

Insufficienza Cardiaca: Hot News

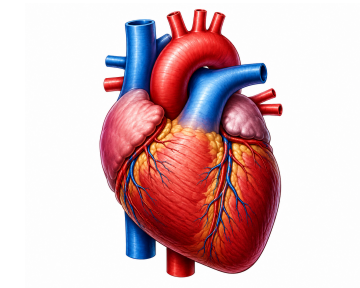
Heart failure next: farmaci, device e dati per una cura personalizzata

**Salerno Elia Nunzio Maria
Aspromonte Nadia**



Heart Failure next

- Farmaci
- Device
- Dati



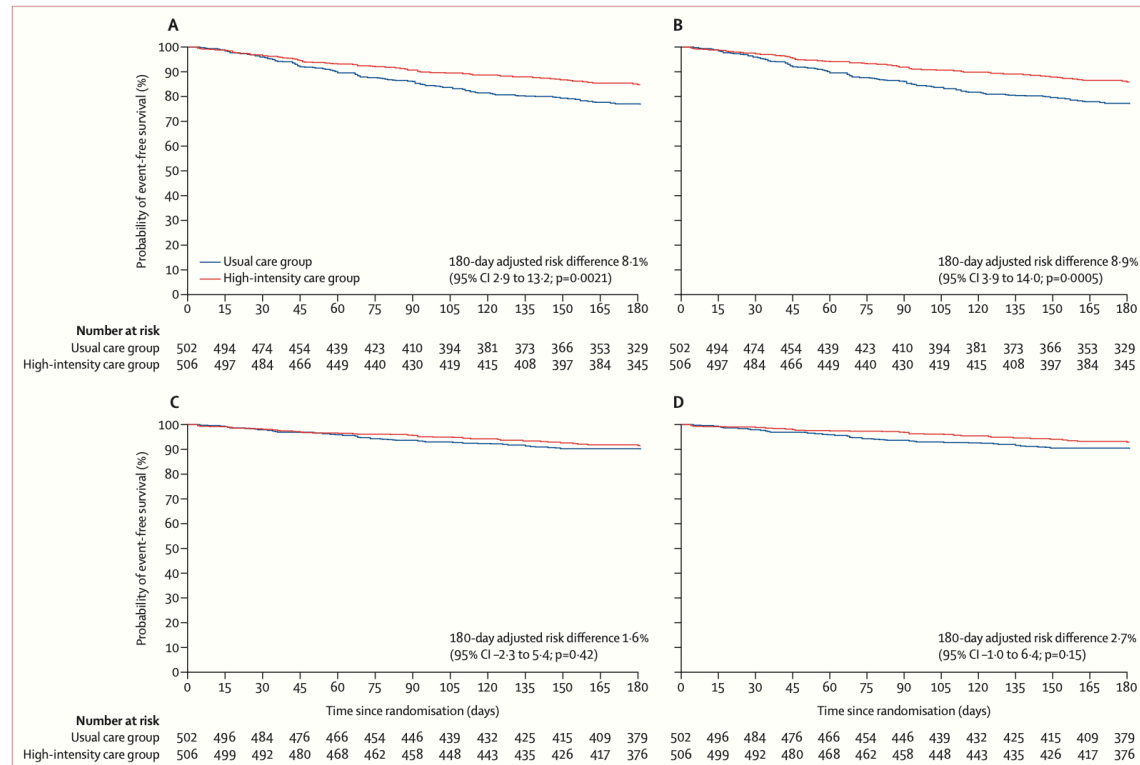


Safety, tolerability, and efficacy of up-titration of guideline-directed medical therapies for acute heart failure (STRONG-HF): a multinational, open-label, randomised, trial

Alexandre Mebazaa, Beth Davison, Ovidiu Chioncel, Alain Cohen-Solal, Rafael Diaz, Gerasimos Filippatos, Marco Metra, Piotr Ponikowski, Karen Shwa, Adriaan A Voors, Christopher Edwards, Maria Novosadova, Koji Takagi, Albertino Damasceno, Hadiza Saidu, Etienne Gayat, Peter S Pang, Jelena Celutkienė, Gad Cotter

	High-intensity care group (n=542)	Usual care group (n=536)	Adjusted treatment effect (95% CI)	Adjusted risk ratio (95% CI)	p value
Primary endpoint					
All-cause death or heart failure readmission by day 180*	74/506 (15.2%)	109/502 (23.3%)	8.1 (2.9 to 13.2)	0.66 (0.50 to 0.86)	0.0021
Secondary endpoints					
Change from baseline to day 90 in EQ-5D VAS†	10.72 (0.88)	7.22 (0.90)	3.49 (1.74 to 5.24)	NA	<0.0001
All-cause death by day 180*	39/506 (8.5%)	48/502 (10.0%)	1.6 (-2.3 to 5.4)	0.84 (0.56 to 1.26)	0.42
All-cause death or heart failure readmission by day 90*	55 (10.4%)	72 (13.8%)	3.4 (-0.4 to 7.3)	0.73 (0.53 to 1.02)	0.081
Prespecified exploratory endpoints					
Cardiovascular death by day 180*	32/506 (6.9%)	44/502 (9.3%)	2.4 (-1.2 to 6.1)	0.74 (0.47 to 1.16)	0.19
Cardiovascular death by day 90*	17 (3.3%)	28 (5.4%)	2.1 (-0.3 to 4.6)	0.60 (0.33 to 1.09)	0.086
All-cause death by day 90*	23 (4.3%)	30 (5.7%)	1.4 (-1.2 to 4.0)	0.76 (0.45 to 1.29)	0.28
Heart failure readmission by day 180*	47/506 (9.5%)	74/502 (17.1%)	7.6 (3.0 to 12.1)	0.56 (0.38 to 0.81)	0.0011
Heart failure readmission by day 90*	36 (6.9%)	48 (9.5%)	2.5 (-0.8 to 5.8)	0.67 (0.43 to 1.04)	0.13
Finkelstein-Schoenfeld hierarchical composite‡	..	..	1.28 (1.13 to 1.46)	NA	0.0002
Proportion of comparisons where group is superior§	40.4%	29.4%	..	..	..
Proportion of comparisons where groups are tied	30.2%	NA	..	..	..
Sensitivity analyses					
All-cause death or heart failure readmission by day 180, excluding COVID-19 deaths*	69/506 (14.1%)	108/502 (23.0%)	8.9 (3.9 to 14.0)	0.61 (0.46 to 0.82)	0.0005
All-cause death by day 180, excluding COVID-19 deaths*	33/506 (7.1%)	47/502 (9.8%)	2.7 (-1.0 to 6.4)	0.72 (0.47 to 1.12)	0.15

Data are n (adjusted Kaplan-Meier %), n/N (down-weighted adjusted Kaplan-Meier %), or mean (SD), unless otherwise stated. For 180-day outcomes, results for patients in cohort 1 are down-weighted.



BRIEF REPORT

Residual Risk Despite Quadruple Medical Therapy for Men vs Women Hospitalized for Heart Failure With Reduced Ejection Fraction

Stephen J. Greene, MD,^{a,b} Haolin Xu, MS,^a Karen Chiswell, PhD,^a G. Michael Felker, MD, MHS,^{a,b} Sabra C. Lewsey, MD, MPH,^c Punag H. Divanji, MD,^d Hans-Peter Goertz, MPH,^d Stephen B. Heitner, MD,^d Javed Butler, MD, MPH, MBA,^{e,f} Gregg C. Fonarow, MD^g

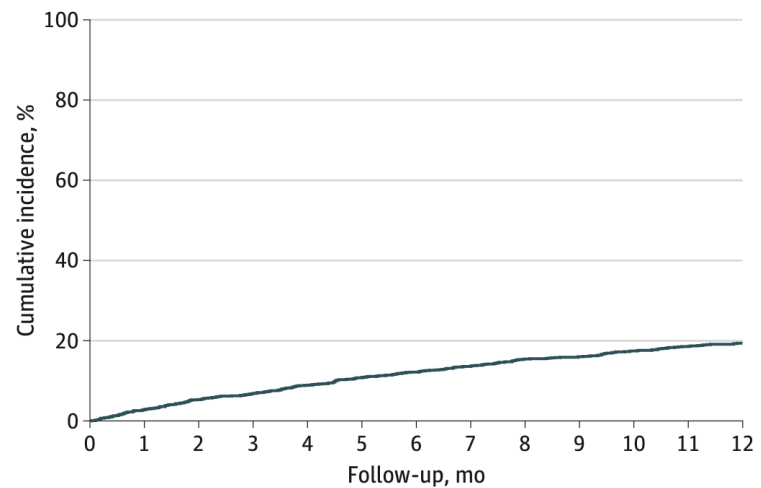
JAMA Cardiology | **Brief Report**

One-Year Outcomes in Patients Hospitalized for Heart Failure With Reduced Ejection Fraction Prescribed Quadruple Medical Therapy at Discharge

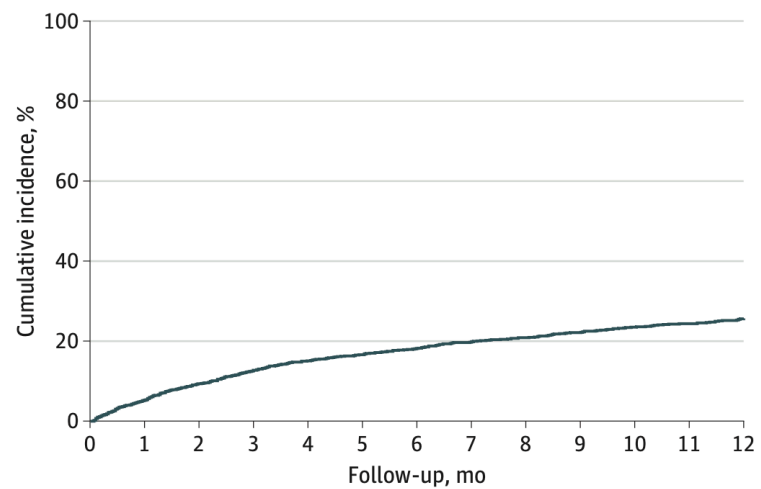
Stephen J. Greene, MD; Haolin Xu, MS; Karen Chiswell, PhD; G. Michael Felker, MD, MHS; Sabra C. Lewsey, MD, MPH; Punag H. Divanji, MD; Hans-Peter Goertz, MPH; Stephen B. Heitner, MD; Sanatan Shreay, PhD; Ambarish Pandey, MD, MPH; Clyde W. Yancy, MD, MSc; Javed Butler, MD, MPH, MBA; Gregg C. Fonarow, MD



