Meeting Nazionale ITACARE-P 2025

La Cardiologia Riabilitativa e Preventiva come snodo fondamentale della cura della persona con cardiopatia

CENTRO CONGRESSI FRENTANI
Roma, 21-22 novembre 2025

Cardiac Contractility Modulation® nei vari fenotipi di insufficienza cardiaca: quali novità nel rapporto tra cardiologia dell'acuto e riabilitazione

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ITACARE-P
ITALIAN ALLIANCE FOR CARDIOVASCULAR
REHABILITATION AND PREVENTION

ESC
European Society
of Cardiology

ESC GUIDELINES

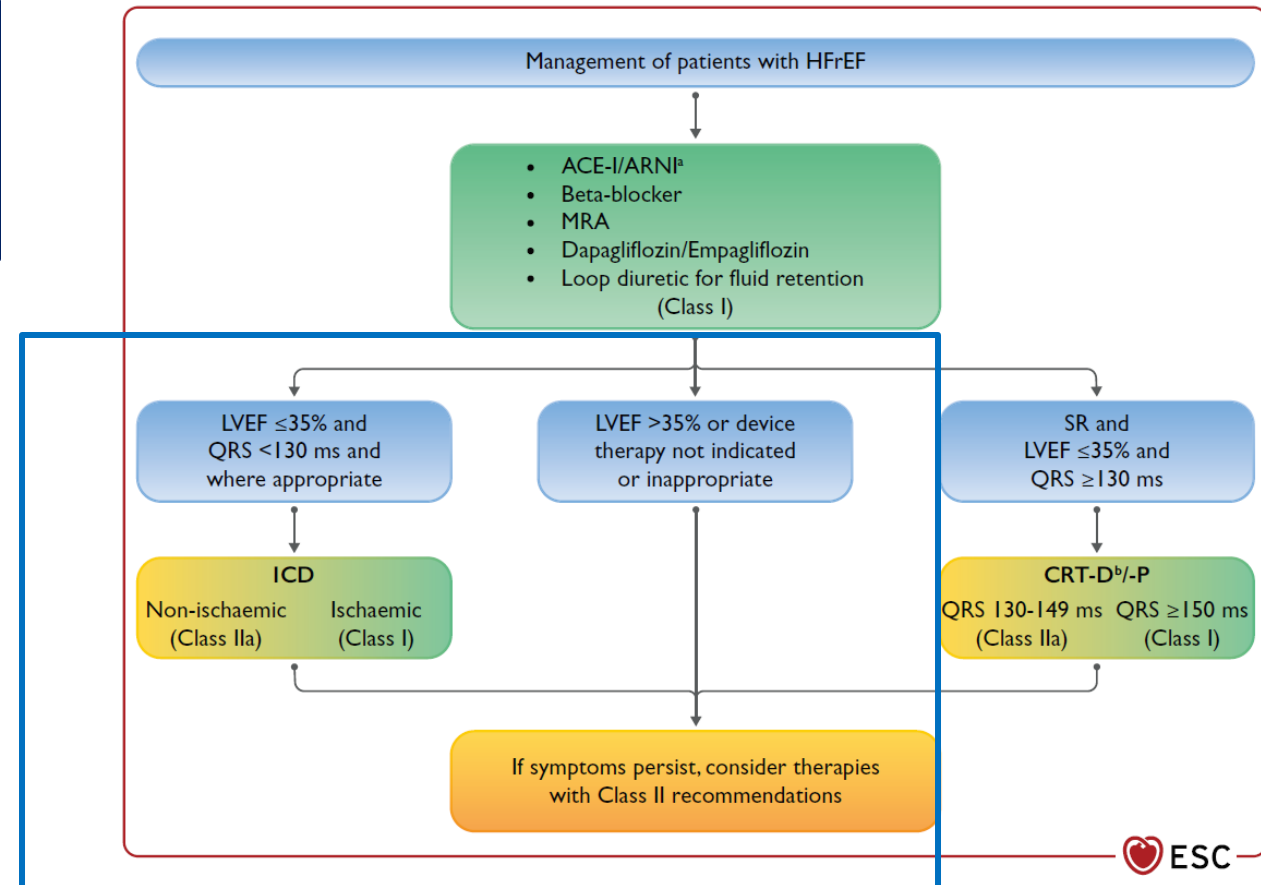## 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

6.3 Devices under evaluation

Cardiac contractility modulation (CCM) has been evaluated in patients with NYHA class III−IV HF, with an LVEF ≥25% to ≤45% and QRS duration <130 ms, and was associated with a small improvement in exercise tolerance and QOL.[241,242]
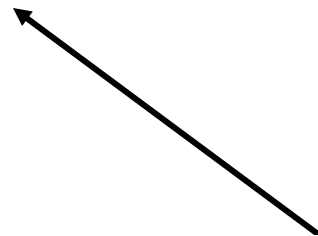
Supplementary Table 9   Interventions aiming to improve quality of life and/or exercise capacity in symptomatic patient with heart failure with reduced ejection fraction

	Intervention	Additional criteria beyond the presence of symptomatic HFrEF (if any)
DRUGS	Sacubitril/valsartan[17,18]	
	Dapagliflozin[19]	
	Diuretics[20]	Fluid overload
	Ferric carboxymaltose i.v.[21−23]	Iron deficiency
	Ivabradine[24−26]	SR >70 b.p.m.
	Trimetazidine[27−29]	
DEVICES AND INVASIVE PROCEDURES	CRT[30,31]	Eligibility for CRT
	Pulmonary vein isolation[32−34]	AF
	Percutaneous correction of severe functional mitral regurgitation[35−38]	Severe functional mitral regurgitation
	Cardiac contractility modulation[39−41]	QRS <130 ms, LVEF 25−45%
	Baroreflex activation therapy[42−44]	
	Phrenic nerve stimulation[45−47]	Central sleep apnoea

Management of patients with HFrEF

- ACE-I/ARNI[a]
- Beta-blocker
- MRA
- Dapagliflozin/Empagliflozin
- Loop diuretic for fluid retention
(Class I)

LVEF ≤35% and QRS <130 ms and where appropriate

LVEF >35% or device therapy not indicated or inappropriate

SR and LVEF ≤35% and QRS ≥130 ms

ICD
Non-ischaemic   Ischaemic
(Class IIa)   (Class I)

CRT-D[b]/-P
QRS 130-149 ms QRS ≥150 ms
(Class IIa)   (Class I)

If symptoms persist, consider therapies with Class II recommendations

ESC

Integration of implantable device therapy in patients with heart failure. A clinical consensus statement from the Heart Failure Association (HFA) and European Heart Rhythm Association (EHRA) of the European Society of Cardiology (ESC)

Wilfried Mullens[1,2]*, Jeroen Dauw[1,3], Finn Gustafsson[4], Alexandre Mebazaa[5],

Cardiac contractility modulation

How does it work?

In whom to implant cardiac contractility modulation?

Cardiac contractility modulation improved the quality of life and exercise capacity in symptomatic patients in sinus rhythm with LVEF <45% and QRS <130 ms in three open-label randomized trials,[68–70] but the effect was rather small. There are no blinded, sham-controlled trials limiting the robustness of the data to influence guidelines.[6] However, the AIM HIGHer clinical trial is a prospective, multicentre, randomized, quadruple-blind, sham-controlled, trial in subjects with HF and an LVEF ≥40% and ≤60% (NCT05064709).

How to implement cardiac contractility modulation?

