



L'Importanza della Terapia Medica Prima dell'Impianto di ICD



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Programma congresso

Venerdì 30 Settembre 2022

8.30 - 10.20

SCOMPENSO CARDIACO CRONICO: UPDATE 2022

*Moderatori: G. Alunni, Perugia - G. Ansalone, Roma
L. Sommariva, Viterbo*

La quadrupla terapia antineurormonale nello scompenso: criticità
C. Tota, Roma

Gestione in acuto dello scompenso cardiaco e poi passaggio ad ARNI: nuove evidenze e timing di trattamento
P. Severino, Roma

L'importanza della terapia medica prima dell'impianto dell'ICD
D. Castagno, Torino

Valvulopatie e insufficienza cardiaca
M. Porcu, Olbia - SS

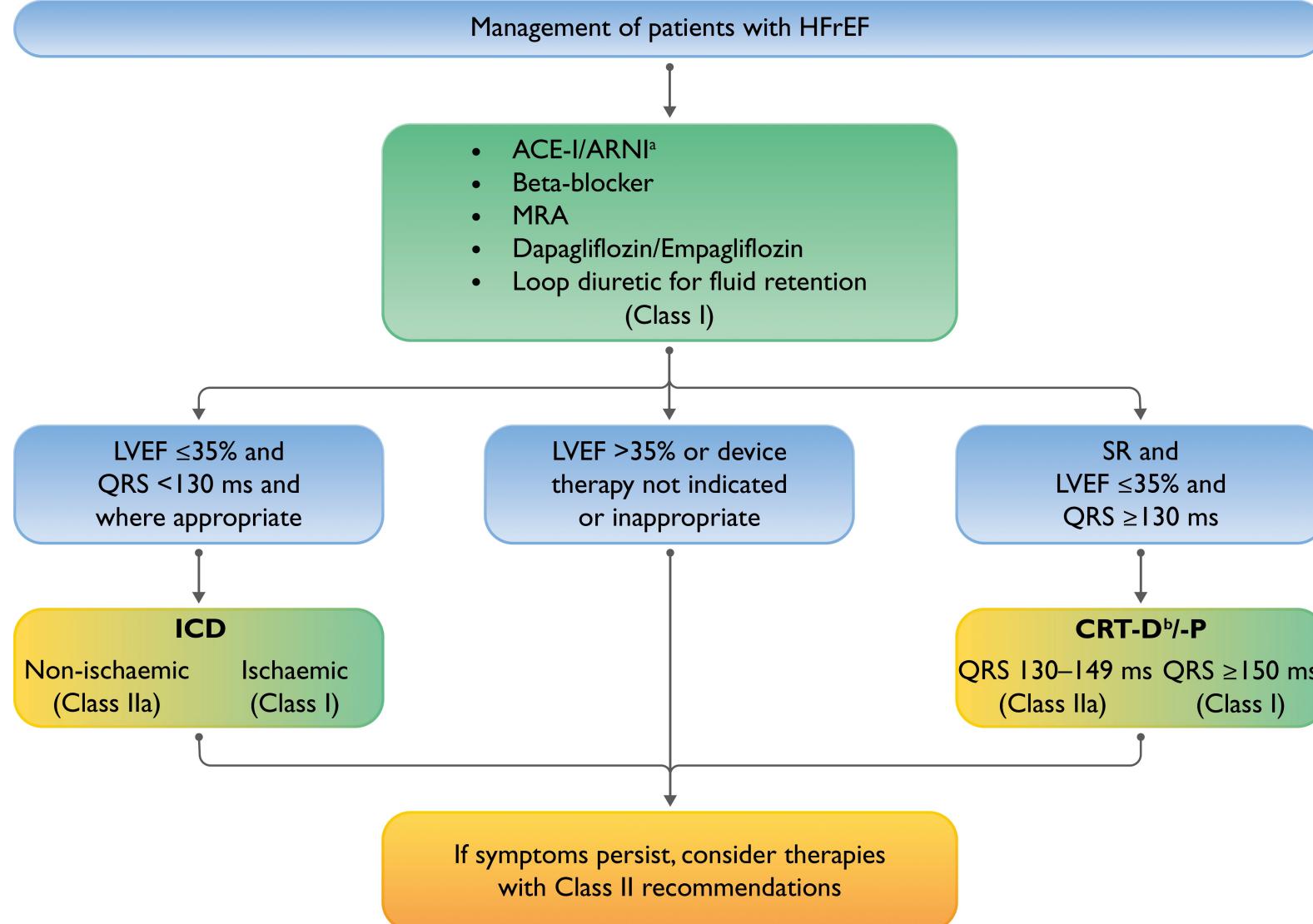
Scompenso cardiaco a funzione cardiaca preservata dal fenotipo alla terapia. L'inizio di una nuova era
E. Gronda, Milano

Quali strategie ospedale-territorio nella diagnosi e terapia dello scompenso. Esiste un reale ruolo per la telemedicina?
A. Di Lenarda, Trieste

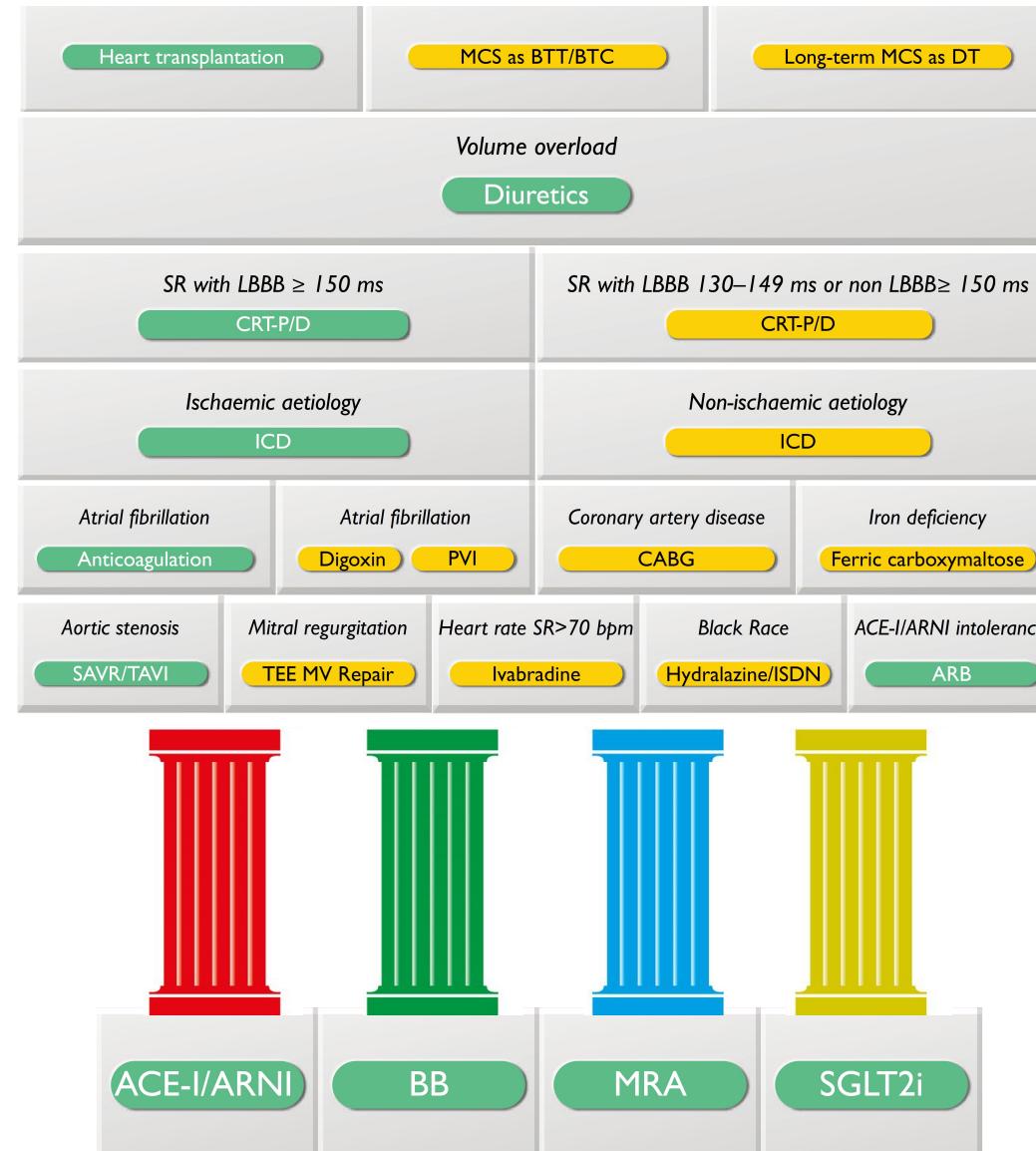
Tachicardiomiopatie. Extrasistolia ventricolare e fibrillazione atriale: dalla diagnosi all'ablazione
G. Viola, Sassari

Insufficienza cardiaca cronica riacutizzata: il ruolo di Vericiguat
M. Volterrani, Roma

2021 ESC Heart Failure Guidelines



Four Pillars of Medical Treatment Before ICD Implantation



Adapted from Eur Heart J 2021; 42:3599-3726

2021 ESC Heart Failure Guidelines

Primary prevention

An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II–III) of an ischaemic aetiology (unless they have had a MI in the prior 40 days—see below), and an LVEF $\leq 35\%$ despite ≥ 3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status.^{161,165}

I

A

An ICD should be considered to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II–III) of a non-ischaemic aetiology, and an LVEF $\leq 35\%$ despite ≥ 3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status.^{161,166,167}

