

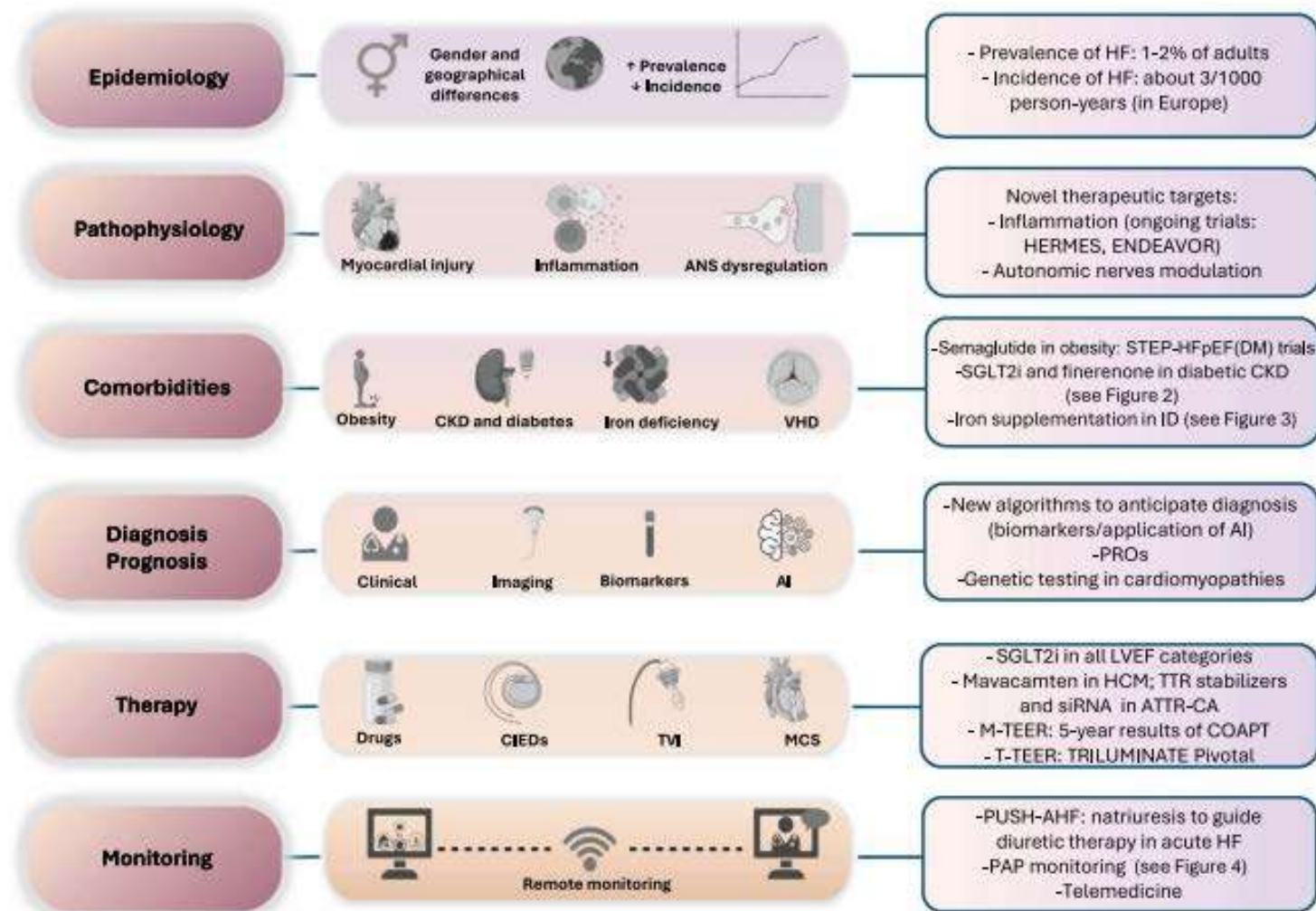
Research Trends In Cardiovascular Medicine and Heart Failure

Servet ALTAY, MD, Professor

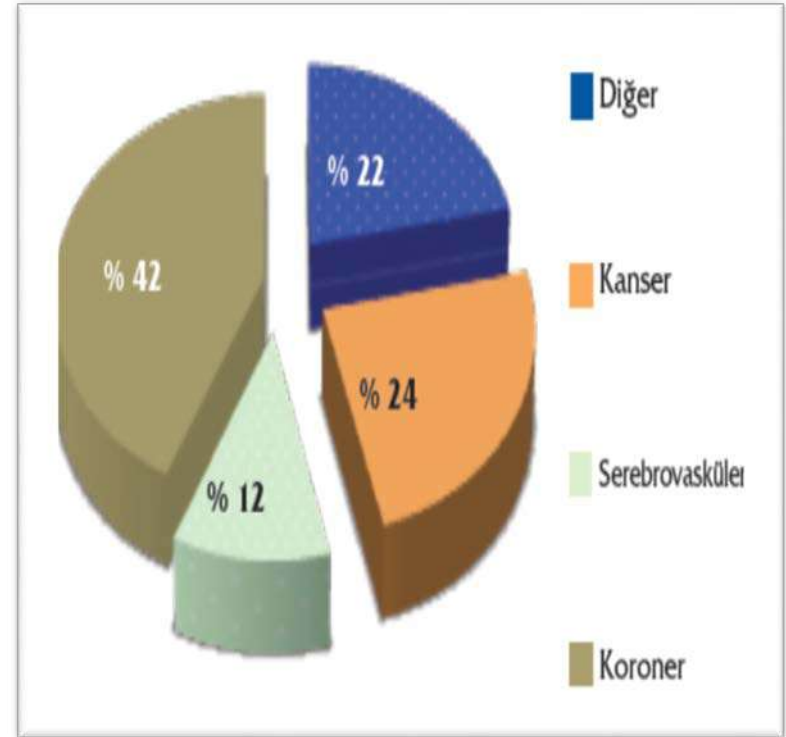
Head of Cardiology Department, Trakya University School of Medicine

Editor in Chief Balkan Medical Journal

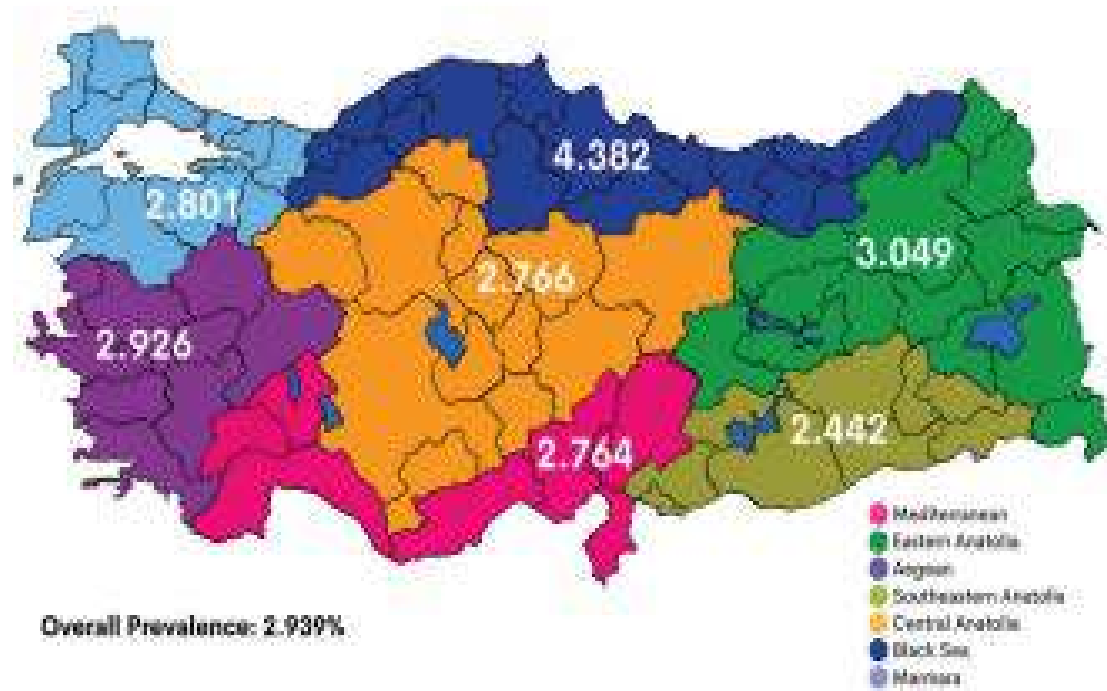
Board Member of Society of Cardiovascular Interventions