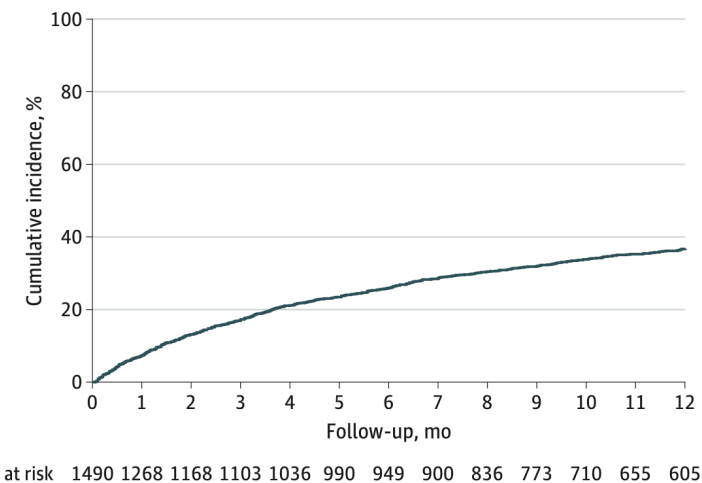
A All-cause mortality



B HF hospitalization

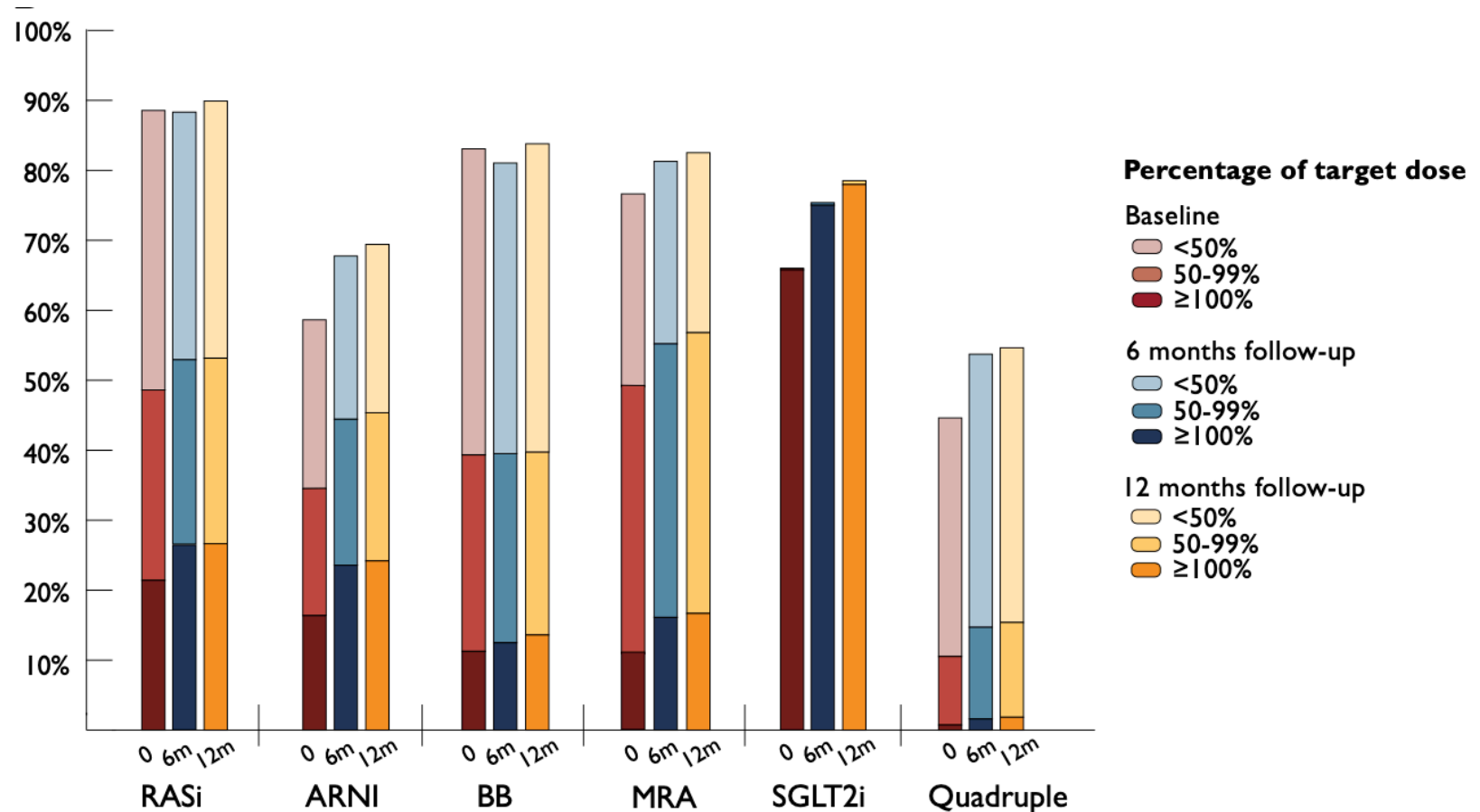


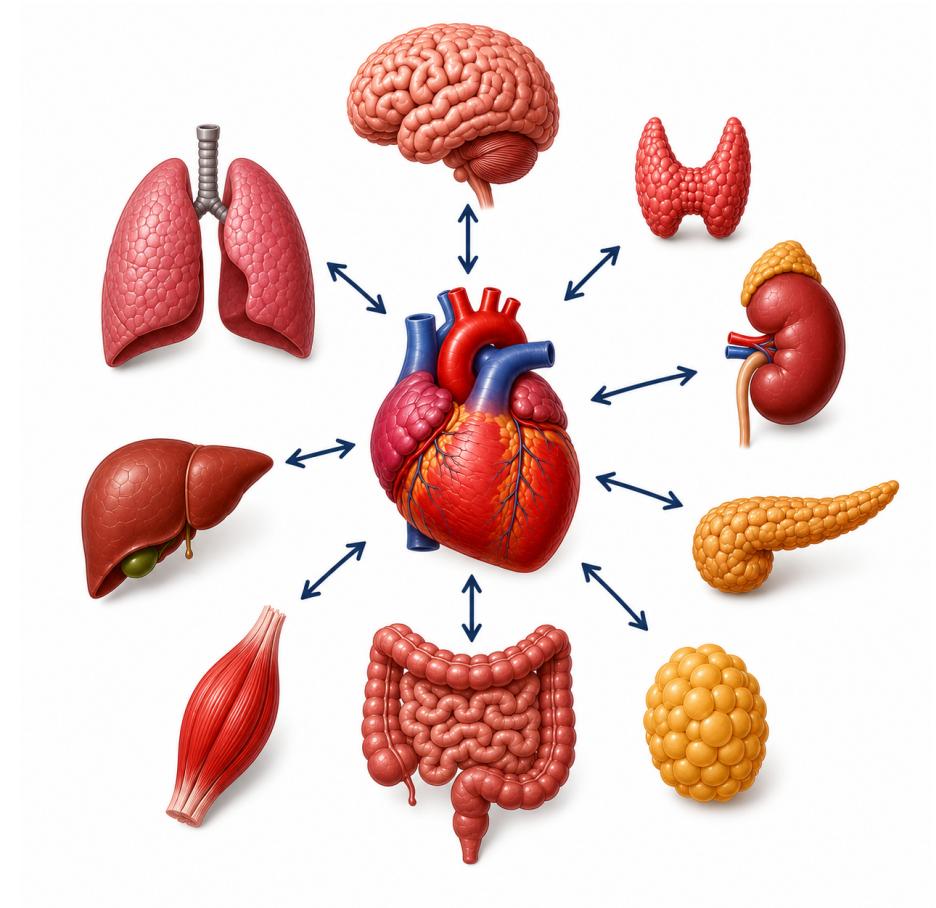
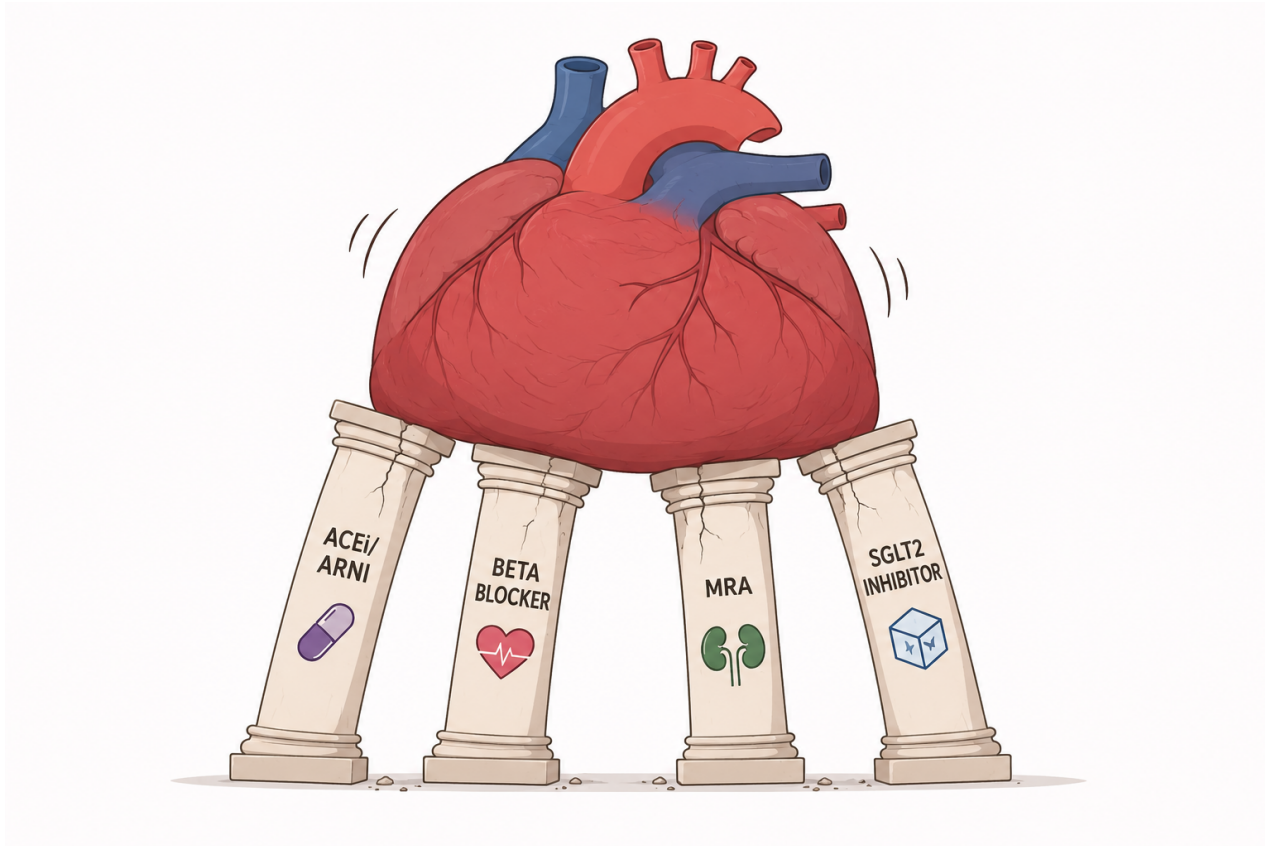
C All-cause mortality or HF hospitalization



Real-life implementation of guideline-recommended medication in heart failure with reduced ejection fraction. Effects on prognosis and left ventricular remodeling. The TITRATE-HF study

Jishnu Malgie^{1†}, Mariëlle I. Wilde^{1†}, Stefan Koudstaal¹, Carlos A. da Fonseca⁴, Henk P. Swart⁵, Clara E.E. van der Wal⁶, Ron Pisters⁸, Gerard C.M. Linssen⁹, Nikola Faber¹⁰, Julio E.C. van de Swaluw¹², Rudolf A. de Boer¹, H. J. B. van der Wal¹ and Jasper J. Bruggema^{1*}



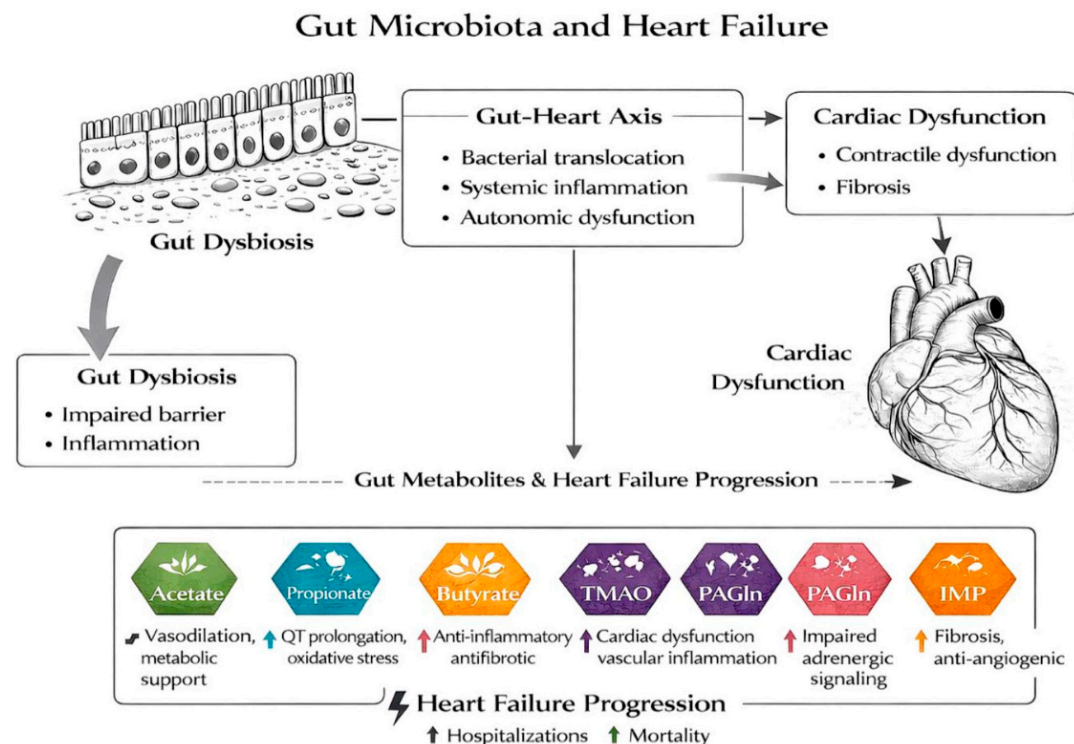


Review

The Heart–Gut Axis in Heart Failure: The Role of Next-Generation Pharmacological Therapies

Elia Nunzio Maria Salerno ^{1,2}, Isabella Fumarulo ^{1,2}, Claudia Mendicino ^{1,2}, Marcello Vaccare
Barbara Garramone ^{1,2}, Francesco Gallo ^{1,2}, Gerardo Volzone ^{1,2}, Andrea Cammuso ^{1,2}, Vincenz
Franco Scaldaferri ^{3,4}, Loris Riccardo Lopetuso ^{5,6}, Antonio Gasbarrini ^{5,7,8}, Francesco Burzotta
and Nadia Aspromonte ^{1,2,6,*}