IIa

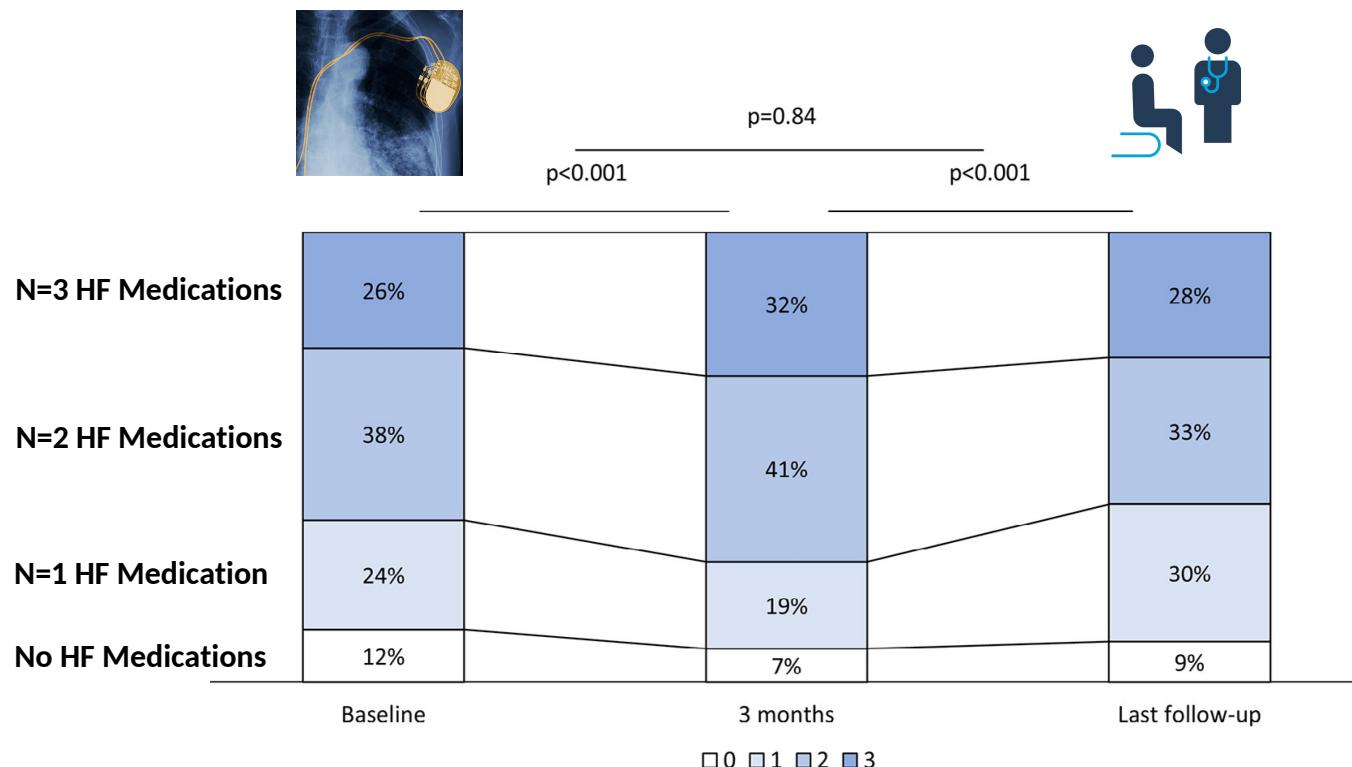
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Underprescription of HF Medications Before ICD Implantation

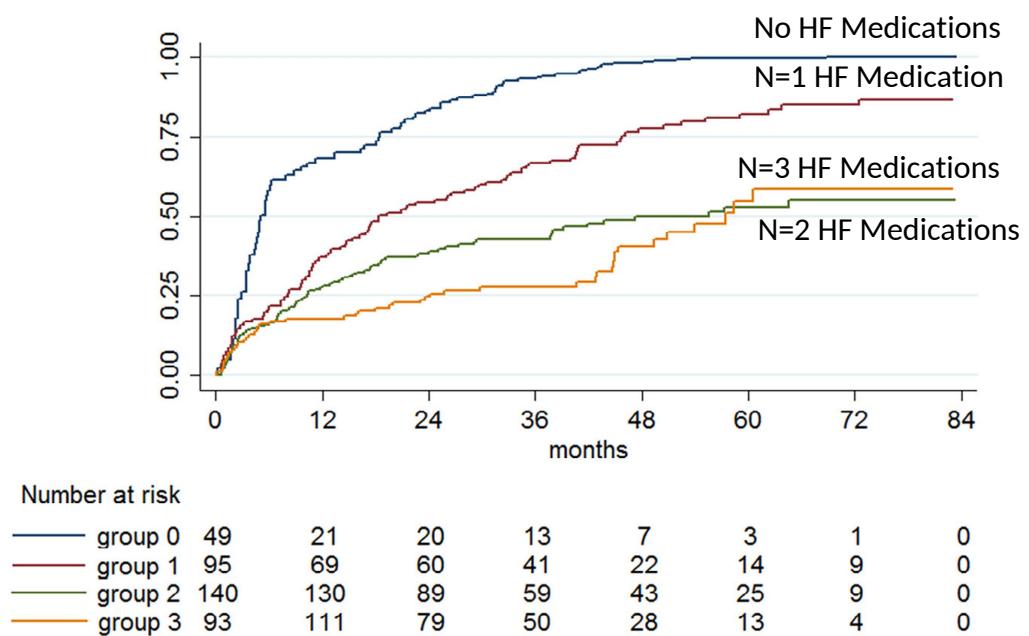


N=378 patients with HF undergoing primary prevention ICD/CRT implantation

Evaluation of Beta-blockers, ACE-I/ARBs, MRAs prescription (alone and in combination)



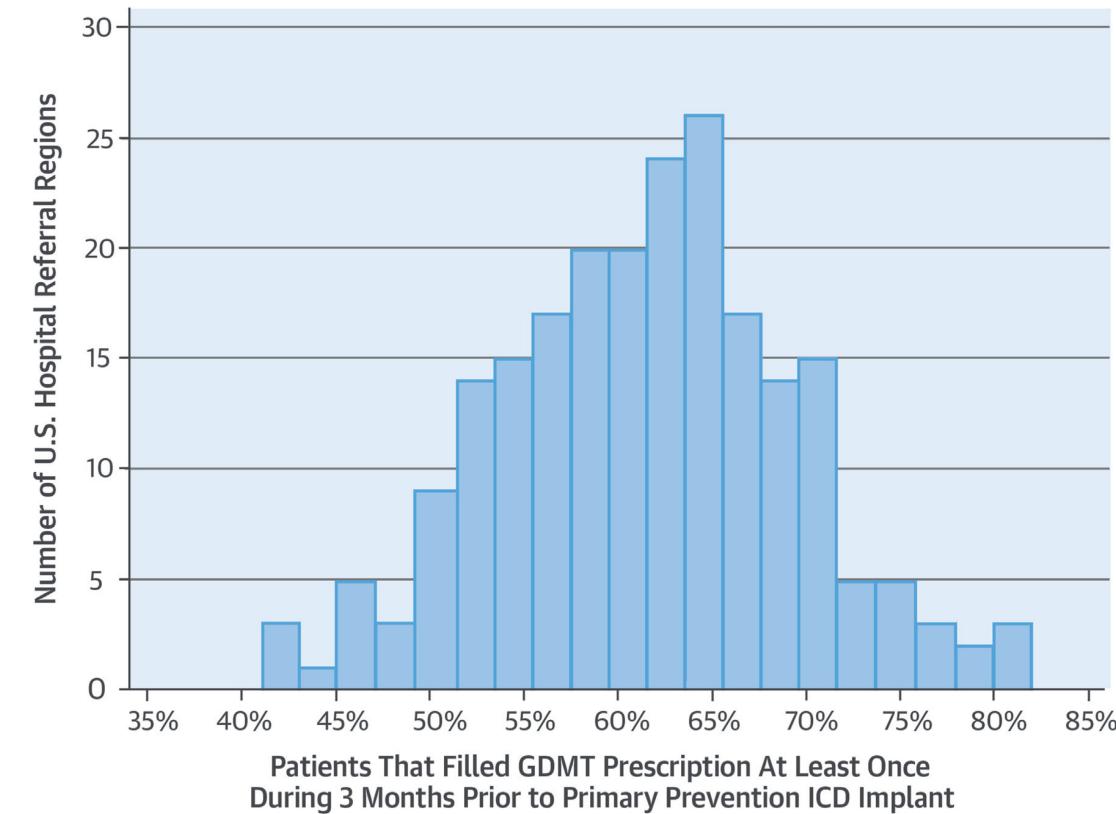
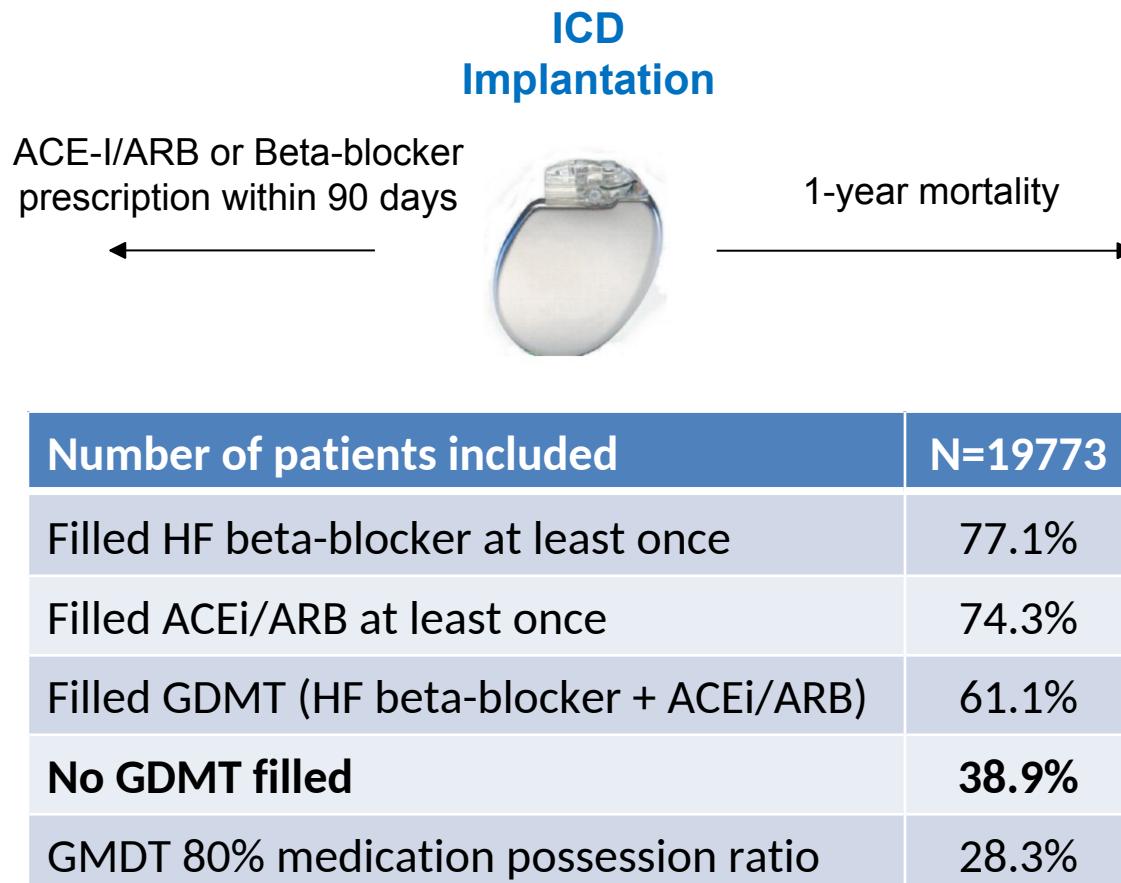
Probability of HF hospitalisation or death



Underprescription of HF Medications Before ICD Implantation



N=19773 patients included in the National Cardiovascular Data ICD Registry
with HF undergoing primary prevention ICD implantation



Effects of HF Drugs on Structural Remodeling

LVEF (%)	Baseline	12 Months	Relative Δ	Trial
RAAS Blockade	25±7	29±8	4, +13.8%	SOLVD
Beta-Blockade	29±1	34±2	5.5, +14.4%	ANZ
MRA	26±1	28±0.4	1.8, +6.9%	Eplerenone