Epidemiology

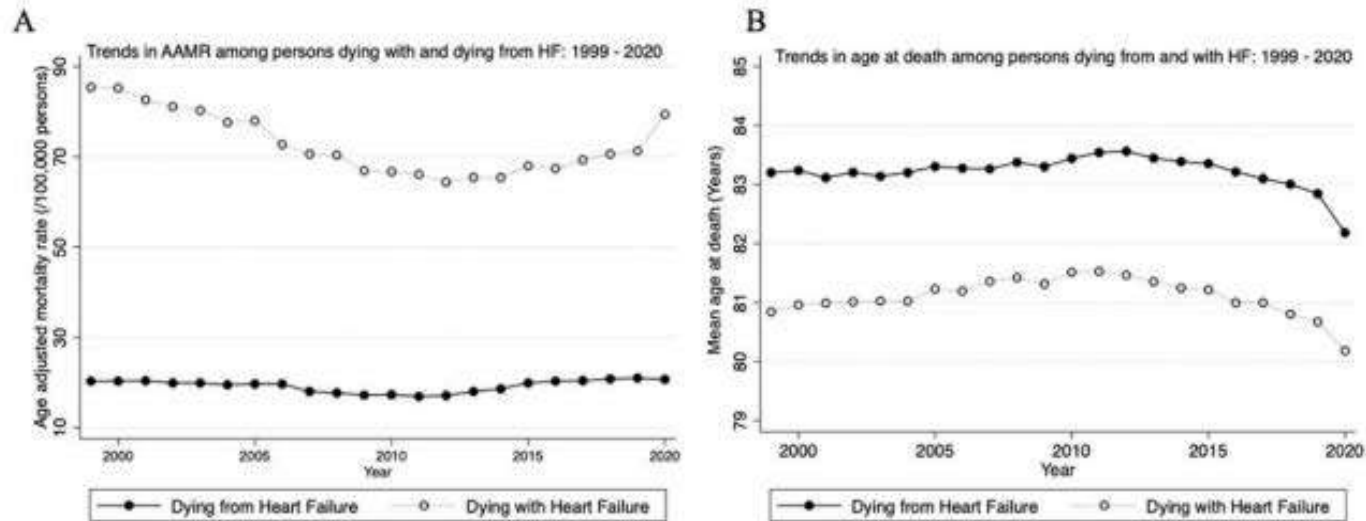


Epidemiology



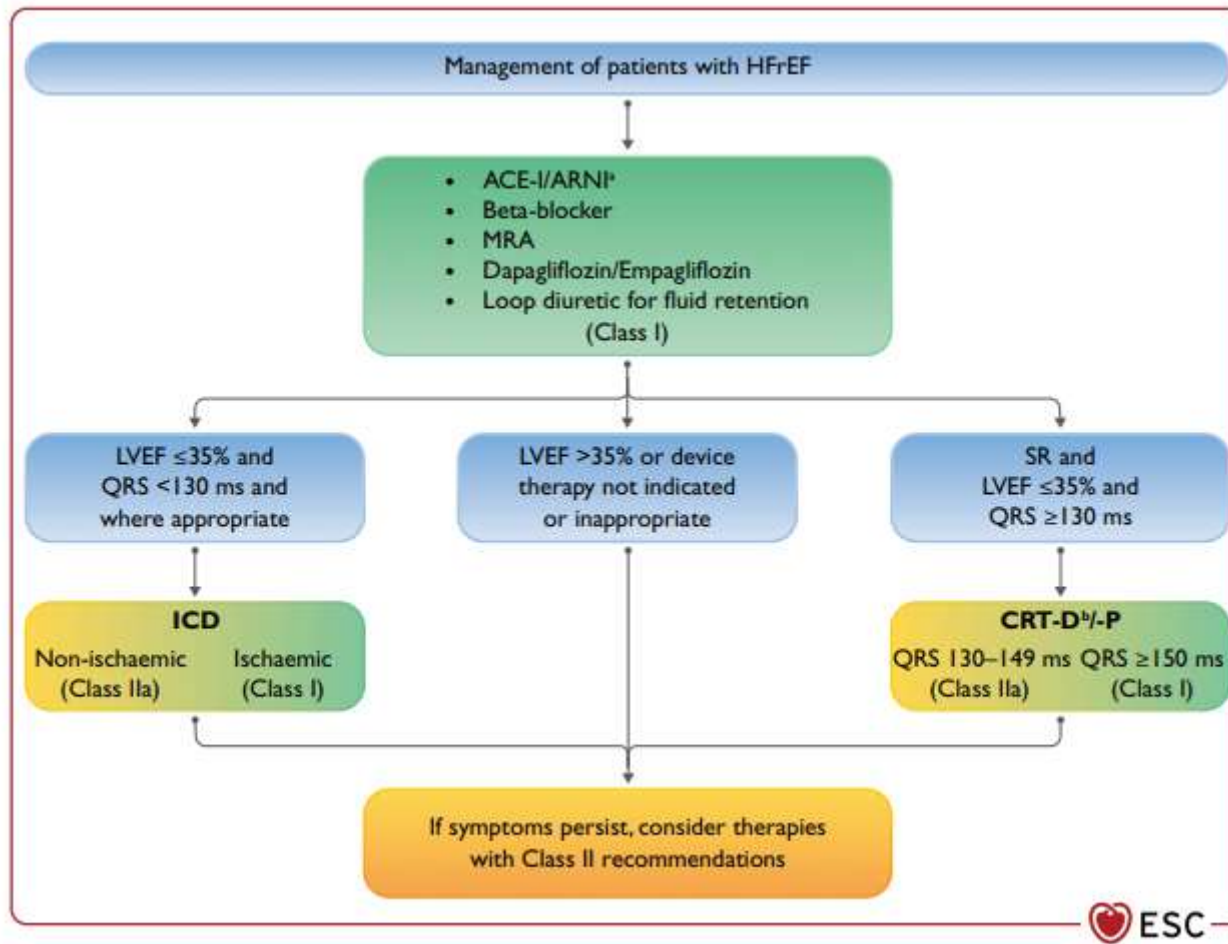
Regional Disparities in Heart Failure Epidemiology and Outcomes: A Comprehensive Study Across Geographical Regions in Türkiye. *Balkan Med J.* 2024 Jan 3;41(1):47-53

Epidemiology

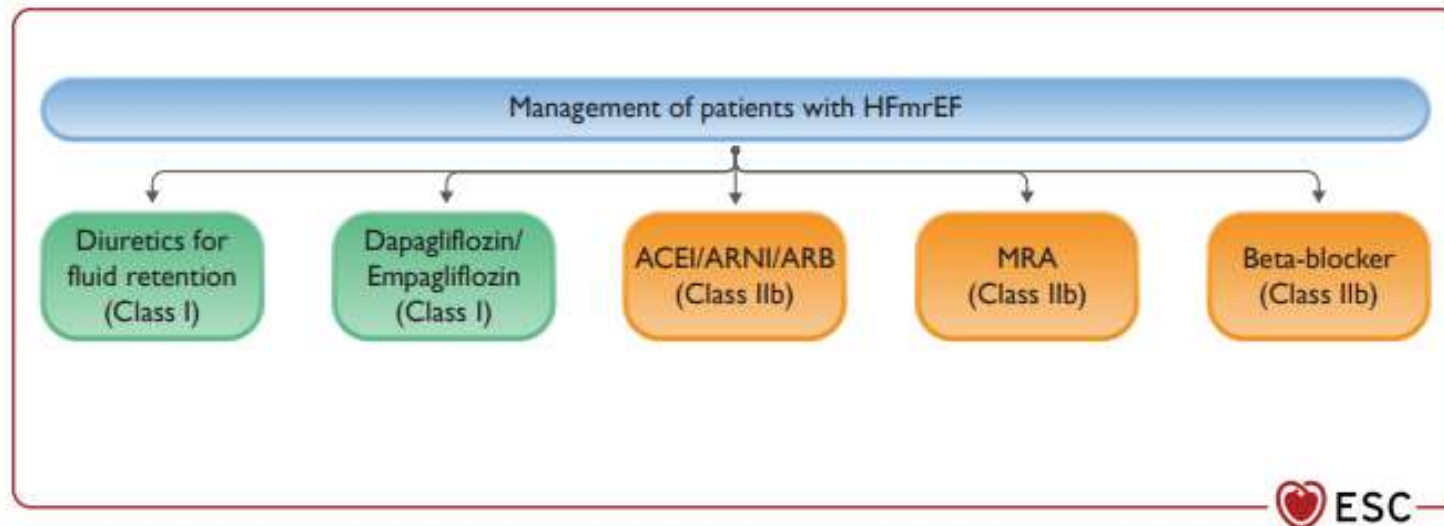


Trends in heart failure mortality in the USA 1999 to 2020, European Heart Journal, Volume 44, Issue Supplement_2, November 2023

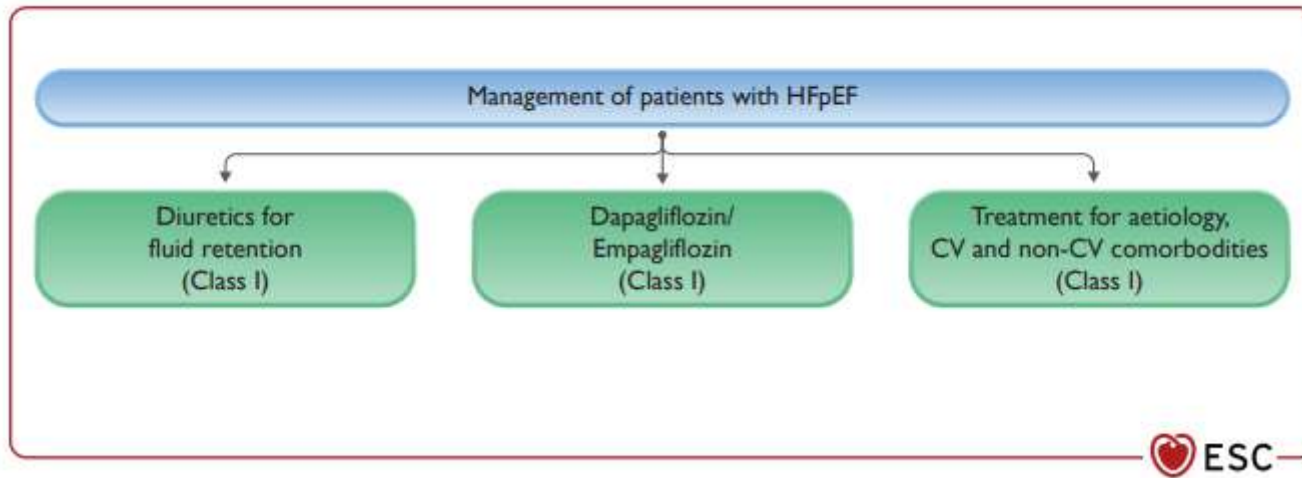
HFrEF Treatment-ESC 2021



HFmEF Treatment-ESC 2023



HFpEF Treatment-ESC 2023



Comorbidities Treatment

- Obesity
- Iron deficiency
- Renal Disease
- Diabetes Mellitus
- VHD

STEP-HF_pEF

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

Study population

HFpEF patients

- left ventricular ejection fraction $\geq 45\%$
- body mass index ≥ 30 kg/m²
- HF symptoms
- functional limitations (New York Heart Association functional class II-IV and Kansas City Cardiomyopathy Questionnaire Clinical Summary Score [KCCQ-CSS] < 90 points)

Where?

13 countries in Asia, Europe, North America and South America  96 sites

Who and what?