Further evidence is needed to guide the role of CCM in routine practice, but in general CCM is only advised in selected patients by experienced operators working within a multidisciplinary HF service capable of follow-up and trouble shooting.
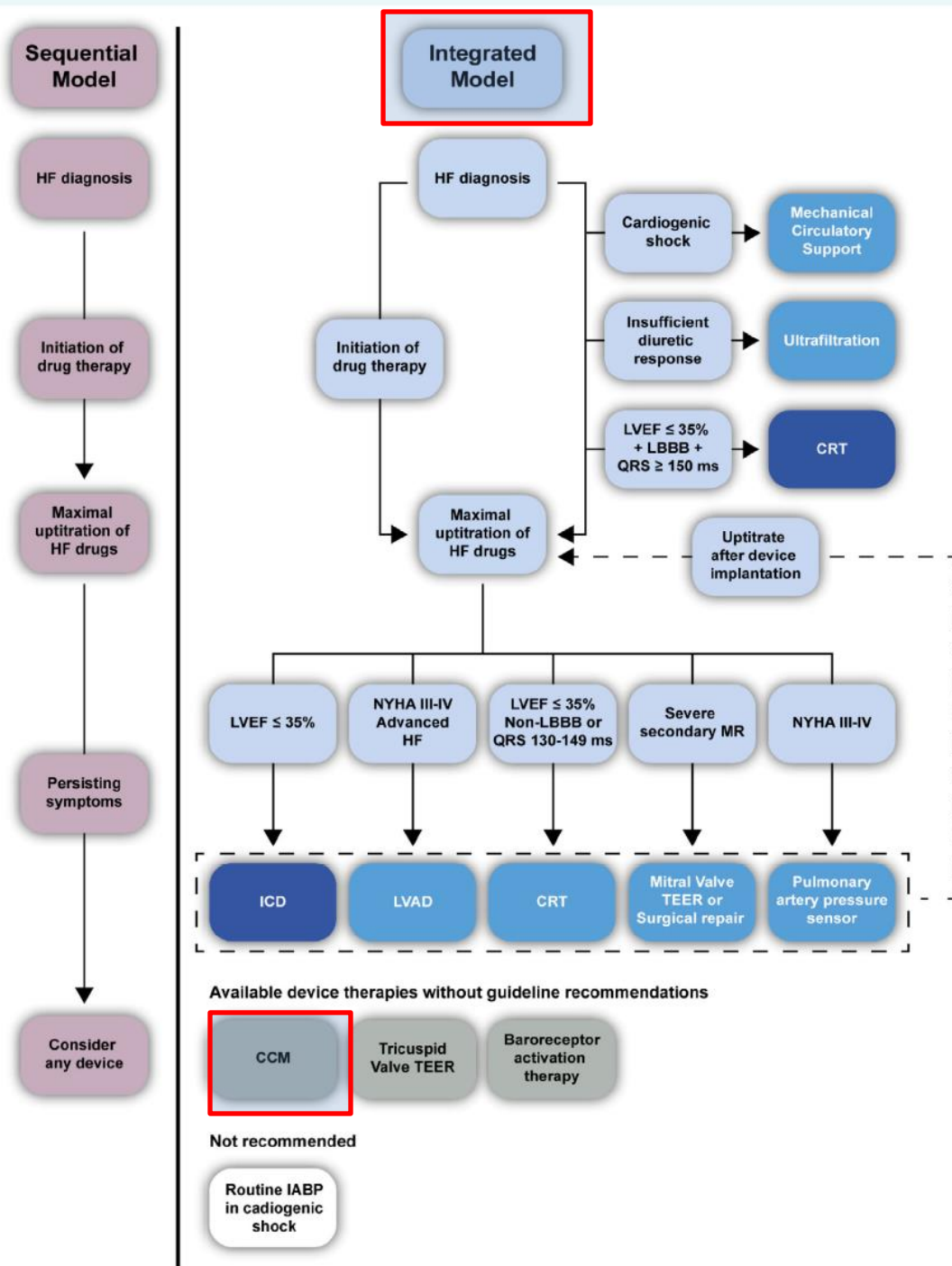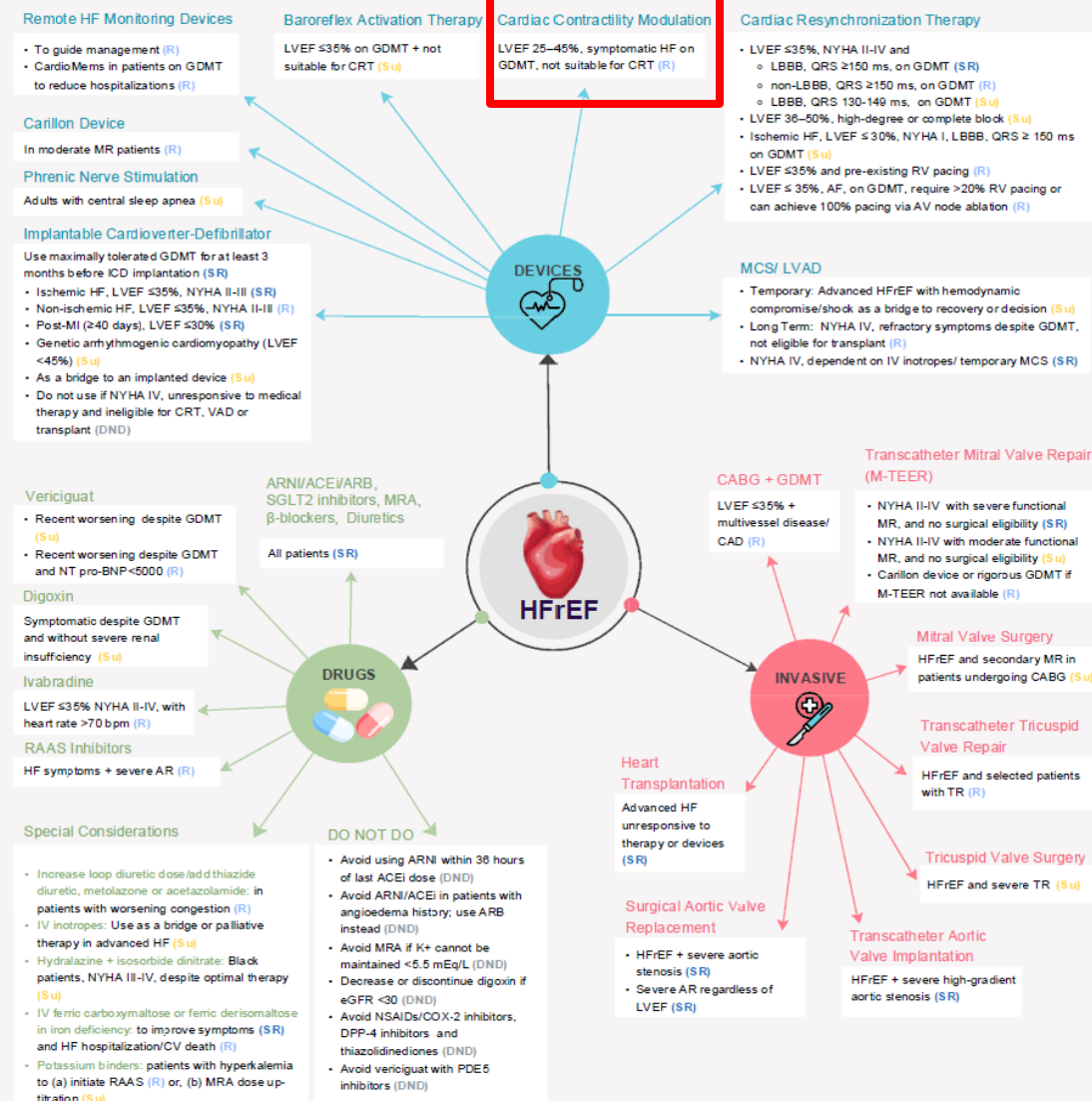
GUIDELINES

iCARDIO Alliance Global Implementation Guidelines on Heart Failure 2025

Vijay Chopra* (India), Muhammad Shahzeb Khan (USA), Magdy Abdelhamid (Egypt), William T. Abraham (USA),

| No.	Guideline Statement	Level of Recommendation
5-13	Use CCM with the Optimizer Smart system to improve symptoms, QOL and exercise tolerance in patients with HF with LVEF 25-45% on GDMT not suitable for CRT.	R

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Recommendations for HFrEF Management

Approved Devices for Stage C and D Chr...

An interdisciplinary team that consists of a general cardiologist, HF cardiologist, interventional cardiologist, structural cardiologist, multimodality imaging cardiologist, electrophysiologist, and cardiothoracic surgeon is crucial for the successful implantation and delivery of device-based therapies in heart failure

Onset of CHF — **Decompensations**

Time

Implantable cardioverter-defibrillator (ICD)
-NYHA I-III
-LVEF ≤ 35%
-Projected survival > 1 year
COR*: 1

Cardiac resynchroni...
-NYHA II-III;
-LVE
-Norr
-QRS ≥ 150 r
CC...

Transcatheter edge-to-edge mitral valve repair (M-TEER)
-NYHA II-Ambulatory IV
-LVEF 20-50%
-Moderate-severe (grade 3+) or severe (grade 4+) secondary MR
-LVESD ≤ 7cm
-Excludes RHF and/or severe PHTN (RVSP > 70 mmHg)
COR*: 2a

AVR (TAVI or SAVR)
-NYHA I-IV
-Asymptomatic patients with severe AS and LVEF < 50%
-Severe high-gradient AS with symptoms (independent of LVEF)
-Symptomatic patients with low-flow, low gradient severe AS with reduced LVEF
-Symptomatic patients with low-flow, low gradient with normal LVEF if AS is the most likely cause of symptoms
COR**: 1

Transcatheter tricuspid valve replacement system OR transcatheter edge-to-edge mitral valve repair (T-TEER)
-NYHA I-IV
-Signs/symptoms of TR or prior hospitalization for HF
- Severe TR
COR*: Not Provided

Remote Hemodynamic Monitoring (CardioMEMs)
-NYHA II-III
-Independent of LVEF
- Hospitalized for HF in the previous year and/or have elevated natriuretic peptides
COR*: 2b

Baroreflex activation therapy (BAT)
-Persistent symptoms with NYHA III or II (with a recent history of Class III)
-LVEF ≤ 35%
- NT-proBNP <1600 pg/ml
-Excludes patients with a guideline indication for CRT
COR*: Not Provided

Cardiac Contractility Modulation (CCM)
-NYHA III
-LVEF 25-45%
-Excludes patients with a guideline indication for CRT
COR*: Not Provided

February 7, 2025

Tamara Syrek Jensen, JD
Director, Coverage & Analysis Group
Centers for Medicare & Medicaid Services
7500 Security Blvd.
Baltimore, MD 21244

RE: CAG-00469N Cardiac Contractility Modulation for Heart Failure

The American College of Cardiology, Heart Rhythm Society, and Heart Failure Society of America represent the physicians and healthcare professionals dedicated to the care of heart failure (HF) patients undergoing cardiac contractility modulation (CCM). These societies strongly support a National Coverage Determination (NCD) for CCM in HF under coverage with evidence development (CED). We appreciate the opportunity to comment on the national coverage analysis (NCA).
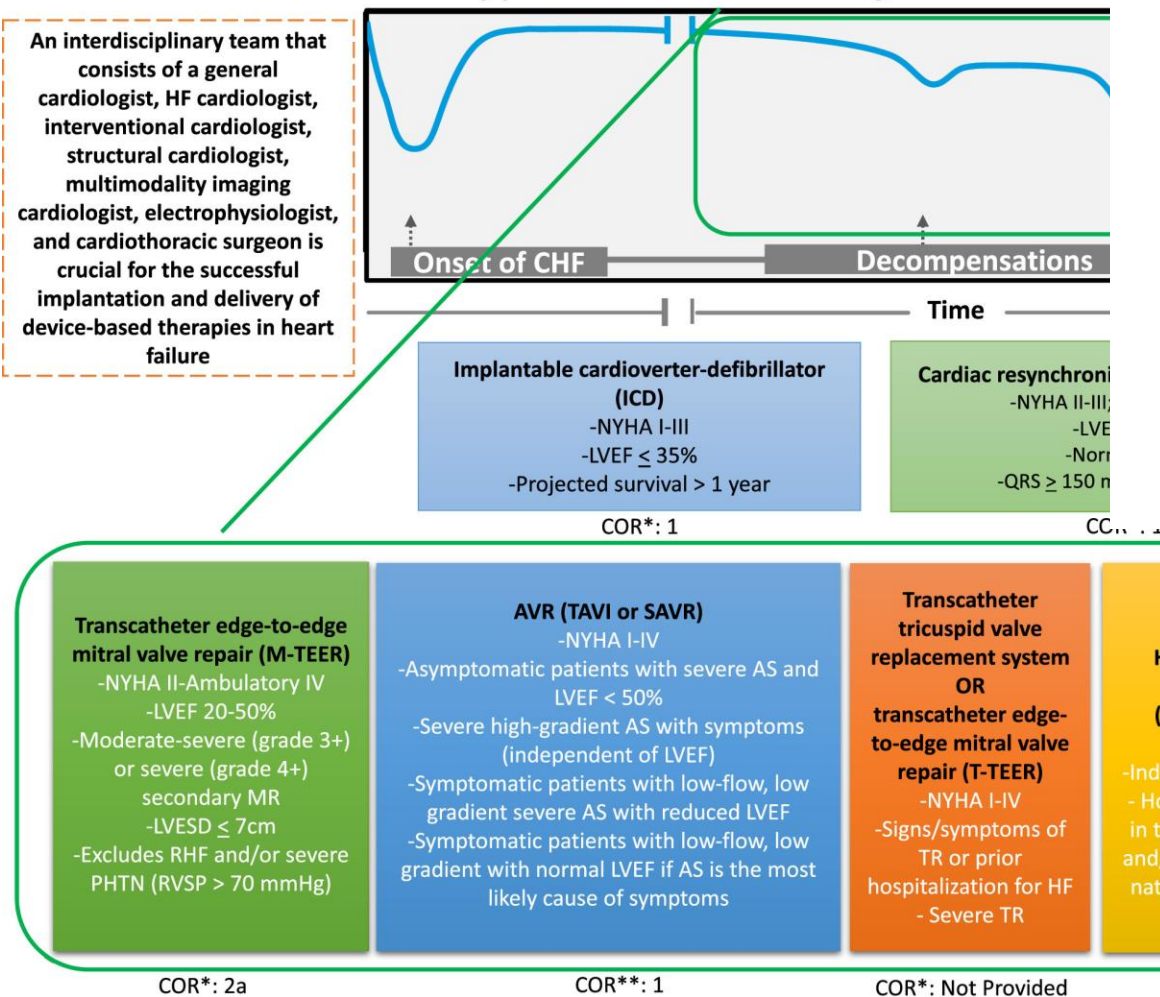
APPROPRIATE USE CRITERIA

