 (64.9%)	148 (67.9%)
Age	50.5 (13.1)	54.1 (13.4)	52.4 (13.3)
Age Median (25th - 75th Percentile)	50.0 (41 - 60)	55.0 (47 - 65)	53.0 (43 - 63)
Age Minimum - Maximum	20 - 75	20 - 74	20 - 75
NYHA Class I	106 (99.1%)	109 (98.2%)	215 (98.6%)
Time from First AF Diagnosis (years)	1.9 (3.4)	2.6 (5.1)	2.2 (4.4)
EHRA I	0 (0.0%)	0 (0.0%)	0 (0.0%)
EHRA II	75 (70.1%)	83 (74.8%)	158 (72.5%)
EHRA III	30 (28.0%)	25 (22.5%)	55 (25.2%)
EHRA IV	2 (1.9%)	1 (0.9%)	3 (1.4%)
Coronary artery disease	2 (1.9%)	1 (0.9%)	3 (1.4%)
Hypertension	33 (30.8%)	40 (36.0%)	73 (33.5%)
Valve Dysfunction	3 (2.8%)	2 (1.8%)	5 (2.3%)
Diabetes	1 (0.9%)	4 (3.6%)	5 (2.3%)
Hyperlipidemia	23 (21.5%)	25 (22.5%)	48 (22.0%)

Values are n (%) or mean (standard deviation).
NYHA, New York Heart Association.
EHRA, European Heart Rhythm Association score.

AAD, Antiarrhythmic Drug
CA, Cryoballoon Catheter Ablation

CRYO-FIRST QUALITY OF LIFE RESULTS

The pre-defined AF-specific quality of life (QoL) analysis compared the QoL benefits of AAD therapy and Arctic Front Advance™ Cardiac Cryoablation as first-line therapies.

CONTEXT

The 2020 European Society of Cardiology (ESC) guidelines on atrial fibrillation (AF) state that PVI should be considered as a first-line therapy to improve symptoms associated with paroxysmal AF (class IIa, level B recommendation)[12].

SYMPTOM EVALUATION

Patient symptoms were assessed using the EHRA score at baseline and follow-up.

AF SPECIFIC QUALITY OF LIFE ANALYSIS

AF-specific health-related QoL was evaluated as a secondary endpoint using the Atrial Fibrillation Effect on Quality-of-Life (AFEQT) questionnaire at baseline and at 1, 3, 6, 9- and 12-months post index treatment.

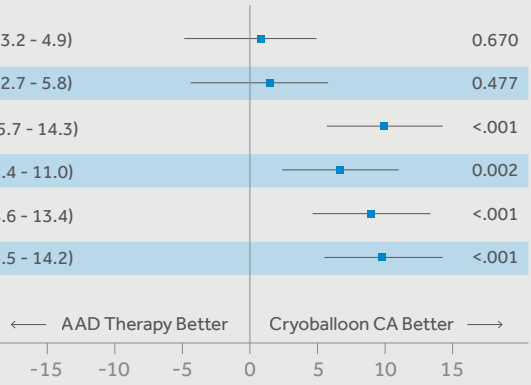
- AFEQT scores range from 0 (complete disability) to 100 (no disability)
- A change in AFEQT score of ± 5 has been associated with a clinically meaningful improvement[13]

CONCLUSION

Cryoablation resulted in a significant improvement in AF-specific health-related quality of life at 12 months compared to AAD therapy in treatment naïve patients with symptomatic PAF.