Primary endpoints

change from baseline to week 52 in KCCQ-CSS



estimated treatment difference 7.8 points
95% CI 4.8 to 10.9
 $p < 0.001$

change from baseline to week 52 in body weight



estimated treatment difference -10.7%
95% CI -11.9% to -9.4%
 $p < 0.001$

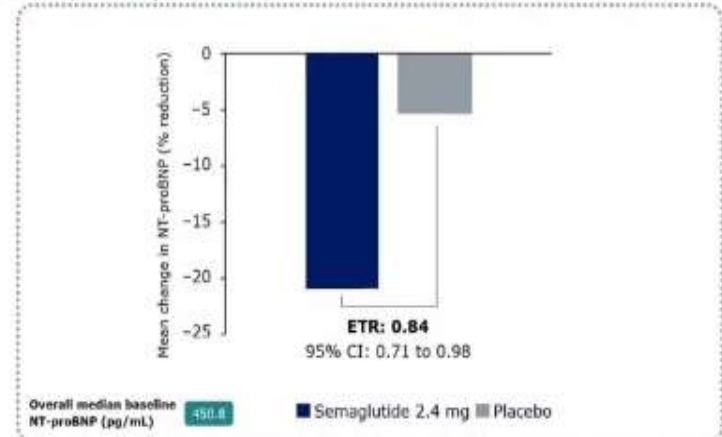
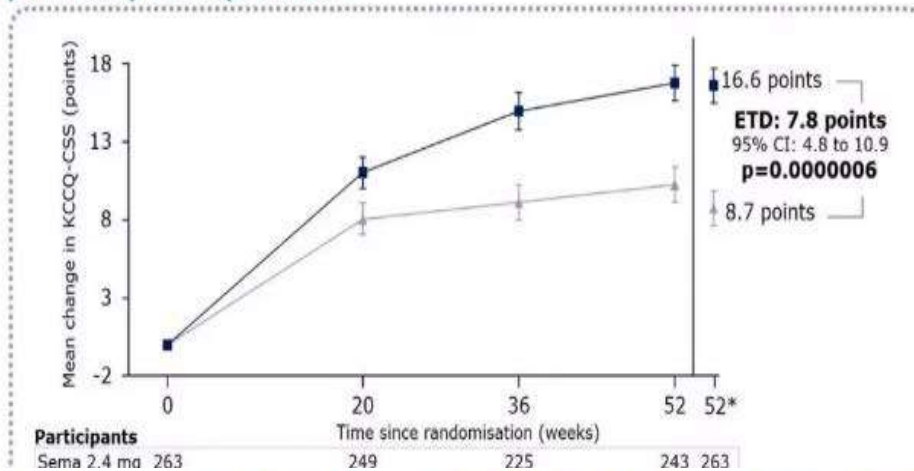
Serious adverse events



STEP-HF_pEF

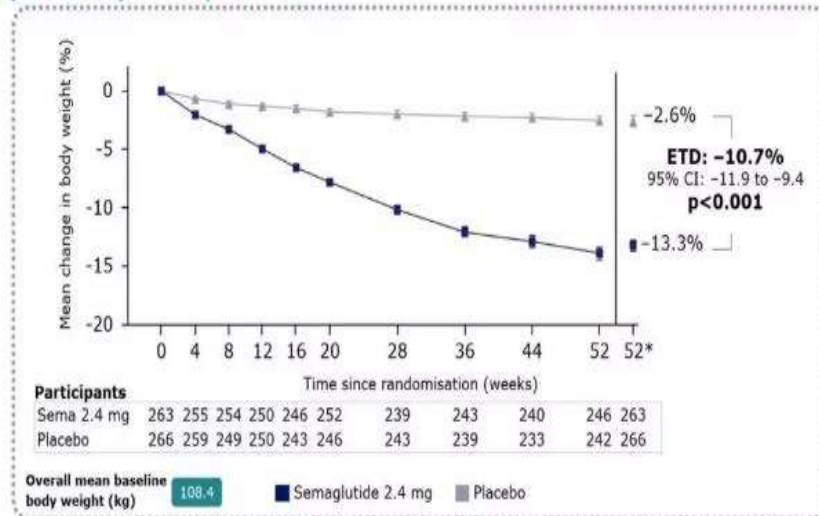
Change from baseline to week 52 in KCCQ-CSS Dual primary endpoints

Change from baseline to week 52 in NT-proBNP Exploratory endpoints



Change from baseline to week 52 in body weight Dual primary endpoints

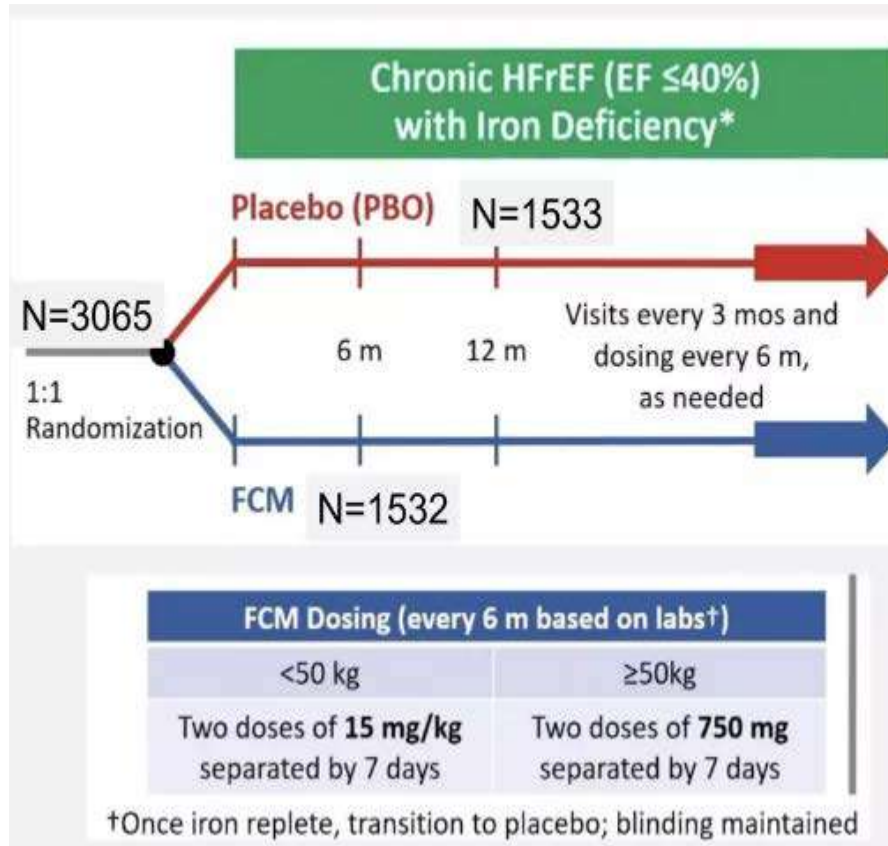
Safety overview On-treatment period



Semaglutide

- Among patients with obesity-related HFpEF and T2DM, semaglutide led to larger reductions in HF-related symptoms and physical limitations and greater weight loss than placebo at 1 year

HEART-FID: Ferric Carboxymaltose in Heart Failure with Iron Deficiency



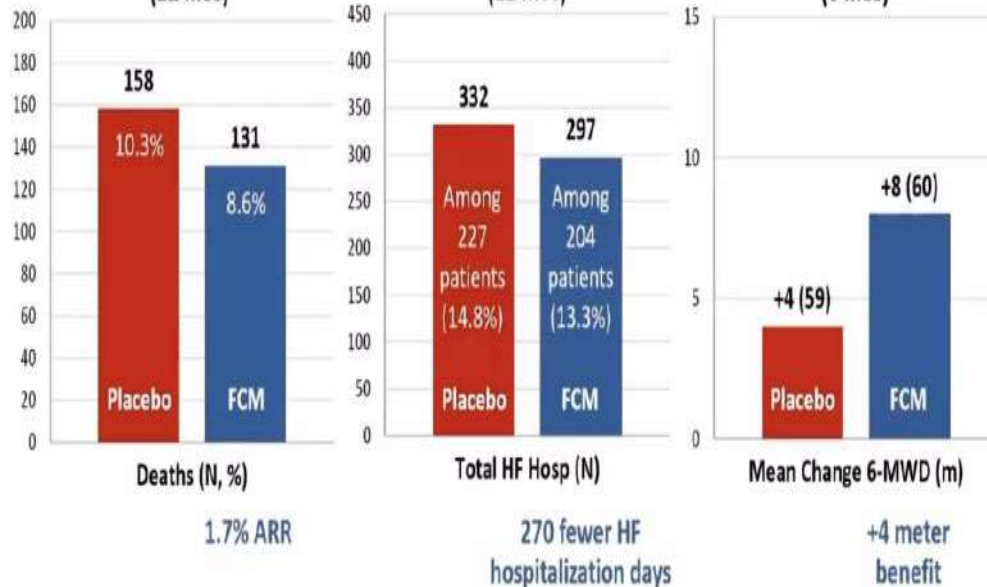
HEART-FID

P-value (Wilcoxon-Mann-Whitney test) = 0.019

All-cause Mortality (12 mos)

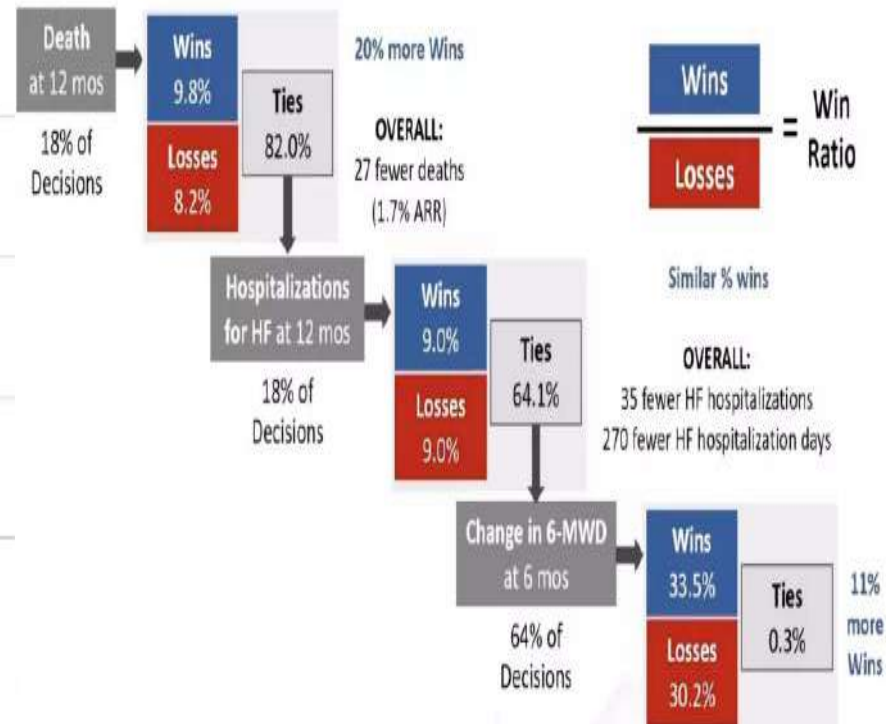
Total HF Hospitalizations (12 mos)