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LVESV index (ml/m ²)	Baseline	12 Months	Relative Δ	Trial
RAAS Blockade	106±42	93±37	13, - 12.3%	SOLVD
Beta-Blockade	73±4	65±5	8, - 10.8%	ANZ
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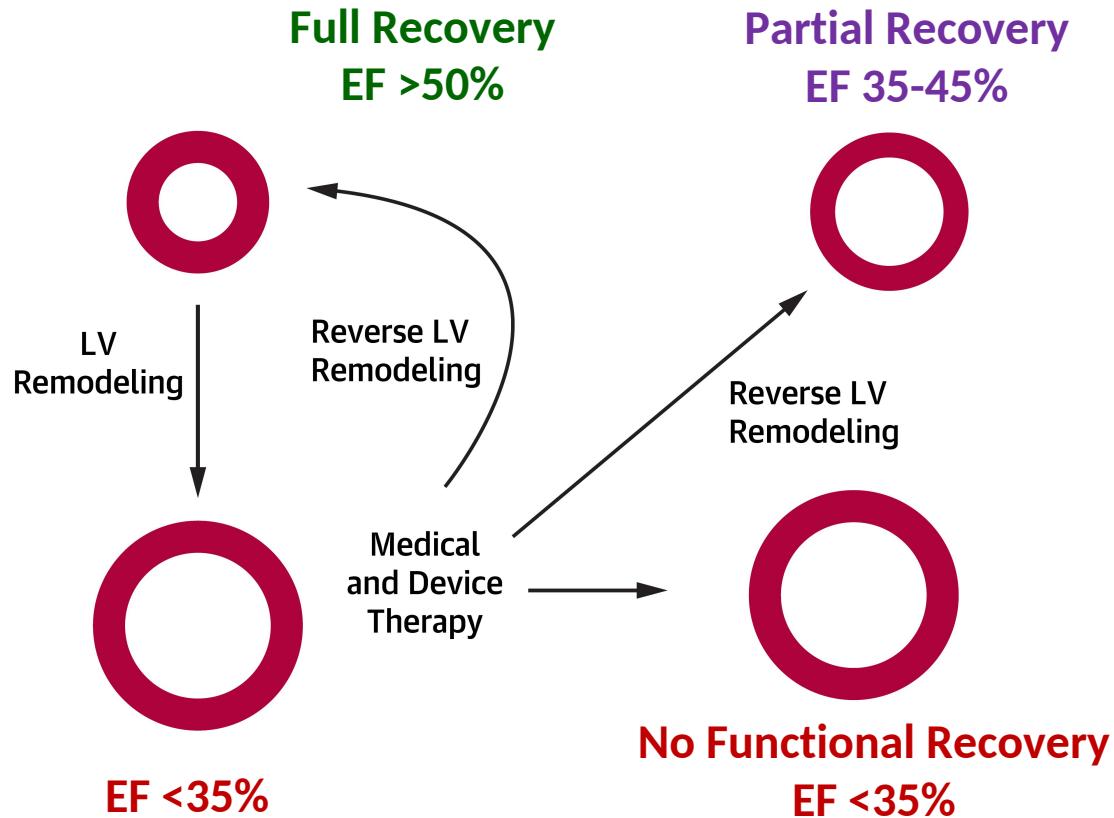
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RAAS Blockade	140±44	127±37	13, - 9.3%	SOLVD
Beta-Blockade	100±5	96±5	4.6, - 4.6%	ANZ
MRA	167±4	163±2	3.7, - 2.2%	Eplerenone

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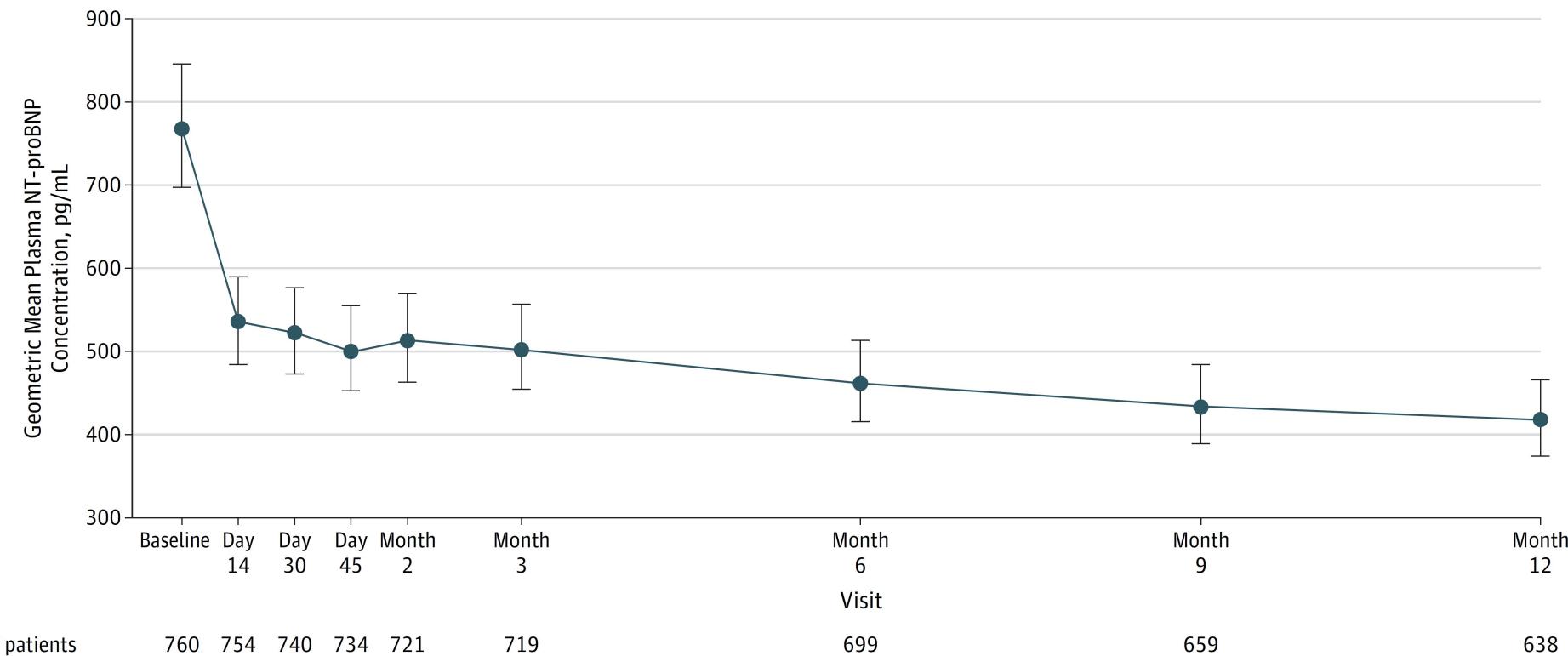
Pathophysiology or LV Function Recovery



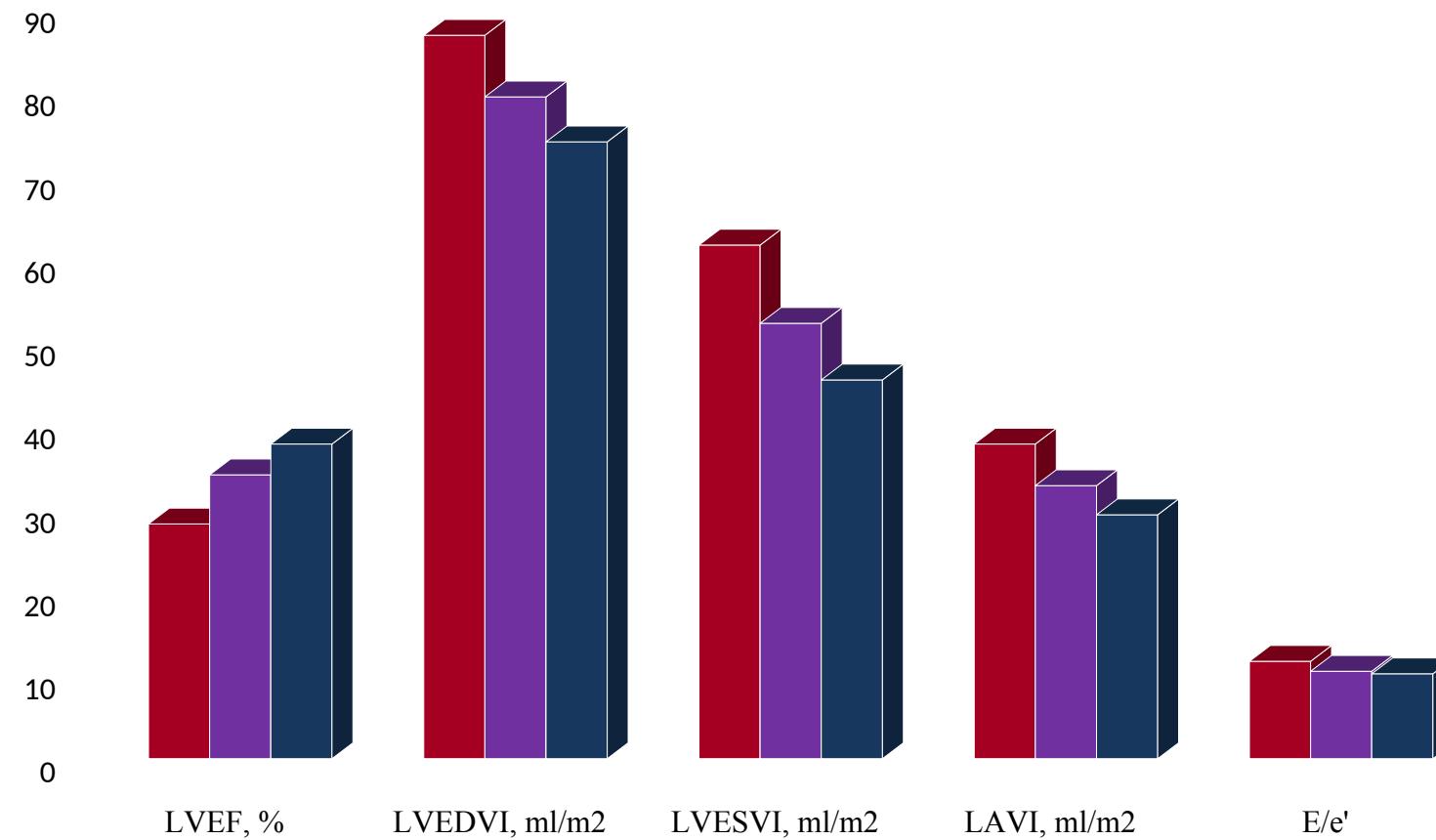
	Beta-blockers	ACE Inhibitors	ARBs	MRAs
Hypertrophy	↓	↓	↓	↓
Fetal gene expression	↓	↓	↓	ND
Myocytolysis	↓	ND	ND	ND
β-adrenergic desensit.	↓	↓	↓	ND
EC coupling	↑	↑	↑	ND
Cytoskeletal proteins	ND	ND	ND	↑
Myocyte apoptosis	↓	↓	↓	ND
MMP activation	↓	↓	↓	↓
Fibrosis	↓	↓	↓	↓
Angiogenesis	↑	↑	↑	↑

