SUPPLEMENTAL MATERIAL

Appendix S1. List of Study Group Investigators, Cryo AF Global Registry Investigators

Jose Luis Gonzalez	Hospital Universitario Fundacion Favaloro, Agrentina
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Clemens Steinwender	Kepler Universitatsklinikum Med Campus III., Austria
Jean-Manuel Herzet	Centre Hospitalier Regional de la Citadelle, Belgium
Peter Peytchev	Onze-Lieve-Vrouwziekenhuis-Campus Aalst, Belgium
Sofian Johar	Gleneagles Jerudong Park Medical Centre, Brunei Darussalam
Juan Manuel Camargo Ballestas	Fundacion Clinica Shaio, Colombia
Petr Neuzil	Nemocnice Na Homolce, Czech Republic
Julian Chun	Cardioangiologisches Centrum Bethanien, Germany
Peter Falk	Herz- und Gefasszentrum Bad Bevensen, Germany
Mike Foresti	Kliniken Maria Hilf GmbH Monchengladbach -KH St. Franziskus, Germany
Sonia Busch	Klinikum Coburg GmbH, Germany
Sascha Stiller	Oberschwaben-Klinik GmbH Krankenhaus St. Elizabeth, Germany
Christian Drephal	Sana Klinikum Lichtenberg, Germany
Georgios Kourgiannidis	Hellenic Airforce 251 General Hospital, Greece
Zoltan Csanadi	Debreceni Egyetem, Hungary
Csaba L. Földesi	Gottsegen György Országos Kardiovaszkuláris Intézet, Hungary
Kristján Guðmundsson	Landspitali - National hospital of Iceland, Iceland
Roberto Rordorf, Enrico Baldi, Antonio Sanzo	Fondazione IRCCS Policlinico San Matteo, Italy
Massimo Tritto	Humanitas Mater Domini, Italy
Gianluca Zingarini	Ospedale Santa Maria della Misericordia di Perguia, Italy
Maria Grazia Bongiorni	Universitaria Pisana - Stabilimento di Cisanello, Italy
Koichiro Kumagai	Fukuoka Sanno Hospital, Japan
Masaomi Kimura	Hirosaki University Hospital, Japan
Osamu Inaba	Japanese Red Cross Saitama Hospital, Japan
Takashi Kurita	Kindai University Hospital, Japan
Atsushi Kobori	Kobe City Medical Center General Hospital, Japan
Kenji Ando	Kokura Kinen Hospital Japan
Satoshi Shizuta	Kyoto University Hospital, Japan
Masahiko Goya	Tokyo Medical and Dental University, Japan
Yasuteru Yamauchi	Yokohama City Minato Red Cross Hospital, Japan
	Salman Al Abdallah Al Dabbous Cardiac Center, Kuwait
Razali Omar	Cardiac Vascular Sentral Kuala Lumpur, Malaysia
Ahmad Fazli Abdul Aziz	Hospital Serdang, Malaysia
Surinder Kaur Khelae	Institut Jantung Negara, Malaysia
Gerardo Rodriguez Diez	Hospital San Angel Inn Universidad, Mexico
Pawel Ptaszynski	Centralny Szpital Kliniczny Uniwersytetu Medycznego w Lodzi
Marcin Kuniewicz	Krakowski Szpit.Specjalist.im.J.Pawla II, Poland
Janusz Romanek	Spital Wojewodzki nr 2, Poland
João José Primo	Centro Hospitalar de Vila Nova de Gaia/Espinho - Unidade I, Portugal

Faisal M.A. Al-Samadi	King Fahad Medical City (KFMC), Saudi Arabia
Dejan Kojic	Insitute for Cardio Vascular Disease Dedinje, Serbia
Chi Keong Ching	National Heart Centre Singapore, Singapore
Robert Hatala	NUSCH a.s. Bratislava, Slovakia
Martin Skamla	Stredoslovensky ustav srdcovych a cievnych chorob a.s, Slovakia
Silvia Misikova	Vychodoslovensky ustav srdcovych a cievnych chorob, a.s, Slovakia
Anthony P.J. Stanley	Netcare Sunninghill Hospital, South Africa
Jesus-Manuel Paylos-Gonzalez	Hospital Universitario Moncloa, Spain
Jen-Yuan Kuo	Mackay Memorial Hospital-Tamsui Branch, Republic of Taiwan
Cheng-Hung Li	Taichung Veterans General Hospital, Republic of Taiwan
Sirin Apiyasawat	Ramathibodi Hospital, Thailand
Arisara Suwanagool	Siriraj Hospital, Thailand
Derick Todd	Liverpool Heart and Chest Hospital, United Kingdom
Richard Schilling	St Bartholomew's Hospital, United Kingdom
Mark Gallagher	St George's University Hospitals - NHS Trust, United Kingdom
Ewan Shepherd	The Newcastle upon Tyne Hospitals - Freeman Hospital, United Kingdom

