

Restoring Reserve: Where Does Vericiguat Fit Today

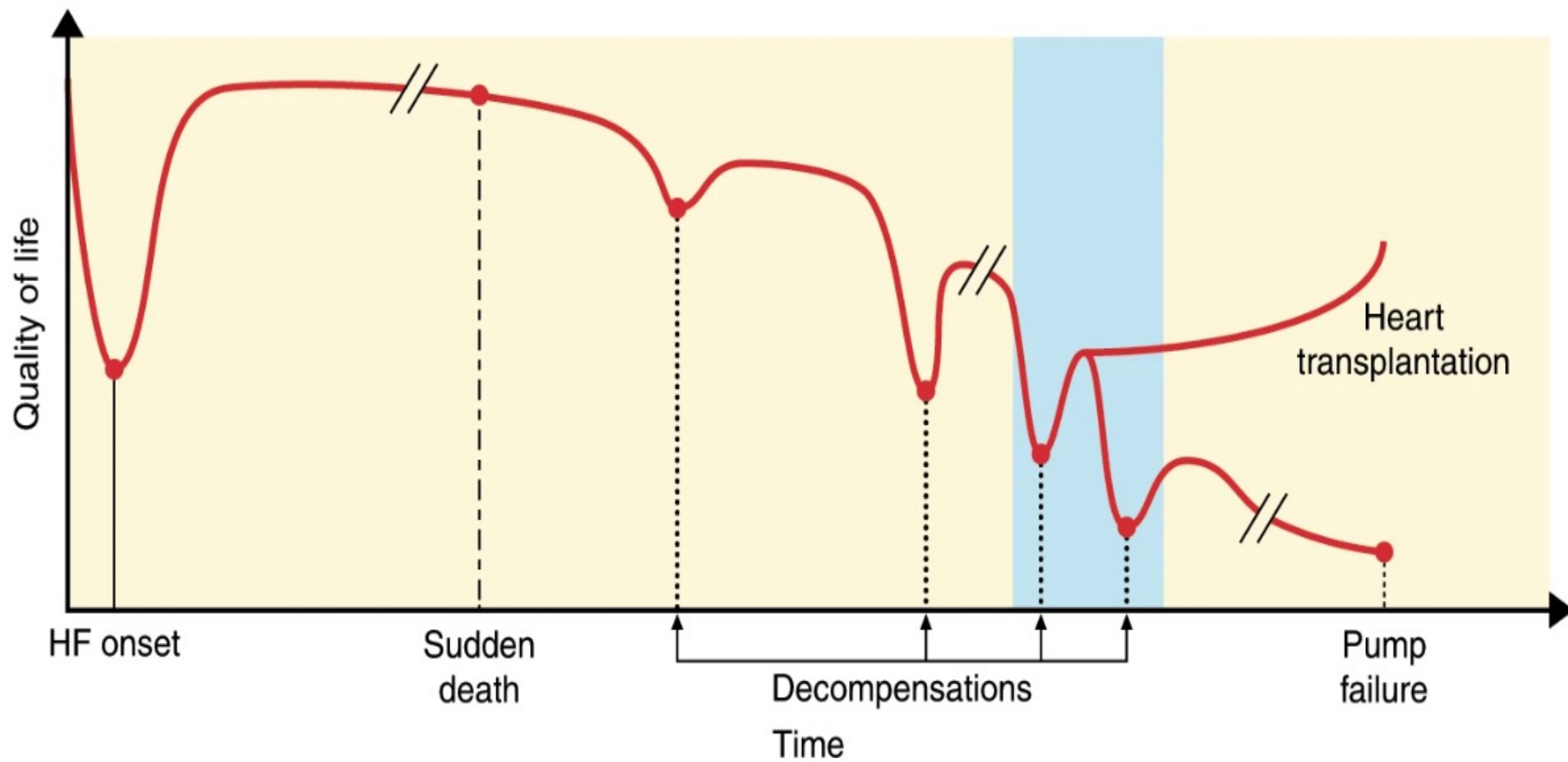
Kenneth Dulnuan, MD

Staten Island University Hospital



NorthwellSM
Cardiovascular Institute