Association of Change in N-Terminal Pro-B-Type Natriuretic Peptide Following Initiation of Sacubitril-Valsartan Treatment With Cardiac Structure and Function in Patients With Heart Failure With Reduced Ejection Fraction

PROVE-HF Single group, open label study, enrolling 794 pts with HFrEF treated with Sacubitril/Valsartan

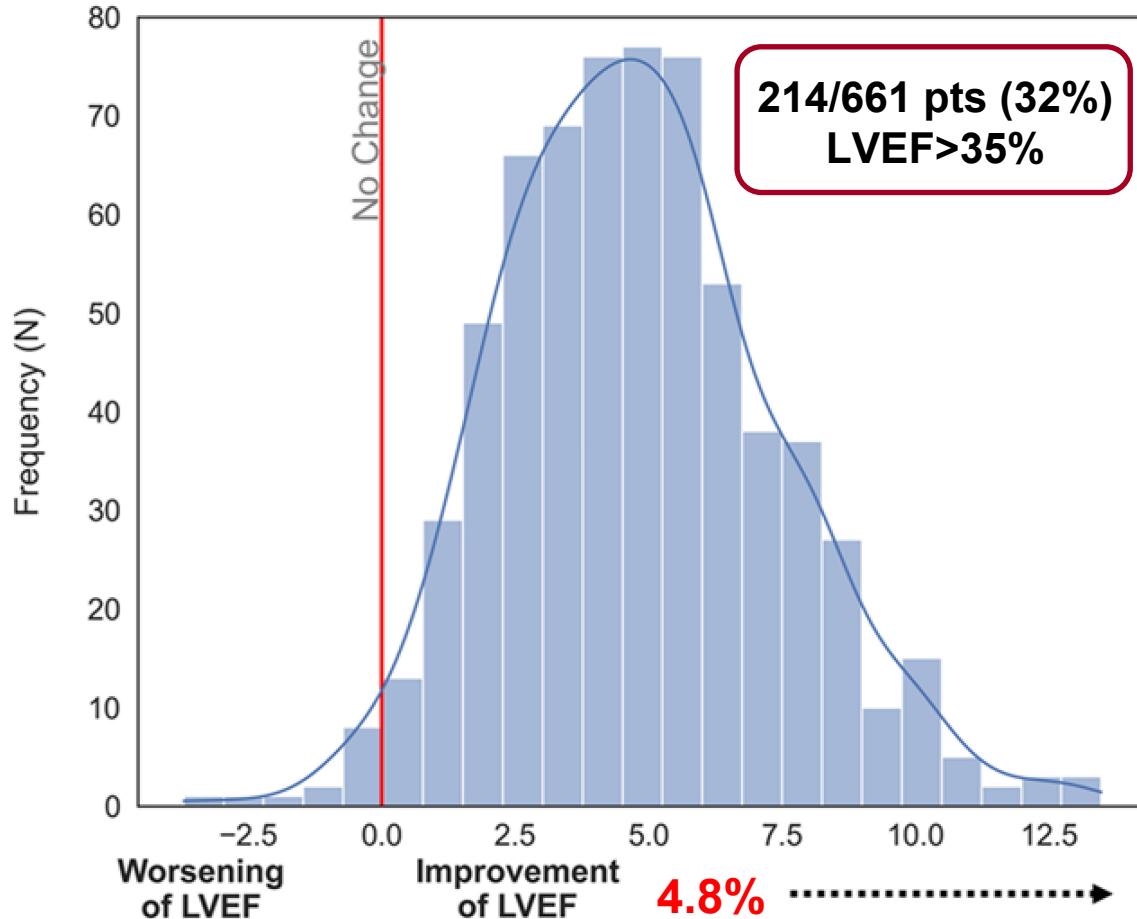


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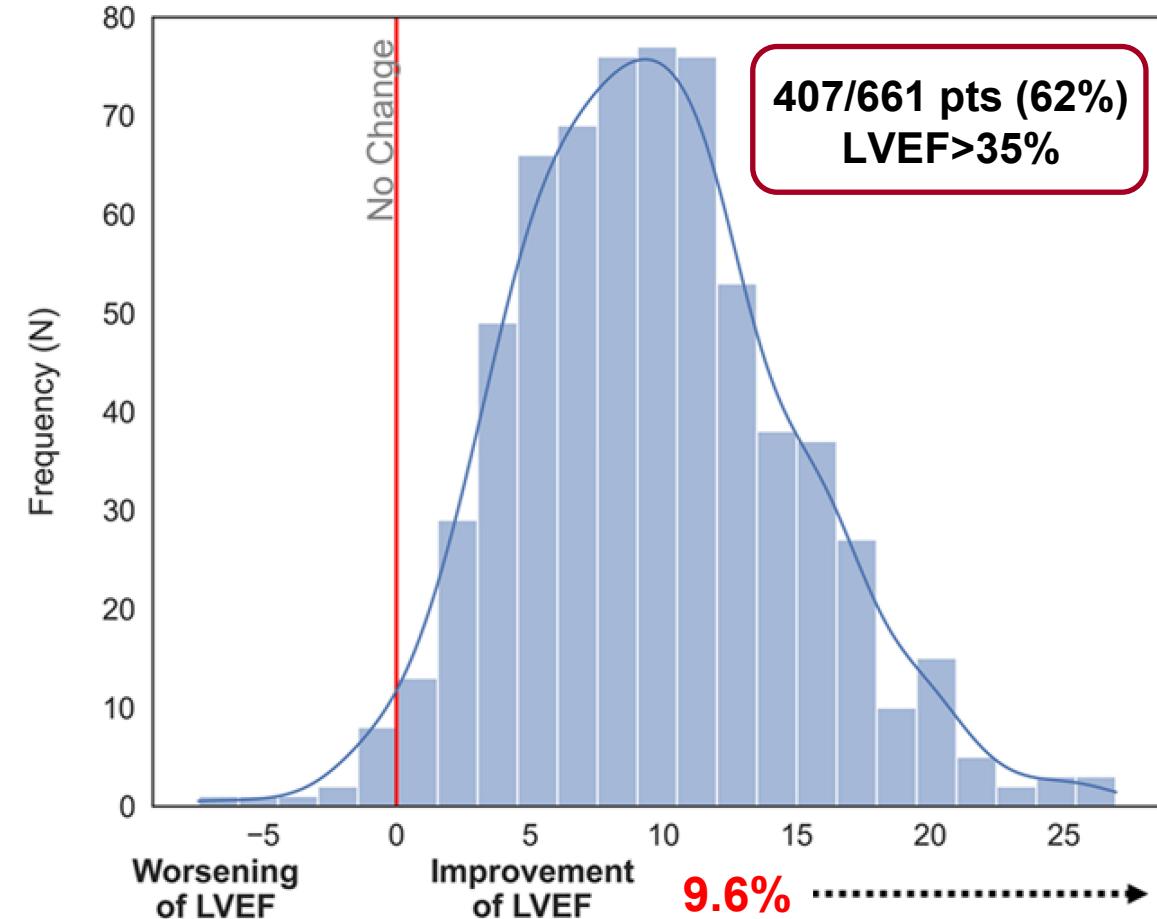


ICD Eligibility After Initiation of Sacubtril/Valsartan

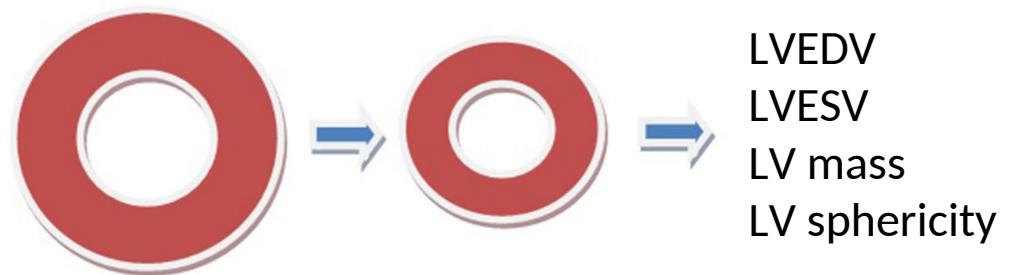
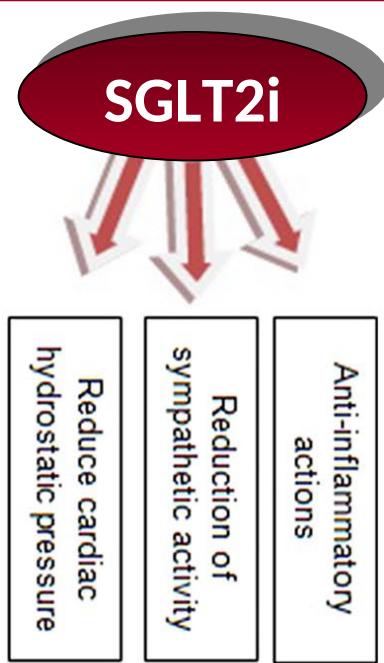
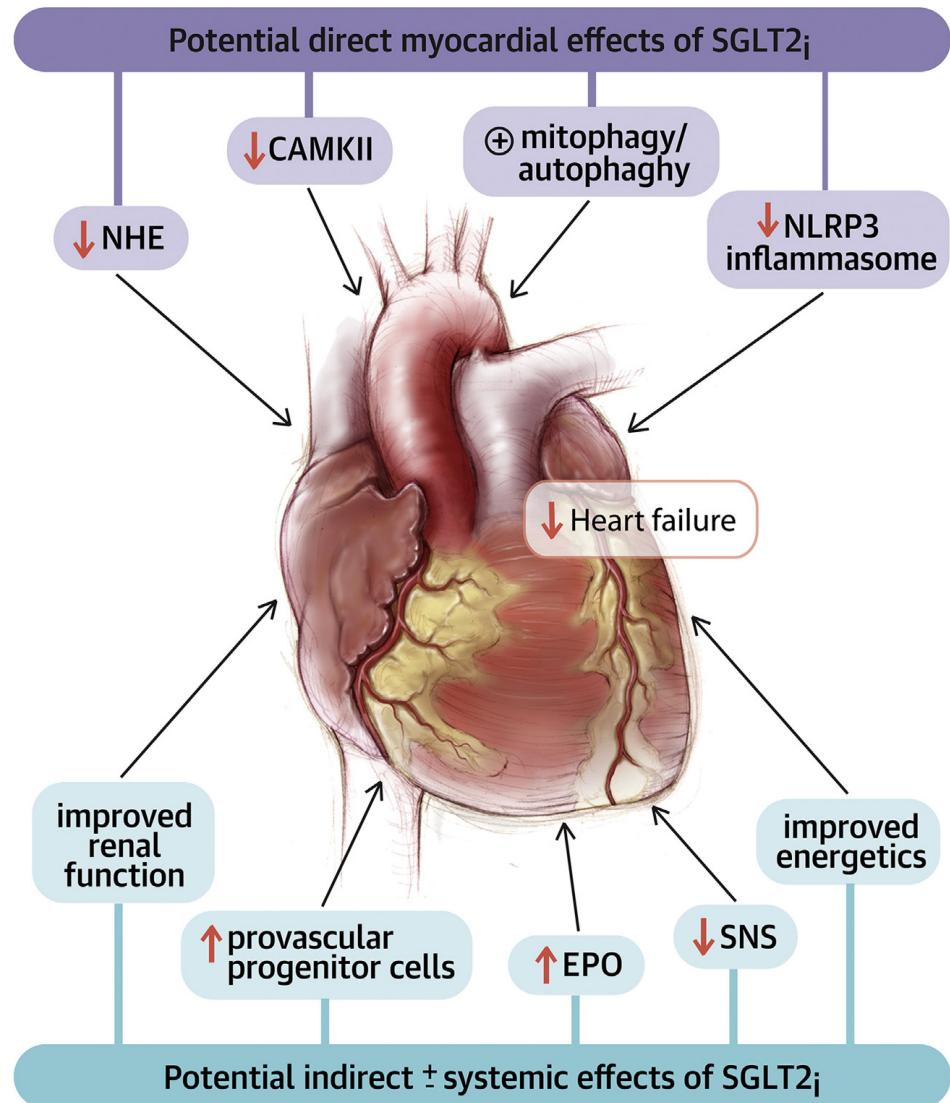
6 months