**ONE SIZE
DOES NOT FIT ALL**



The NEW ENGLAND JOURNAL of MEDICINE

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MAY 14, 2020

VOL. 382 NO. 20

Vericiguat in Patients with Heart Failure and Reduced Ejection Fraction

Paul W. Armstrong, M.D., Burkert Pieske, M.D., Kevin J. Anstrom, Ph.D., Justin Ezekowitz, M.B., B.Ch., Adrian F. Hernandez, M.D., M.H.S., Javed Butler, M.D., M.P.H., M.B.A., Carolyn S.P. Lam, M.B., B.S., Ph.D., Piotr Ponikowski, M.D., Adriaan A. Voors, M.D., Ph.D., Gang Jia, Ph.D., Steven E. McNulty, M.S., Mahesh J. Patel, M.D., Lothar Roessig, M.D., Joerg Koglin, M.D., Ph.D., and Christopher M. O'Connor, M.D., for the VICTORIA Study Group*

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VOL. 85, NO. 2, 2025

ORIGINAL RESEARCH

Finerenone in Patients With a Recent Worsening Heart Failure Event



The FINEARTS-HF Trial

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SEPTEMBER 21, 2023

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Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity

M.N. Kosiborod, S.Z. Abildstrøm, B.A. Borlaug, J. Butler, S. Rasmussen, M. Davies, G.K. Hovingh, D.W. Kitzman, M.L. Lindegaard, D.V. Møller, S.J. Shah, M.B. Treppendahl, S. Verma, W. Abhayaratna, F.Z. Ahmed, V. Chopra, J. Ezekowitz, M. Fu, H. Ito, M. Lelonek, V. Melenovsky, B. Merkely, J. Núñez, E. Perna, M. Schou, M. Senni, K. Sharma, P. Van der Meer, D. von Lewinski, D. Wolf, and M.C. Petrie, for the STEP-HFpEF Trial Committees and Investigators*

ORIGINAL ARTICLE



Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity

Authors: Milton Packer, M.D., , Michael R. Zile, M.D., Christopher M. Kramer, M.D., Seth J. Baum, M.D., Sheldon E. Litwin, M.D., Venu Menon, M.D., Junbo Ge, M.D., , for the SUMMIT Trial Study Group* [Author Info & Affiliations](#)

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ORIGINAL ARTICLE



Digitoxin in Patients with Heart Failure and Reduced Ejection Fraction

Authors: Udo Bavendiek, M.D., Anika Großhennig, M.S., Johannes Schwab, M.D., Dominik Berliner, M.D., Andreas Rieth, M.D., Lars S. Maier, M.D., Thomas Gaspar, M.D., **+28**, for the DIGIT-HF Study Group* [Author Info & Affiliations](#)

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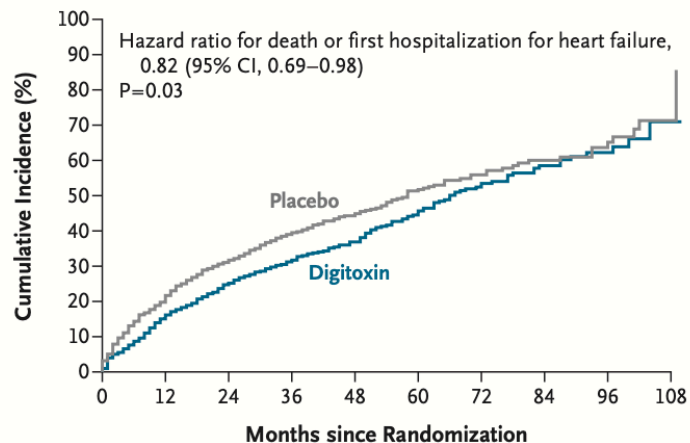
- HFrEF sintomatico
- NYHA II-IV
- FE $\leq 40\%$
- In terapia ottimale contemporanea
- 1240 pazienti
- Follow-up mediano circa 36 mesi

Endpoint primario: composito di morte per tutte le cause o primo ricovero per riacutizzazione di HF

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Digitoxin (N = 613)	Placebo (N = 599)
Age — yr	66.0 $\pm$ 11.1	65.8 $\pm$ 11.4
Female sex — no. (%)	122 (19.9)	125 (20.9)
Region — no. (%)		
Germany	545 (88.9)	533 (89.0)
Austria	19 (3.1)	14 (2.3)
Serbia	49 (8.0)	52 (8.7)
NYHA functional class — no. (%) [†]		
II	181 (29.5)	178 (29.7)
III	408 (66.6)	399 (66.6)
IV	24 (3.9)	22 (3.7)
Left ventricular ejection fraction — %	28.4 $\pm$ 6.9	28.9 $\pm$ 6.7
Left ventricular ejection fraction <30% — no. (%)	315 (51.4)	278 (46.4)
Main cause of heart failure — no./total no. (%)		
Ischemic	323/608 (53.1)	310/592 (52.4)
Nonischemic or unknown	285/608 (46.9)	282/592 (47.6)
Body-mass index [‡]	29.3 $\pm$ 5.7	28.9 $\pm$ 5.6
Heart rate — beats/min	73.7 $\pm$ 11.9	74.1 $\pm$ 12.3
Systolic blood pressure — mm Hg	120.5 $\pm$ 18.6	121.4 $\pm$ 18.8
Atrial fibrillation — no. (%)	169 (27.6)	161 (26.9)
eGFR		
Mean — ml/min/1.73 m ²	65.0 $\pm$ 23.0	65.2 $\pm$ 23.7
≤ 60 ml/min/1.73 m ² — no./total no. (%)	263/612 (43.0)	257/599 (42.9)
Device therapy — no./total no. (%)		
Implantable cardioverter–defibrillator therapy	415/613 (67.7)	364/598 (60.9)
Cardiac-resynchronization therapy	162/613 (26.4)	144/597 (24.1)
Heart failure medication — no. (%)		
Beta-blocker	593 (96.7)	567 (94.7)
Angiotensin-converting–enzyme inhibitor	222 (36.2)	213 (35.6)
Angiotensin-receptor blocker	113 (18.4)	115 (19.2)
Angiotensin receptor–neprilysin inhibitor	248 (40.5)	231 (38.6)
Mineralocorticoid receptor antagonist	466 (76.0)	458 (76.5)
Sodium–glucose cotransporter 2 inhibitor [§]	121 (19.7)	113 (18.9)
Cardiac glycoside	3 (0.5)	6 (1.0)

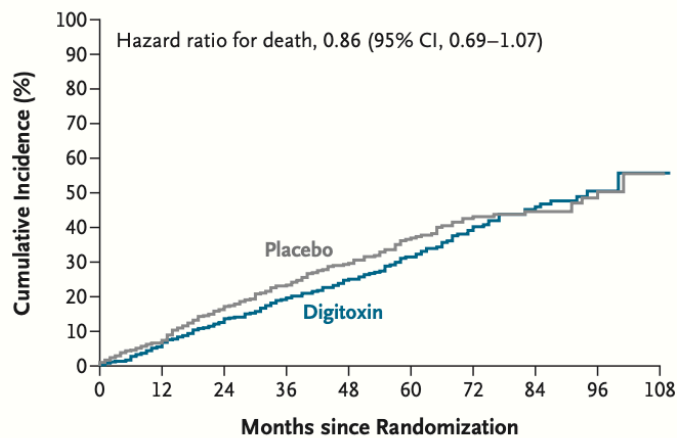
A Death from Any Cause or First Hospitalization for Heart Failure



No. at Risk

Placebo	599	421	309	234	184	126	78	47	24	4
Digitoxin	613	460	346	276	208	144	92	55	25	3

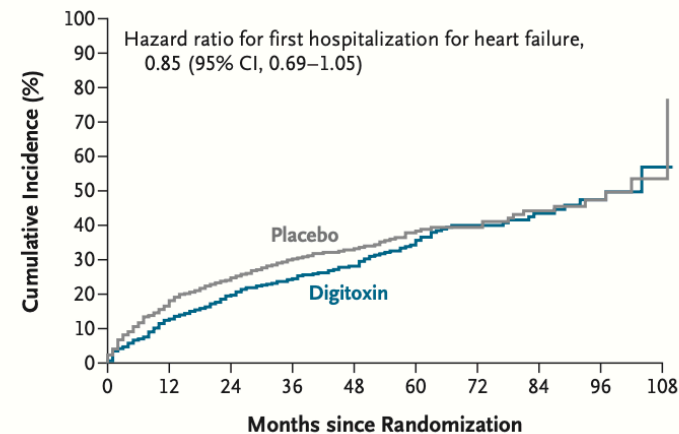
B Death from Any Cause



No. at Risk

Placebo	599	485	370	291	229	162	103	60	29	4
Digitoxin	613	507	398	317	239	172	113	70	28	4

C First Hospitalization for Heart Failure



No. at Risk

Placebo	599	421	309	234	184	126	78	47	24	4
Digitoxin	613	460	346	276	208	144	92	55	25	3



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Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure

J.R. Teerlink, R. Diaz, G.M. Felker, J.J.V. McMurray, M. Metra, S.D. Solomon, K.F. Adams, I. Anand, A. Arias-Mendoza, T. Biering-Sørensen, M. Böhm, D. Bonderman, J.G.F. Cleland, R. Corbalan, M.G. Crespo-Leiro, U. Dahlström, L.E. Echeverria, J.C. Fang, G. Filippatos, C. Fonseca, E. Goncalvesova, A.R. Goudev, J.G. Howlett, D.E. Lanfear, J. Li, M. Lund, P. Macdonald, V. Mareev, S. Momomura, E. O'Meara, A. Parkhomenko, P. Ponikowski, F.J.A. Ramires, P. Serpytis, K. Sliwa, J. Spinar, T.M. Suter, J. Tomcsanyi, H. Vandekerckhove, D. Vinereanu, A.A. Voors, M.B. Yilmaz, F. Zannad, L. Sharpsten, J.C. Legg, C. Varin, N. Honarpour, S.A. Abbasi, F.I. Malik, and C.E. Kurtz, for the GALACTIC-HF Investigators*

