



# First-Line cryoablation trials for paroxysmal AF: STOP-AF FIRST, EARLY AF and CRYO-FIRST

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# CONFLICTS OF INTEREST

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- Consulting fees and speaking honoraria: Boston Scientific Inc., Farapulse Inc., Galaxy Medical Inc., Biosense&Webster
- Contracted research: Boston Scientific Inc., Farapulse Inc., Galaxy Medical Inc., Biosense&Webster

# Why ablation as a first line?

- Why the rush?
- Why PVI as an early treatment option
- Less AF means less LA remodeling/less fibrosis
- Long term AAD therapy is road to nowhere + the earlier we intervene, the greater the chance patient will be PVI responder

**SINUS RHYTHM MATTERS ON THE LONGER RUN!!!!**

# RHYTHM or RATE CONTROL PUZZLE SOLVED?

## The NEW ENGLAND JOURNAL of MEDICINE

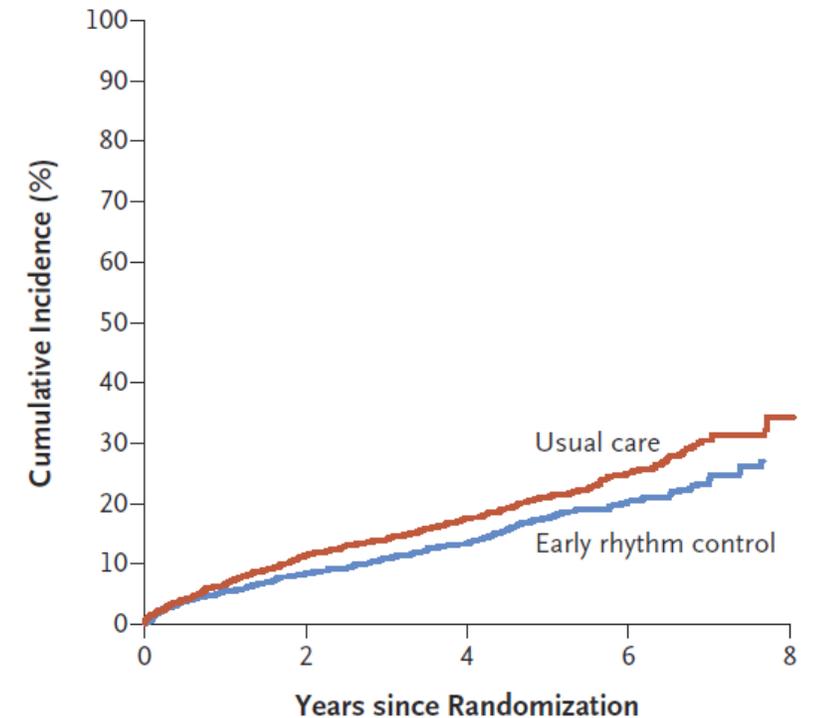
ESTABLISHED IN 1812

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### Early Rhythm-Control Therapy in Patients with Atrial Fibrillation

P. Kirchhof, A.J. Camm, A. Goette, A. Brandes, L. Eckardt, A. Elvan, T. Fetsch, I.C. van Gelder, D. Haase, L.M. Haegeli, F. Hamann, H. Heidbüchel, G. Hindricks, J. Kautzner, K.-H. Kuck, L. Mont, G.A. Ng, J. Rekosz, N. Schoen, U. Schotten, A. Suling, J. Taggeselle, S. Themistoclakis, E. Vettorazzi, P. Vardas, K. Wegscheider, S. Willems, H.J.G.M. Crijns, and G. Breithardt, for the EAST-AFNET 4 Trial Investigators\*



#### No. at Risk

Usual care	1394	1169	888	405	34
Early rhythm control	1395	1193	913	404	26

The first primary outcome was a composite of death from cardiovascular causes, stroke, or hospitalization with worsening of heart failure or acute coronary syndrome.