Change in 6-MWD (6 mos)

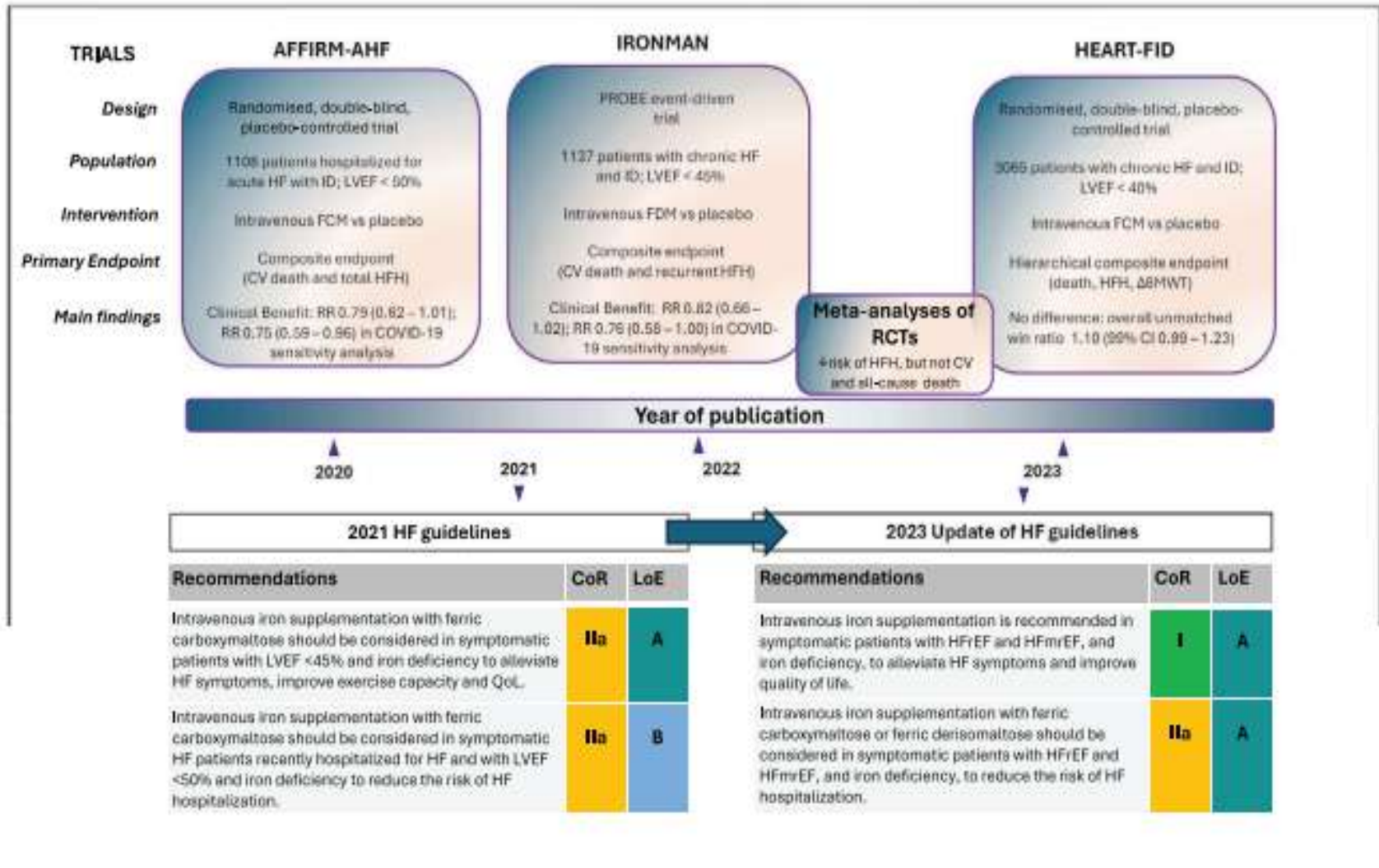


Overall Win Ratio (99%CI) = 1.10 (0.99, 1.23)




1st Imputed Dataset:



Iron Deficiency of HF



CKD and DM

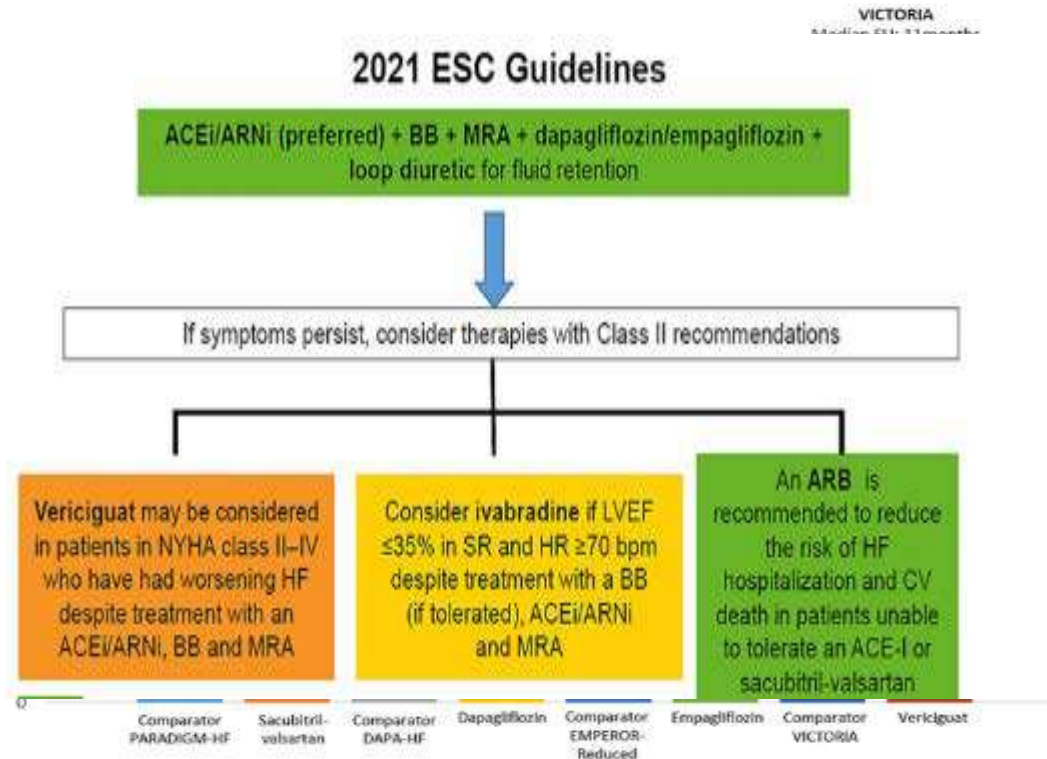
		SGLT2I			FINERENONE
		DAPA-CKD	EMPA-KIDNEY	META-ANALYSIS	FIDELITY pooled analysis
POPULATION		CKD (eGFR 25-75 ml/min/m ² and ACR ratio ≥ 200 mg/g); with/without T2DM	CKD (eGFR 20-45 or 45-90 ml/min/m ² and ACR ratio ≥ 200 mg/g); with/without T2DM	4 trials: T2DM and high CV risk 5 trials: HF 4 trials: CKD	Patients with diabetic CKD (FIDELIO-DKD and FIGARO-DKD trials)
 HF hospitalizations		HR for the composite of CV death or HFH: 0.71 (95% CI, 0.55-0.92)	HR for CV death or HFH: 0.84; 95% CI 0.67-1.07	- Overall HR for CV death or HFH: 0.77 (0.74-0.81) - Considering only CKD trials: HR 0.74 (0.66-0.82) and 0.95 (0.65-1.40) in patients with and without T2DM, respectively	HFH: HR 0.78 (0.66-0.92) CV composite (CV death, non-fatal MI, non-fatal stroke, or HFH): HR 0.86 (0.78-0.95)
 CV death			HR for CV death: 0.84 (0.60-1.19)	Overall HR for CV death: 0.86 (0.81-0.92)	CV death: HR 0.88 (0.76-1.02)
 Kidney Outcomes		Sustained decline in eGFR of ≥50%, ESKD*, CV or renal death: HR 0.61 (0.51-0.72)	Progression of CKD or CV death: HR 0.72 (0.64-0.82)	RR for the risk of kidney disease progression: 0.63 (0.58-0.69), with similar RRs in patients with and without T2DM	Kidney failure, sustained ≥57% decrease in eGFR from baseline over ≥4 weeks, or renal death: HR 0.78 (0.66-0.92)

CKD and DM

Recommendation Table 4 — Recommendations for the prevention of heart failure in patients with type 2 diabetes mellitus and chronic kidney disease

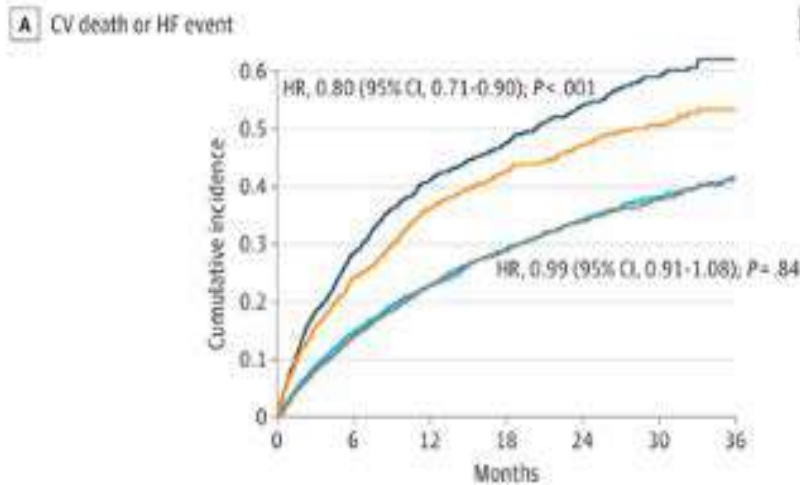
Recommendations	Class ^a	Level ^b
In patients with T2DM and CKD, ^c SGLT2 inhibitors (dapagliflozin or empagliflozin) are recommended to reduce the risk of HF hospitalization or CV death. ^{5,7,35}	I	A
In patients with T2DM and CKD, ^c finerenone is recommended to reduce the risk of HF hospitalization. ^{10,11,34,40}	I	A