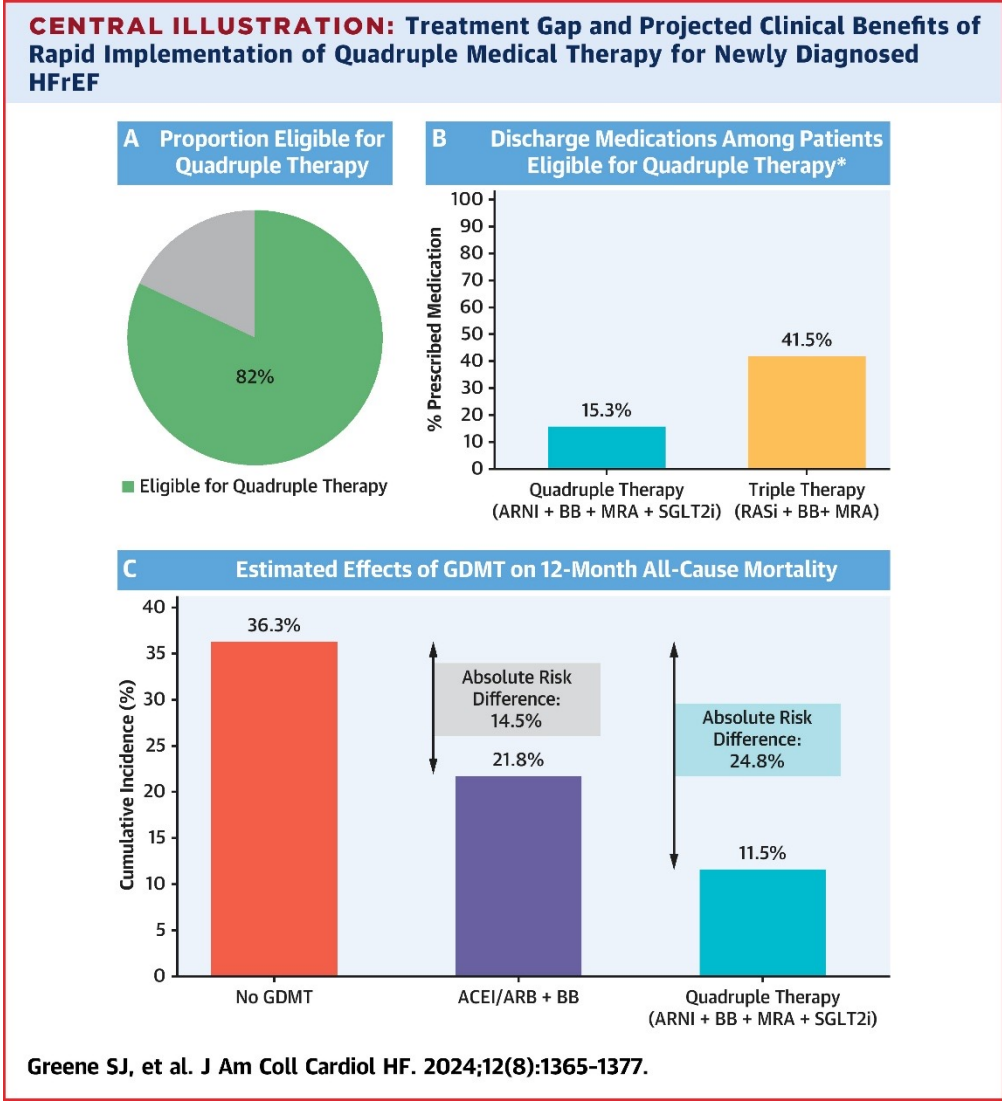
April 16, 2026



FOUR-PILLAR GDMT

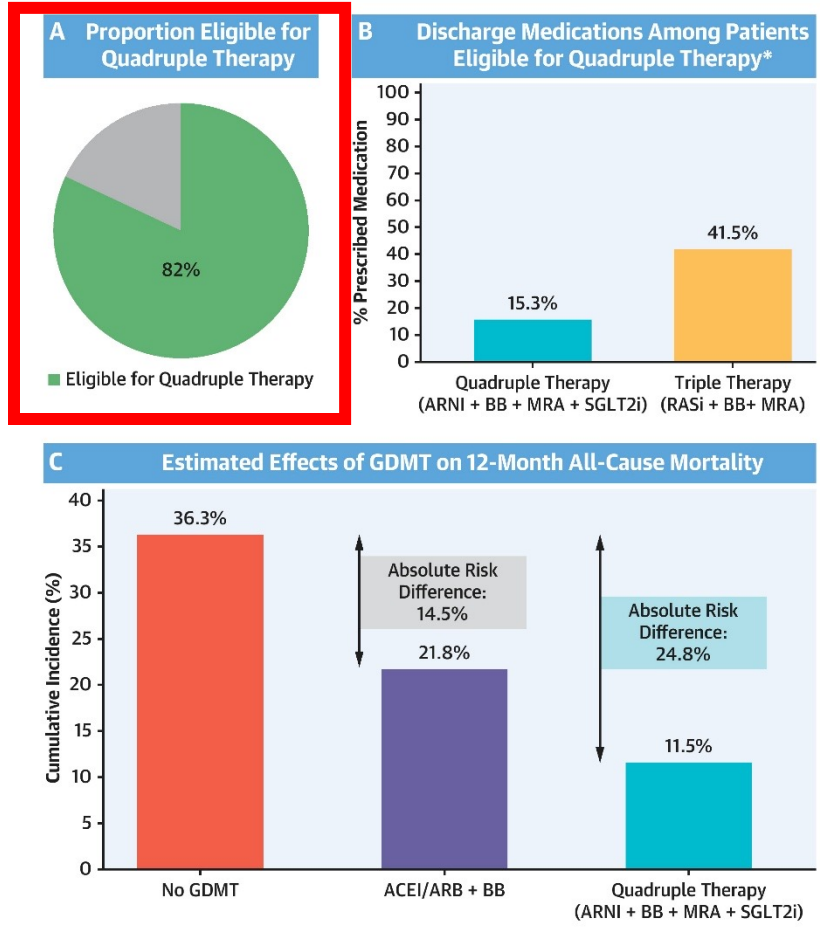


FOUR-PILLAR GDMT



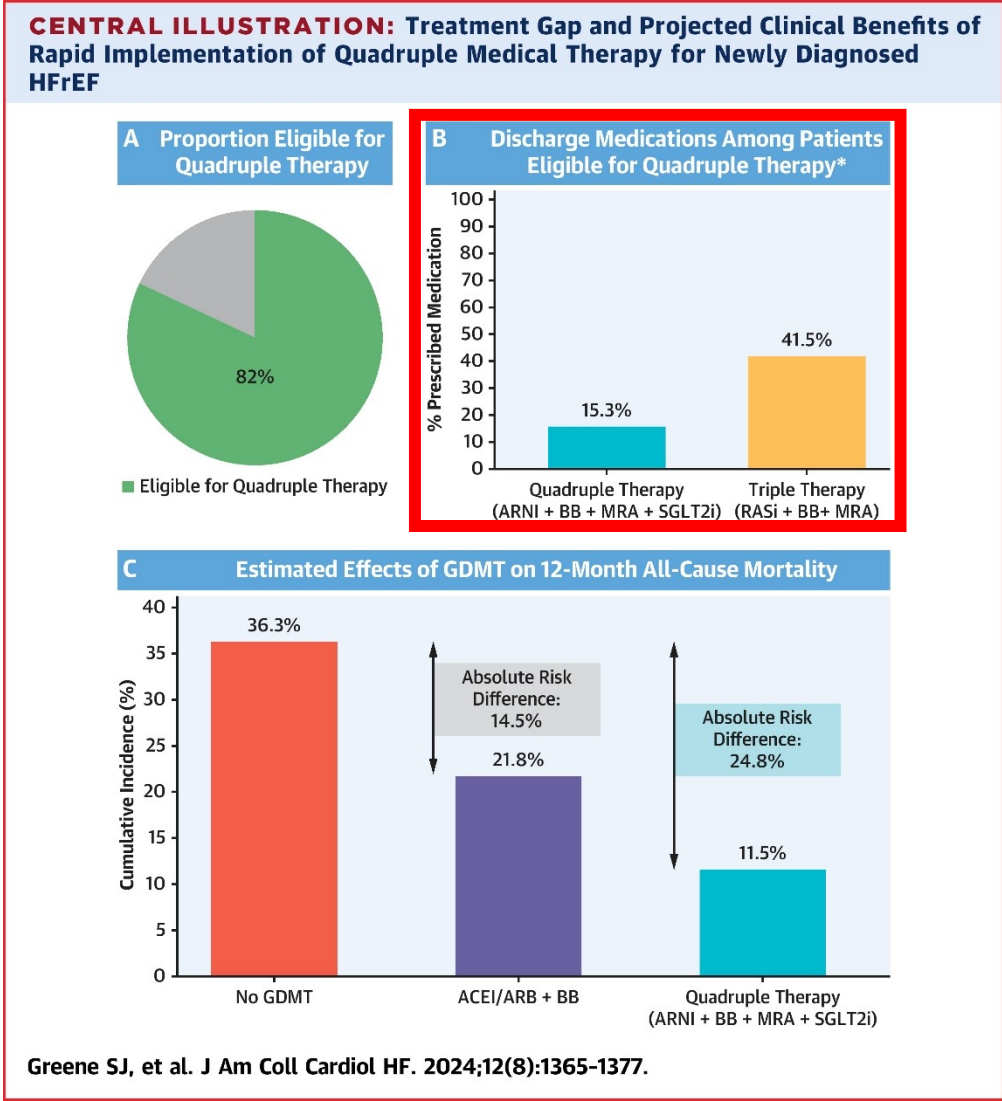
FOUR-PILLAR GDMT

CENTRAL ILLUSTRATION: Treatment Gap and Projected Clinical Benefits of Rapid Implementation of Quadruple Medical Therapy for Newly Diagnosed HFrEF