ACC/AHA/ASE/HFSA/HRS/SCAI/ SCCT/SCMR 2025 Appropriate Use Criteria for Implantable Cardioverter- Defibrillators, Cardiac Resynchronization Therapy, and Pacing

A Report of the American College of Cardiology Solution Set Oversight Committee, American Heart Association, American Society of Echocardiography, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance

TABLE 10.1   Heart Failure and CCM

Indication		Appropriate Use Score (1-9)	
NYHA Functional Class		**II**	**III-IV**
CCM, Not Candidate for CRT (QRS <130 ms)			
289.	■ LVEF <25%	M (4)	M (4)
290.	■ LVEF 25%-≤35%	M (4)	M (5)
291.	■ LVEF 36%-≤45%	M (4)	M (4)

CCM = cardiac contractility modulation; CRT = cardiac resynchronization therapy; LVEF = left ventricular ejection fraction; M = May Be Appropriate; NYHA = New York Heart Association.

FIGURE 25 Summary of Table 10.1, Heart Failure and CCM
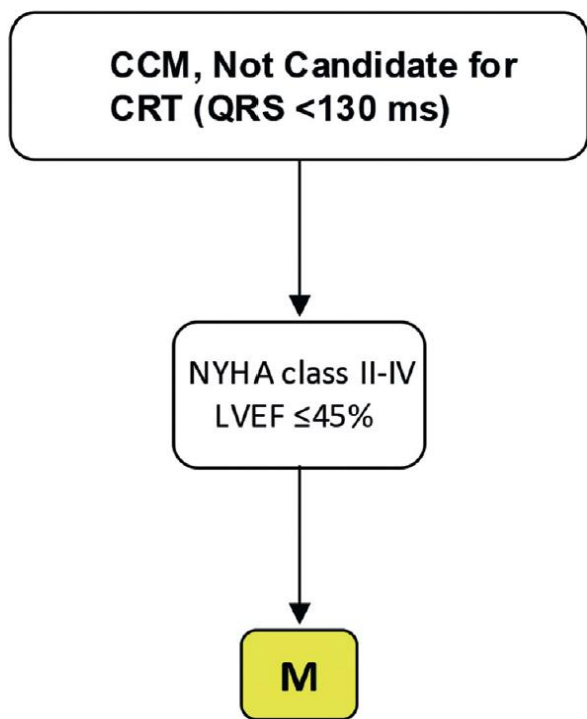
CCM = cardiac contractility modulation; CRT = cardiac resynchronization therapy; LVEF = left ventricular ejection fraction; M = May Be Appropriate; NYHA = New York Heart Association.

Current CE Mark Indication

The **OPTIMIZER Smart®** and the **OPTIMIZER Smart Mini®** Systems are indicated to:

improve clinical status, functional capacity, and quality of life

and

prevent hospital admissions

in patients who are older than 18 years of age with symptomatic heart failure due to systolic left ventricular dysfunction, despite appropriate medical therapy

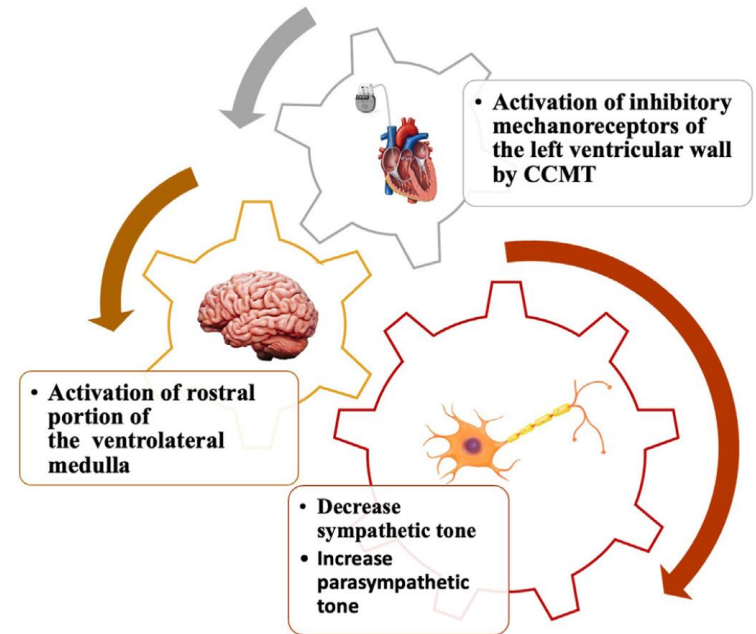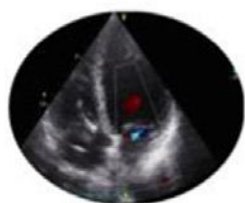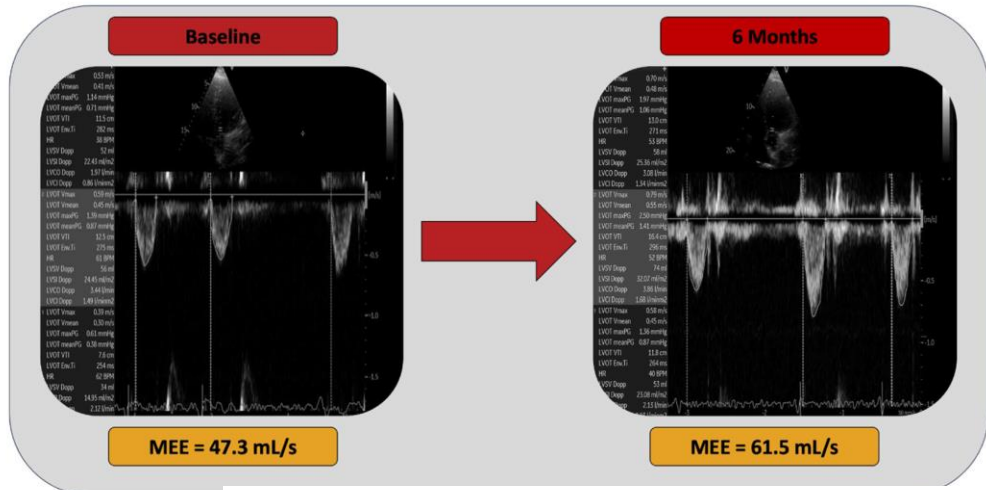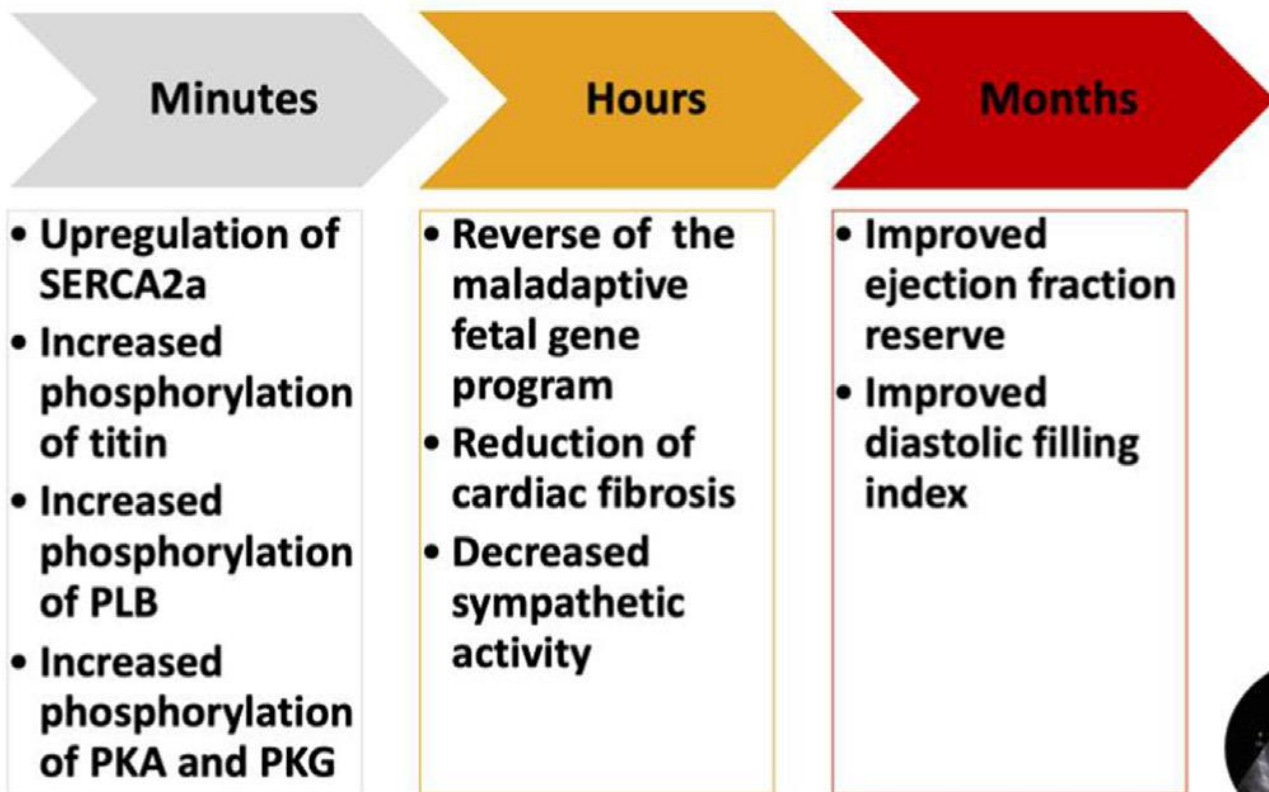# Impulse Dynamics Receives European CE Mark For Expanded Indication For Diastolic Heart Failure

by Impulse Dynamics | Mar 28, 2025 | Press Releases

CCM therapy is now indicated for symptomatic heart failure patients with diastolic or systolic ventricular dysfunction, offering a broader range of patients a new option for improving quality of life and reducing heart failure hospitalization