# AF ablation delays progression to PerAF



ESC

European Society of Cardiology  
doi:10.1093/europace/euaa298

Europace (2020) 00, 1–8

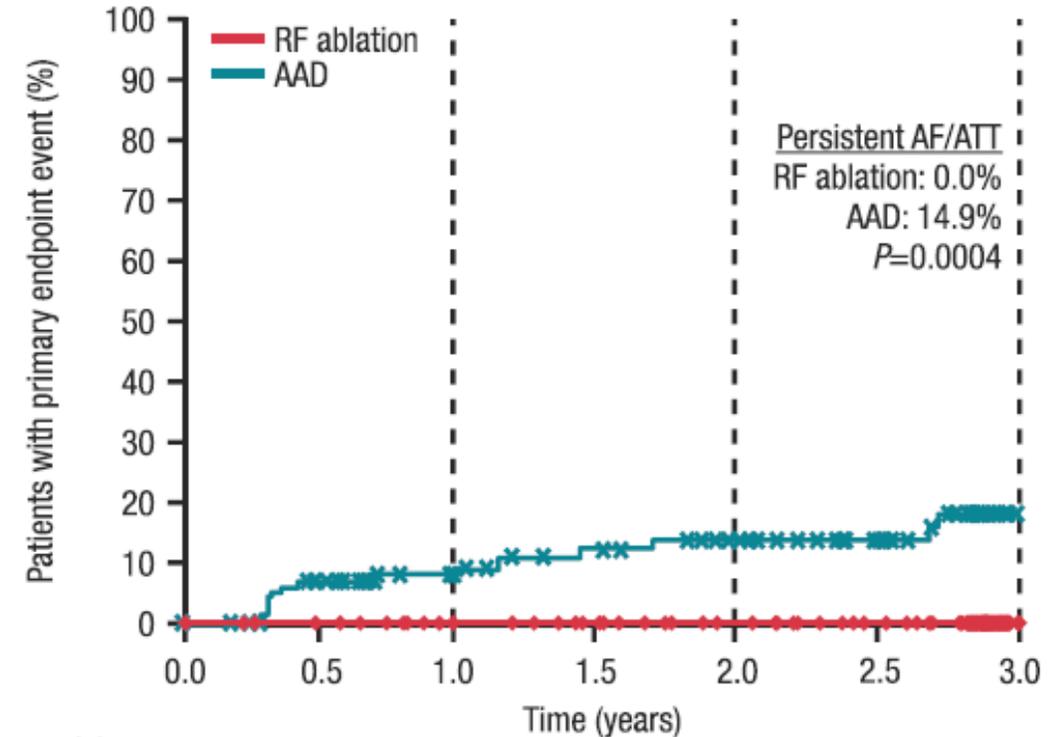
CLINICAL RESEARCH

## Catheter ablation or medical therapy to delay progression of atrial fibrillation: the randomized controlled atrial fibrillation progression trial (ATTEST)

Karl-Heinz Kuck<sup>1\*</sup>, Dmitry S. Lebedev<sup>2</sup>, Evgeny N. Mikhaylov<sup>2</sup>, Alexander Romanov<sup>3</sup>, László Gellér<sup>4</sup>, Oskars Kalējs<sup>5</sup>, Thomas Neumann<sup>6</sup>, Karapet Davtyan<sup>7</sup>, Young Keun On<sup>8</sup>, Sergey Popov<sup>9</sup>, Maria Grazia Bongiorno<sup>10</sup>, Michael Schlüter<sup>11</sup>, Stephan Willems<sup>12</sup>, and Feifan Ouyang<sup>1\*</sup>

D

ITT population (HRS 2017)



# patients at risk

	0.0	0.5	1.0	1.5	2.0	2.5	3.0
RF ablation	128	95	88	80	68	58	34
AAD	127	98	86	75	66	55	34

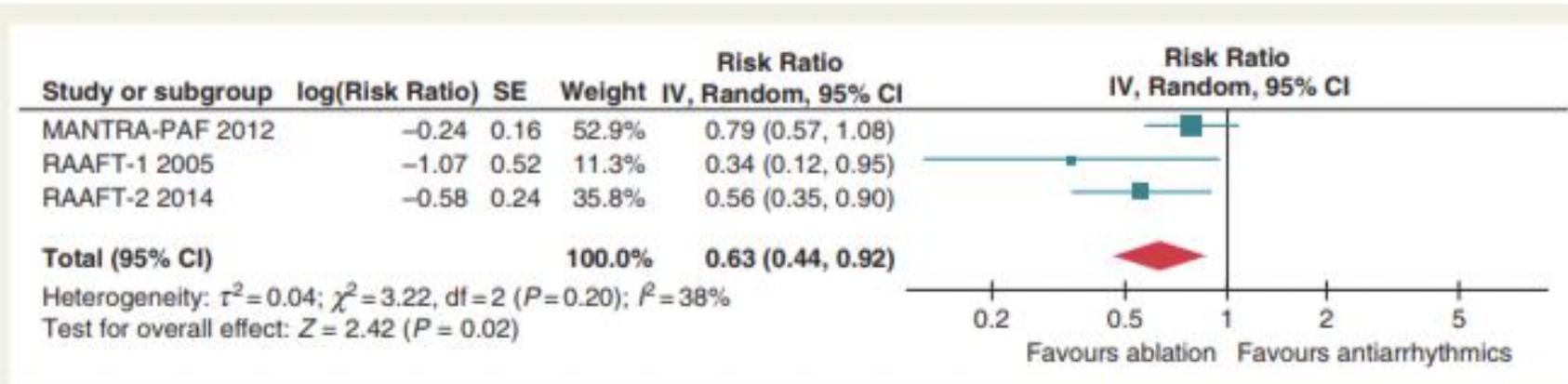
# How does the cryoballoon fit into the AF story?