12 months



Effect of Gliflozins on Cardiac Structure and Function



Lopaschuk GD, et al. JACC Bas Transl Sci 2020; 5:632-644
Correale M, et al. Clin Drug Invest 2022; 42: 567-579

How Can Optimization of Medical Treatment Avoid Unnecessary Implantable Cardioverter-Defibrillator Implantations in Patients With Idiopathic Dilated Cardiomyopathy Presenting With “SCD-HeFT Criteria?”

Baseline Evaluation

Eligible for ICD
162 pts
 β -blockers 0%
ACE-I 41%

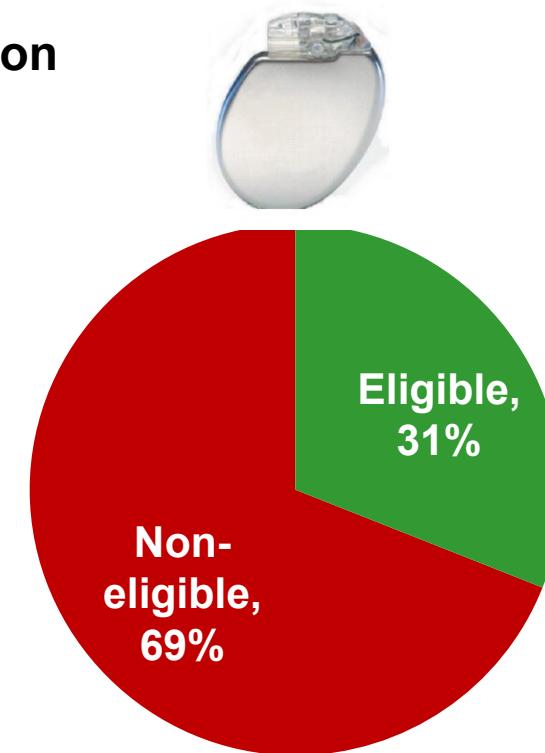


3-9 months Re-evaluation

3 pts (2%)
NYHA IV

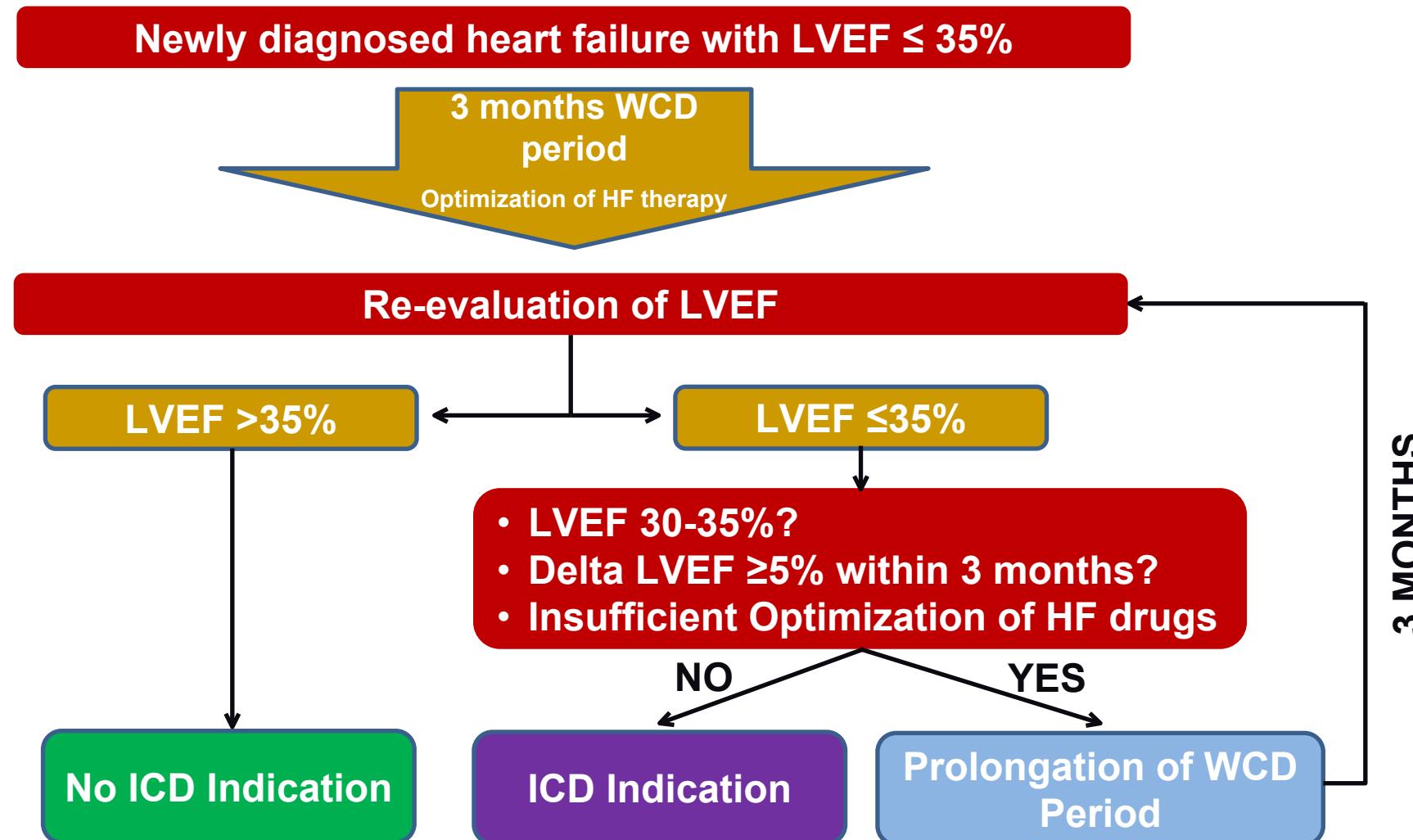
Eligible for ICD
50 pts (31%)
 β -block 85%, ACE-I 94%

Non-eligible for ICD
109 pts (67%)
 β -block 90%, ACE-I 95%



Avoiding Untimely Implantable Cardioverter/Defibrillator Implantation by Intensified Heart Failure Therapy Optimization Supported by the Wearable Cardioverter/Defibrillator—The PROLONG Study

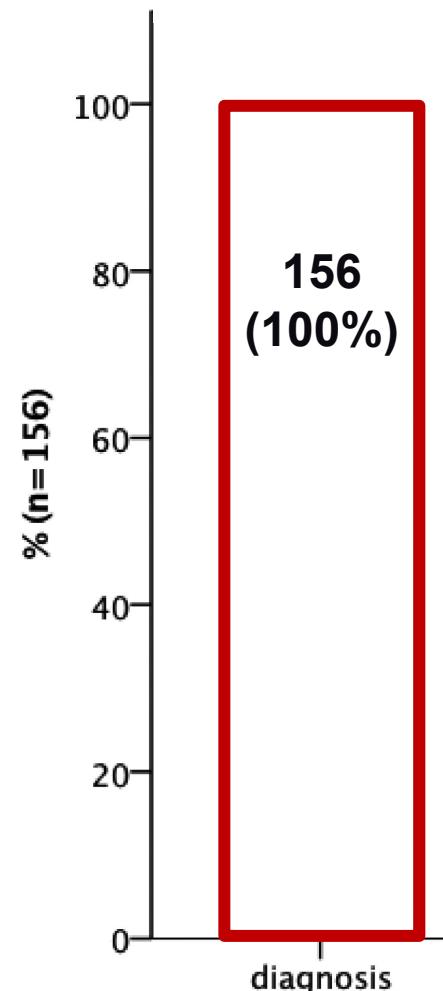
David Duncker, MD; Thorben König, MD; Stephan Hohmann, MD; Johann Bauersachs, MD; Christian Veltmann, MD



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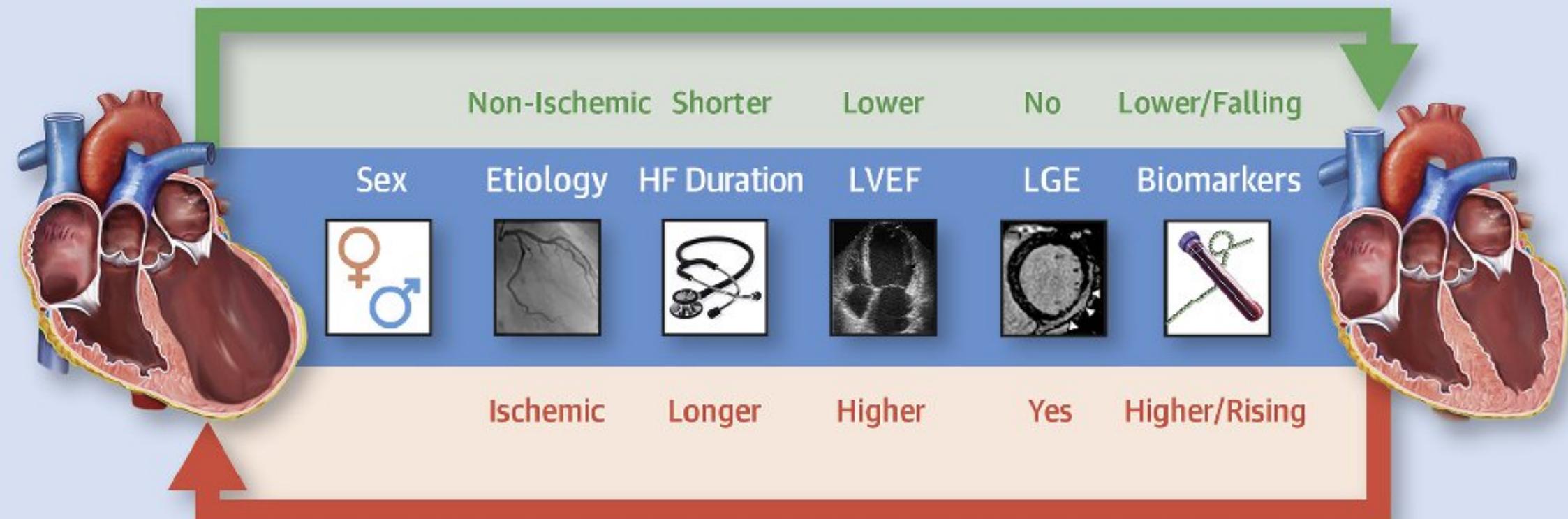
	Baseline N=156	3-months FUP N=153
NYHA	2.8	2.0
Mean LVEF%	24	35
Heart rate, bpm	80	69
CMP Aetiology		
Nonischaemic	55%	-
Ischaemic	29%	-
Peripartum	12%	-
Myocarditis	4%	-
Beta-blocker dosage (% target dose)	47	63
RAS antagonist dosage (% target dose)	45	65
MRA dosage (% target dose)	49	55