MARLTON, N.J., March 28, 2025 (GLOBE NEWSWIRE) — Impulse Dynamics plc, a global medical device company dedicated to improving the lives of people with heart failure (HF), is proud to announce that it received European CE Mark approval for an expanded indication for the Optimizer® Smart Mini system, which delivers the company's proprietary CCM® therapy. This new indication now offers millions of patients with diastolic HF a way to alleviate debilitating symptoms, improving their quality of life and reducing hospitalizations related to heart failure. [i]
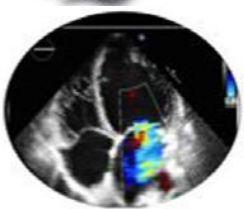
Meccanismo di azione della terapia CCM

Minutes
- Upregulation of SERCA2a
- Increased phosphorylation of titin
- Increased phosphorylation of PLB
- Increased phosphorylation of PKA and PKG

Hours
- Reverse of the maladaptive fetal gene program
- Reduction of cardiac fibrosis
- Decreased sympathetic activity

Months
- Improved ejection fraction reserve
- Improved diastolic filling index

Baseline — MEE = 47.3 mL/s

6 Months — MEE = 61.5 mL/s

- Activation of inhibitory mechanoreceptors of the left ventricular wall by CCMT
- Activation of rostral portion of the ventrolateral medulla
- Decrease sympathetic tone
- Increase parasympathetic tone

A comprehensive individual patient data meta-analysis of the effects of cardiac contractility modulation on functional capacity and heart failure-related quality of life
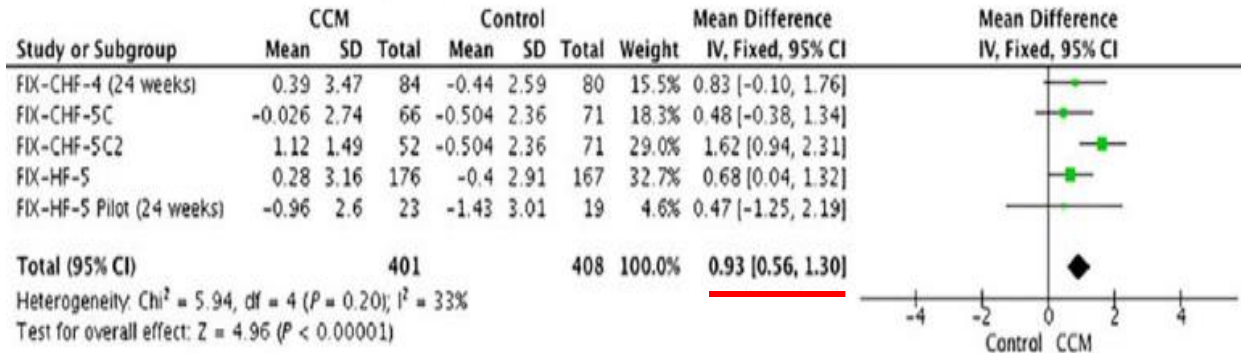
Francesco Giallauria[1]*, Gianluigi Cuomo[1], Alessandro Parlato[1], Nirav Y. Raval[2], Jürgen Kuschyk[3] and Andrew JS Stewart Coats[4]

	RX-HF-5 pilot		FIX-CHF-4		FIX-HF-5		FIX-HF-5C		FIX-HF-5C2	
First author	Neelagaru SB[26]		Borggrefe MM[27]		Kadish A[28]		Abraham WT[29]		Wiegn P[32]	
Year of publication	2006		2008		2011		2018		2020	
Total study cohort sample size (N)	49		164		428		160		60	
Randomized	Yes		Yes		Yes		Yes		No	
Double blinded	No		Yes		Yes		No		No	
	CCM	Control	CCM	Control	CCM	Control	CCM	Control[c]	CCM	Control[c]
Age (years)	52 ± 15	60 ± 12	59 ± 10	60 ± 10	58 ± 13	59 ± 12	63 ± 11	63 ± 11	66 ± 9	63 ± 11
Male (%)	68	71	89	81	73	71	73	79	88	79
Ischaemic CHF (%)	64	67	64	56	65	67	62	59	68	59
EF (%)[a]	24.9 ± 6.5	31.4 ± 7.4	29.3 ± 6.6	29.8 ± 7.8	25.7 ± 6.8	26.1 ± 6.5	33 ± 6	33 ± 5	34 ± 6	33 ± 5
NYHA class III (%)	100	96	72	66	91	86	86	91	98	91
Peak VO$_2$ (mL/kg/min)	14.3 ± 2.8	16.0 ± 2.9	14.1 ± 3.0	13.6 ± 2.7	14.7 ± 3.0	14.7 ± 2.9	15.5 ± 2.6	15.4 ± 2.8	15.0 ± 2.9	15.4 ± 2.8
6MWT (m)	321 ± 82	352 ± 95	386 ± 103	394 ± 102	326 ± 82	324 ± 92	317 ± 88	324 ± 90	NA	324 ± 90
MLWHFQ score	56.4 ± 24.8	52.1 ± 21.4	38.9 ± 27.4	36.5 ± 27.1	60.5 ± 23.0	57.4 ± 22.6	56 ± 23	57 ± 23	NA	57 ± 23
Interventions	CCM (OPTIMIZER system) signals on; control; signals off		CCM (OPTIMIZER system) allocated to on/off (Group 1: on to off; Group 2: off to on)		CCM (OPTIMIZER system) and optimal medical therapy[b] vs. optimal medical therapy alone (control)		CCM (OPTIMIZER system) and optimal medical therapy vs. optimal medical therapy alone (control)		The OPTIMIZER Smart system with 2-lead	
Outcomes	Peak VO$_2$, 6MWT, MLWHFQ. Others: NYHA classification, Holter monitoring		Peak VO$_2$, 6MWT, MLWHFQ. Others: NYHA classification, LV function		Peak VO$_2$, 6MWT, MLWHFQ. Others: NYHA classification, LVEF, LV end-diastolic dimension, VAT, composite of all-cause mortality and all-cause hospitalizations		Peak VO$_2$, 6MWT, MLWHFQ. Others: safety		Peak VO$_2$. Others: NYHA, safety	
Follow-up visits	12, 24 weeks		Phase I: 12 weeks; Phase II: 24 weeks		12, 24, 50 weeks		12, 24 weeks		12, 24 weeks	

861 pts in totale per valutazione del pVO$_2$, della QoL e 6MWT

A comprehensive individual patient data meta-analysis of the effects of cardiac contractility modulation on functional capacity and heart failure-related quality of life

Francesco Giallauria[1]*, Gianluigi Cuomo[1], Alessandro Parlato[1], Nirav Y. Raval[2], Jürgen Kuschyk[3] and Andrew JS Stewart Coats[4]

Effetti statisticamente significativi e clinicamente utili della terapia CCM sono emersi rispetto a :
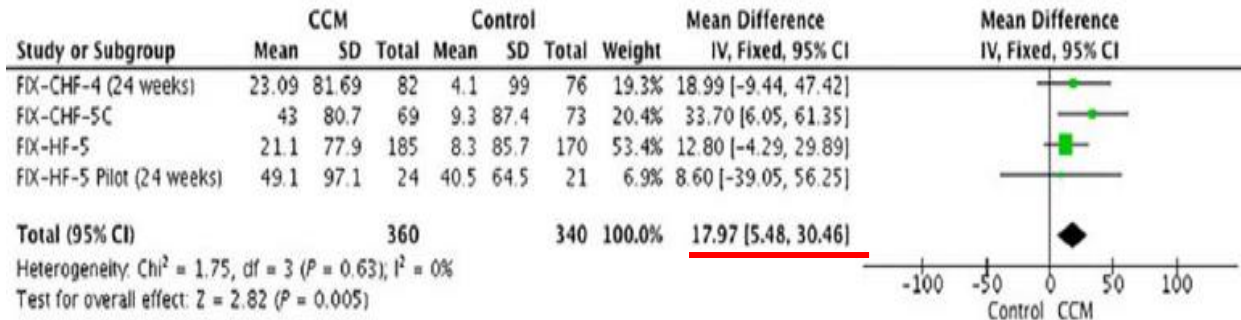- Capacità Funzionale (CPET, peak VO_2)
- Capacità di Esercizio (6MWT)
- Qualità della Vita (MLWHFQ)

Tutti gli endpoint hanno dimostrato differenze non significative tra pazienti con età > 60 anni e quelli con età ≤ 60 anni

Panel A. Peak VO_2 (ml/kg/min)

Study or Subgroup	CCM Mean	CCM SD	CCM Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
FIX-CHF-4 (24 weeks)	0.39	3.47	84	-0.44	2.59	80	15.5%	0.83 [-0.10, 1.76]
FIX-CHF-5C	-0.026	2.74	66	-0.504	2.36	71	18.3%	0.48 [-0.38, 1.34]
FIX-CHF-5C2	1.12	1.49	52	-0.504	2.36	71	29.0%	1.62 [0.94, 2.31]
FIX-HF-5	0.28	3.16	176	-0.4	2.91	167	32.7%	0.68 [0.04, 1.32]
FIX-HF-5 Pilot (24 weeks)	-0.96	2.6	23	-1.43	3.01	19	4.6%	0.47 [-1.25, 2.19]
Total (95% CI)			401			408	100.0%	0.93 [0.56, 1.30]

Heterogeneity: Chi² = 5.94, df = 4 (P = 0.20); I² = 33%
Test for overall effect: Z = 4.96 (P < 0.00001)

Panel B. 6MWT distance (m)