Table S1: List of participating centers

Country	Center	Number of Patients
Total number of subjects		**1303**
Argentina	Hospital Universitario Fundacion Favaloro	67
	Instituto Cardiovascular de Buenos Aires (ICBA)	93
Austria	Kepler Universitatsklinikum Med Campus III.	20
Belgium	Centre Hospitalier Regional de la Citadelle	83
	Onze-Lieve-Vrouwziekenhuis-Campus Aalst	2
Brunei Darussalam	Gleneagles Jerudong Park Medical Centre	1
Colombia	Fundacion Clinica Shaio	1
Czech Republic	Nemocnice Na Homolce	24
Germany	Cardioangiologisches Centrum Bethanien	47
	Herz- und Gefasszentrum Bad Bevensen	19
	Kliniken Maria Hilf GmbH Monchengladbach -KH St. Franziskus	28
	Klinikum Coburg GmbH	11
	Oberschwaben-Klinik GmbH Krankenhaus St. Elizabeth	4
	Sana Klinikum Lichtenberg	46
Greece	Hellenic Airforce 251 General Hospital	11
Hungary	Debreceni Egyetem	9
	Gottsegen György Országos Kardiovaszkuláris Intézet	63
Iceland	Landspitali - National hospital of Iceland	1
Italy	Fondazione IRCCS Policlinico San Matteo	9
	Humanitas Mater Domini	10
	Ospedale Santa Maria della Misericordia di Perguia	15
	Universitaria Pisana - Stabilimento di Cisanello	24
Japan	Fukuoka Sanno Hospital	36
	Hirosaki University Hospital	29
	Japanese Red Cross Saitama Hospital	39
	Kindai University Hospital	35

Country	Center	Number of Patients
	Kobe City Medical Center General Hospital	29
	Kokura Kinen Hospital	30
	Kyoto University Hospital	35
	Tokyo Medical and Dental University	26
	Yokohama City Minato Red Cross Hospital	38
Kuwait	Salman Al Abdallah Al Dabbous Cardiac Center	25
Malaysia	Cardiac Vascular Sentral Kuala Lumpur	3
	Hospital Serdang	3
	Institut Jantung Negara	22
Mexico	Hospital San Angel Inn Universidad	18
Poland	Centralny Szpital Kliniczny Uniwersytetu Medycznego w Lodzi	52
	Krakowski Szpit.Specjalist.im.J.Pawla II	18
	Spital Wojewodzki nr 2	4
Portugal	Centro Hospitalar de Vila Nova de Gaia/Espinho - Unidade I	4
Saudi Arabia	King Fahad Medical City (KFMC)	29
Serbia	Insitute for Cardio Vascular Disease Dedinje	18
Singapore	National Heart Centre Singapore	6
Slovakia	NUSCH a.s. Bratislava	14
	Stredoslovensky ustav srdcovych a cievnych chorob a.s	26
	Vychodoslovensky ustav srdcovych a cievnych chorob, a.s	47
South Africa	Netcare Sunninghill Hospital	27
Spain	Hospital Universitario Moncloa	17
Taiwan, Republic of	Mackay Memorial Hospital-Tamsui Branch	4
	Taichung Veterans General Hospital	8
Thailand	Ramathibodi Hospital	4
	Siriraj Hospital	3
United Kingdom	Liverpool Heart and Chest Hospital	56
	St Bartholomew's Hospital	3

Country	Center	Number of Patients
	St George's University Hospitals - NHS Trust	2
	The Newcastle upon Tyne Hospitals - Freeman Hospital	5

In the Cryo AF Global Registry, patients were classified at enrollment as either a heart failure patient or no heart failure by their clinician. For those with heart failure, a NYHA assessment was performed during baseline testing. Table 1 summarizes the baseline characteristics by NYHA classification. A progression and greater incidence of comorbidities are observed from no heart failure to NYHA I supporting the investigator classification of heart failure for the NYHA I patients.

Table S2. Patient Baseline Characteristics.