Soluble guanylate cyclase stimulators

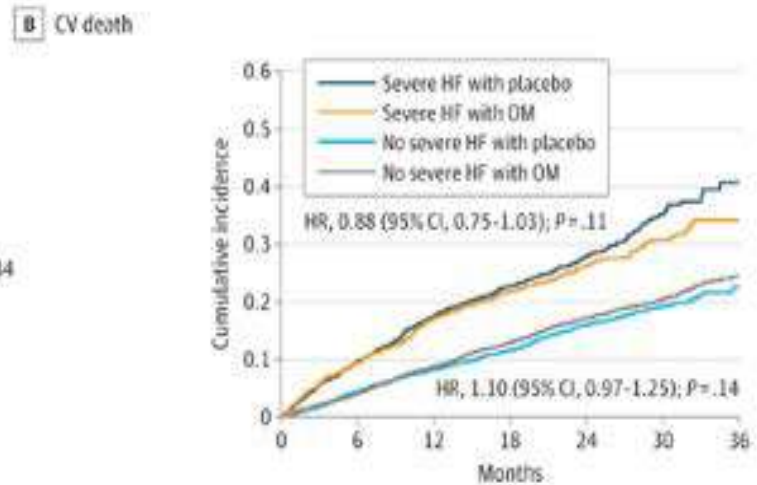


Myosin Activators

- Selective cardiac myosin activator omecamtiv mecarbil
- GALACTIC-HF Trial



No. at risk	0	6	12	18	24	30	36
No severe HF with placebo	2960	2492	2228	1602	1003	479	97
Severe HF with placebo	1152	808	650	464	290	119	13
No severe HF with OM	3014	2565	2271	1651	1051	516	96
Severe HF with OM	1106	814	671	480	320	137	31



No. at risk	0	6	12	18	24	30	36
No severe HF with placebo	2960	2793	2641	1991	1273	628	131
Severe HF with placebo	1152	1022	911	687	450	192	26
No severe HF with OM	3014	2857	2671	2022	1326	659	132
Severe HF with OM	1106	976	874	656	438	186	40

Acute Heart Failure

DICTATE-AHF: Early Dapagliflozin Initiation in Acute Heart Failure

Study population

Adult patients with

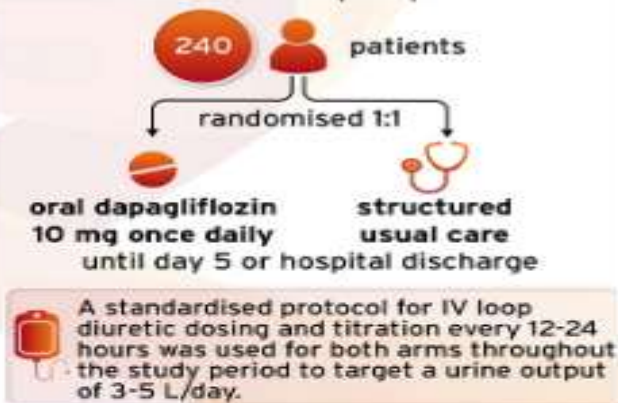
- type 2 diabetes
- estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73m²
- admitted to hospital with ADHF
- current or planned treatment with intravenous (IV) loop diuretics



Protocol amended in September 2021 to allow enrolment of patients with or without type 2 diabetes and to decrease the eGFR inclusion criterion to 25 mL/min/1.73m² due to new safety data in these groups.

Who and what?

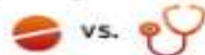
Within 24 hours of hospital presentation:



Primary endpoint

Diuretic efficiency (diuretic response) expressed as the cumulative change in weight per cumulative loop diuretic dose (IV and oral) from enrolment to day 5 or discharge, if sooner.

After adjusting for baseline weight:



odds ratio 0.65, 95% CI 0.41 to 1.01, p=0.06

Exploratory endpoints

24-hour natriuresis increased with



24-hour urine output increased with

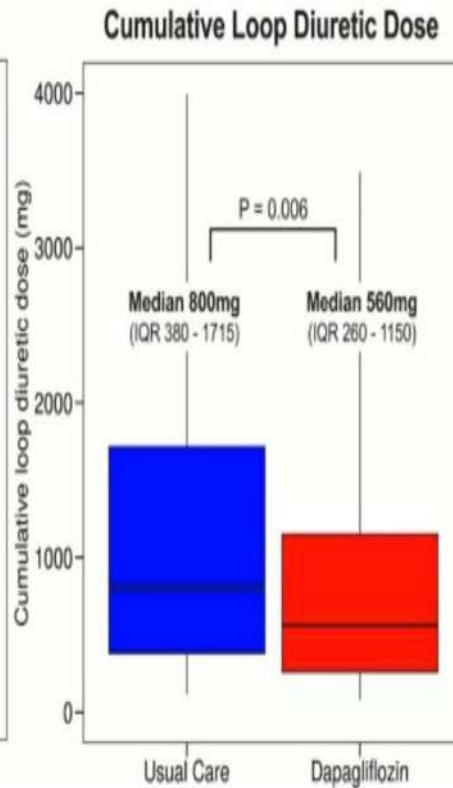
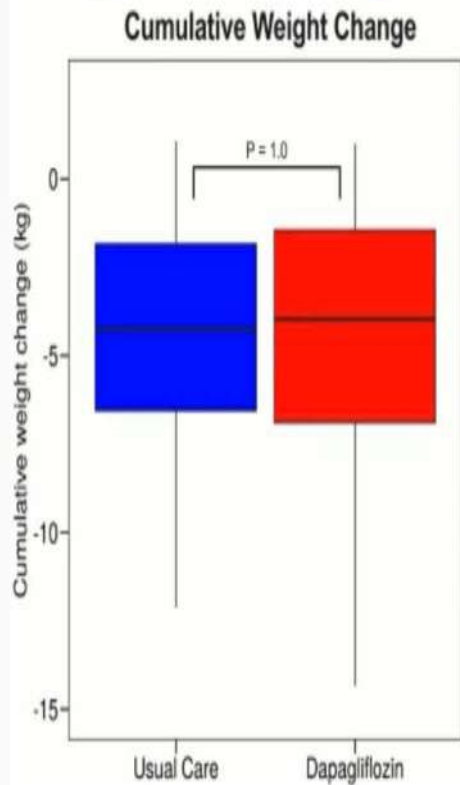


time to hospital discharge decreased with

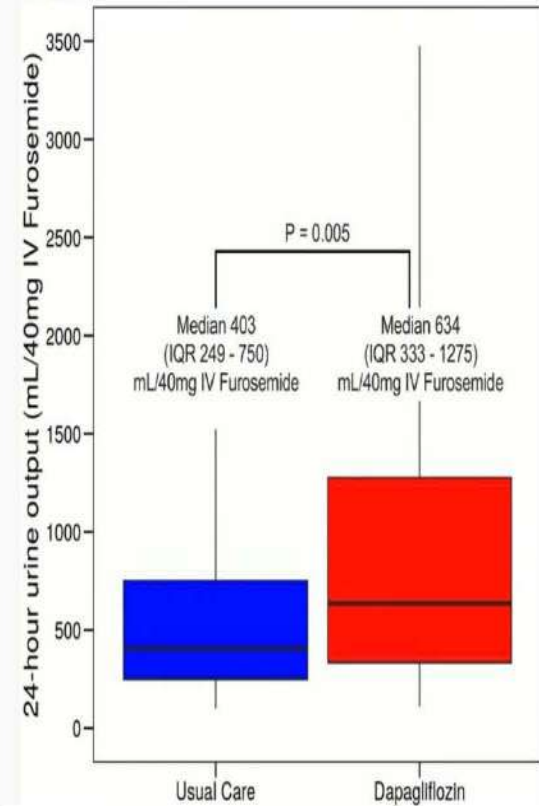


DICTATE-AHF: Early Dapagliflozin Initiation in Acute Heart Failure

Primary Outcome Components



Improved 24-Hour Diuresis with Dapagliflozin



The Pragmatic Urinary Sodium-based treatment algorithm in Acute Heart Failure (PUSH-AHF) trial

Study population

Patients

- AHF requiring treatment with intravenous (IV) loop diuretics

The inclusion and exclusion criteria were intentionally broad to enrol a contemporary, representative, all-comer AHF population.

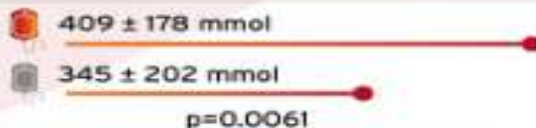
Where?



University Medical Centre Groningen, the Netherlands

Primary endpoints: $p < 0.025$ for each was considered statistically significant

24-hour natriuresis

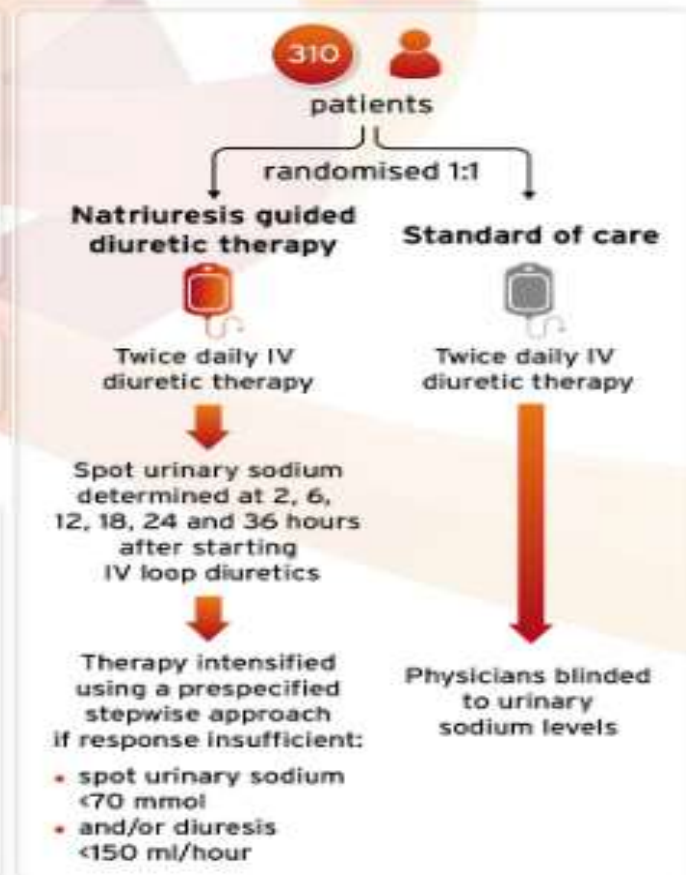


Combined endpoint of time to all-cause mortality or HF rehospitalisation at 180 days



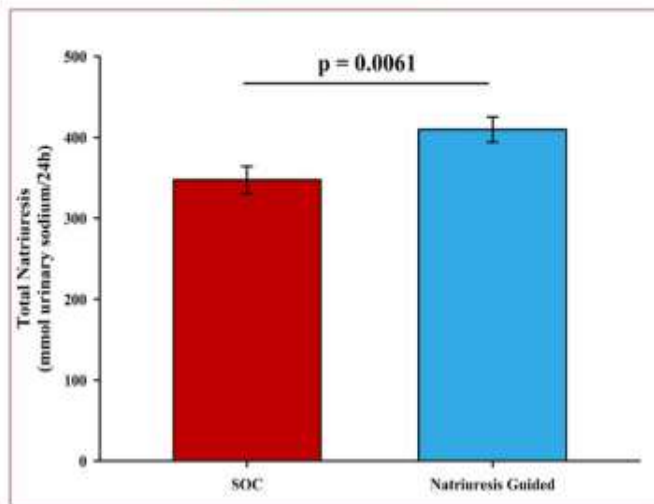
Hazard ratio 0.92; 95% CI 0.62 to 1.38; $p = 0.6980$

Who and what?