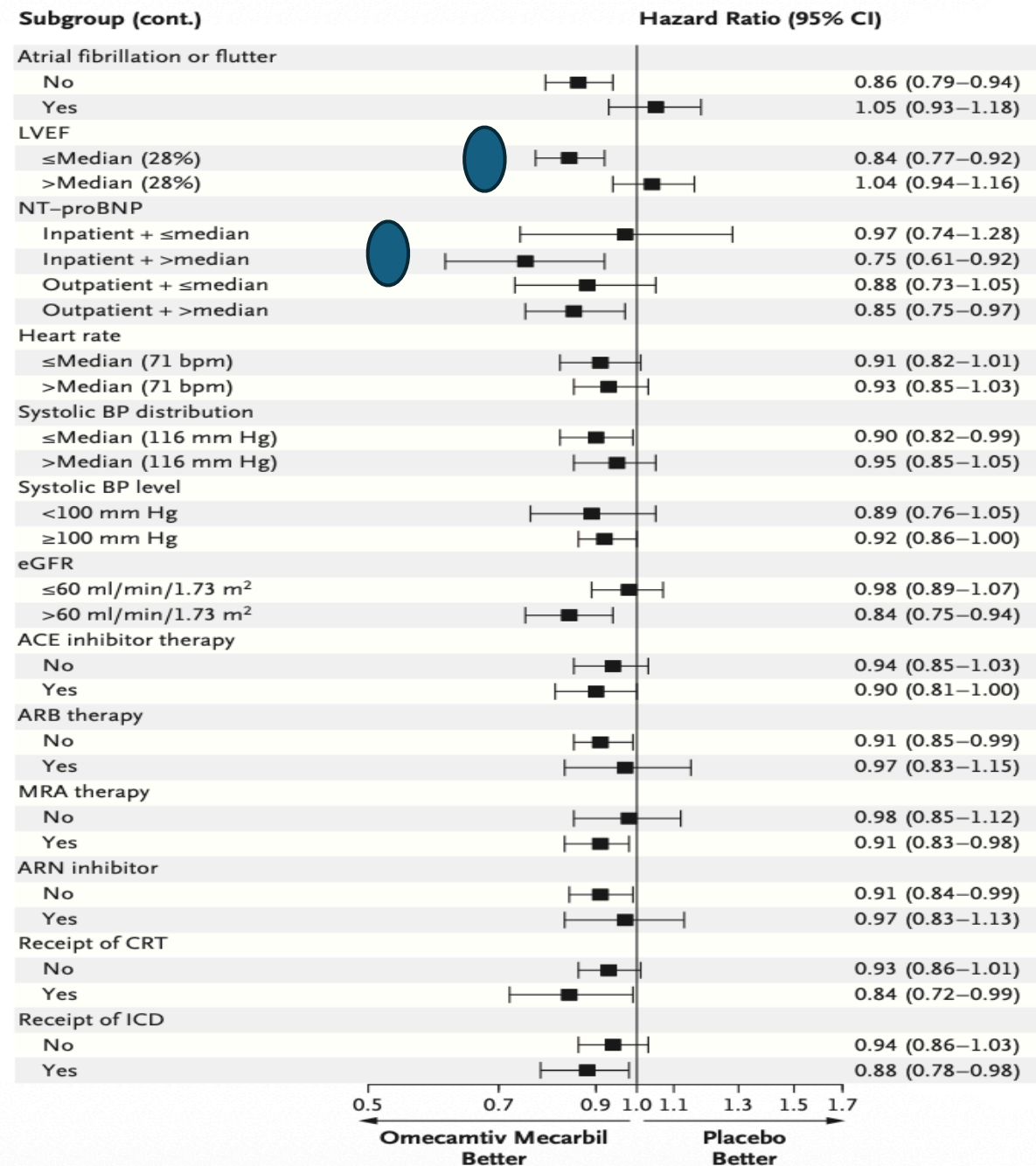
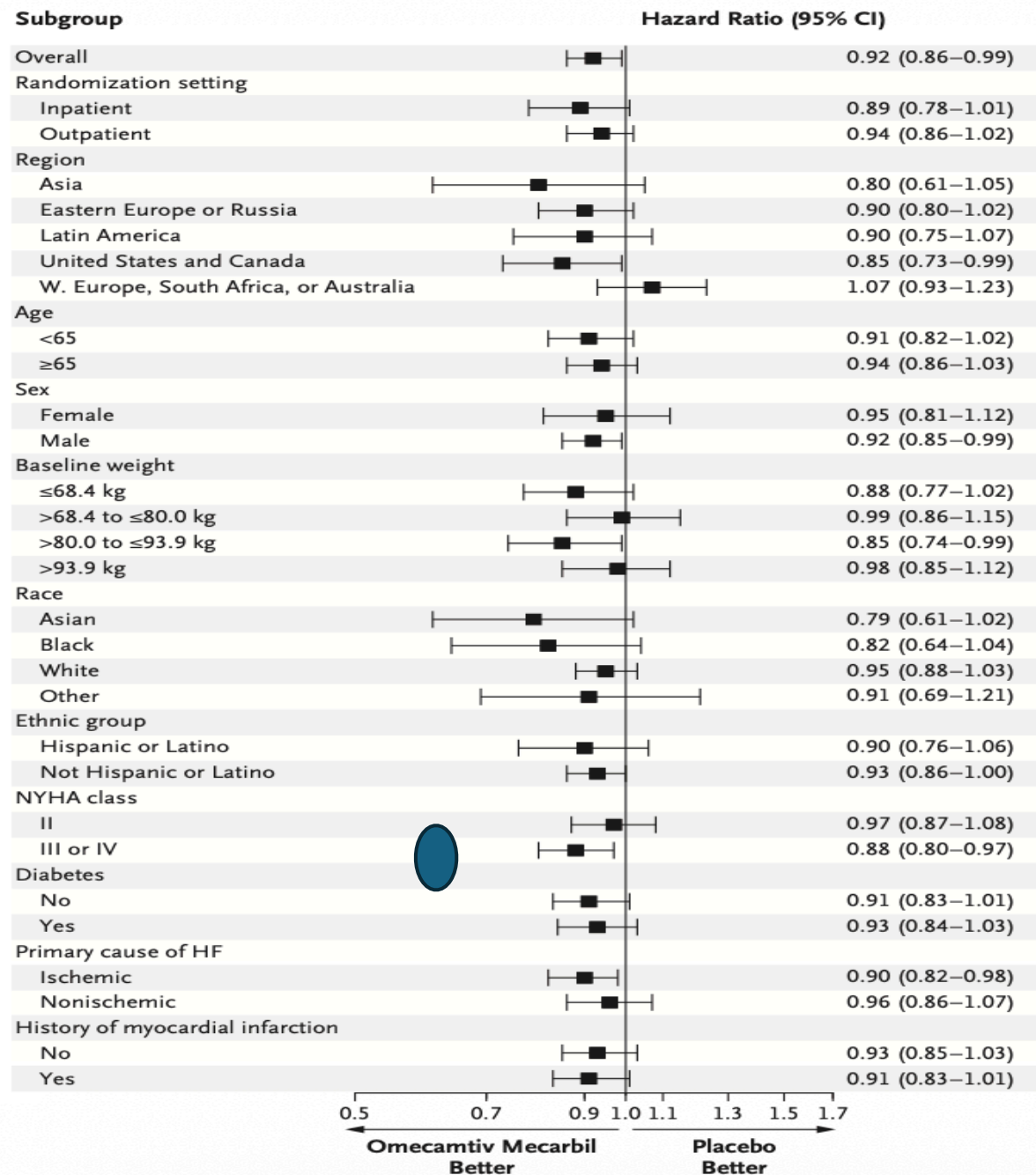


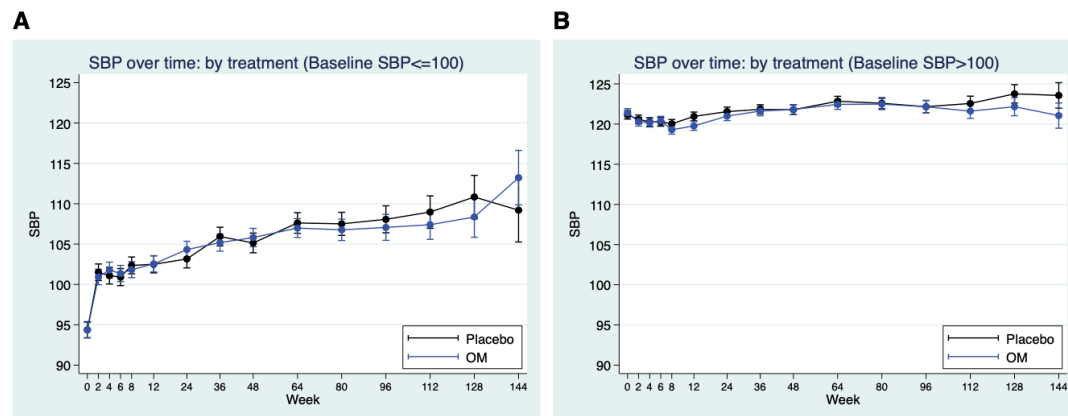
Table 2. Primary and Secondary Cardiovascular Outcomes.*

Variable	Omecamtiv Mecarbil (N = 4120)		Placebo (N = 4112)		Hazard Ratio or Difference (95% CI)†	P Value
	Value	Events	Value	Events		
		no./100 patient-yr		no./100 patient-yr		
Primary composite outcome — no. (%)‡	1523 (37.0)	24.2	1607 (39.1)	26.3	0.92 (0.86 to 0.99)	0.03
Cardiovascular death as first event	346 (8.4)		371 (9.0)			
Hospitalization for heart failure as first event	1107 (26.9)		1133 (27.6)			
Urgent outpatient visit for heart failure as first event	70 (1.7)		103 (2.5)			
Secondary outcomes						
Cardiovascular death — no. (%)	808 (19.6)	10.9	798 (19.4)	10.8	1.01 (0.92 to 1.11)	0.86§
Change in KCCQ total symptom score at wk 24						0.03§
Inpatients	23.7±0.7	NA	21.2±0.7	NA	2.5 (0.5 to 4.5)	
Outpatients	5.8±0.3	NA	6.3±0.3	NA	−0.5 (−1.4 to 0.5)	
First hospitalization for heart failure — no. (%)	1142 (27.7)	18.0	1179 (28.7)	19.1	0.95 (0.87 to 1.03)	NA
Death from any cause — no. (%)	1067 (25.9)	14.4	1065 (25.9)	14.4	1.00 (0.92 to 1.09)	NA
Exploratory outcome						
Heart-failure event — no. (%)	1177 (28.6)	18.7	1236 (30.1)	20.3	0.93 (0.86 to 1.00)	NA

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Omecamtiv Mecarbil (N = 4120)	Placebo (N = 4112)
Age — yr	64.5±11.3	64.5±11.4
Female sex — no. (%)	875 (21.2)	874 (21.3)
Race or ethnic group — no. (%)†		
White	3196 (77.6)	3201 (77.8)
Asian	355 (8.6)	355 (8.6)
Black	285 (6.9)	277 (6.7)
Other	284 (6.9)	279 (6.8)
Geographic region — no. (%)		
Eastern Europe or Russia	1344 (32.6)	1337 (32.5)
Western Europe, South Africa, or Australasia	961 (23.3)	960 (23.3)
Latin America	787 (19.1)	787 (19.1)
United States or Canada	693 (16.8)	693 (16.9)
Asia	335 (8.1)	335 (8.1)
Inpatient setting — no. (%)	1044 (25.3)	1040 (25.3)
Clinical features		
Atrial fibrillation or flutter — no. (%)	1146 (27.8)	1099 (26.7)
Type 2 diabetes mellitus — no. (%)	1652 (40.1)	1657 (40.3)
Ischemic heart failure — no. (%)	2193 (53.2)	2222 (54.0)
Left ventricular ejection fraction — %	26.6±6.3	26.5±6.3
NYHA classification — no. (%)		
II	2195 (53.3)	2173 (52.8)
III	1801 (43.7)	1815 (44.1)
IV	124 (3.0)	124 (3.0)
Median total symptom score on KCCQ (IQR)‡	68.8 (49.0–87.5)	68.8 (49.0–87.5)
Outpatient	74.0 (54.2–90.6)	75.0 (56.3–91.7)
Inpatient	54.2 (34.4–72.9)	52.1 (31.3–69.8)
Systolic blood pressure — mm Hg	116.3±15.4	116.6±15.3
Heart rate — beats/min	72.4±12.2	72.3±12.1
Median NT-proBNP (IQR) — pg/ml	1977 (980–4061)	2025 (1000–4105)
Median cardiac troponin I (IQR) — ng/liter	27 (12–52)	27 (13–52)
Median eGFR (IQR) — ml/min/1.73m ²	58.8 (44.3–74.3)	58.7 (43.8–73.7)
Heart-failure therapy — no. (%)		
ACE inhibitor, ARB, or ARN inhibitor	3583 (87.0)	3576 (87.0)
ARN inhibitor	819 (19.9)	782 (19.0)
Beta-blocker	3881 (94.2)	3883 (94.4)
Mineralocorticoid-receptor antagonist	3199 (77.6)	3198 (77.8)
SGLT2 inhibitor	104 (2.5)	114 (2.8)
Cardiac-resynchronization therapy	592 (14.4)	566 (13.8)
Implantable cardioverter-defibrillator	1326 (32.2)	1288 (31.3)



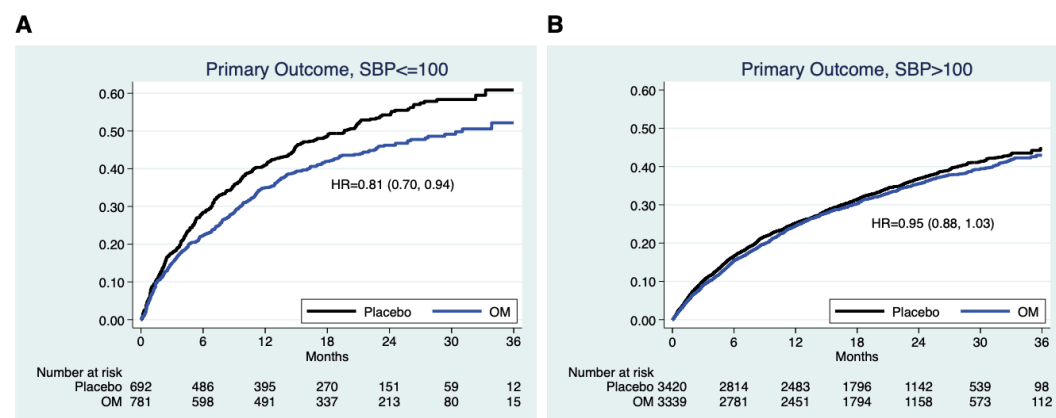


European Heart Journal (2022) 43, 5006–5016
<https://doi.org/10.1093/eurheartj/ehac293>

FASTTRACK CLINICAL RESEARCH
Heart failure and cardiomyopathies

Effects of omecamtiv mecarbil in heart failure with reduced ejection fraction according to blood pressure: the GALACTIC-HF trial