Avoiding Untimely Implantable Cardioverter/Defibrillator Implantation by Intensified Heart Failure Therapy Optimization Supported by the Wearable Cardioverter/Defibrillator—The PROLONG Study



Predicting Reverse LV Remodeling

Reverse Remodeling



Adverse Remodeling

Waiting Period Before ICD Implantation

Primary prevention

An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II–III) of an ischaemic aetiology (unless they have had a MI in the prior 40 days—see below), and an LVEF $\leq 35\%$ despite ≥ 3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status.^{161,165}

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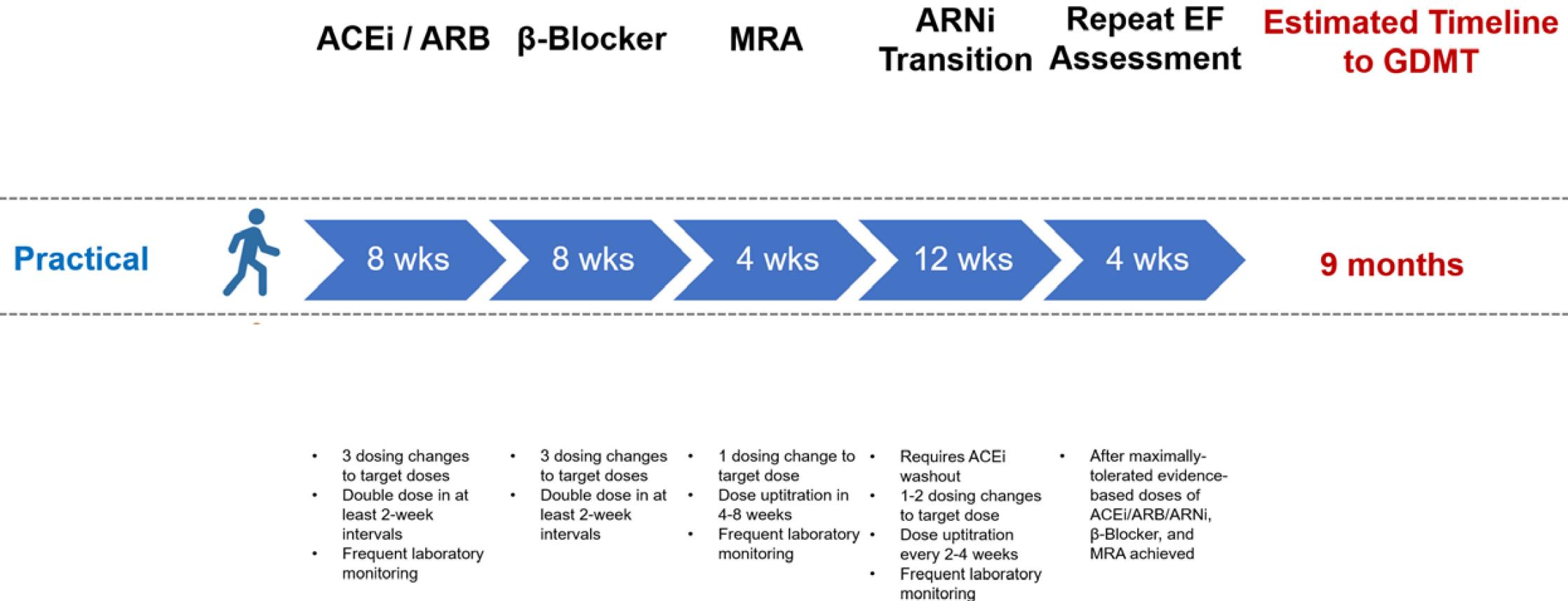
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How Long Does It Take to Optimize Medical Therapy?

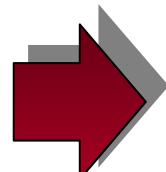
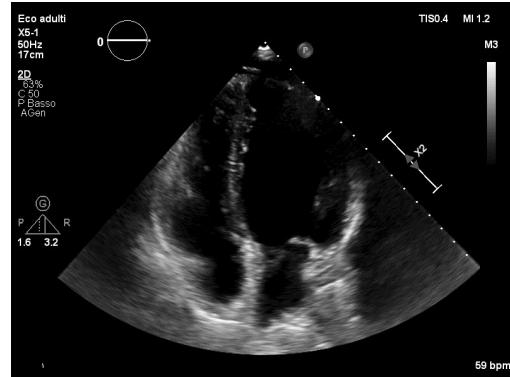


Clinical Case

♀, 36 years, first HF hospitalisation 12/21 - NGS TruSight Cardio: **TNNI3 C3-Vus**

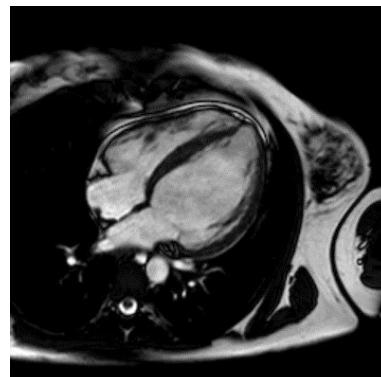
Echo at discharge 01/22

LVEF 21%



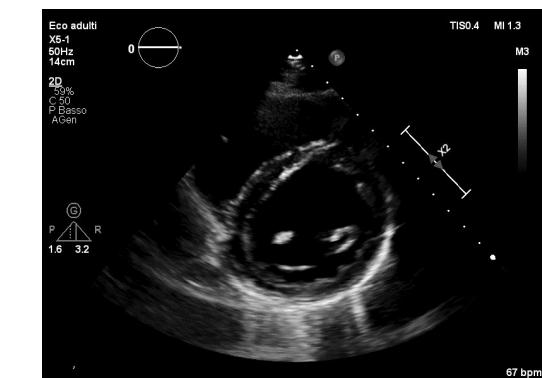
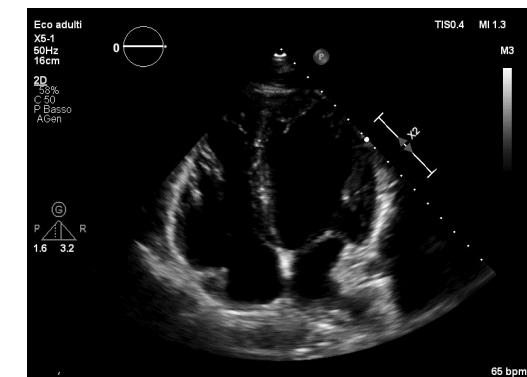
CMR 02/22