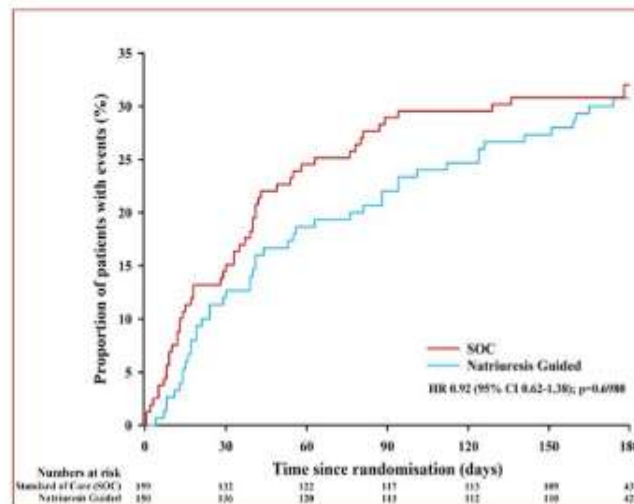


The Pragmatic Urinary Sodium-based treatment algorithm in Acute Heart Failure (PUSH-AHF) trial

Natriuresis

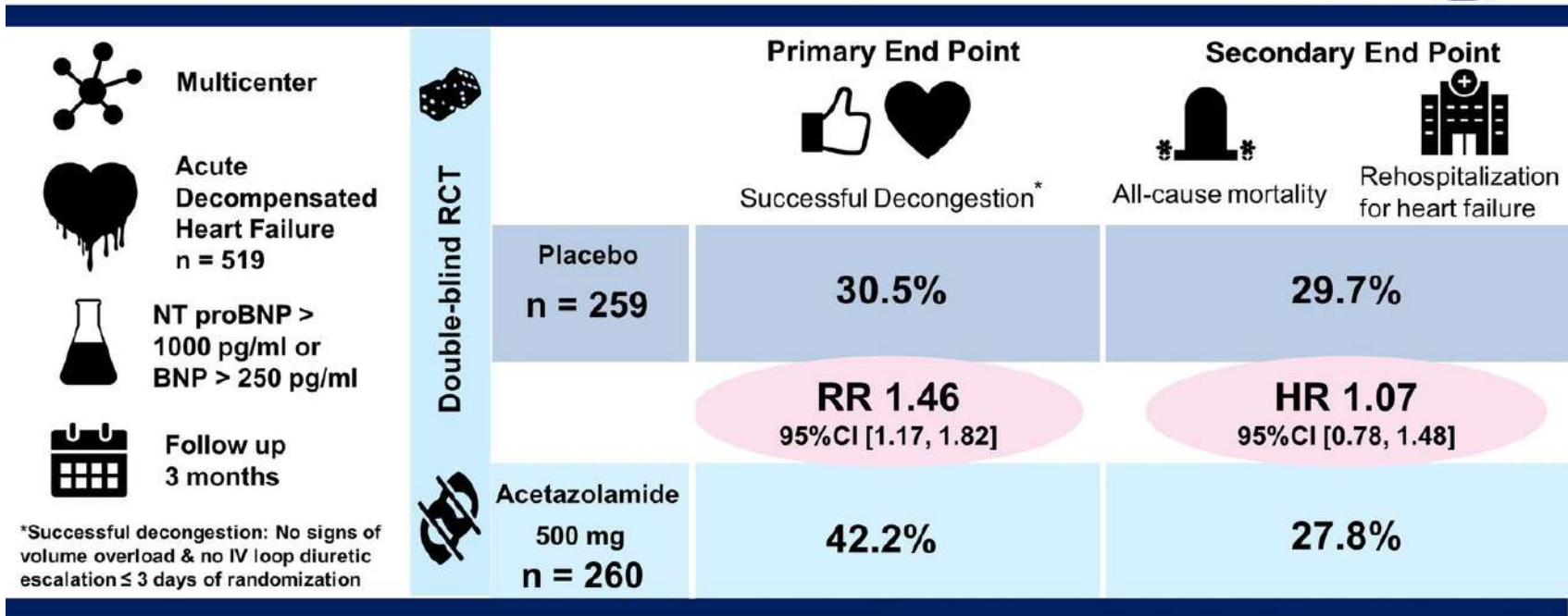


180-day all-cause mortality or adjudicated heart failure rehospitalization



Acetazolamide

Does Acetazolamide Help Decongest in Acute Decompensated Heart Failure with Volume Overload (ADVOR)?



Conclusion: The addition of acetazolamide to loop diuretic therapy in patients with acute decompensated heart failure resulted in a greater incidence of successful decongestion

Mullens W, Dauw J, Martens et al. ADVOR Study Group. Acetazolamide in Acute Decompensated Heart Failure with Volume Overload. N Engl J Med. 2022 Aug 27. doi: 10.1056/NEJMoa2203094. Visual Abstract by @Api_chew

ATTRibute-CM: Study Design

Key eligibility criteria

- Subjects with diagnosed ATTR-CM (WT or variant)
- NYHA Class I-III
- ATTR-positive biopsy or 99mTc scan
- Light chain amyloidosis excluded if diagnosis by 99mTc

Screening and randomization

800 mg acoramidis HCl twice daily

N = 421

placebo twice daily

N = 211

Efficacy assessment included 611 participants in the pre-specified mITT population (eGFR ≥ 30 mL/min/1.73 m²)

Tafamidis usage allowed after Month 12

30-month primary endpoint:

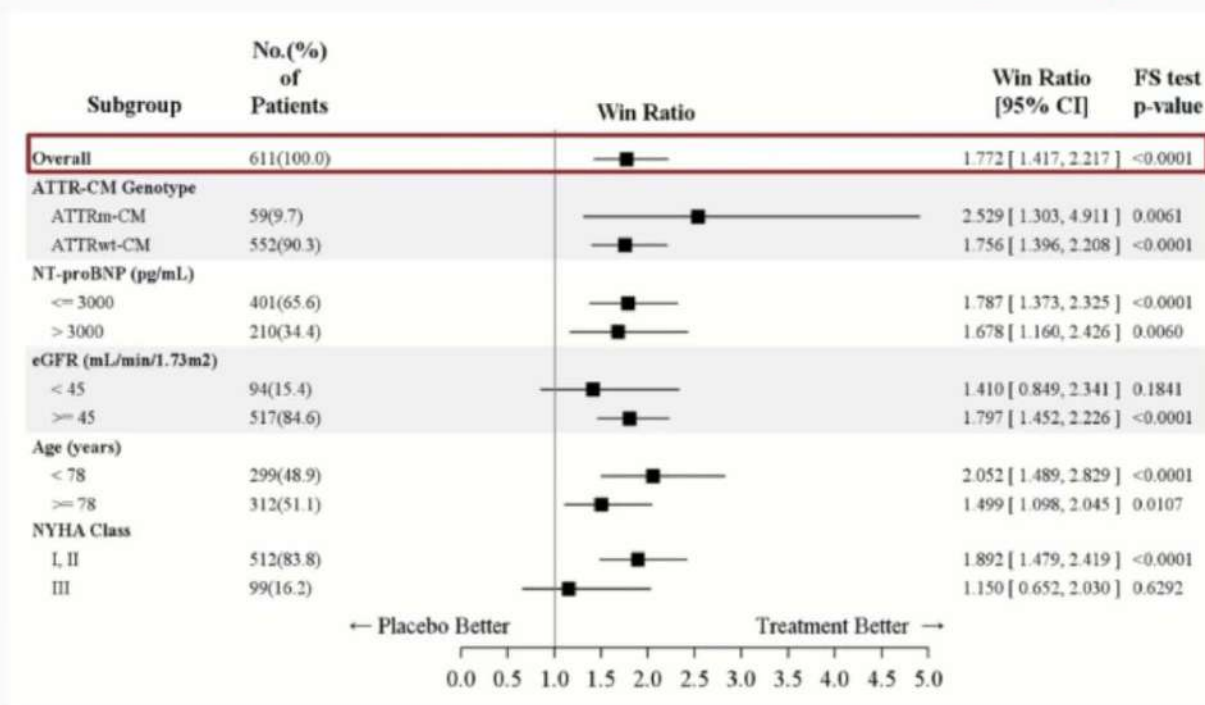
Hierarchical analysis consisting of all-cause mortality, cumulative frequency of CVH, change from baseline in NT-proBNP, and change from baseline in 6MWD

800 mg acoramidis HCl twice daily

Open-label extension

6MWD = Six-minute walk distance; NYHA = New York heart association; 99mTc = Technetium labeled pyrophosphate (PYP) or bisphosphonate (e.g., DPD); mITT = Modified intent-to-treat. eGFR = Estimated glomerular filtration rate. ClinicalTrials.gov identifier: NCT03860935.

ATTRibute-CM: Primary Outcome Overall and by Subgroups



FS = Finkelstein-Schoenfeld; CI = Confidence interval.