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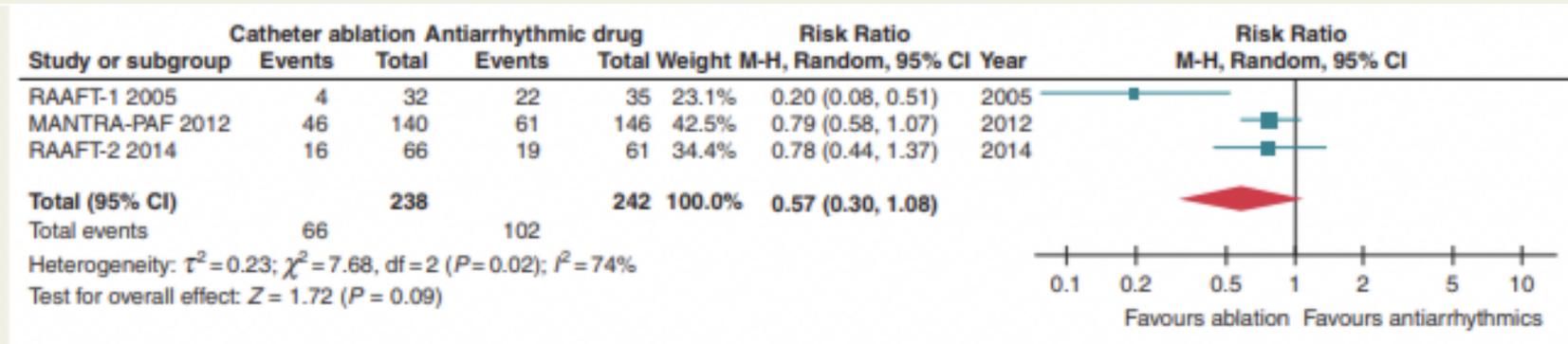
- Cryoballoon is a good PVI tool (all PVs durably isolated in 60-70% of patients)
- ...reasonably effective
- ...reasonably safe
- ...reproducible procedural time
- ...easy to master (compared to point by point ablation)

# Meta analysis of 3 trials using RFA:

- Prior first-line studies have evaluated “old generation” point-by-point radiofrequency catheter ablation<sup>1-3</sup>



**Figure 2** Forest plot showing the risk of recurrence of atrial fibrillation after radiofrequency ablation or antiarrhythmic drug treatment in three randomized studies. RAAFT-2 study included also the occurrence of atrial tachycardia and flutter.



**Figure 3** Forest plot showing the risk of symptomatic atrial fibrillation after radiofrequency ablation or antiarrhythmic drug treatment in three randomized studies.

1. Wazni OM et al. JAMA 2005;293:2634-40.
2. Cosedis Nielsen J et al. N Engl J Med 2012;367:1587-95.
3. Morillo CA et al. JAMA 2014;311:692-700.
4. Hakalahti A et al. Europace 2015;17:370-8.

# 2020/2021 – 3 new trials using CB - PVI only

## EARLY AF<sup>1</sup>

- **303 pts** randomized to PVI or AAD
- Primary endpoint: **freedom from any AA**
- FUP – **ILR**

## STOP AF FIRST<sup>2</sup>

- **203 pts** randomized to PVI or AAD
- Primary endpoint: **freedom from any AA**
- FUP – **weekly TTM+TTM with symptoms**