LVEF 18%



Echo at follow-up 7/22

LVEF 42%

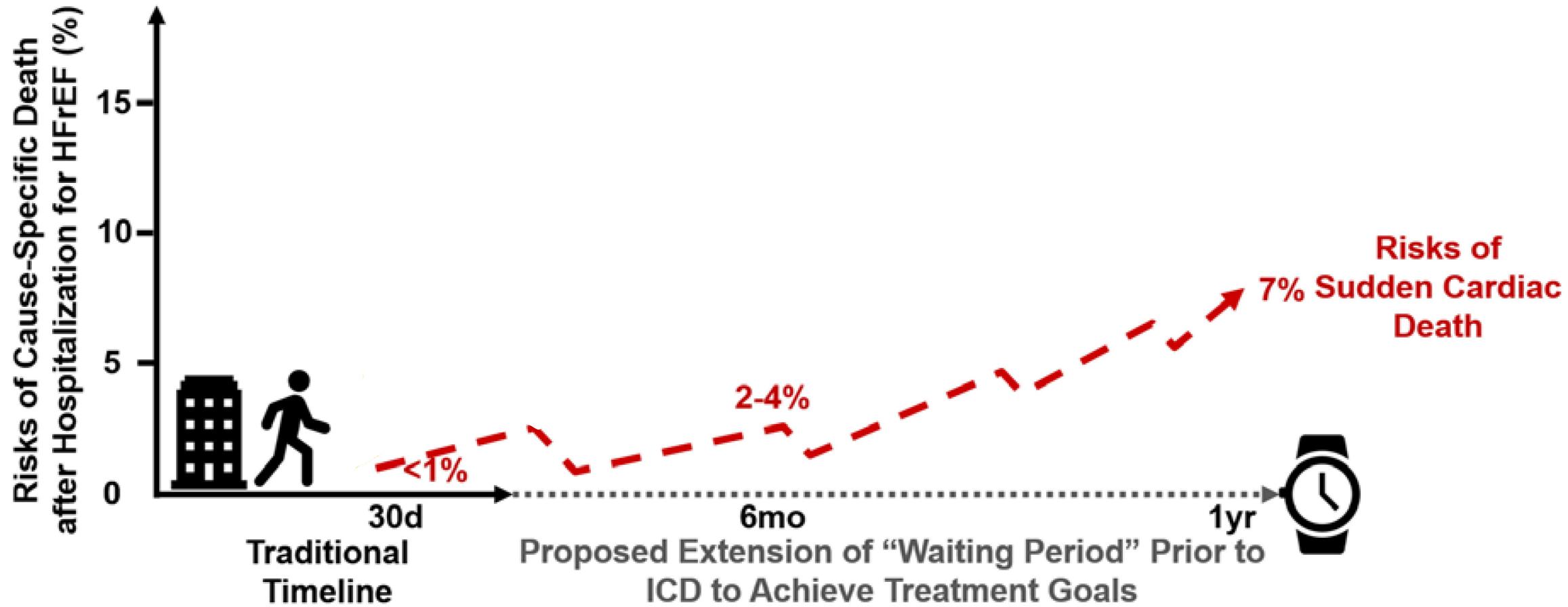


Courtesy of Dr. Stefano Pidello

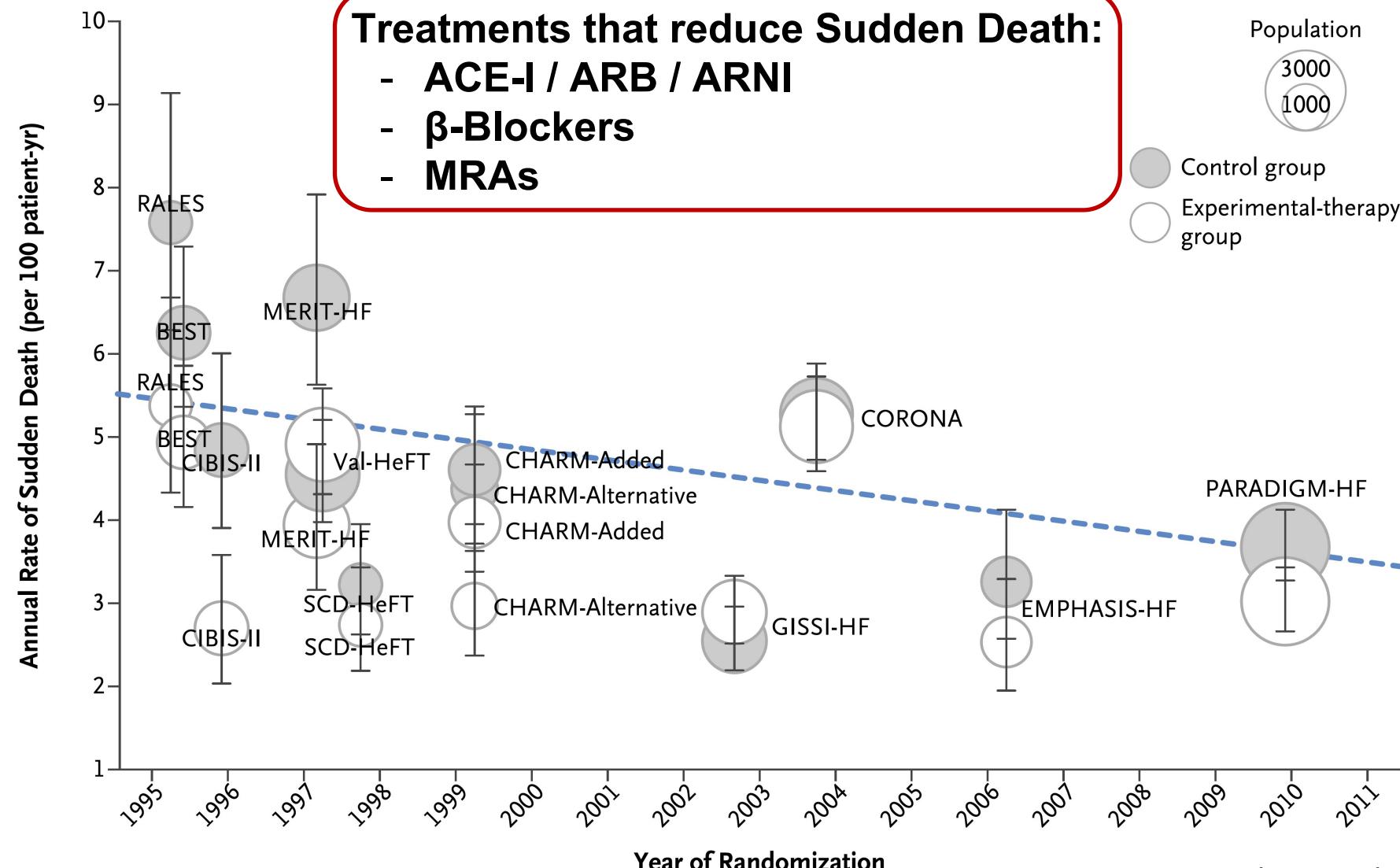
A large African elephant is standing in a conference room. A group of approximately ten people are seated around a long, rectangular conference table, engaged in a meeting. The room has large windows on one side, a decorative ceiling light fixture, and wood-paneled walls. The elephant is positioned on the right side of the frame, partially obscuring the wall.

SCD
Risk

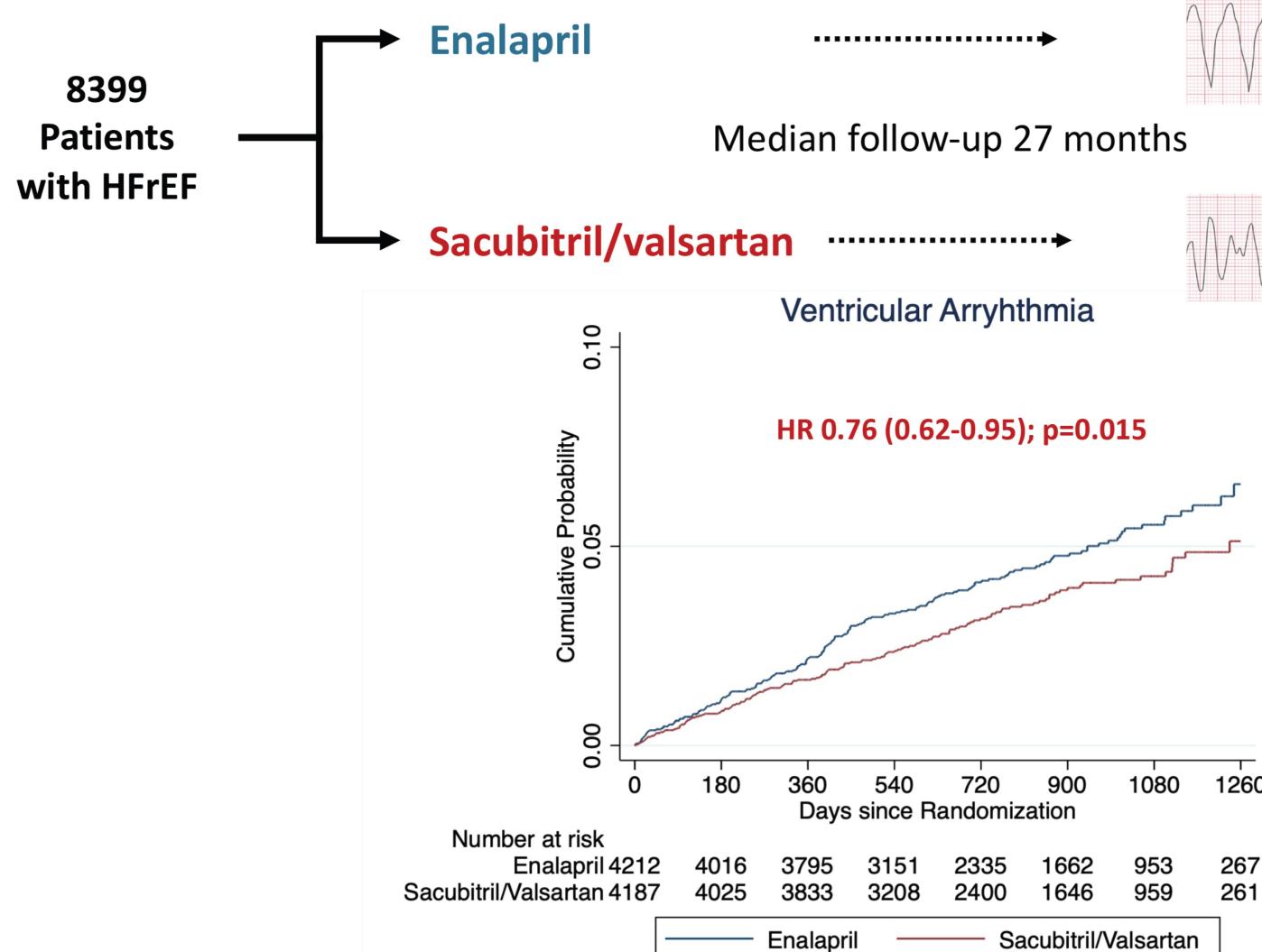
Risk of SCD After Hospitalisation for HFrEF



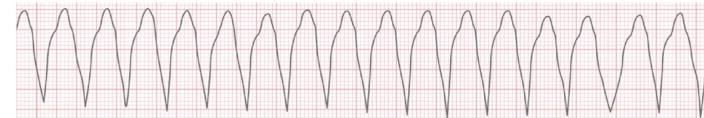
Declining Incidence of Sudden Cardiac Death



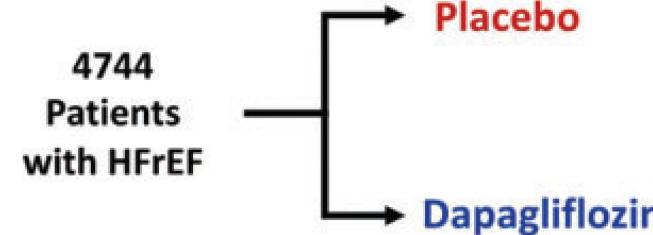
Effect of Sacubitril/valsartan on Ventricular Arrhythmias



Investigator Reports (Adverse Events)



Effect of Dapagliflozin on VTs, Cardiac Arrest and SCD



Median follow-up 18.2 months

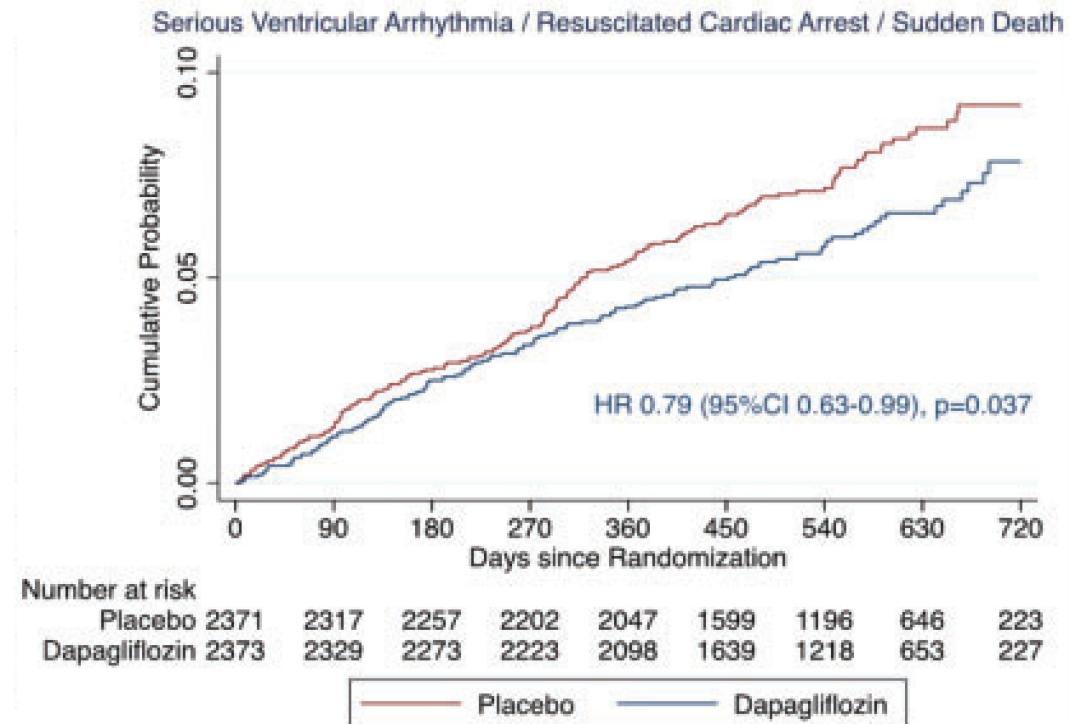
Investigator Reports (Serious Adverse Events)