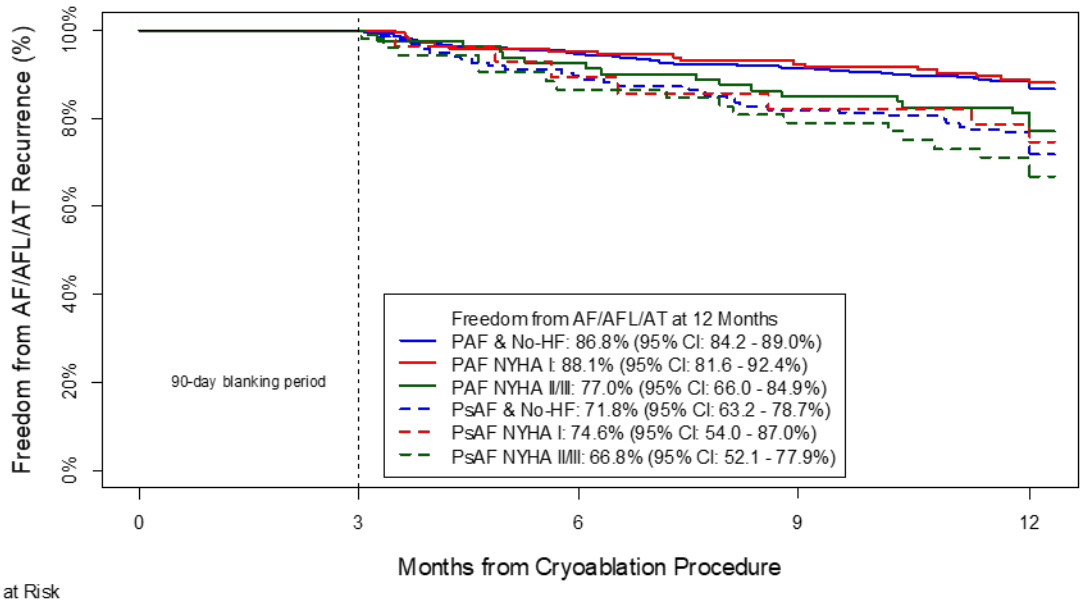
Subject Characteristics	No Heart Failure (N = 985)	Heart Failure NYHA I (N = 179)	Heart Failure NYHA II/III (N = 139)	p-value (No HF vs NYHA I)
Female sex (N (%))	331 (33.6%)	81 (45.3%)	64 (46.0%)	< 0.01
Age in years (mean ± STD)	60 ± 12	63 ± 11	64 ± 11	< 0.01
Body mass index in kg/m^2 (mean ± STD)	27 ± 5	27 ± 5	29 ± 6	0.86
CHA_2DS_2-VASc Score (mean ± SD)	1.6 ± 1.4	3.2 ± 1.5	3.6 ± 1.7	< 0.01
Paroxysmal AF (N (%))	844 (85.7%)	150 (83.8%)	86 (61.9%)	0.49
Years diagnosed with AF (mean ± STD)	3.3 ± 5.1	3.5 ± 4.9	2.9 ± 3.7	0.54
History of Atrial Flutter	50 (5.1%)	7 (3.9%)	1 (0.7%)	0.71
History of Atrial Tachycardia	12 (1.2%)	2 (1.1%)	1 (0.7%)	1.00
Left atrial diameter in cm (mean ± STD)	40 ± 7	43 ± 10	45 ± 8	< 0.01
Left ventricular ejection fraction in % (mean ± STD)	62 ± 7	62 ± 10	53 ± 14	0.89
LVEF <= 40%	6 (0.6%)	6 (3.4%)	28 (20.1%)	
LVEF 40-50%	15 (1.5%)	5 (2.8%)	12 (8.6%)	
LVEF >= 50%	816 (82.8%)	138 (77.1%)	88 (63.3%)	
Not reported (N,%)	148 (15.0%)	30 (16.8%)	11 (7.9%)	
Number of failed AADs (mean ± STD)	0.8 ± 0.7	0.8 ± 0.8	0.8 ± 0.7	0.82
First-line cryoablation (N (%))	306 (31.1%)	51 (28.5%)	38 (27.3%)	0.48
Hypertension (N (%))	484 (49.1%)	111 (62.0%)	105 (75.5%)	< 0.01
Prior cardiac device implant (N (%))	33 (3.4%)	9 (5.0%)	20 (14.4%)	0.28
Prior myocardial infarction (N (%))	17 (1.7%)	4 (2.2%)	8 (5.8%)	0.55
Prior stroke/transient ischemic attack (N (%))	56 (5.7%)	14 (7.8%)	10 (7.2%)	0.30
Coronary artery disease (N (%))	60 (6.1%)	22 (12.3%)	24 (17.3%)	< 0.01
Diabetes (N (%))	100 (10.2%)	19 (10.6%)	35 (25.2%)	0.89
Sleep apnea (N (%))	31 (3.1%)	8 (4.5%)	6 (4.3%)	0.37

AF: atrial fibrillation; HF: heart failure; NYHA Class: New York Heart Association functional classification; CHA_2DS_2-VASc Score: congestive heart failure, hypertension, age (2 points), diabetes, previous stroke/transient ischemic attack (2 points), vascular disease; LVEF: left ventricular ejection fraction; AAD: anti-arrhythmic drug.