Marco Metra ^{1*}, Matteo Pagnesi ¹, Brian L. Claggett ², Rafael Díaz ³, G. Michael Felker ⁴, John J.V. McMurray ⁵, Scott D. Solomon ², Diana Bonderman ⁶, James C. Fang ⁷, Cândida Fonseca ⁸, Eva Goncalvesova ⁹, Jonathan G. Howlett ¹⁰, Jing Li ¹¹, Eileen O'Meara ¹², Zi Michael Miao ², Siddique A. Abbasi ¹³, Stephen B. Heitner ¹⁴, Stuart Kupfer ¹⁴, Fady I. Malik ¹⁴, and John R. Teerlink ¹⁵, on behalf of the GALACTIC-HF Investigators





Analisi ad interim: fine 2026-metà
2027

- 1800 pazienti
- FE <30%
- NT-proBNP ≥ 1000 pg/mL
- evento HF negli ultimi 6 mesi
- pazienti già in GDMT ottimizzata

Endpoint primari:

- CV death + HF events
- CV death
- worsening HF
- LVAD
- trapianto cardiaco
- stroke



Coadministered Cagrilintide and Semaglutide in Adults with Overweight or Obesity

Authors: W. Timothy Garvey, M.D., Matthias Blüher, M.D., Cynthia Karenina Osorto Contreras, M.D., Melanie J. Davies, M.D., Eva Winning Lehmann, M.D., Ph.D., Kirsi H. Pietiläinen, M.D., Ph.D., Domenica Rubino, M.D., Paolo Sbraccia, M.D., Ph.D., Thomas Wadden, Ph.D., Niels Zeuthen, M.Sc., and John P.H. Wilding, D.M., for the REDEFINE 1 Study Group* [Author Info & Affiliations](#)

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The Cardiometabolic HF revolution

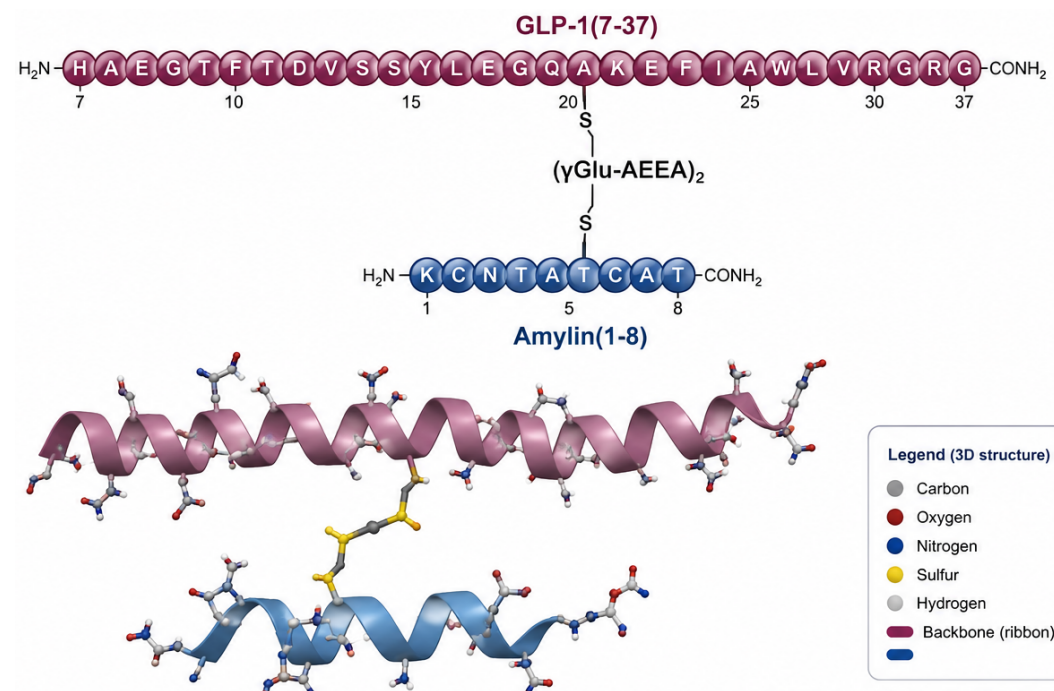
Zenagamtide (NNC0487-0111)

- Agonista GLP-1
- Agonista dell'amilina
- HFpEF e HFmrEF
- BMI > 30 kg/m²
- NYHA II-IV
- Terapia medica ottimizzata

Endpoint primario:

- morte cardiovascolare
- ricovero per HF
- Visite urgenti per HF

Inizio arruolamento: metà del 2026 (durata follow-up circa 3 anni)



- Triplo agonista: **GLP-1 receptor/ GIP receptor/Glucagon receptor**

May 21, 2026

In TRIUMPH-1, participants on 12 mg retatrutide lost an average of 70.3 lbs (28.3%) over 80 weeks with 45.3% of participants achieving $\geq 30\%$ weight loss, a level long associated with bariatric surgery

Individuals with a baseline BMI ≥ 35 who participated in a study extension continued to lose weight, and achieved up to an average of 85.0 lbs (30.3%) weight loss at 104 weeks

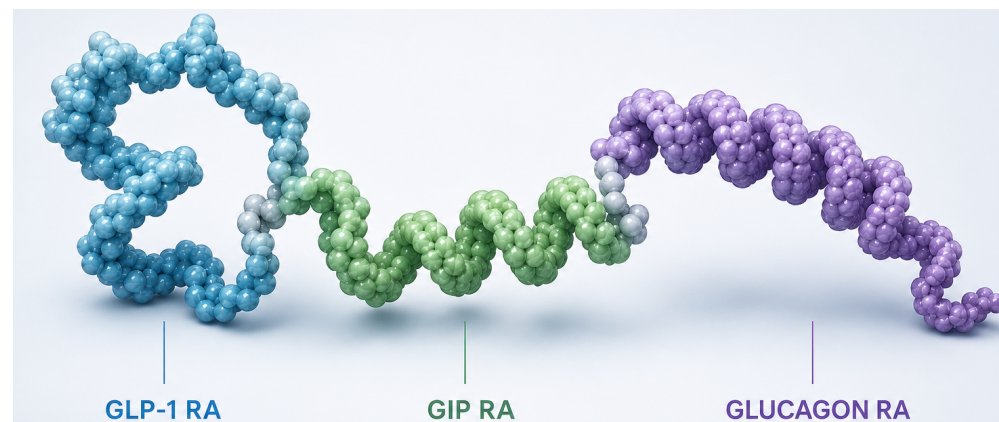
At the 4 mg dose, reached with only a single escalation step, participants lost an average of 47.2 lbs (19.0%) at 80 weeks with a lower observed discontinuation rate due to adverse events vs. placebo

- TRIUMPH-3 trial: Obesità + Malattia cardiovascolare (2000 pazienti circa, endpoint differenza di peso) → risultati previsti entro il 2026



The Effect of Retatrutide Once Weekly on Cardiovascular Outcomes and Kidney Outcomes in Adults Living With Obesity (TRIUMPH-Outcomes)

- ~10000 pazienti
- BMI ≥ 27
- ASCVD e/o CKD
- circa 10.000 pazienti
- follow-up ~5 anni



Endpoint primari

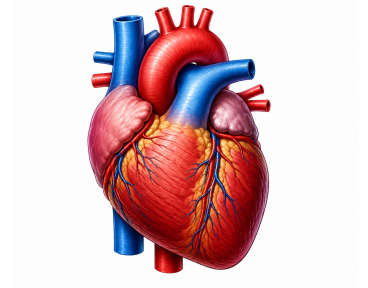
- MACE
- progressione della malattia renale

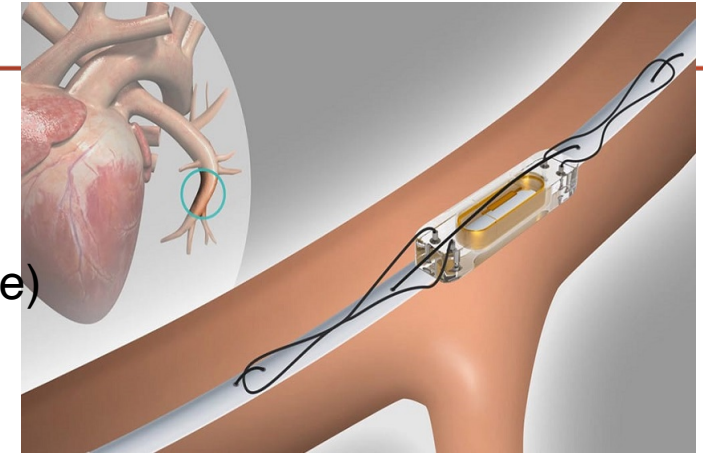
Risultati previsti tra 2028 e il 2029



Heart Failure next

- Farmaci
- Device
- Dati





L'aumento della PAP precede la comparsa dei sintomi (2-4 fino a 6 settimane)



- CHAMPION (2011) → 550 pz, NYHA III. Riduzione del 28% delle ospedalizzazioni per HF
- GUIDE-HF (2020) → Trial negativo per endpoint primario su morte, ricovero e visite urgenti per HF (trial eseguito durante pandemia)
- MONITOR-HF (2023) → 348 pz, NYHA III. Significativo miglioramento del KCCQ e delle ospedalizzazioni per HF
- PASSPORT-HF (Ongoing trial) → 554 pz, NYHA III.

Endpoint primario: riospedalizzazioni per HF o morte a 12 mesi → **Risultati previsti per fine 2026 e 2027**



Misurazione in posizione seduta

In posizione supina: aumenta il ritorno venoso → aumenta il precarico → aumentano le pressioni di riempimento → la PAP è leggermente più alta

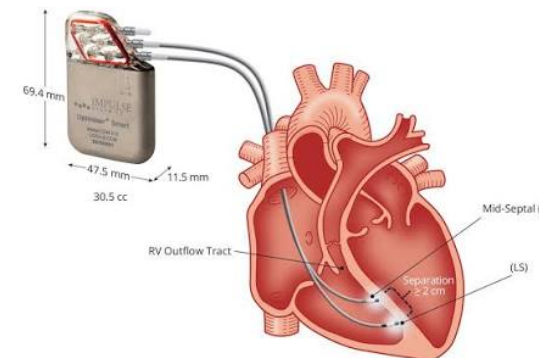
- Pressione
 - Frequenza
 - Peso
 - Saturazione
-
- PROACTIVE-HF (2024) → 456 pz, NYHA III. Endpoint raggiunto su ospedalizzazioni e morte (Non è un trial randomizzato)
 - PROACTIVE-HF 2 (ongoing trial) → NYHA II-III. Introduzione del “patient self-management + precision monitoring → **Primi dati intermedi 2027-2028**
 - **Altri ongoing trials:** PREDICT-HF (NCT05200338), POST-Acute HF (NCT05635181), AT-HOME HF (NCT05329286)



- Erogazione di impulsi elettrici durante il periodo refrattario assoluto



- Migliora l'handling del calcio intracellulare
- Aumenta la fosforilazione di proteine contrattili
- Non aumenta il consumo di ossigeno
- Può favorire il reverse remodeling



HFrEF-HFmrEF sintomatico
QRS stretto
Non candidato a CRT
Terapia medica ottimizzata

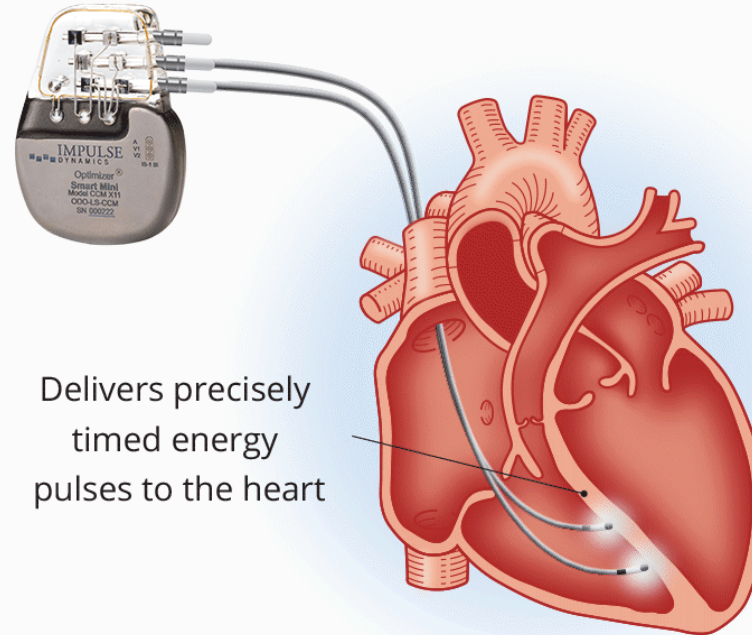
- FIX-HF-5C (2018) → 160 pz. Miglioramento di peak VO_2 , 6MWT, qualità di vita e riduzione delle ospedalizzazioni per HF a 6 mesi
- FIX-GDMT-HF (Ongoing trial) → 200 pz. Endpoint primario: change in QMS → **Risultati principali nel 2027**
- AIM HIGHer (Ongoing trial) → 1500 pz, FE 40-70% → **Risultati previsti nel 2029**



HF is a BIG Problem. *CCM*[®] is a BIG breakthrough.