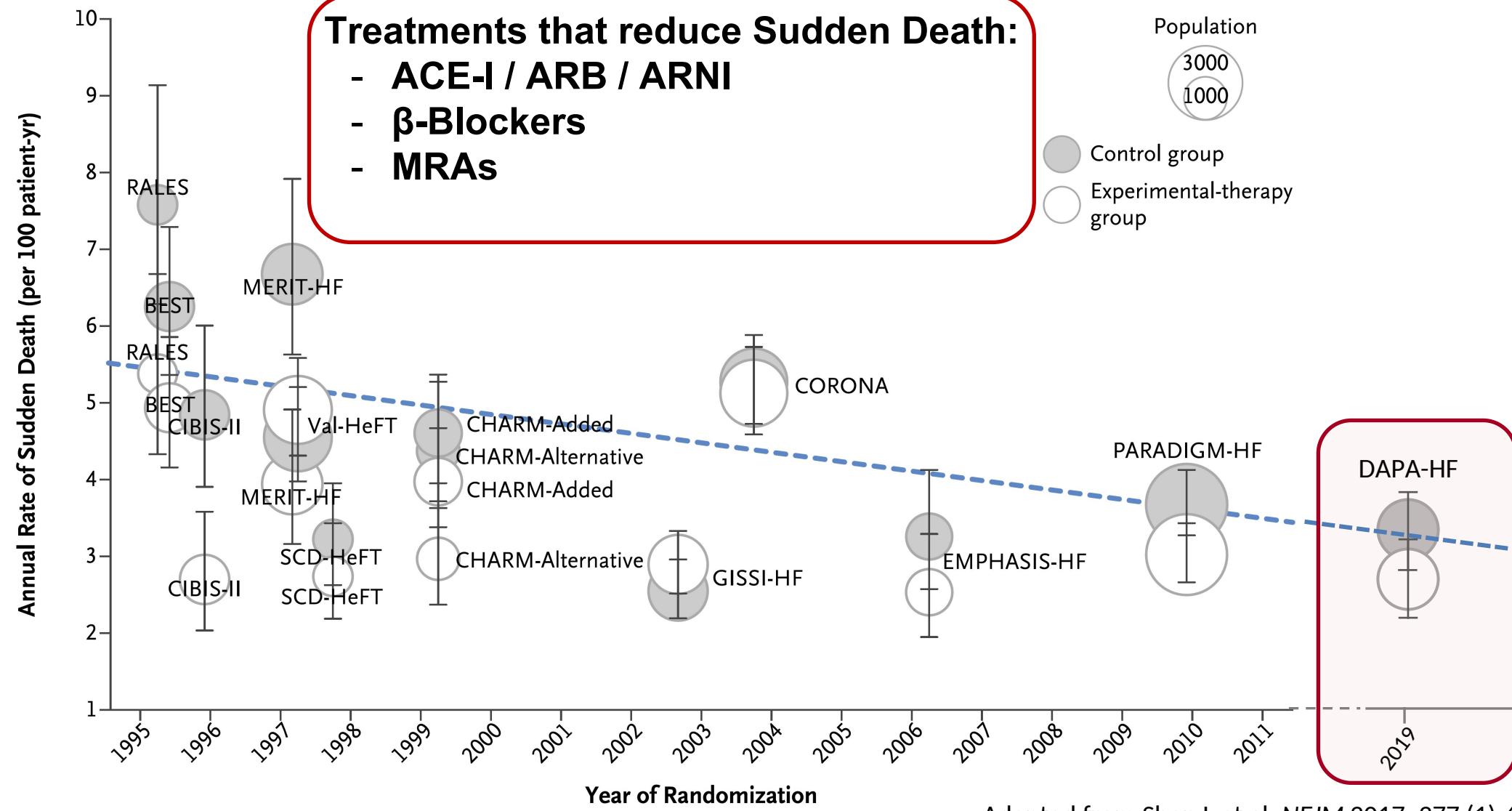
Backward stepwise logistic regression multivariable model to predict any serious ventricular arrhythmia, resuscitated cardiac arrest or sudden death

Predictor Variable*	Odds Ratio (95% CI)	p Value**	χ^2
Log-transformed NT-proBNP (per 1 unit increase)	1.54 (1.34 – 1.77)	<0.001	36.0
Previous Ventricular Arrhythmia	1.93 (1.41 – 2.64)	<0.001	16.8
LVEF (per 5% increase)	0.86 (0.78 – 0.94)	0.001	11.9
Systolic BP (per 10mmHg)	0.88 (0.81 – 0.96)	0.004	8.1
Previous MI	1.42 (1.11– 1.82)	0.005	7.8
Sex- male	1.53 (1.10 – 2.12)	0.012	6.3
BMI (per 1 kg/m ² increase)	1.03 (1.00 – 1.05)	0.020	5.4
Sodium (per 1 mmol/L increase)	0.96 (0.92 – 0.99)	0.039	4.3
Non-white race	0.85 (0.72 – 0.99)	0.038	4.3
Dapagliflozin	0.80 (0.63 – 1.02)	0.067	3.4
Cardiac Resynchronization Therapy	0.64 (0.39 – 1.04)	0.070	3.3
Previous HF hospitalization	0.99 (0.78 – 1.27)	0.985	0.0

*Randomized treatment and history of heart failure hospitalization were fixed factors in the model. **The p-value threshold was set at p<0.1



Declining Incidence of Sudden Cardiac Death

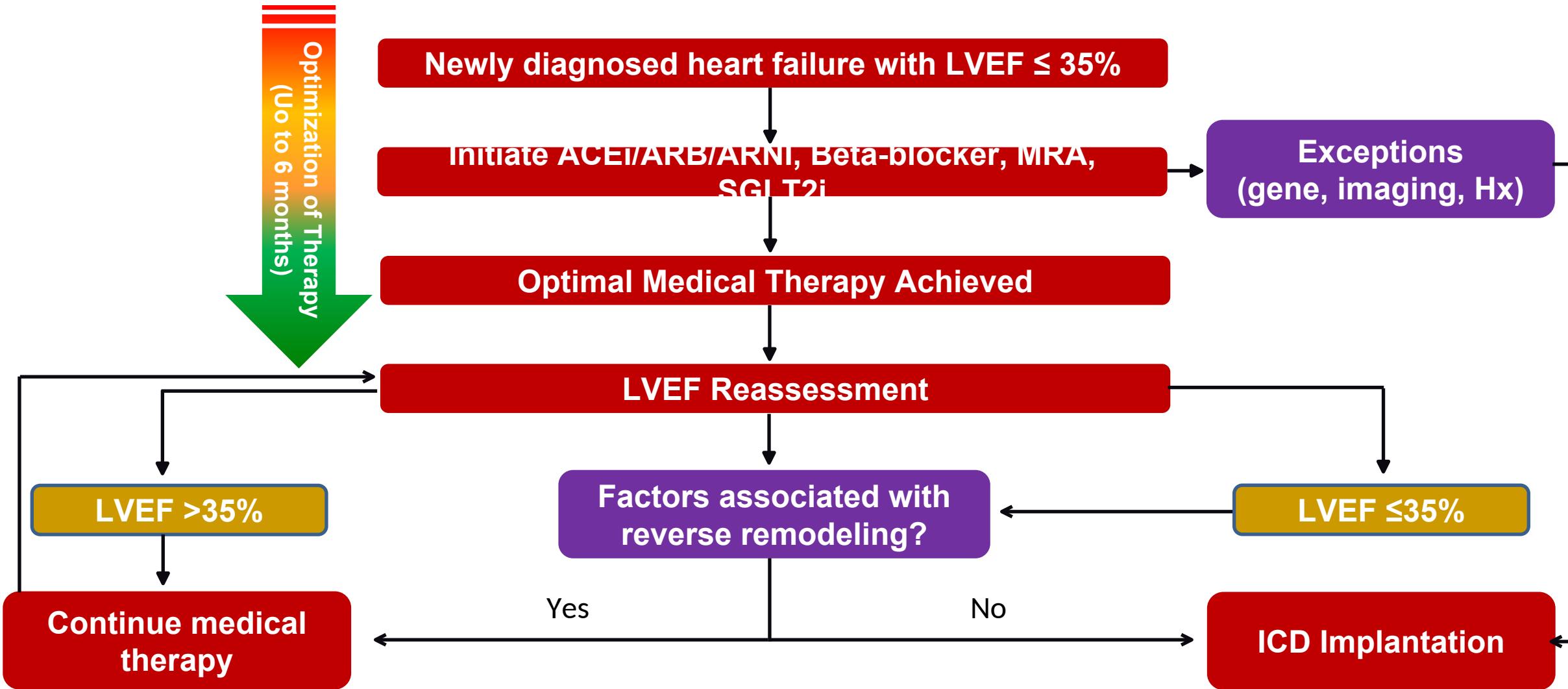


Adapted from Shen L et al. NEJM 2017; 377 (1):41-51

Clinical Exceptions to Waiting Time and LVEF<35%

Pathology / Gene Mutation	Protein	Cardiac Phenotype	Consensus Statement/Guideline Recommendations on Primary Prevention ICD
Sarcoidosis	NA	Conduction system disease Cardiomyopathy Atrial and ventricular arrhythmias	ICD reasonable (class IIa) if LVEF 36-49% and significant LGE or RVEF<40% or high degree AV block
FLNC	Filamin C	Ventricular cardiomyopathy	Consider ICD when LVEF<45%
LMNA	Lamin A/C	Conduction system disease Atrial fibrillation Ventricular cardiomyopathy	ICD reasonable when cardiac pacing is required or when 2 or more of the following: 1) male 2) NSVT 3) LVEF<45%
PLN	Phosholamban	Ventricular cardiomyopathy associated with low QRS voltage	Consider ICD when LVEF<45% or in case of NSVT

Proposed Timeline Before ICD Implantation



Take Home Messages

Despite compelling evidence, use of guideline directed medical therapy before primary prevention ICD implantation remains suboptimal

Allowing time for initiation, uptitration and optimization of multidrug regimen is crucial to evaluate its effect on reverse ventricular remodeling

Identification of subgroup of patients who may (or may not) benefit from longer waiting time can maximize ICD net clinical benefit



Thank you for your attention!