Study or Subgroup	CCM Mean	CCM SD	CCM Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
FIX-CHF-4 (24 weeks)	23.09	81.69	82	4.1	99	76	19.3%	18.99 [-9.44, 47.42]
FIX-CHF-5C	43	80.7	69	9.3	87.4	73	20.4%	33.70 [6.05, 61.35]
FIX-HF-5	21.1	77.9	185	8.3	85.7	170	53.4%	12.80 [-4.29, 29.89]
FIX-HF-5 Pilot (24 weeks)	49.1	97.1	24	40.5	64.5	21	6.9%	8.60 [-39.05, 56.25]
Total (95% CI)			360			340	100.0%	17.97 [5.48, 30.46]

Heterogeneity: Chi² = 1.75, df = 3 (P = 0.63); I² = 0%
Test for overall effect: Z = 2.82 (P = 0.005)

Panel C. MLWHFQ

Study or Subgroup	CCM Mean	CCM SD	CCM Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
FIX-CHF-4 (24 weeks)	-10.07	16.73	84	-6.78	18.41	78	28.7%	-3.29 [-8.72, 2.14]
FIX-CHF-5C	-21.2	23.7	70	-10.2	18.5	78	17.7%	-11.00 [-17.91, -4.09]
FIX-HF-5	-15.56	19.15	180	-5.76	21.24	188	49.6%	-9.80 [-13.93, -5.67]
FIX-HF-5 Pilot (24 weeks)	-18.29	23.47	24	-15.96	27.87	24	4.0%	-2.33 [-16.91, 12.25]
Total (95% CI)			358			368	100.0%	-7.85 [-10.76, -4.94]

Heterogeneity: Chi² = 4.92, df = 3 (P = 0.18); I² = 39%
Test for overall effect: Z = 5.29 (P < 0.00001)

A Randomized Controlled Trial to Evaluate the Safety and Efficacy of Cardiac Contractility Modulation

William T. Abraham, MD,[a] Karl-Heinz Kuck, MD,[b] Rochelle L. Goldsmith, PhD,[c] JoAnn Lindenfeld, MD,[d] Vivek Y. Reddy, MD,[e] Peter E. Carson, MD,[f] Douglas L. Mann, MD,[g] Benjamin Saville, PhD,[h] Helen Parise, ScD,[i] Rodrigo Chan, MD,[j] Phi Wiegn, MD,[k] Jeffrey L. Hastings, MD,[k] Andrew J. Kaplan, MD,[l] Frank Edelmann, MD,[m] Lars Luthje, MD,[m] Rami Kahwash, MD,[n] Gery F. Tomassoni, MD,[o] David D. Gutterman, MD,[p] Angela Stagg, BS,[q] Daniel Burkhoff, MD, PhD,[r] Gerd Hasenfuß, MD[s]

Analisi combinata (FIX-HF-5+FIX-HF-5C) su 389 pazienti: 293 con Fe < 35%, 96 con FE≥35%
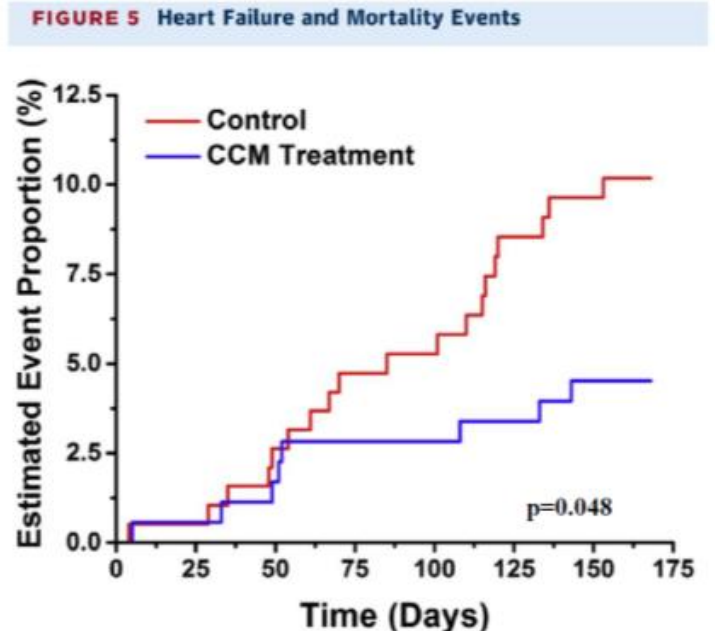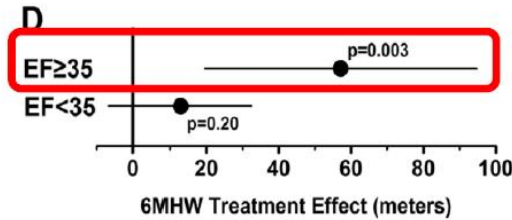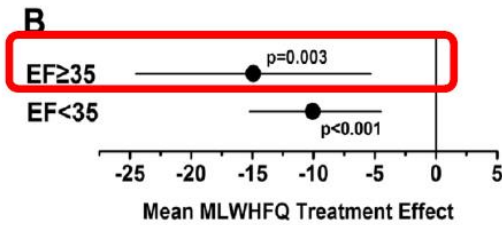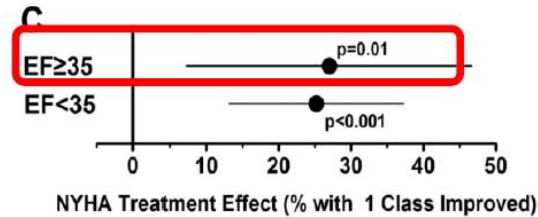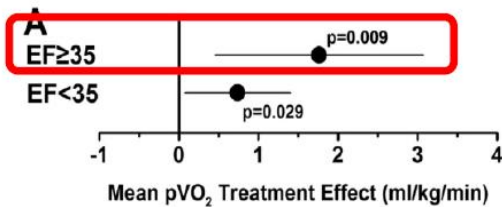
- Benefici della terapia CCM in **tutte le classi di FE**
- Responder migliori in FE>35%: +1,76 mL/Kg/min VO2 picco, (+0,9 mL/Kg/min in tutta la popolazione)
- **81% dei pazienti trattati con CCM con miglioramento ≥1 classe NYHA, di cui il 50% con miglioramento di 2 classi funzionali.**

FIGURE 5 Heart Failure and Mortality Events

A 24 settimane, il gruppo CCM aveva maggiore sopravvivenza libera da morte cardiaca e ospedalizzazioni per SC: 97,1% nel gruppo studio vs 89,2% nel gruppo controllo

Long-term clinical experience with cardiac contractility modulation therapy delivered by the Optimizer Smart system

Jürgen Kuschyk[1], Peter Falk[2], Thomas Demming[2], Oliver Marx[3], Deborah Morley[4], Ishu Rao[4], and Daniel Burkhoff[5]*

CCM-REG Registry Study N=503

LVEF ≤25% *n*= 178

LVEF 26–34% *n*= 164

LVEF ≥35% *n*= 161
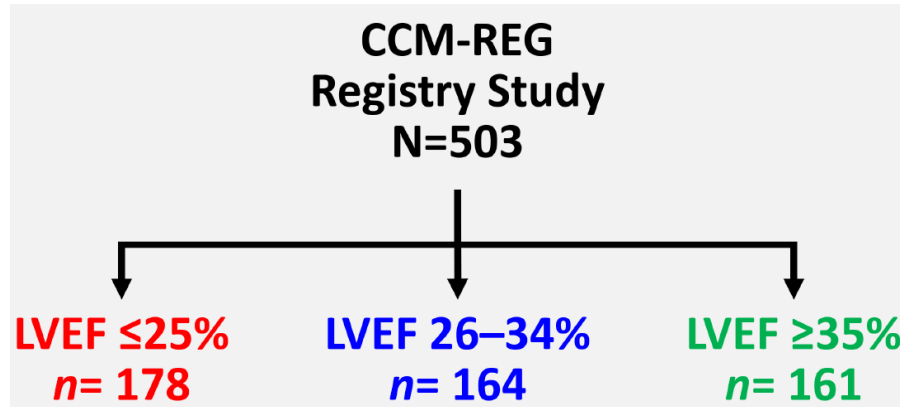
Registro a lungo termine (24 mesi) real-world di pazienti impiantati con dispositivo CCM secondo CE Mark (HF sistolico cronico sintomatico→ FE ≤ 45%, NYHA>II) per valutazione impatto sulla mortalità, QoL, eventi SCC, FE Vsx e QoL.

Età media 66 anni, 60% ischemici, NYHA III 82%, FE 30%, FA 30%.

Il 75% dei pazienti già portatori di ICD

Long-term clinical experience with cardiac contractility modulation therapy delivered by the Optimizer Smart system

Jürgen Kuschyk[1], Peter Falk[2], Thomas Demming[2], Oliver Marx[3], Deborah Morley[4], Ishu Rao[4], and Daniel Burkhoff[5]*

Table 3 Hospitalization rates the year prior to Optimizer implant compared to the 2 years following Optimizer implant in the entire cohort and in the five subgroups of interest