## CRYO FIRST<sup>3</sup>

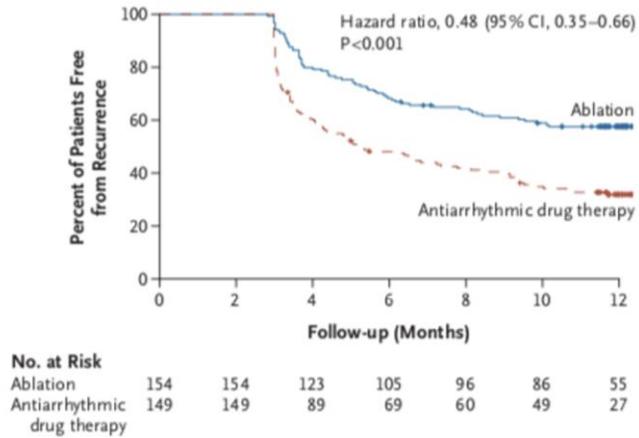
- **220 pts** randomized to PVI or AAD
- Primary endpoints: **Freedom from any AA**
- QoI
- FUP – **7 day Holter ECGs**

<sup>1</sup>Andrade J. et al. N Engl J Med 2021; 384:305-315

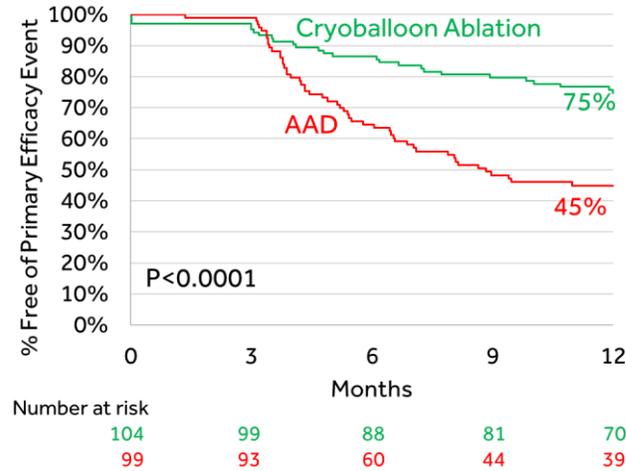
<sup>2</sup>Wazni O. et al. N Engl J Med 2021; 384:316-324