ADJUSTED MEAN DIFFERENCE IN AFEQT SCORES

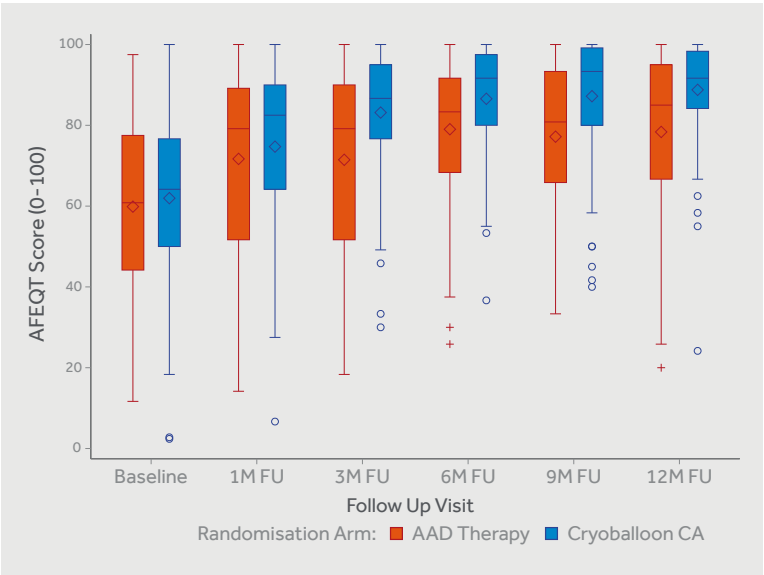
Follow up Visit	AAD Therapy	Cryoballoon CA	Adjusted Mean Diff. (95% CI)	p-value
Baseline	107	105	0.9 (-3.2 - 4.9)	0.670
1M FU	98	90	1.5 (-2.7 - 5.8)	0.477
3M FU	96	89	10.0 (5.7 - 14.3)	<.001
6M FU	94	90	6.7 (2.4 - 11.0)	0.002
9M FU	93	87	9.0 (4.6 - 13.4)	<.001
12M FU	92	89	9.9 (5.5 - 14.2)	<.001



A statistically significant and clinically meaningful improvement for the AFEQT summary score was observed after Cryoballoon catheter ablation compared to AAD therapy at 3, 6, 9 and 12 months.

The adjusted mean difference was calculated using mixed models for continuous outcomes to account for repeated measures using patient as the subject.

MEAN AND MEDIAN AFEQT SCORE



Clinically meaningful improvements in health-related QoL were observed in both treatment groups at 12 months.

- QoL was similar between groups at baseline (AAD: 59.9±20.6; Cryoballoon CA: 62.0±19.5)
- At 12 months, the AFEQT score was 78.1±19.8 in the AAD arm and 88.9±12.8 in the Cryoballoon CA arm.

Boxes indicate the interquartile range (IQR), with the mid-line representing the median and the diamond representing the mean. Whiskers extend from each box to the farthest point within ± 1.5 × the IQR. Observations outside this range are considered outliers and denoted by small circles.

SYMPTOM EVALUATION

More patients in the cryoablation group (86.5%) were without symptoms (EHRA score 1) at 12 months compared to the patients in the AAD group (70.4%, P=0.017).

CA, Cryoballoon Catheter Ablation

AF IS PROGRESSIVE IN NATURE

33 million people are estimated to have AF globally, with 14-17 million AF patients anticipated in Europe by 2030[2].

If left untreated, AF is associated with an increased risk of death, stroke, heart failure, and an array of symptoms that can negatively impact patient quality of life[2-6]. Accordingly, improving rhythm control and reducing AF symptoms are important clinical priorities.

For patients with symptomatic paroxysmal AF, antiarrhythmic drugs (AAD) are often prescribed as the first-line therapy. However, these drugs fail to prevent AF recurrence in up to 50% of patients[7]. Some of these patients go on to receive catheter ablation. Importantly, prior studies suggest that a shorter diagnosis to ablation time is associated with lower rates of atrial arrythmia recurrence, repeat procedures, and cardiovascular hospitalization[8-11].

These observations paired with evidence that catheter ablation can halt AF progression more effectively than AAD therapy[11] has sparked debate around the optimal first-line therapy for symptomatic AF patients.

The positive results from the Cryo-FIRST study demonstrate: Cryoballoon ablation is safe and superior to AAD therapy in reducing AF recurrence in this first-line patient population[1].

The Cryo-FIRST trial safety and efficacy results[1] are consistent with the 800+ articles in peer-reviewed journals from the Arctic Front™ family of cryoablation catheters.

See the device manuals for detailed information regarding the instructions for use, indications, contraindications, warnings, precautions, and potential adverse events.

For further information, contact your local Medtronic representative.
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The Arctic Front Advance™ and the Arctic Front Advance Pro™ Cardiac Cryoablation Catheter systems are indicated for the treatment of patients with atrial fibrillation.

For applicable products, consult instructions for use on:
www.medtronic.com/manuals

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