Subgroup	Pre-treatment (1 year prior)				Post-treatment (0–730 days)				P-value
	Patients	Patient-years	Events	Event rate	Patients	Patient-years	Events	Event rate	
All patients									
All cardiovascular events	503	503	523	1.04	503	729	287	0.39	<0.0001
Heart failure events			371	0.74			179	0.25	<0.0001
Non-heart failure cardiovascular events			152	0.30			108	0.15	<0.0001
LVEF ≤25%									
All cardiovascular events	178	178	227	1.28	178	233	123	0.53	<0.0001
Heart failure events			182	1.02			90	0.39	<0.0001
Non-heart failure cardiovascular events			45	0.25			33	0.14	0.0106
LVEF 26–34%									
All cardiovascular events	164	164	157	0.96	164	255	99	0.39	<0.0001
Heart failure events			102	0.62			59	0.23	<0.0001
Non-heart failure cardiovascular events			55	0.34			40	0.16	0.0002
LVEF ≥35%									
All cardiovascular events	161	161	139	0.86	161	242	65	0.27	<0.0001
Heart failure events			87	0.54			30	0.12	<0.0001
Non-heart failure cardiovascular events			52	0.32			35	0.14	0.0002
Normal sinus rhythm									
All cardiovascular events	349	349	342	0.98	349	530	200	0.38	<0.0001
Heart failure events			229	0.66			130	0.25	<0.0001
Non-heart failure cardiovascular events			113	0.32			70	0.13	<0.0001
Atrial fibrillation									
All cardiovascular events	154	154	181	1.18	154	198	87	0.44	<0.0001
Heart failure events			142	0.92			49	0.25	<0.0001
Non-heart failure cardiovascular events			39	0.25			38	0.19	0.2189
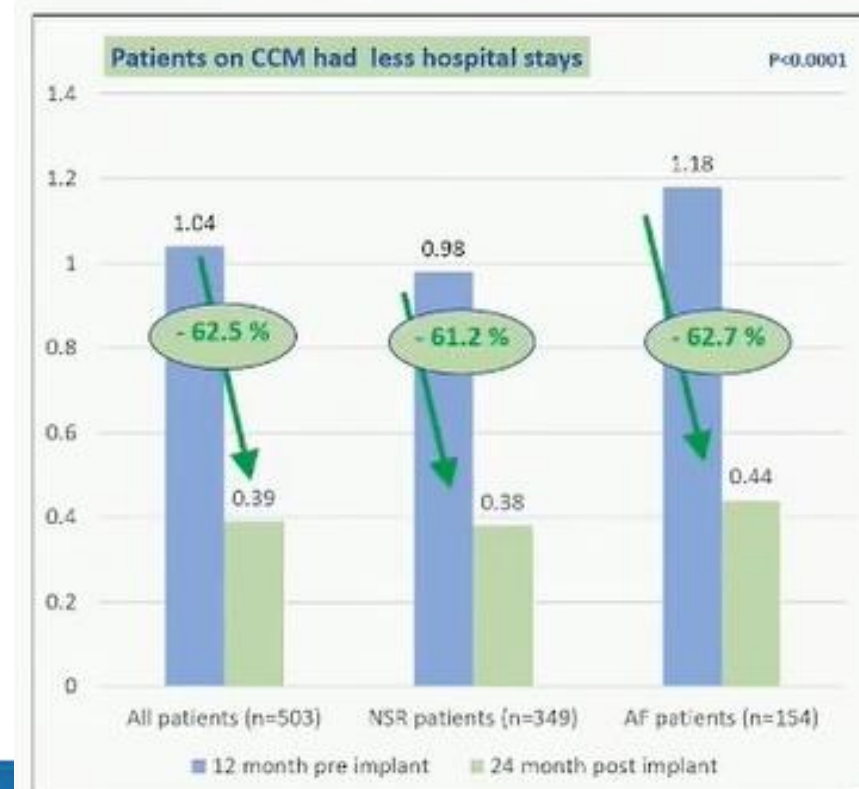
LVEF, left ventricular ejection fraction.

Reduces *hospitalization*

Patients on CCM had less hospital stays — P<0.0001

- All patients (n=503): 1.04 → 0.39, −62.5%
- NSR patients (n=349): 0.98 → 0.38, −61.2%
- AF patients (n=154): 1.18 → 0.44, −62.7%

■ 12 month pre implant ■ 24 month post implant

Long-term clinical experience with cardiac contractility modulation therapy delivered by the Optimizer Smart system

Jürgen Kuschyk[1], Peter Falk[2], Thomas Demming[2], Oliver Marx[3], Deborah Morley[4], Ishu Rao[4], and Daniel Burkhoff[5]*
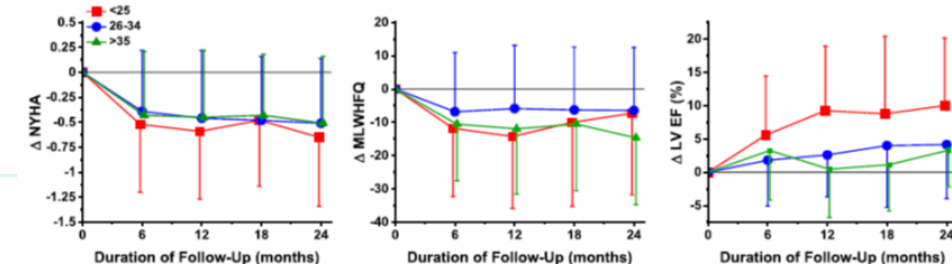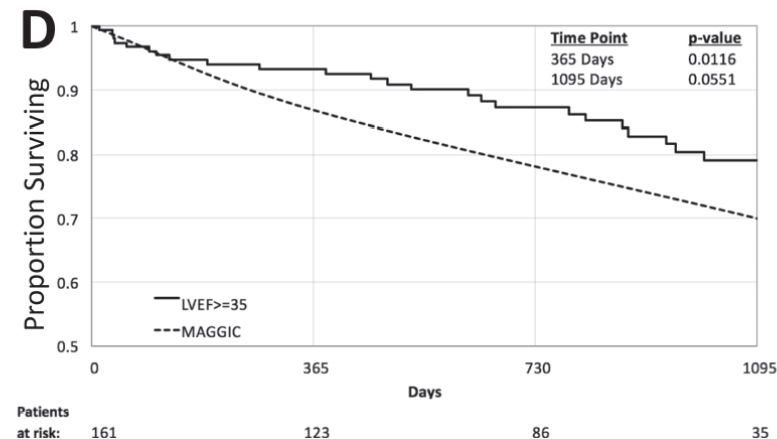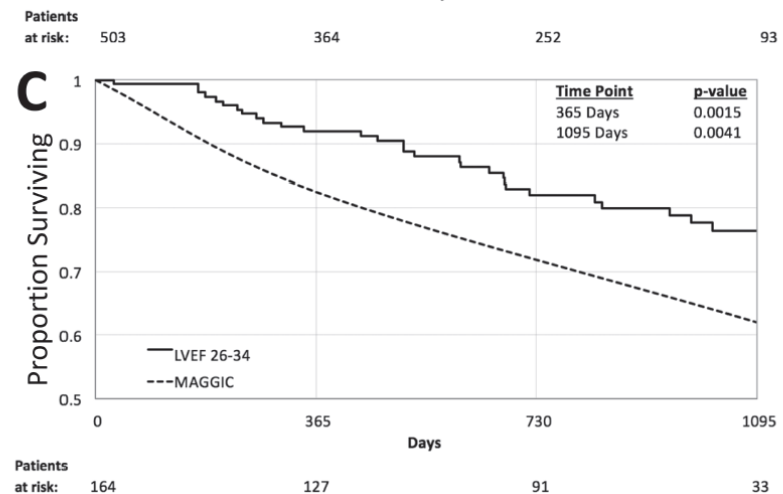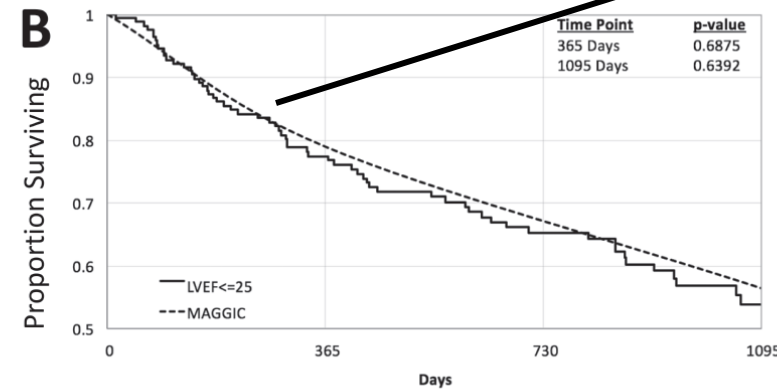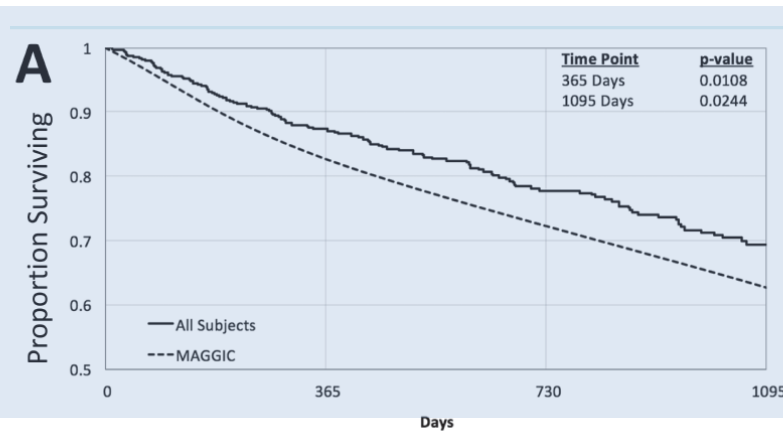
Ad un FUP massimo di 3 anni, la sopravvivenza osservata nella coorte generale dei pazienti con CCM è migliore di quella stimata con MAGICC score (Panel A), ma il dato è guidato dalle classi di FE>25% (Panel C e D).
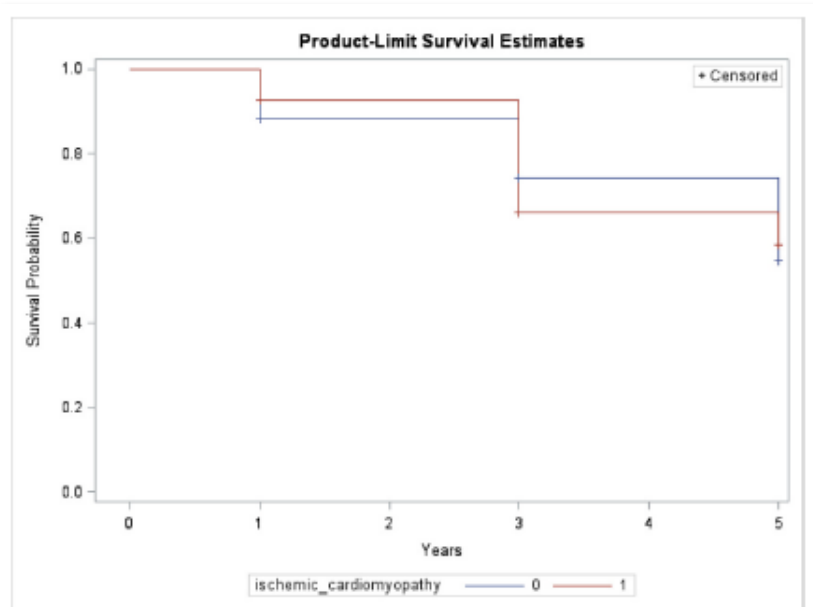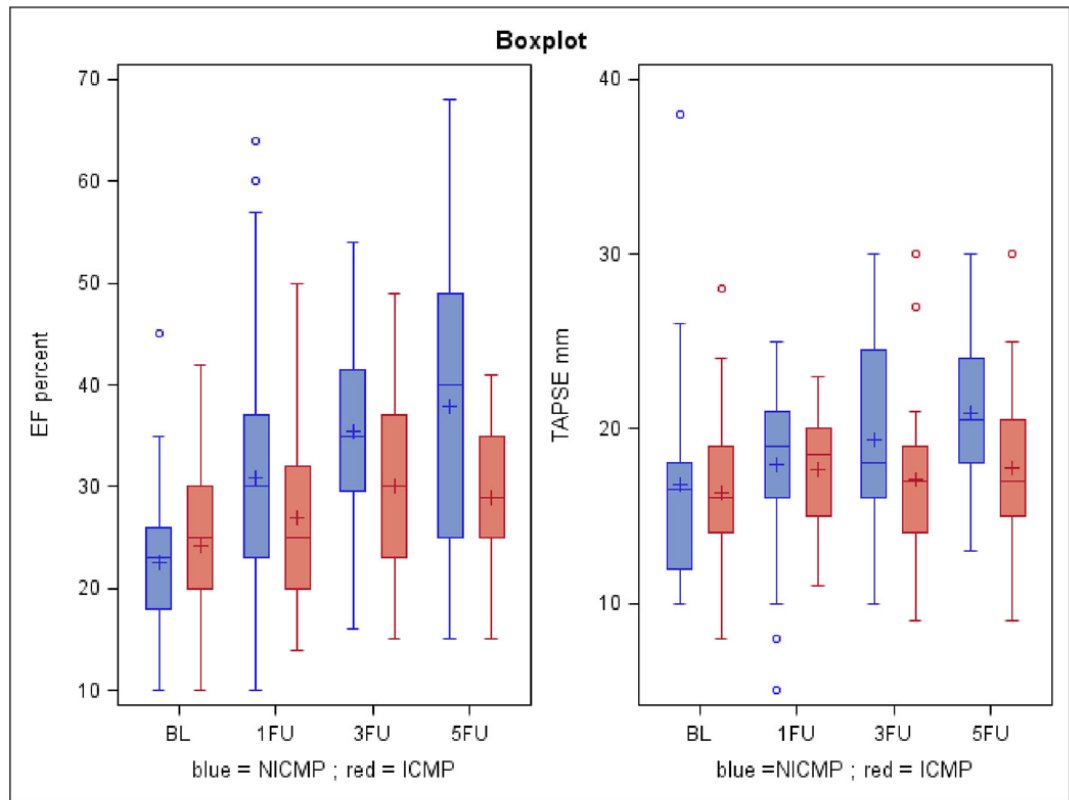
Ischemic *vs.* Non-Ischemic HF