<sup>3</sup>Kuniss M. et al. Europace 2021;00:1-9

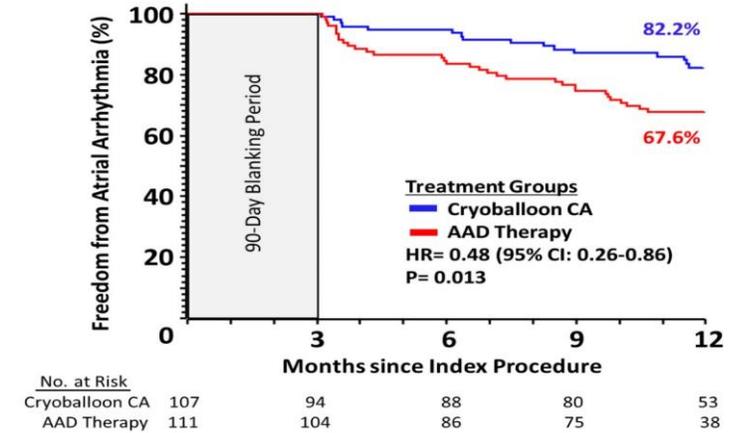
# Primary efficacy endpoint



## EARLY AF



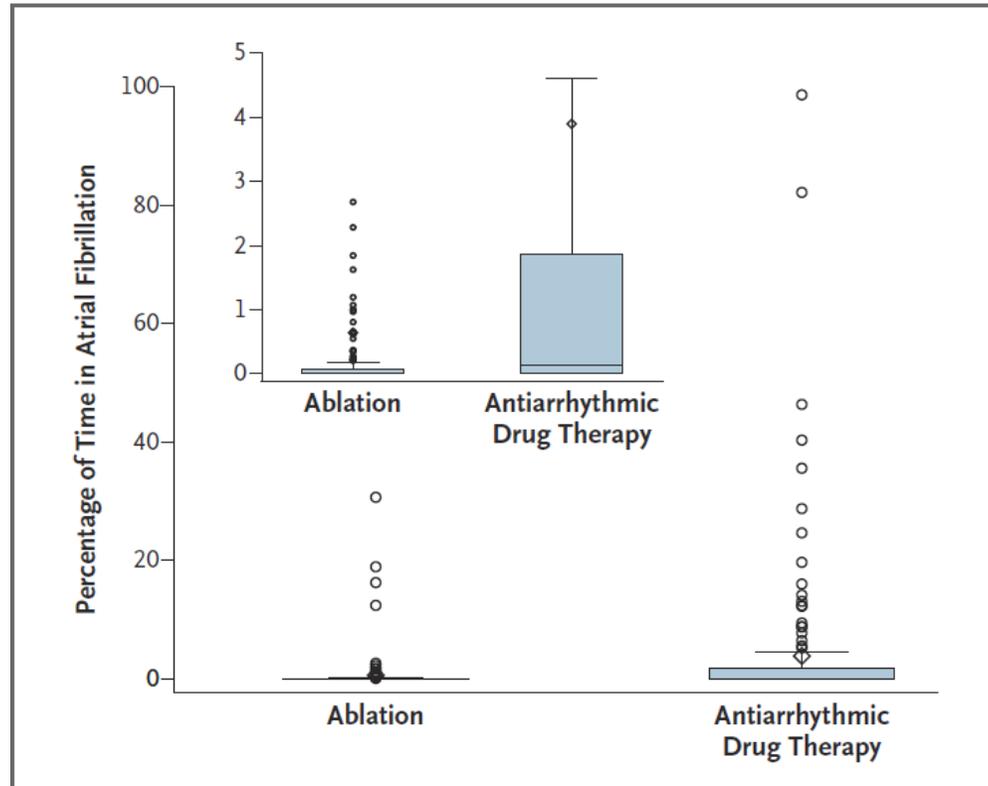
## STOP AF FIRST



## CRYO FIRST

- Consistent RR reduction cca 50% - absolute numbers differ depending on FU method

# AF burden- an important metric for the long term outcomes



**EARLY AF**

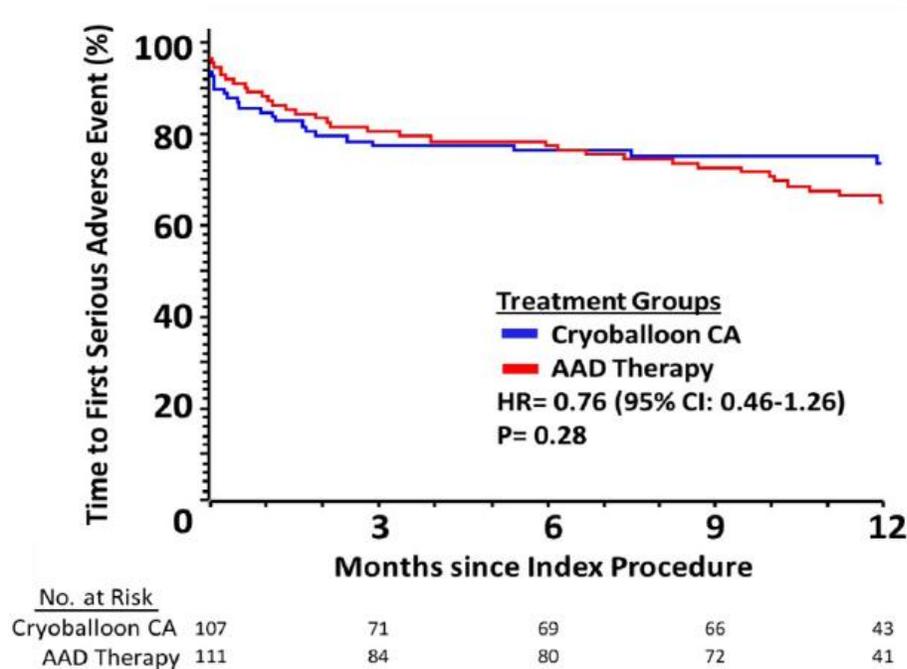
Andrade J. et al. N Engl J Med 2021; 384:305-315

# Secondary efficacy outcomes - QoL

	Ablation Group (N = 154)	Antiarrhythmic Drug Group (N = 149)	Treatment Effect (95% CI)
Secondary quality-of-life end points§			
Change from baseline in AFEQT score¶			
At 6 mo	24.4±1.6	17.9±1.6	10.5±2.2
At 12 mo	26.9±1.9	22.9±2.0	8.0±2.2
Change from baseline in EQ-5D score			
At 6 mo	0.08±0.02	0.07±0.02	0.03±0.03
At 12 mo	0.12±0.02	0.06±0.02	0.07±0.03
Change from baseline in EQ-VAS score**			
At 6 mo	6.10±1.17	4.97±1.19	2.05±1.68
At 12 mo	7.73±1.44	5.71±1.46	2.94±1.69