Mavacamten

- Cardiac myosin adenosine triphosphatase inhibitor
- VALOR-HCM trial ,HCM and symptomatic LVOTO, improvements in LVOT gradients and symptoms,need for septal reduction therapy
- EXPLORER-HCM trial showed peak oxygen uptake
- EXPLORER-HCM and MAVA-LTE studies showed that mavacamten benefits were reproduced and maintained regardless of beta-blocker use

Resting/provocable LVOTO ≥ 50 mmHg

Symptoms

Beta-blockers or verapamil
may be considered
(Class IIb)

Beta-blockers
(Class I)

Still symptomatic or intolerant/contraindication to beta-blockers

Verapamil
(Class I)

OR

Diltiazem
(Class I)

Still symptomatic

Disopyramide
(Class I)

OR

Mavacamten
(Class IIa)

Still symptomatic

Septal reduction therapies
(Class I)

Anti-inflammator Therapy

- Il-6 antagonist: **Ziltivecimab**(HERMES study)
- Selective myeloperoxidase inhibitor:
Mitiperstat (ENDEAVOR Study)

Omega-3 Supplementation

Omega-3 Supplementation and Heart Failure

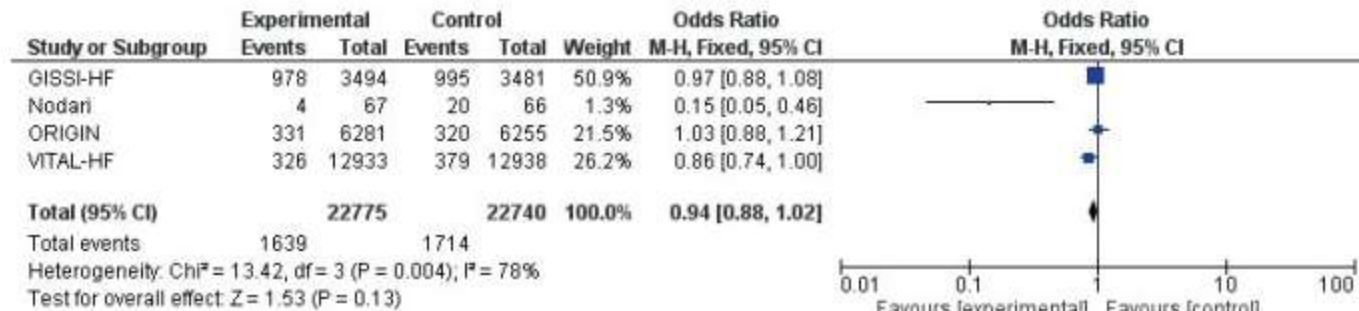
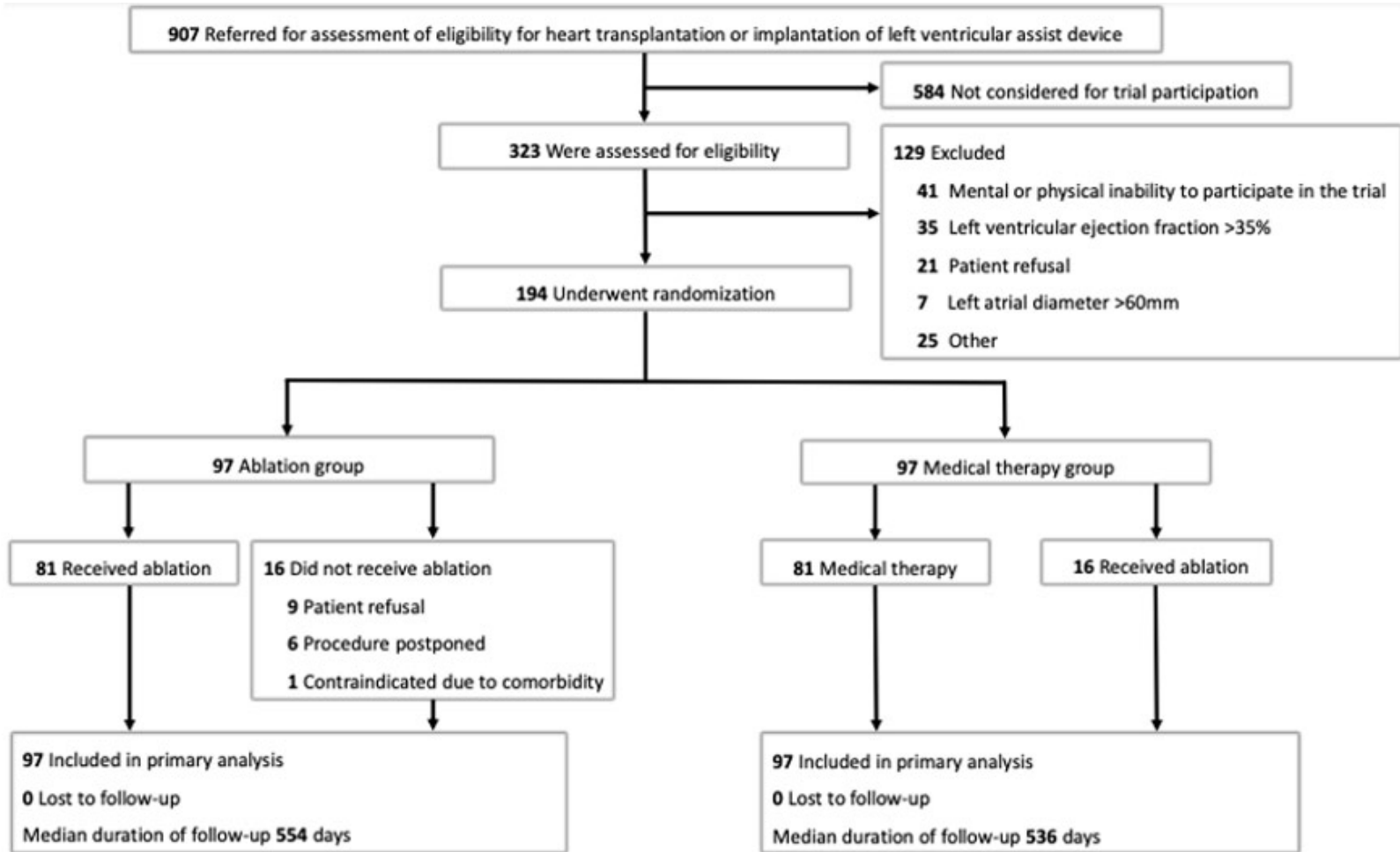


Fig. 6. Meta-analysis with individual study results

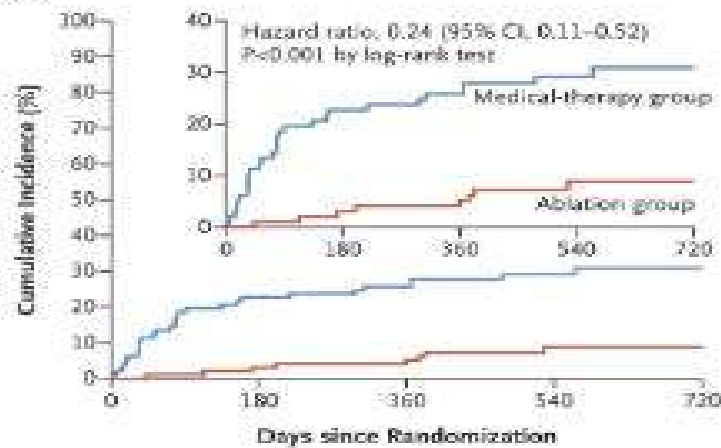
AF ABLATION: CASTLE-HTx



CASTLE-HTx - Supplementary data - Figure S1. Enrollment, Randomization, and Follow-up