Fig. 3. Survival over the 5-year follow-up.
Red line = patients with ischemic cardiomyopathy; blue line = patients with non-ischemic cardiomyopathy; p = 0.81.

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- Nessuna differenza significativa in termini di sopravvivenza a 5 anni,
- I **non-ischemici** mostrano un miglioramento della funzione sistolica significativamente maggiore

Septal myocardial scar burden predicts the response to cardiac contractility modulation in patients with heart failure

Uzair Ansari[1,3,4✉], Daniel Overhoff[2,5], Daniel Burkhoff[6], Christian Fastner[1,3,4], Gökhan Yücel[1,3,4], Susanne Röger[1,3,4], Boris Rudic[1,3,4], Volker Liebe[1,3,4], Martin Borggrefe[1,3,4], Ibrahim Akin[1,3,4], Jürgen Kuschyk[1,3,4], Theano Papavassiliu[1,3,4] & Erol Tülümen[1,3,4,7]

Variable	LVEF change	Responder (n = 26)	Non-responder (n = 32)	p-value*
LVEF change [%]		9.2 ± 6.3	0.4 ± 1.2	**< 0.01**
TAPSE change [mm]		2.1 ± 2.4	0.2 ± 1.4	**< 0.01**
MLWHF change		− 11.3 ± 16.5	− 19.5 ± 18.6	0.20
NT-pro BNP (pg/mL) change		− 1995 ± 2921	68.4 ± 4170	0.06
NYHA change, n (%)	− 2	6 (23.1%)	3 (9.4%)	**0.04**
	− 1	16 (61.5%)	14 (43.8%)	
	0	4 (15.4%)	13 (40.6%)	
	+ 1	–	2 (6.3%)	
Lead stimulation, n (%)	Single	8 (30.8%)	10 (31.3%)	0.96
	Dual	18 (69.2%)	22 (68.8%)	
LGE of at least 25% at lead position (both single and dual)	LGE > 25% (Group A)	4 (15.4%)	8 (25.8%)	0.33
	LGE < 25% (Group B)	22 (84.6%)	23 (74.2%)	

Table 3. Responder vs. non-responder based on LVEF change. *LGE* late gadolinium enhancement, *NYHA* New York Heart Association, *FU* follow-up. Values in bold are statistically significant. *Pearson Chi-square test.

Check for updates

Bridging the gap in the symptomatic heart failure patient journey: insights from the Italian scenario

Matteo Ziacchi[a], Alberto Spadotto [a], Stefano Ghio[b], Marta Pellegrino[c], Luciano Potena[a], Daniele Masarone[d], Marco Merlo[e], Davide Stolfo[e], Maria Michela Caracciolo[f], Corinna Inserra[g], Fabrizio Ammirati[h], Michele Ciccarelli[i], Furio Colivicchi[j], Stefano Bianchi[k], Giuseppe Patti[l], Fabrizio Oliva[m], Giuseppe Arcidiacono[n], Roberto Rordorf[b], Daniela Pini[c], Giuseppe Pacileo[d], Antonio D'Onofrio[d], Giovanni Battista Forleo[f], Matteo Mariani[g], Francesco Adamo[h], Alessandro Alonzo[j], Matteo Ruzzolini[k], Chiara Ghiglieno[l], Manlio Cipriani[m], Giorgio Firetto[n], Nadia Aspromonte[o,p], Francesco Clemenza[p], Gaetano Maria De Ferrari[q], Michele Senni[r], Maria Grazia Bongiorni[s], Claudio Tondo[t], Massimo Grimaldi[u], Francesco Giallauria[v], Francesco Rametta[w], Procolo Marchese[x], Mauro Biffi[a] and Gianfranco Sinagra[e]
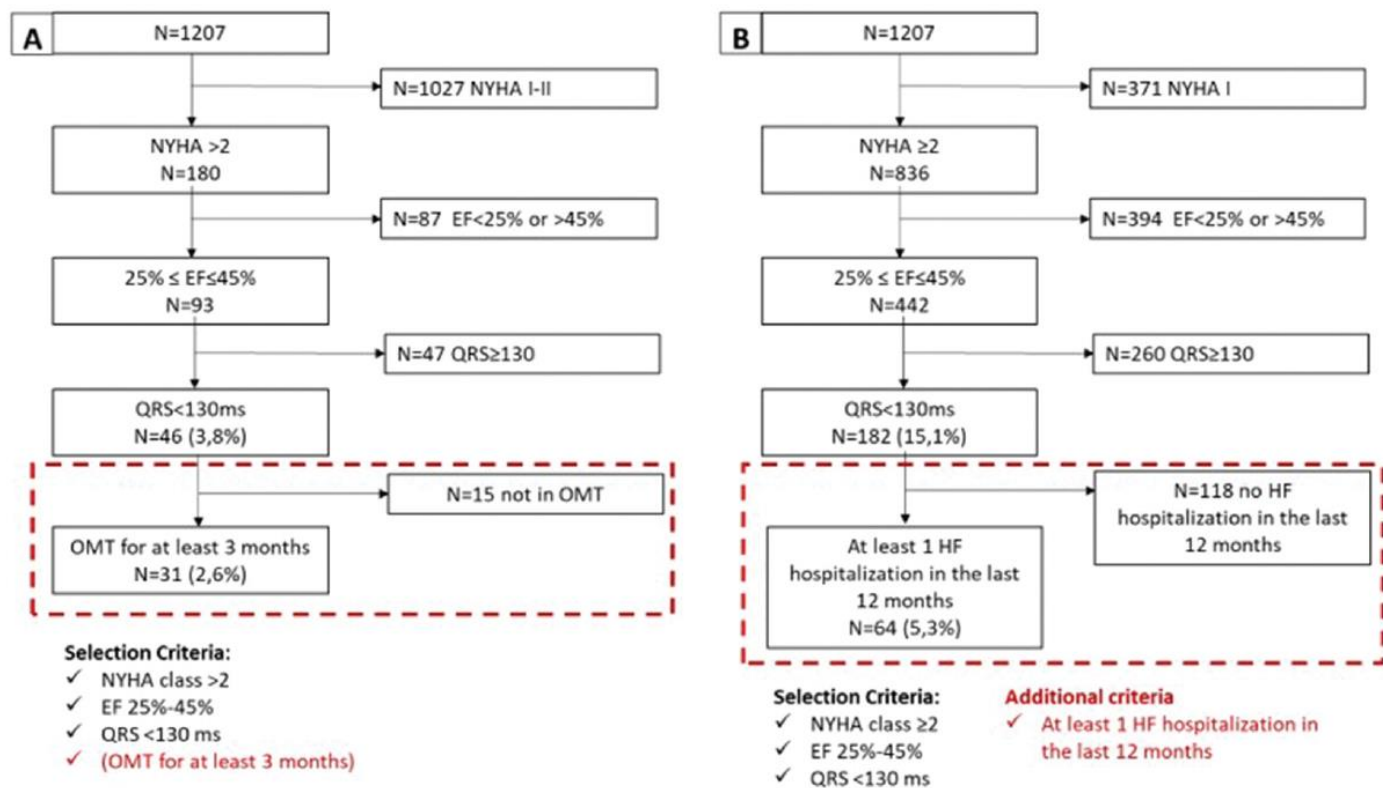
Figure 4. Patients eligible to CCM implant according to different selection criteria. A: patients selection according to FDA selection criteria. B: patients selection according to CCM Italian registry criteria (NYHA>3 or NYHA 2 + HF hospitalization in the last year).