Cardiac Contractility Modulation therapy

has been shown to:
improve quality of life
reduce HF symptoms
reduce HF hospitalizations



Delivers precisely
timed energy
pulses to the heart

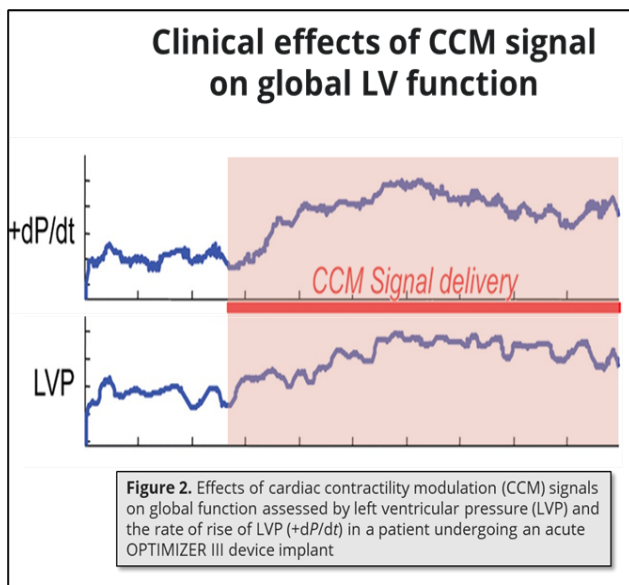
- CCM[®] is a therapy that delivers impulses in the Absolute Refractory Period to **improve contractility**
- through a **rechargeable** device, with a **20-year** battery life
- that can be implanted with the **safety & simplicity** of a typical CRM device

For Systolic HF Patients, NYHA Class II-III-IV, symptomatic despite GDMT (EU indication)

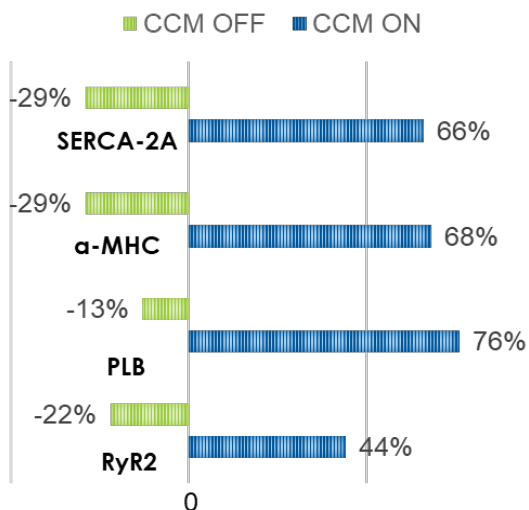
**Contractility improves
(minutes - hours)**

**Gene profile normalizes
(hours - weeks)**

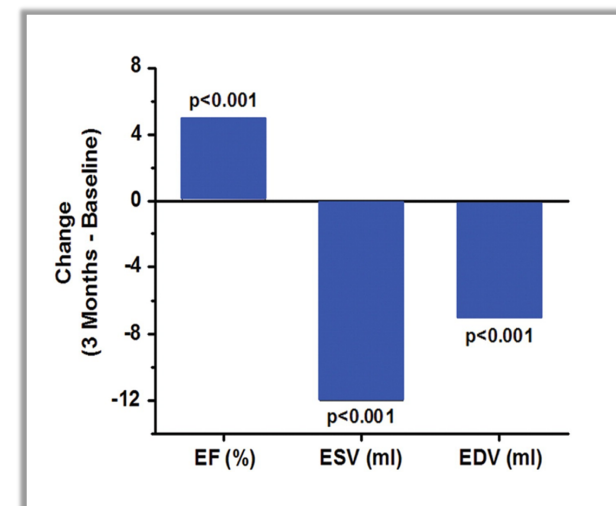
**Reverse remodeling
(weeks - months)**



Burkhoff, Daniel, et al. "Electric currents applied during the refractory period can modulate cardiac contractility in vitro and in vivo." *Heart failure reviews* 6 (2001): 27-34.

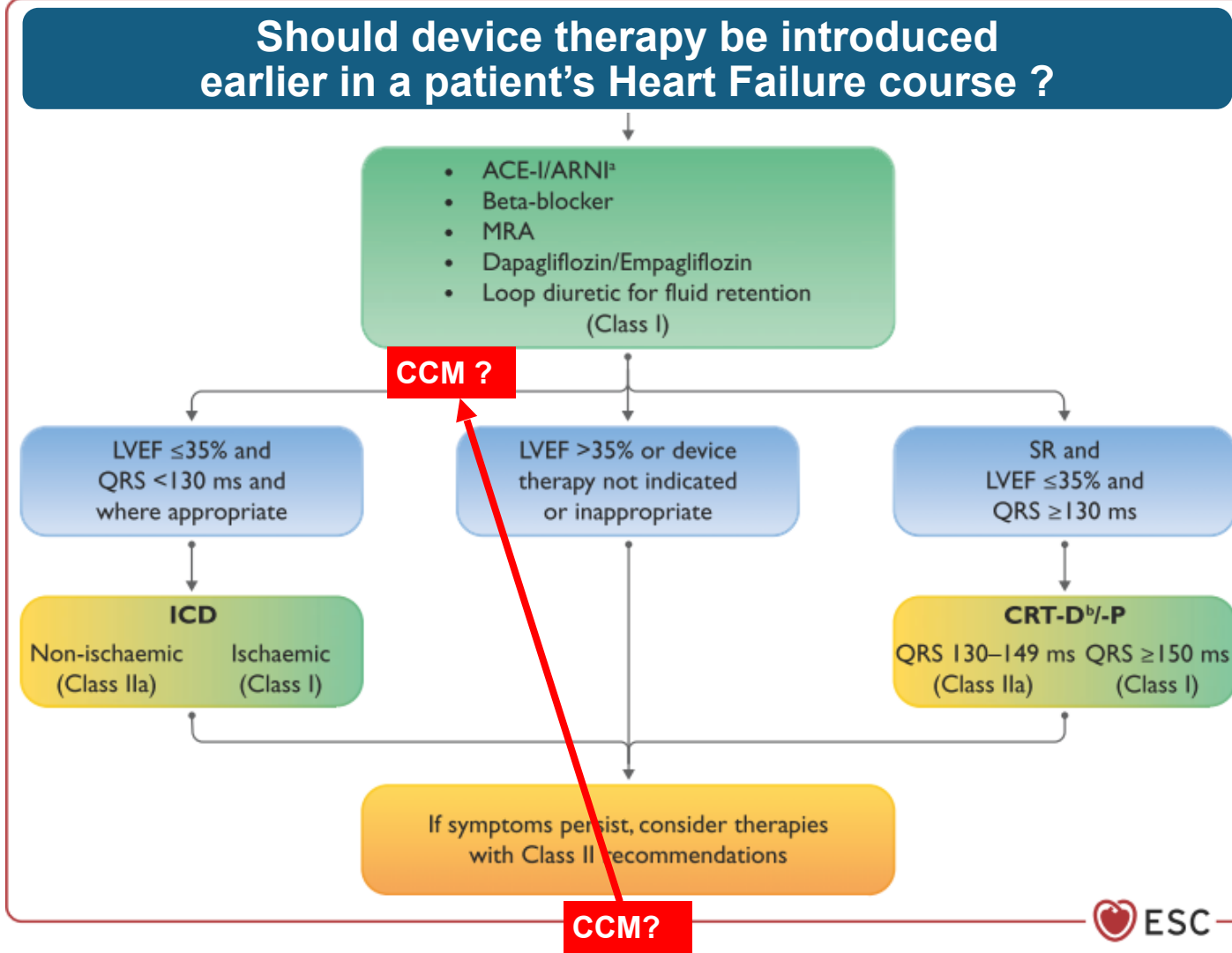


Butter, Christian, et al. "Cardiac contractility modulation electrical signals improve myocardial gene expression in patients with heart failure." *Journal of the American College of Cardiology* 51.18 (2008): 1784-1789.



Yu, Cheuk-Man, et al. "Impact of cardiac contractility modulation on left ventricular global and regional function and remodeling." *JACC: Cardiovascular Imaging* 2.12 (2009): 1341-1349.





STUDY HYPOTHESIS

CCM therapy use in patients with symptomatic HF can augment their use and dosing of GDMT medications

The FIX-GDMT Trial

European Heart Journal (2021) 42, 35993726



FIX-GDMT-HF Clinical Trial

CCM & Uptitration of Guideline-Directed Medical Therapy (GDMT) in Patients with Heart Failure

Study Objective

Evaluate the impact of CCM therapy on the initiation and up-titration of GDMT in patients with heart failure

Primary Endpoint

- Change in Quad Medicare Score (QMS) from baseline (pre-CCM) to 6-month follow-up (post-CCM)

Secondary Endpoints

- Change in loop diuretic dose
- Change in eGFR
- Change in systolic blood pressure
- Adverse events associated with CCM
- Change in heart rate among patients with concomitant CRM device
- Percentage of patients receiving maximal GDMT following CCM
- GDMT adherence measured by change in QMS

Study Design

Prospective, non-randomized, comparison analysis of medication use and dosing at pre- and post-CCM therapy.
100 subjects (Investigational Arm) and 100 subjects (Registry Arm) enrolled in EU and USA

Trial open to enrollment as of March 2025

Key Inclusion Criteria

- Symptomatic HFrEF patients with **LVEF $\leq 40\%$** ; (& $\geq 25\%$ USA only)
- Patients **can have an active concomitant CRT device** provided the following:
 - Device implanted >1 year & NYHA Class II to IV

Key Exclusion Criteria

- Quad Medication Score (QMS) >5
- eGFR <15
- CRT responders or have Class I indication for CRT device
- Severe stenotic valve disease



Gemelli
Fondazione Policlinica Universitaria Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore

**International
Principal Investigator**
Nadia Aspromonte, MD
Gemelli University
Polyclinic
Foundation
Rome, Italy



Simula una una pressione arteriosa elevata stimolando i barocettori carotidei



Aumento dell'attività parasimpatica



Riduzione delle catecolamine, della vasocostrizione e dell'attivazione RAAS

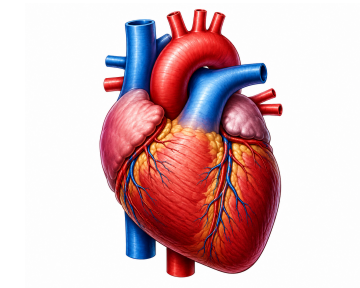


- BeAT-HF (2020) → 245 pz, HFrEF, NYHA III. Miglioramento su qualità di vita, 6MWT, NYHA e NT-proBNP. Non differenze su mortalità e ricoveri.
- BENEFIT-HF (Ongoing trial) → 2500 pz, FE <50%, HFrEF, NYHA II-III. Endpoint primario composito di mortalità totale e eventi di scompenso → **Risultati previsti 2029-2031**



Heart Failure next

- Farmaci
- Device
- Dati



Non-Invasive Cardiac System (NiCas)

Whole-body bioimpedance cardiography



ELSEVIER

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Advances in Medical Sciences

journal homepage: www.elsevier.com/locate/advms



Original research article

Can non-invasive cardiac hemodynamics and fluid content system (NiCaS) parameters predict Acute Heart Failure outcomes in Caucasian and Asian patients in the emergency department?