CASTLE-HTx

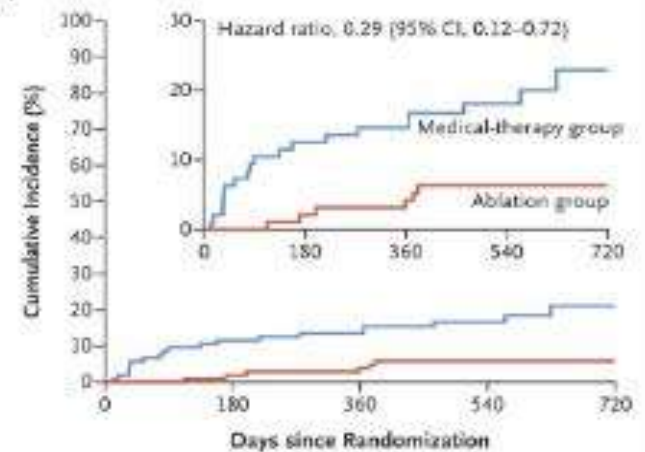
A Primary End Point



No. at Risk

Medical-therapy group	97	75	72	41	12
Ablation group	97	94	88	50	20

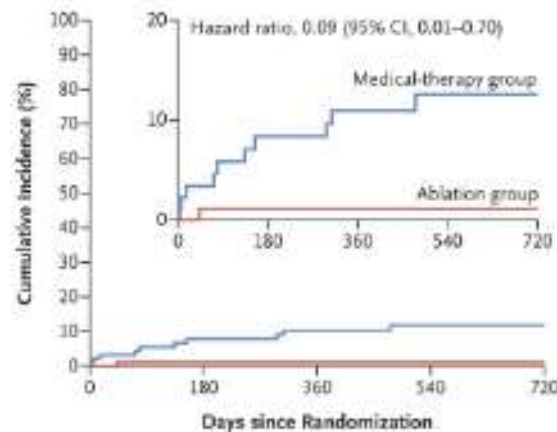
B Death from Any Cause



No. at Risk

Medical-therapy group	97	85	83	45	13
Ablation group	97	95	93	51	20

C Implantation of a Left Ventricular Assist Device



No. at Risk

Medical-therapy group	97	79	76	42	12
Ablation group	97	94	92	51	20

CRT Upgrade

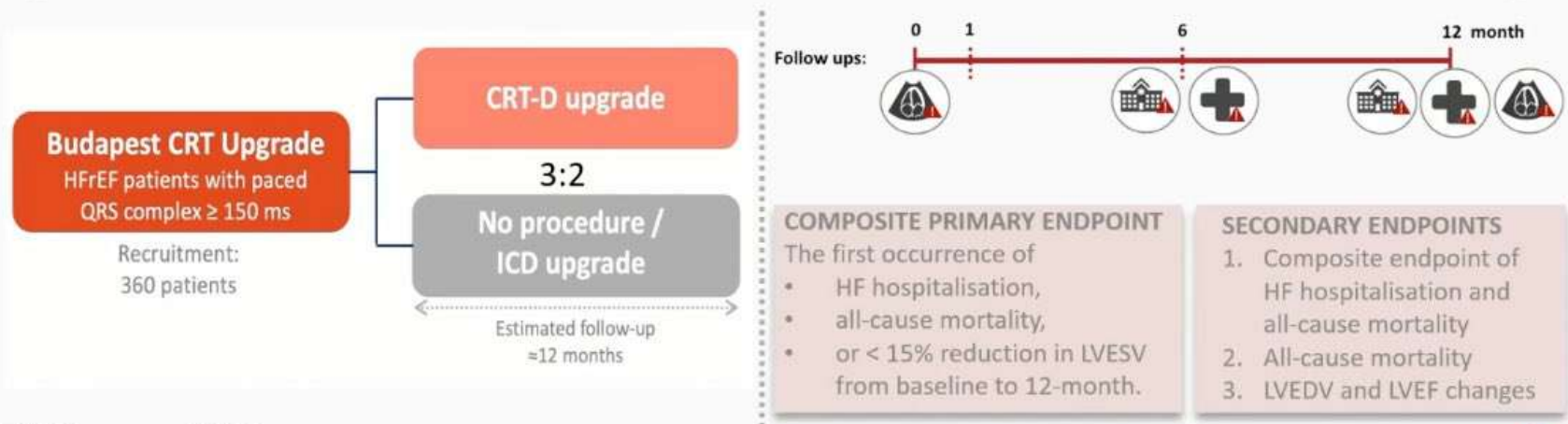
BUDAPEST CRT Upgrade - Study design



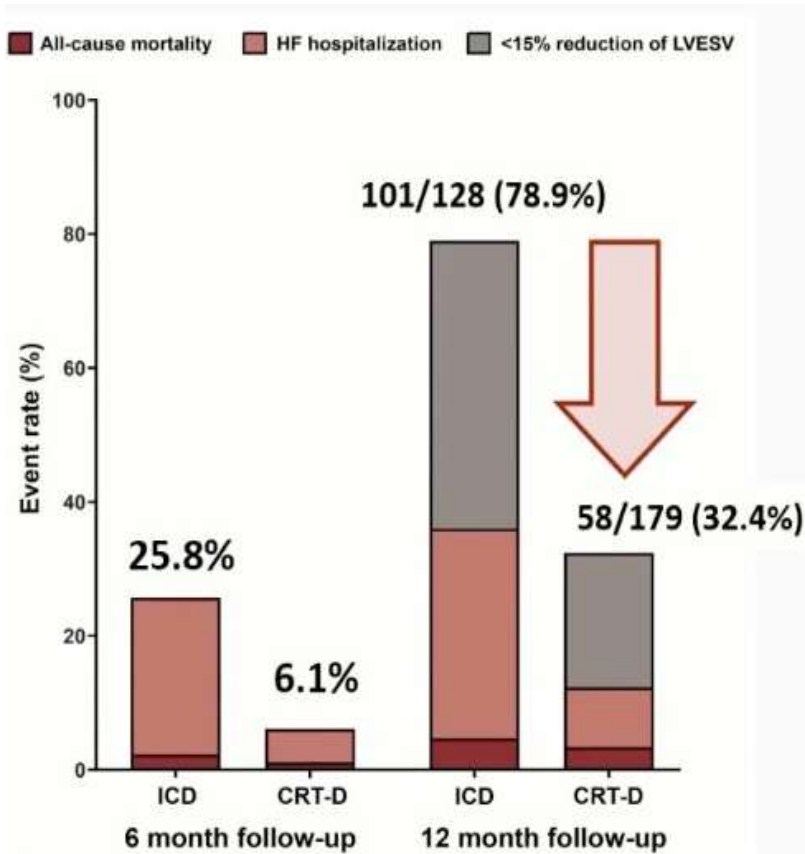
A Multicentre, Randomised, Controlled, Investigator-initiated Trial testing the hypothesis that CRT-D upgrade compared to ICD only would be associated with improved clinical outcomes

Key Inclusion Criteria: HFrEF patients with a prior pacemaker or ICD, RV pacing 20-100%, paced QRS complex ≥ 150 ms and GDMT

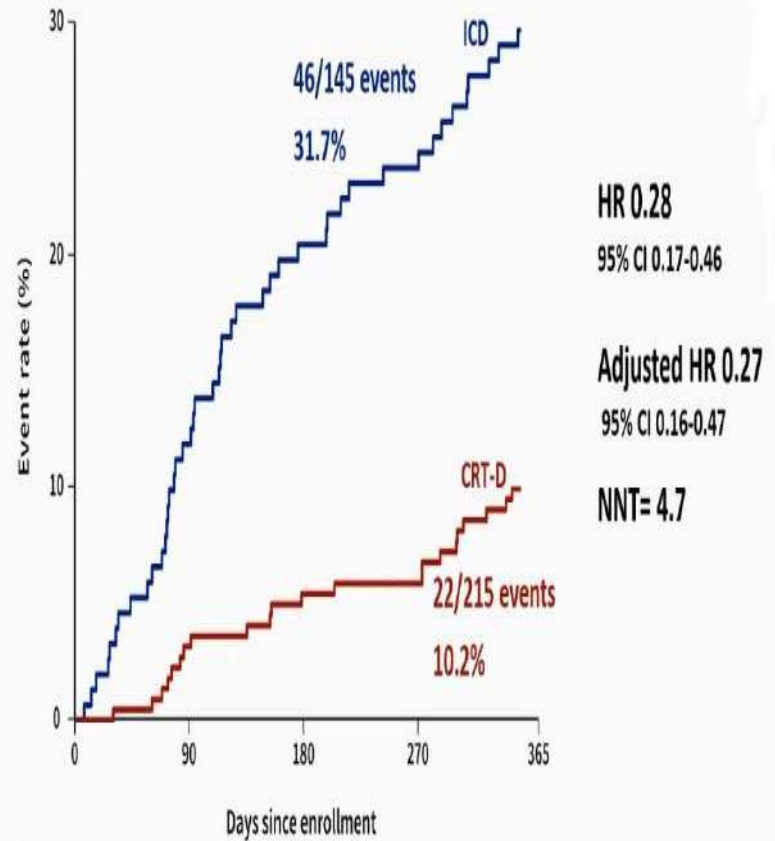
Key Exclusion Criteria: intrinsic QRS with LBBB morphology, severe renal dysfunction, severe RV dilatation, ACS events



BUDAPEST CRT Upgrade



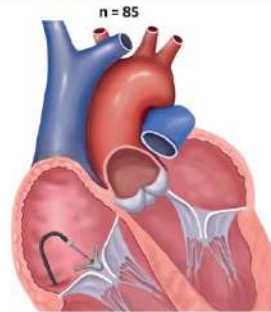
Secondary Endpoint: All-cause mortality or HF hospitalisation



T-TEER and M-TEER

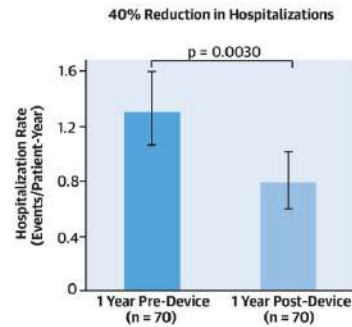
CENTRAL ILLUSTRATION: 1-Year Outcomes From the TRILUMINATE Trial

TRILUMINATE Study



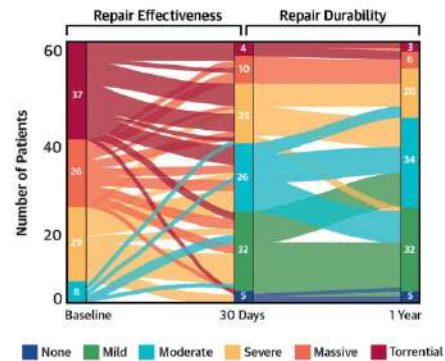
n = 85
Major Adverse Events: 7.1%
Cardiovascular Mortality: 4.8%

Clinical Implications



Durability of Repair

TR Reduction at 1 Year ≥ 1 : 87%



Lurz, P. et al. J Am Coll Cardiol. 2021;77(3):229-39.

New Perspectives

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Review Article | Published: 10 April 2024

Cardiovascular disease and cancer: shared risk factors and mechanisms

[Nicholas S. Wilcox](#), [Uri Amit](#), [Jacob B. Reibel](#), [Eva Berlin](#), [Kendyl Howell](#) & [Bonnie Ky](#) 

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Future Research Area

Cureus
Part of **SPRINGER NATURE**

Open Access Review
Article

DOI: 10.7759/cureus.59661

Artificial Intelligence and Its Role in Diagnosing Heart Failure: A Narrative Review

Review began 04/25/2024
Review ended 05/01/2024

Diptiman Medhi ¹, Sushmitha Reddy Kamidi ², Kannuru Paparaju Mamatha Sree ³, Shifa Shaikh ⁴,
Shanida Rasheed ⁵, Abdul Hakeem Thengu Murichathil ⁶, Zahra Nazir ⁷

> [Balkan Med J.](#) 2023 May 8;40(3):151-152. doi: 10.4274/balkanmedj.galenos.2023.06042023.
Epub 2023 Apr 7.

The Role of Artificial Intelligence in Coronary Artery Disease and Atrial Fibrillation

Mert İlker Hayiroğlu ¹, Servet Altay ²

Affiliations + expand

PMID: 37025078 PMCID: PMC10175890 DOI: 10.4274/balkanmedj.galenos.2023.06042023

medical and surgical interventions specific to HF patients rely significantly on early identification of HF. Hospitalization and treatment costs for HF are high, with readmissions increasing the burden. AI can help improve diagnostic accuracy by recognizing patterns and using them in multiple areas of HF management. AI has shown promise in offering early detection and precise diagnoses with the help of ECG analysis, advanced cardiac imaging, leveraging biomarkers, and cardiopulmonary stress testing. However, its challenges include data access, model interpretability, ethical concerns, and generalizability across diverse populations. Despite these ongoing efforts to refine AI models, it suggests a promising future for HF diagnosis. After applying exclusion and inclusion criteria, we searched for data available on PubMed, Google Scholar, and the Cochrane Library and found 150 relevant papers. This review focuses on AI's significant contribution to HF diagnosis in recent years, drastically altering HF treatment and outcomes.

Thank you for attention...