Cardiac contractility modulation in patients with heart failure: The added value of cardiac rehabilitation in identification, management, and follow-up

Matteo Ruzzolini [a,*,1], Francesco Giallauria [b,1], Francesco Fattirolli [c], Elio Venturini [d], Francesco Maranta [e], Gian Francesco Mureddu [f], Pasqualina Calisi [g], Raffaele Griffo [h], Carlo Vigorito [b], Pompilio Faggiano [i], Marco Ambrosetti [j], Daniele Masarone [k]
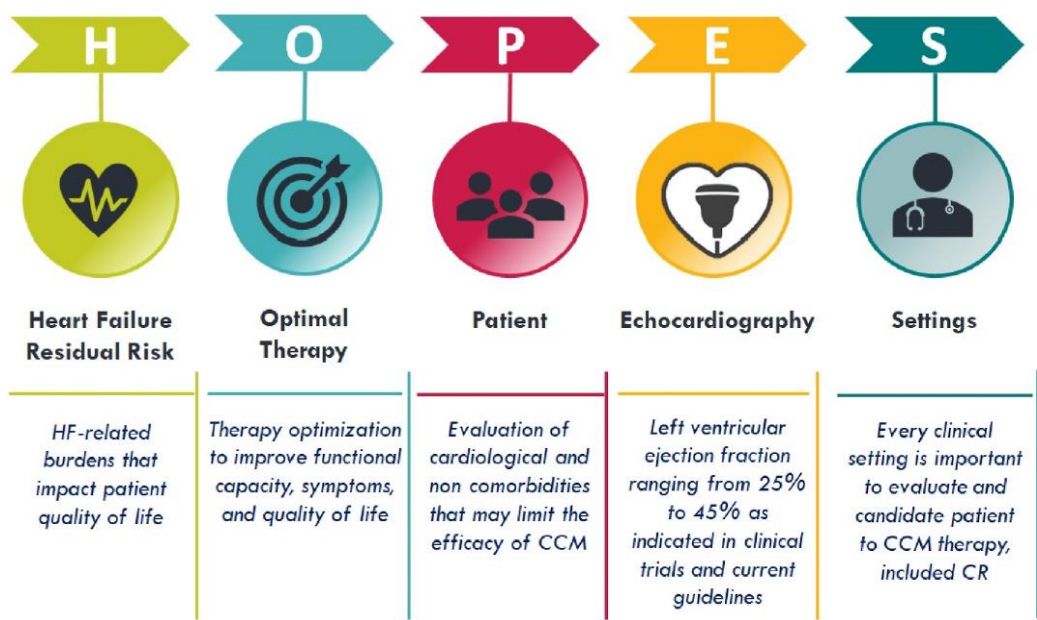
Fig. 2. HOPES algorithm to simplify CCM patient selection.

Fig. 3. CCM patient selection process summarized in 5 points.

Cardiac contractility modulation therapy improves health status in patients with heart failure with preserved ejection fraction: a pilot study (CCM-HFpEF)

Cecilia Linde[1]*, Marcin Grabowski[2], Piotr Ponikowski[3], Ishu Rao[4], Angela Stagg[5], and Carsten Tschöpe[6]
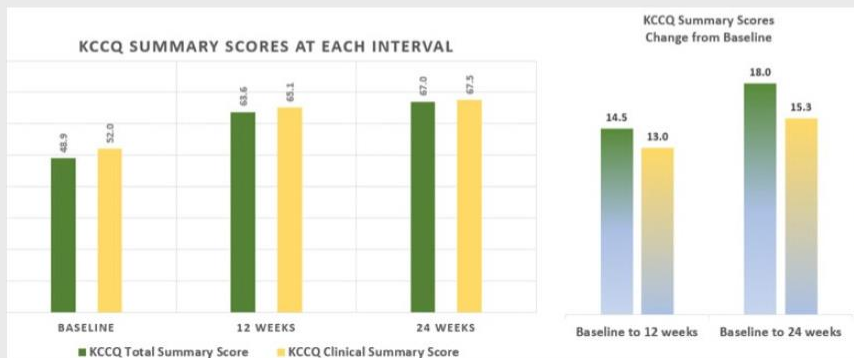
Criteri di inclusione:
- Classe NYHA II – III;
- OMT per HF stabile da 3 mesi;
- NT-proBNP:
- > 220 pg/ml in RS
- > 600 pg/ml in AF

Endpoint primario di efficacia: valutazione del cambio di KCCQ dal baseline a 24 settimane

End-point primario di sicurezza:

Tasso di libertà da eventi: 93,6%

EHJHF://doi.orhttpsg/10.1002/ejhf.2619

CCM-HFpEF Study

**Table 4** Secondary efficacy endpoints (with last observation carried forward)

Parameter	Baseline	24 weeks	Baseline–24 weeks	*p*-values for baseline–24 weeks t-test	Wilcoxon signed-rank test	Normality test
Echocardiography						
LAVi (ml/m^2)	48.2 ± 14.0 (47)	45.9 ± 14.4 (44)	−2.8 ± 8.2 (44) (−5.3 to −0.3)	0.014	0.034	0.046
Septal E/e′	15.3 ± 4.4 (47)	14.5 ± 5.2 (42)	−0.9 ± 4.7 (42) (−2.4 to 0.6)	0.111	0.038	0.022
Septal e′	5.7 ± 1.2 (47)	5.6 ± 1.6 (43)	−0.0 ± 1.5 (43) (−0.5 to 0.4)	0.417	0.336	0.008
NT-proBNP (pg/ml)[a]	702.0 (470–1005) (46) (230.0–6814)	730.0 (394–1140) (42) (152.0–4720)	23.0 (43) (−85.0 to −283.1) (−2399 to 1710)	NA	0.077	NA
NYHA class	2.6 ± 0.5 (47)	2.2 ± 0.6 (46)	−0.5 ± 0.6 (46) (−0.6 to −0.3)	<0.001	<0.001	<0.001

Values are given as mean ± standard deviation (N), and 95% confidence interval.

LAVi, left atrial volume index; NA, not available; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association.

[a]One was an outlier and removed from this analysis. For NT-proBNP we present median (interquartile range) and minimum – maximum values.

HF hospitalization

67% reduction

Percent of patients experiencing at least 1 HFH
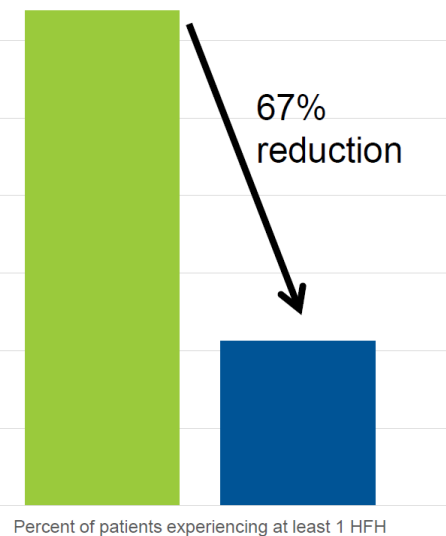
1y pre implant vs 1y post implant

CCM-D: Integra Trial – Preliminary data

STUDY DESIGN & PATIENT CHARACTERISTICS

300 Patients

Stage C/D heart failure patients with EF ≤ 40% and Class I/II ICD indication

On GDMT

No CRT / pacing indication

No PR interval >375ms /AV block

75 US sites

Primary Efficacy Objective

100 Subjects — Evaluate device effectiveness in converting VF at implant

Completed: n = 101 across 24 sites

62.5 years	28.7%	30.0%	106.8 ms	52.5%
Mean Age	% Female	Mean LVEF	Mean QRS	Ischemic

Additional analysis: NYHA functional class change at 6-month in patients with paired data

In progress

Safety objective evaluation in an additional 200 patients

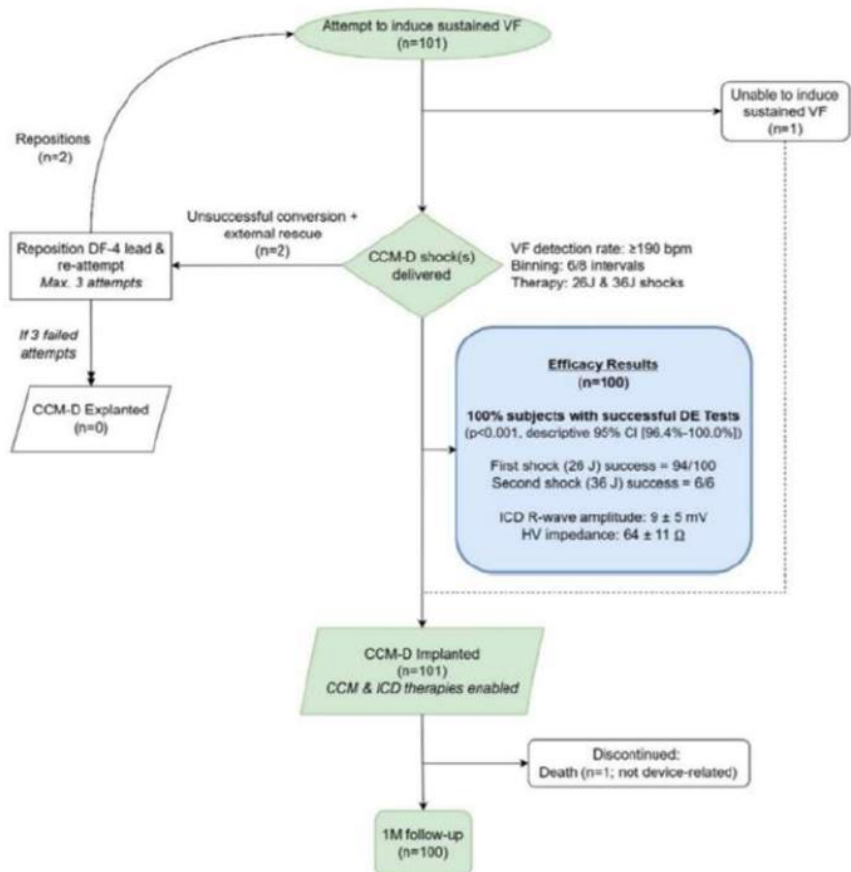Evaluate device-related complications and appropriateness of arrhythmia treatment through 6-month follow-up

CCM-D: Integra Trial – Preliminary data

100%
Patients **Successfully defibrillated** with CCM-D (p<0.001, descriptive 95% CI [96.4%-100.0%])

No inappropriate CCM/ICD interaction occurred using novel hybridized circuits

55% of Class III/IV patients (N=44) improved - nearly identical to the **57%** improvement seen with CRT-D treatment arm in COMPANION*

Proportion of NYHA III/IV Patients with NYHA Improvement from Baseline at 6-Months

55% "Integra-D(CCM-D)"

57% "COMPANION(CRT-D arm)"

*Bristol et al. Cardiac-Resynchronization Therapy with or without an Implantable Defibrillator in Advanced Chronic Heart Failure. N Engl J Med 2004,350:2140-50

Preliminary 6-month data shows that **HF symptoms improved or remained stable in majority (88%) of patients**

GRAZIE!!!