# Primary safety outcomes

## TIME TO FIRST SERIOUS ADVERSE EVENT:



PVI group, n=107

No stroke

No tamponade

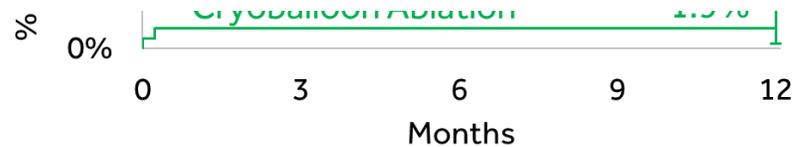
No persistent PN palsy

1 TIA

# Primary safety outcomes



Event  
Any serious adverse event related to the trial regimen — no. of patients (%)\*



Months	0	3	6	9	12
Number at risk	104	102	100	100	97

PVI group, n=154

No stroke

Ablation Group  
(N=154)

Antiarrhythmic Drug Group  
(N=149)

5 (3.2)

6 (4.0)

3 persistent PN palsy  
(resolved at 1 month FU)

No TIA

EARLY AF

Andrade J. et al. N Engl J Med 2021; 384:305-315

# Primary safety outcomes

PVI group. n=104

Table 4. Serious Adverse Events.\*

Serious Adverse Event	Ablation (N=104)		Drug Therapy (N=99)	
	<i>no. of events</i>	<i>no. of patients (%)</i>	<i>no. of events</i>	<i>no. of patients (%)</i>
Any serious adverse event	22	15 (14)	16	14 (14)

No persistent PN  
palsy at 12 months  
FU

No AE fistula

# Summary

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3 recent RCTs (STOP AF FIRST, CRYO FIRST and EARLY AF) show:

## SAFETY ASPECT

PVI with cryoballoon as an early treatment option for paroxysmal AF patients is as safe as the AAD treatment

...when performed at high volume centers, with high volume operators (industry picked!!!)

# Summary

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3 recent RCTs (STOP AF FIRST, CRYO FIRST and EARLY AF) show:

## AF SUPPRESSION ASPECT

PVI with cryoballoon as an early treatment option for paroxysmal AF patients results in better control of AF (treatment effect preserved irrespective of FU strategy)

...when performed at high volume centers, with high volume operators

# Impact to the guidelines

First-line therapy		
AF catheter ablation for PVI should/may be considered as first-line rhythm control therapy to improve symptoms in selected patients with symptomatic:		
<ul style="list-style-type: none"> <li>Paroxysmal AF episodes, <sup>240–242,614,615</sup> or <b>+ CryoFirst, STOP AF first, Early AF + EAST AFNET4&amp;ATTEST</b></li> </ul>	<b>IIa</b>	<b>B</b>
<ul style="list-style-type: none"> <li>Persistent AF without major risk factors for AF recurrence. <sup>253–255,264,598–601,609,610,633,636,641,724,745,746,832</sup></li> </ul>	<b>IIb</b>	<b>C</b>
as an alternative to AAD class I or III, considering patient choice, benefit, and risk.		
AF catheter ablation:		
<ul style="list-style-type: none"> <li>Is recommended to reverse LV dysfunction in AF patients when tachycardia-induced cardiomyopathy is highly probable, independent of their symptom status. <sup>666,675,676</sup></li> </ul>	<b>I</b>	<b>B</b>
<ul style="list-style-type: none"> <li>Should be considered in selected AF patients with HF with reduced LVEF to improve survival and reduce HF hospitalization. <sup>612,659,662–666,668–671,817–826</sup></li> </ul>	<b>IIa</b>	<b>B</b>
AF catheter ablation for PVI should be considered as a strategy to avoid pacemaker implantation in patients with AF-related bradycardia or symptomatic pre-automaticity pause after AF conversion considering the clinical situation. <sup>816–818</sup>	<b>IIa</b>	<b>C</b>

# Personal take on these 3 RCTs with CB for PAF

WILL THIS DATA CHANGE MY PRACTICE? **NO**

DO THESE TRIALS BRING IN ANY NEW DATA? **NO**

DO THESE TRIALS SUGGEST THE CRYOBALLOON SUPREMACY OVER  
OTHER WIDELY AVAILABLE ABLATION PLATFORMS/APPROACHES?

**YES**

**Is there a reason for CB product managers to laugh???**



PFA single shot PVI