Figure S1 displays the Kaplan-Meier estimate of 12-month freedom from AF/AT/AFL recurrence in subgroups based on NYHA classification. In a Cox regression sub-analysis of the HF cohort and NYHA classification, 12-month freedom from atrial arrhythmia recurrence was not statistically different between patients with No-HF vs HF NYHA Class I vs HF NYHA Class II/III (P=0.08).

AF: atrial fibrillation; AFL: atrial flutter; AT: atrial tachycardia; PAF: paroxysmal atrial fibrillation; PsAF: persistent atrial fibrillation; HF: heart failure; No-HF: no heart failure; NYHA Class: New York Heart Association functional classification.

Figure S1. Freedom from atrial arrhythmia recurrence over 12-months by NYHA subgroup

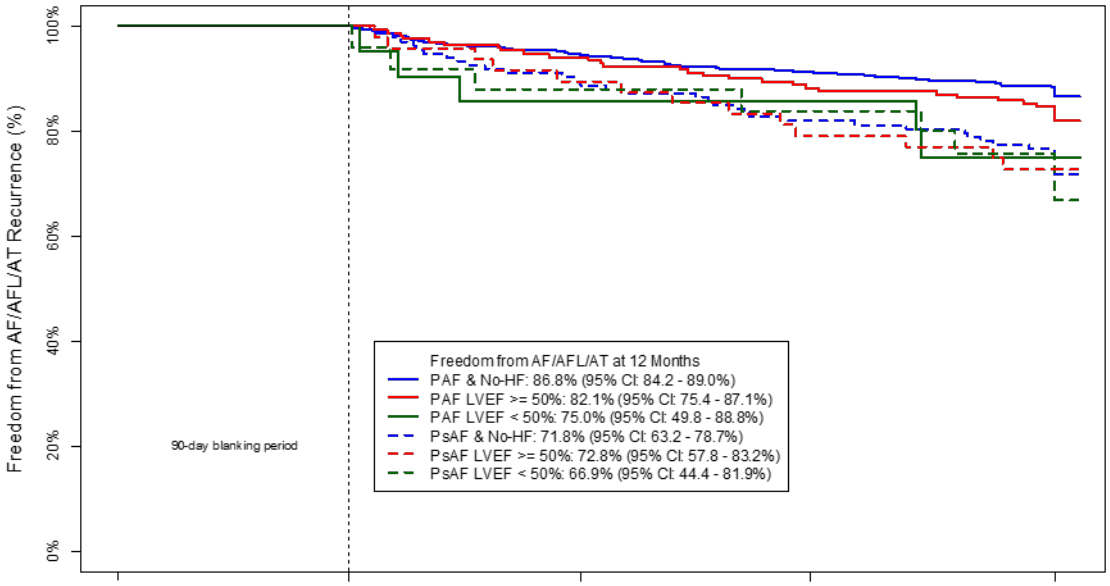


Number at Risk					
PAF & No-HF	844	809	755	716	659
PAF NYHA I	150	145	138	132	118
PAF NYHA II / III	86	81	74	67	60
PsAF & No-HF	141	136	118	108	95
PsAF NYHA I	29	28	25	23	20
PsAF NYHA II / III	53	52	45	41	34

Figure S2 displays the Kaplan-Meier estimate of 12-month freedom from AF/AT/AFL recurrence in subgroups based on LVEF (no-HF, HF & preserved LVEF, HF & reduced LVEF). In a Cox regression sub-analysis of the cohorts, 12-month freedom from atrial arrhythmia recurrence was not statistically different between patients with No-HF vs HF-pEF vs HF-rEF (P=0.23).

AF: atrial fibrillation; AFL: atrial flutter; AT: atrial tachycardia; PAF: paroxysmal atrial fibrillation; PsAF: persistent atrial fibrillation; No-HF: no heart failure; LVEF: left ventricular ejection fraction

Figure S2. Freedom from atrial arrhythmia recurrence over 12-months by LVEF subgroup



Number at Risk

PAF & No-HF	844	809	755	716	659
PAF LVEF >= 50%	177	172	161	149	132
PAF LVEF < 50%	25	21	18	17	13
PsAF & No-HF	141	136	118	108	95
PsAF LVEF >= 50%	49	48	43	38	33
PsAF LVEF < 50%	26	25	22	21	17