Muhammad Anshory^{a,g}, Win Sen Kuan^b, M. Saifur Rohman^c, Yoga Waranugraha^c, Putri Annisa Kamila^c, Agustin Iskandar^{d,g}, Hani Susianti^{d,g}, Ying Wei Yau^b, Crystal Harn Wei Soh^b, Khalid Mohammed Ali^e, Mui Teng Chua^b, Salvatore Di Somma^{f,g,*}

^a Internal Medicine Department, Saiful Anwar General Hospital, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia

^b Emergency Medicine Department, National University Hospital, National University Health System, Singapore

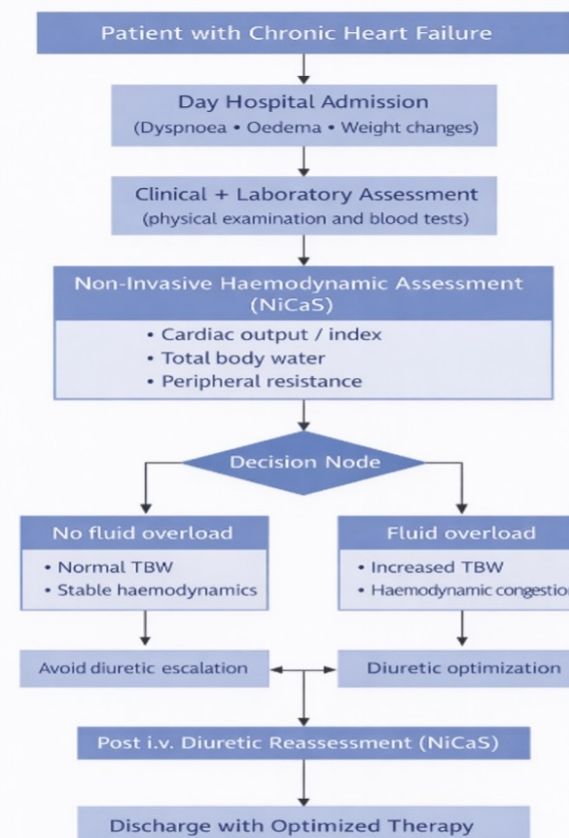
^c Cardiology Department, Saiful Anwar General Hospital, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia

^d Clinical Pathology Department, Saiful Anwar General Hospital, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia

^e Kingston Hospital NHS Foundation Trust, Kingston upon Thames, United Kingdom

^f Department of Medical-Surgery Sciences and Translational Medicine, Sapienza University of Rome, Rome, Italy

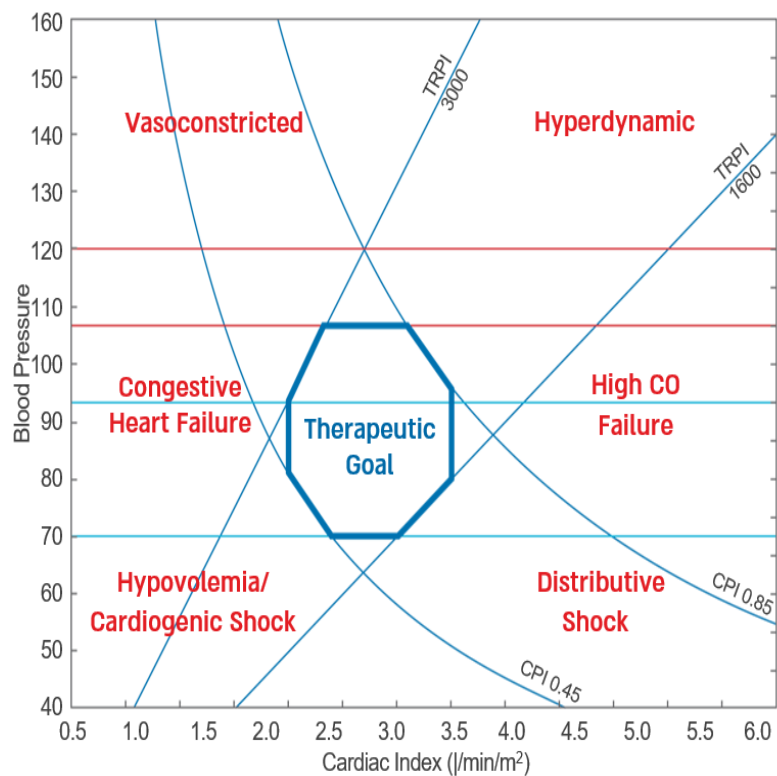
^g Great Network, Global Research on Acute Conditions Team, Rome, 00191, Italy



Phenotyping



Monitoring



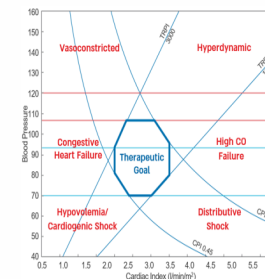
NICaS (Non Invasive Cardiac System) di Innovamed Sphere

NICaS+

Monitorare in maniera non invasiva e riproducibile dei parametri cardiovascolari, respiratori e dei liquidi (Sistema a bio impedenza full body).

Misurazioni in tempo reale:

- Frequenza Cardiaca (HR)
- Gittata Sistolica (SV)
- Gittata Cardiaca (CO)
- Resistenza Periferica Totale
- Indice di Contrattilità Cardiaca
- Acqua Corporea Totale
- Frequenza Respiratoria



WIN HF

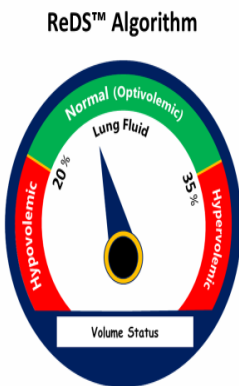
National Congress on Heart Failure:
Advances and Innovation



Remote

ReDS guided Congestion Management

- Valutazione di
elettromagnet
del tessuto pc



Normal lung measures 20-35%
Device range is 15-60%

ReDS reading	Action
≤20%	Hold diuretics
21-35%	Maintain current diuretic dosing 1. If the patient was on IV diuretic and is without significant edema, he/she can be converted to the equivalent oral dose 2. If the patient still has significant edema, IV diuretics will be continued
36-45%	Increase diuretics 1. If on oral diuretic change to IV 2. If dose of diuretic is equivalent to >200 mg furosemide IV then add a distal loop diuretic (metolazone or thiazide)
≥46%	Consider iv loop diuretics 1. All diuretics will need to be IV and titrated to demonstrate a response of at least 250 cc urine in the 2 hours post treatment. If not then the dose of IV diuretics will be doubled

+ GDMT
optimization

Alvarez-Garcia, J, Lala, A, Rivas-Lasarte, M. et al. Remote Dielectric Sensing Before and After Discharge in Patients With ADHF: The ReDS-SAFE HF Trial. J Am Coll Cardiol HF. 2024 Apr, 12 (4) 695–706.



dielétriche
ne polmonare



National Congress on Heart Failure:
Advances and Innovation



Association between lung fluid levels estimated by remote dielectric sensing and lung ultrasound in patients with heart failure

[Shan Huang](#)^{1,†}, [Guangfeng Sun](#)^{2,†}, [Yulin Wu](#)¹, [Hongfei Jiang](#)¹, [Weiliang Zhu](#)¹, [Penglong Wu](#)¹, [Manxin Lin](#)¹, [Fanqi Meng](#)^{1,*}

▶ [Author information](#) ▶ [Article notes](#) ▶ [Copyright and License information](#)

PMCID: PMC12894278 PMID: [41694306](#)

Univariate and multivariate linear regression analysis for sum of B lines.

Variables	Univariate Analysis		Multivariate Analysis	
	Beta Value (95% CI)	p Value	Beta Value (95% CI)	p Value
ReDS, %	0.572 (0.457–0.687)	<0.001*	0.569 (0.458–0.680)	<0.001*
NT-ProBNP, pg/mL	1.416 (0.604–2.229)	<0.001*	1.424 (0.721–2.128)	<0.001*
BMI, kg/m ²	−0.188 (−0.475–0.098)	0.196	-	-
LVEDD, mm	0.061 (−0.050–0.172)	0.279	-	-
Creatinine, umol/L	0.006 (−0.001–0.012)	0.09	−0.002(−0.008–0.003)	0.383
LVEF, %	0.021 (−0.068–0.109)	0.645	-	-

Remote Dielectric Sensing (ReDS)



- Valutazione del contenuto di liquido nel polmone tramite onde elettromagnetiche a bassa energia che misurano le proprietà dielettriche del tessuto polmonare → Misurazione indiretta di congestione polmonare
- SMILE-HF (2019): 268 pz, indipendentemente dalla FE. Riduzione delle riospedalizzazioni per HF del 58% rispetto al gruppo di controllo
- REDS-SAFE HF (2024) → 101 pz con scompenso acuto. Standard Care Vs Dimissione guidata da ReDS. Endpoint primario composito: visita urgente HF, riospedalizzazione per HF, morte.



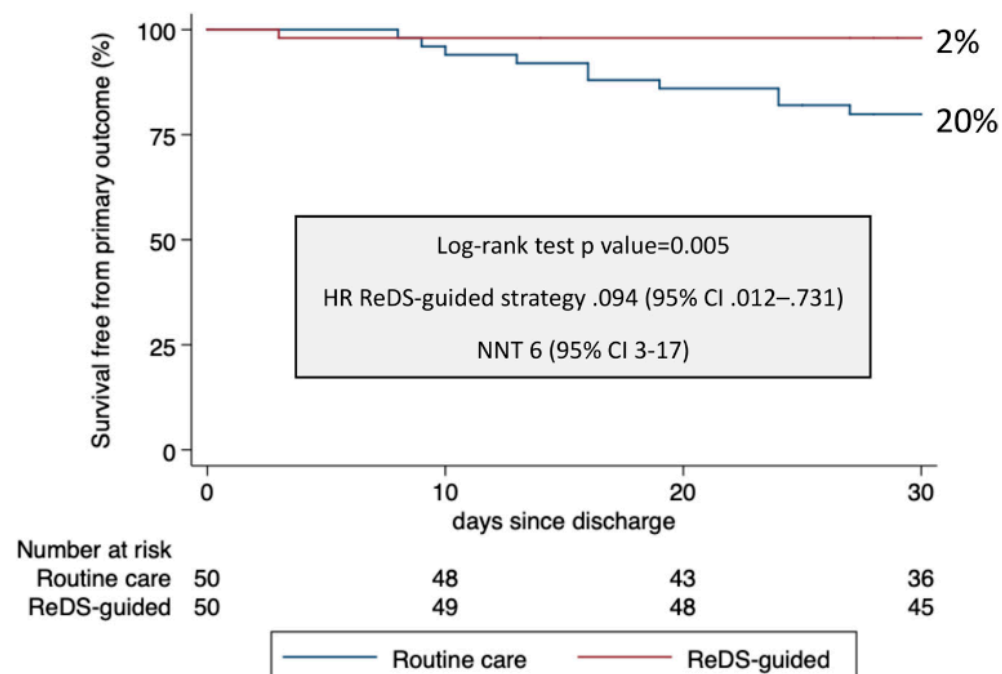
Remote Dielectric Sensing Before and After Discharge in Patients With ADHF

The ReDS-SAFE HF Trial

Jesus Alvarez-Garcia, MD, PhD,^{a,b} Anuradha Lala, MD,^{c,d} Mercedes Rivas-Lasarte, MD, PhD,^{b,e}
Clemencia De Rueda, MD,^{a,b} Danielle Brunjes, PhD,^{c,d} Sara Lozano-Jimenez, MD,^{b,e} Cristina Garcia-Sebastian, MD,^{a,b}
Sumeet Mitter, MD,^{c,d} Paloma Remior, MD,^a Marta Jimenez-Blanco Bravo, MD,^{a,b} Susana Del Prado, MD, PhD,^{a,b}
Maya Barghash, MD,^{c,d} Eduardo González-Ferrer, MD,^{a,b} Jennifer Ullman, RN,^{c,d} Marta Cobo, MD,^{b,e}
Javier Segovia-Cubero, MD, PhD,^{b,e} José Luis Zamorano, MD, PhD,^{a,b} Sean P. Pinney, MD,^{c,d} Donna Mancini, MD^c



FIGURE 4 Kaplan-Meier Survival Curve for 30-Day Primary Outcome



Time to the primary endpoint. Differences were driven by a decrease in the number of HF readmissions. NNT = number needed to treat; other abbreviation as in [Figure 2](#).

Remote Dielectric Sensing (ReDS)



- Valutazione del contenuto di liquido nel polmone tramite onde elettromagnetiche a bassa energia che misurano le proprietà dielettriche del tessuto polmonare → Misurazione indiretta di congestione polmonare
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- REDS-SAFE HF (2024) → 101 pz con scompenso acuto. Standard Care Vs Dimissione guidata da ReDS. Endpoint primario composito: visita urgente HF, riospedalizzazione per HF, morte.
- RADAR-HF, NCT03586336 (Ongoing trial): 100 Pz. Diuresi guidata da ReDS Vs usual care. Ottimizzazione della decogestione → **Risultati previsti tra il 2026 e il 2027**



Satelia

• Remote patient monitoring (RPM)

- Sintomi riferiti dal paziente
- Peso corporeo
- Questionari strutturati



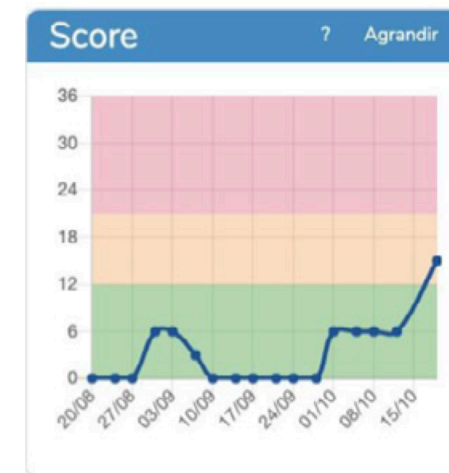
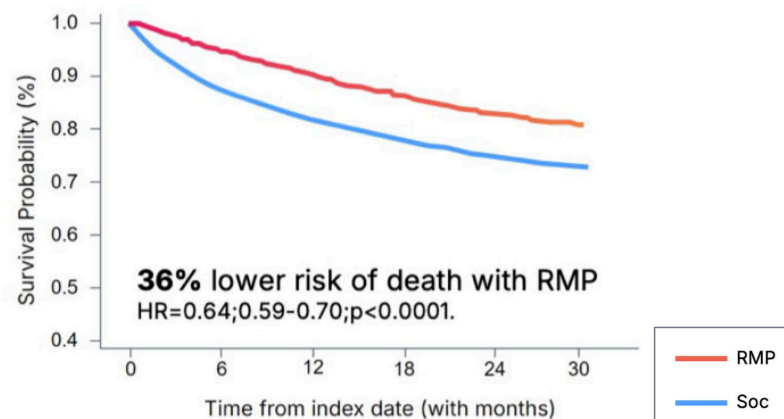
European Journal of Heart Failure (2025) 27, 1658–1669
doi:10.1002/ehf.3563

RESEARCH ARTICLE

Association of a remote monitoring programme with all-cause mortality and hospitalizations in patients with heart failure: National-scale, real-world evidence from a 3-year propensity score analysis of the TELESAT-HF study

Nicolas Girerd^{1*}, Vanessa Barbet², Marie-France Seronde³, Hélène Benchimol⁴, Annabelle Jagu⁵, Jean-Michel Tartière⁶, Olivier Hanon^{7,8}, François Picard⁹, Stéphane Lafitte⁹, Magali Lemaître², Nicolas Pages¹⁰, Sophie Nisse-Durgeat¹⁰, and Patrick Jourdain¹¹

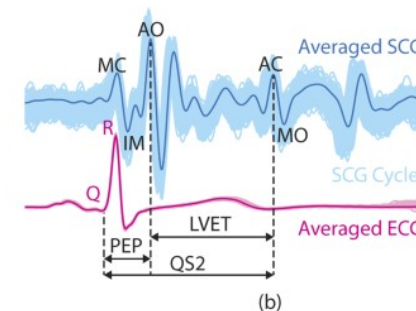
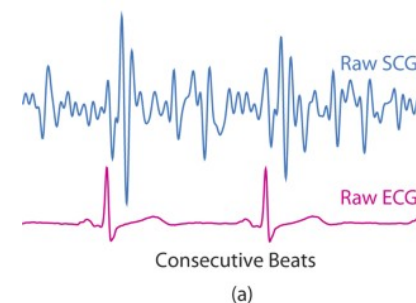
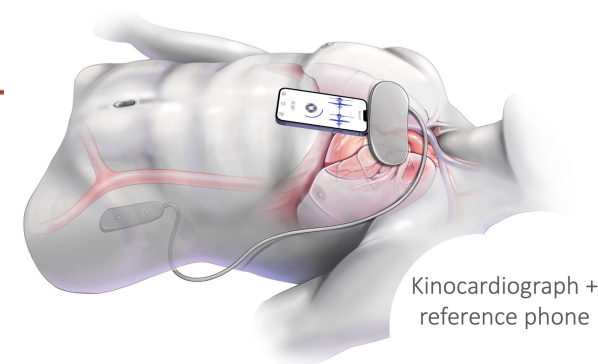
(A) Overall



Seismocardiografia (SCG)

Registrazione delle micro-vibrazioni toraciche

- Contrattilità
- Cardiac Output
- Stroke Volume
- Congestione



Heart Failure Reviews (2025) 30:1099–1101
<https://doi.org/10.1007/s10741-025-10514-1>

MINI REVIEW



SEISMIC-HF 1: key findings from AHA24 and implications for remote cardiac monitoring

Baljash Cheema^{1,2} · Anjan Tibrewala^{1,2}

Accepted: 15 April 2025 / Published online: 23 April 2025
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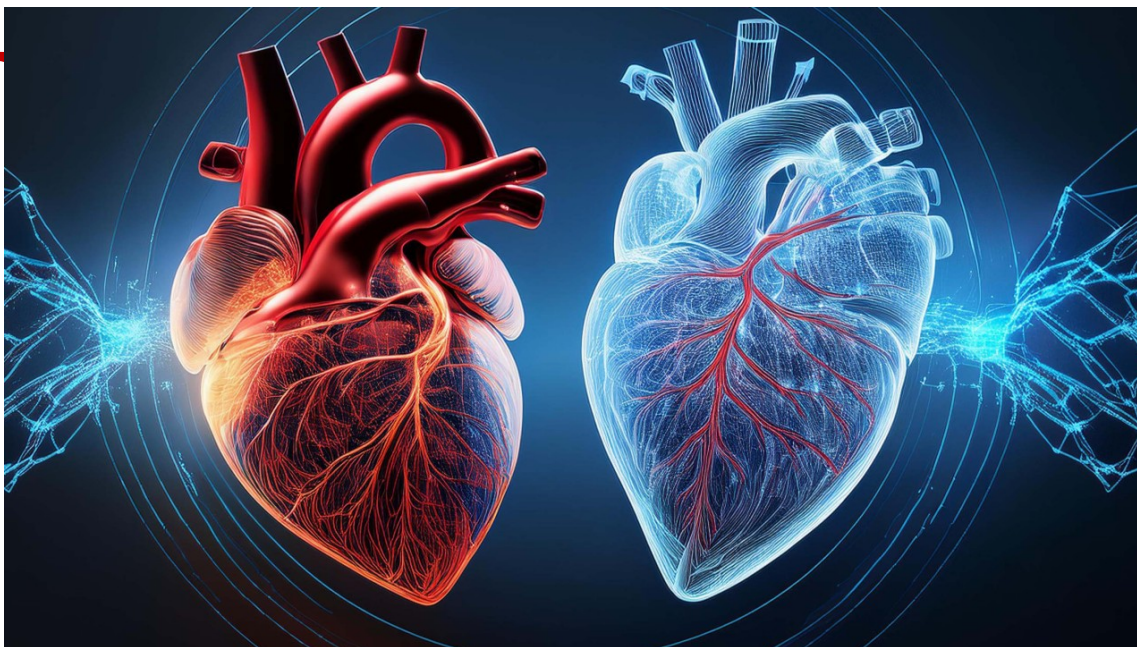
- SEISMIC-HF 2 (Ongoing trial): Performance diagnostica sui valori di PCWP→
Arruolamento iniziato nel 2025



Digital Twin

INPUT

- Clinica
- Imaging
- Emodinamica
- Biomarcatori



OUTPUT

- Rischio di worsening
- Risposta ai farmaci
- Risposta ai device
- Evoluzione della malattia

[Journal of the American Heart Association](#)



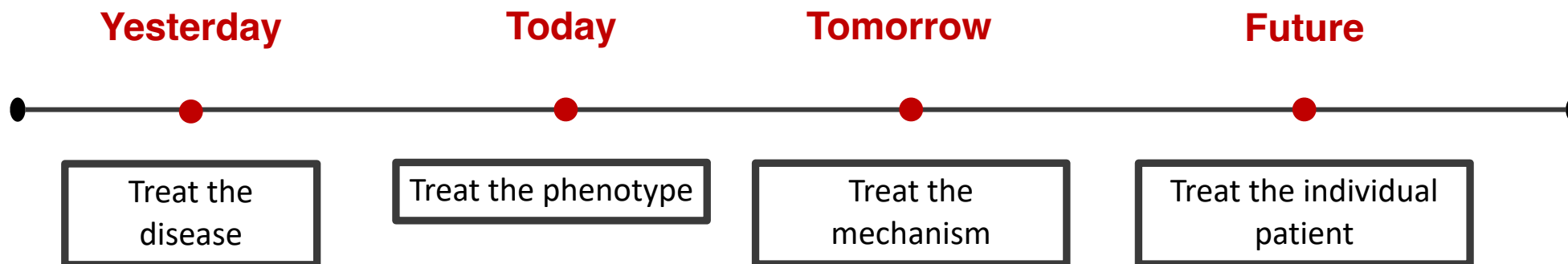
CONTEMPORARY REVIEW

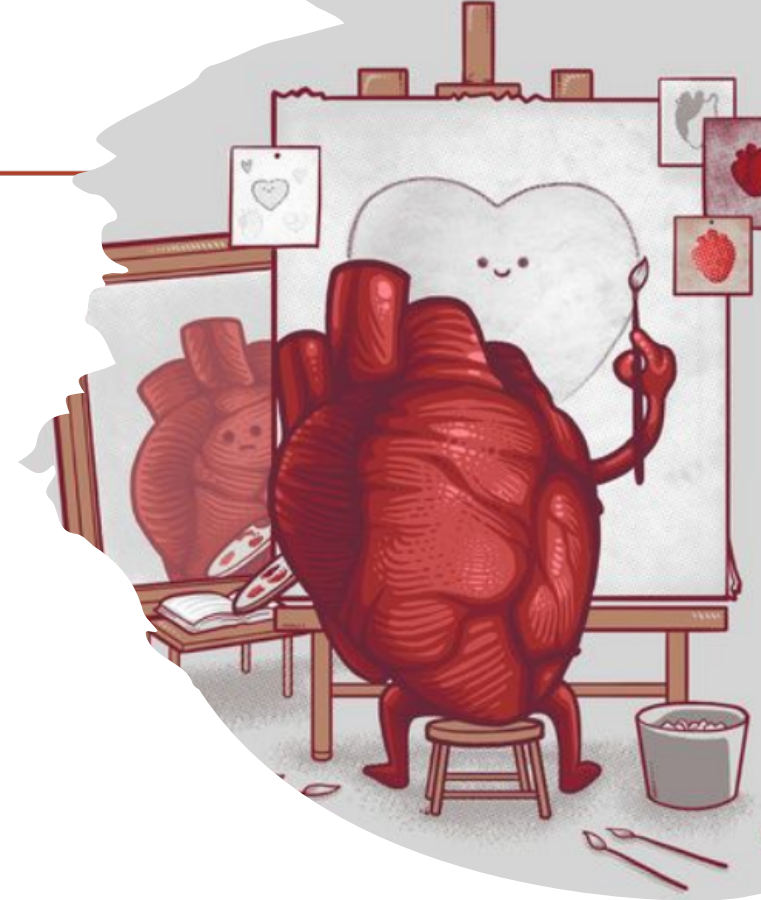
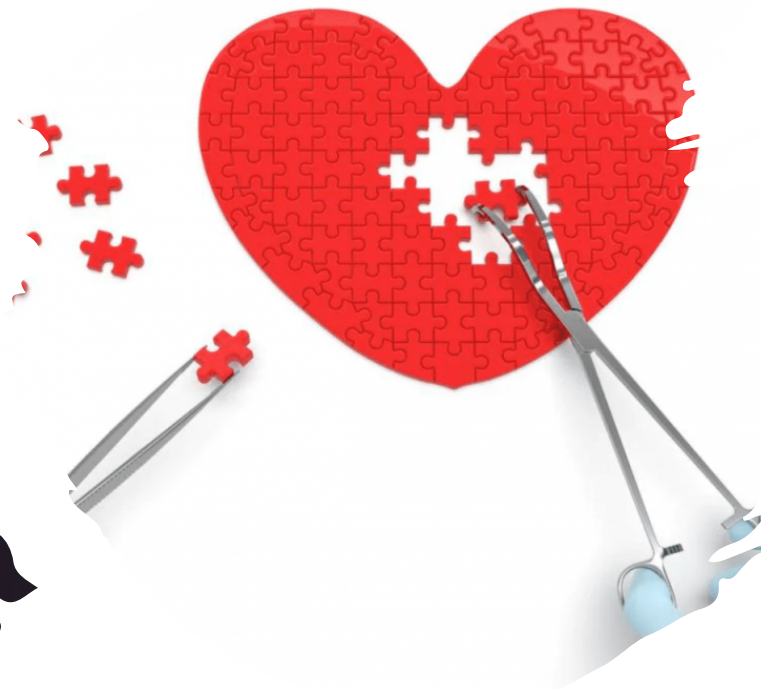
Building Digital Twins for Cardiovascular Health: From Principles to Clinical Impact

Kaan Sel , PhD^{*}; Deen Osman , BSc^{*}; Fatemeh Zare , BSc; Sina Masoumi Shahrabak , BSc; Laura Brattain , PhD[†]; Jin-Oh Hahn , PhD[†]; Omer T. Inan , PhD[†]; Ramakrishna Mukkamala , PhD[†]; Jeffrey Palmer , PhD[†]; David Paydarfar, MD[†]; Roderic I. Pettigrew, PhD, MD[†]; Arshed A. Quyyumi , MD[†]; Brian Telfer , PhD[†]; Roozbeh Jafari , PhD



Heart Failure Next...





Grazie per l'attenzione