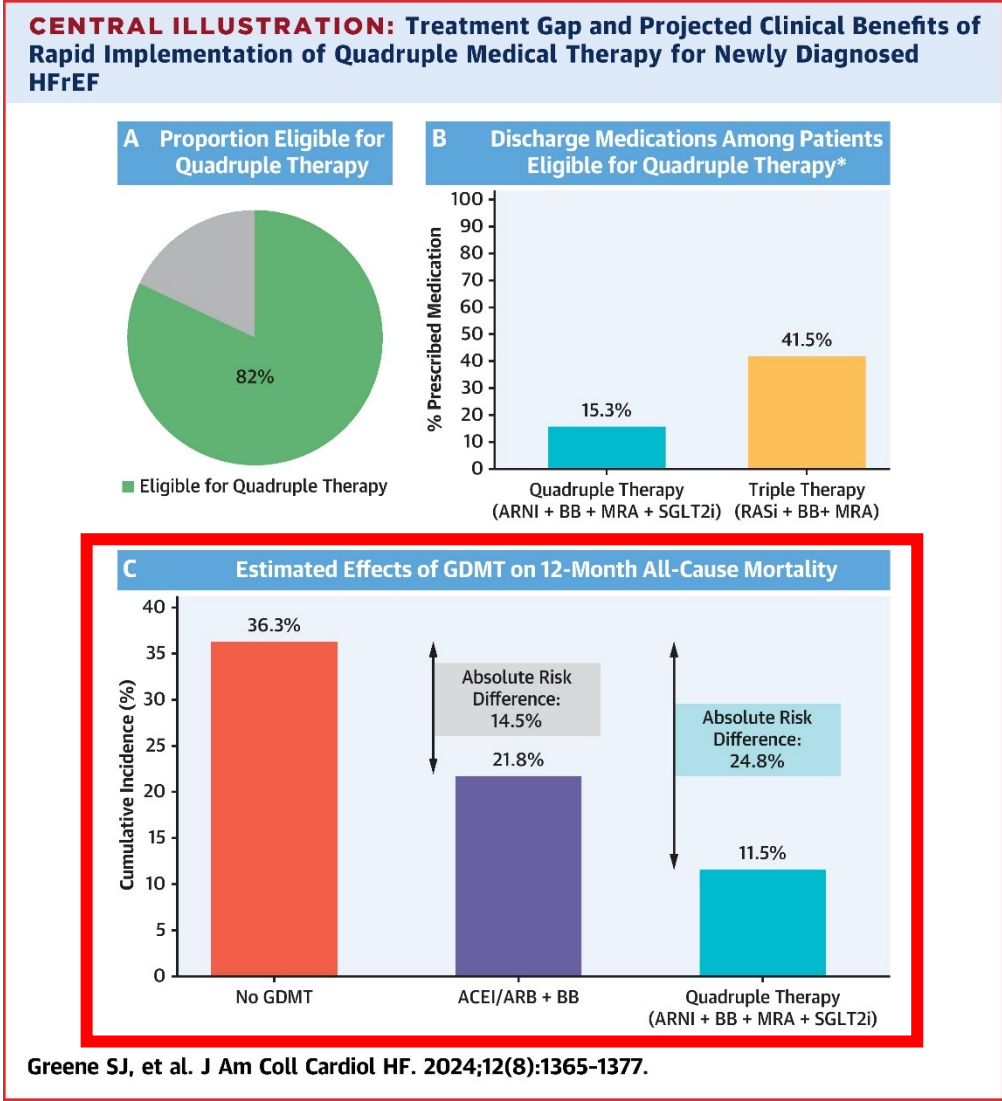


Greene SJ, et al. J Am Coll Cardiol HF. 2024;12(8):1365-1377.

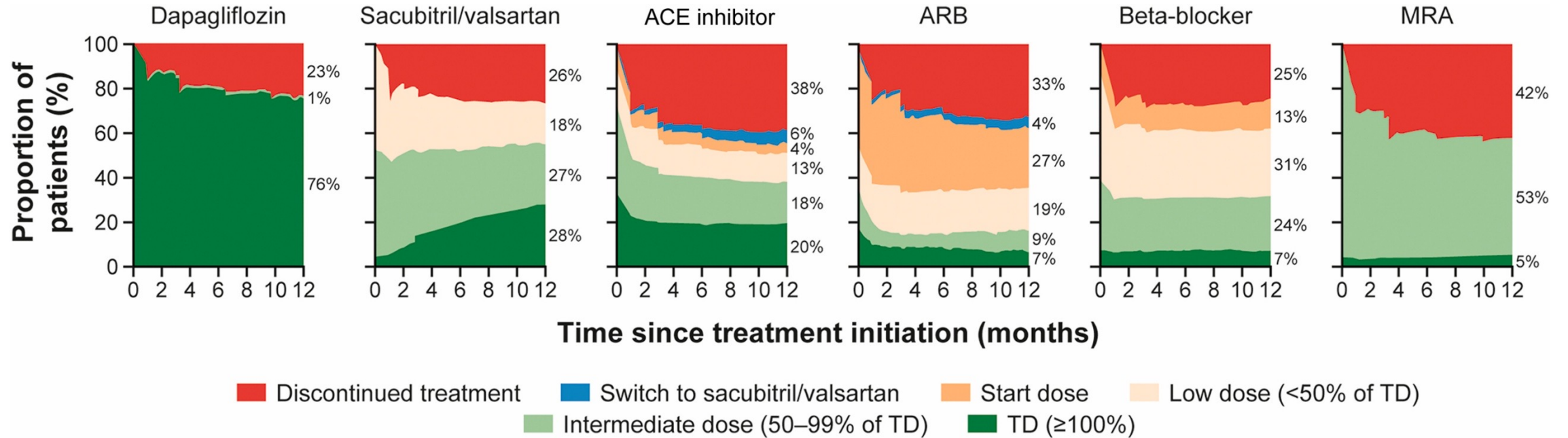
FOUR-PILLAR GDMT



FOUR-PILLAR GDMT



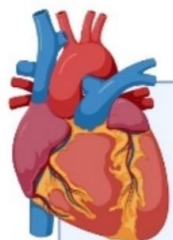
FOUR-PILLAR GDMT



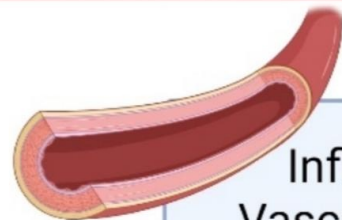


FIFTH PILLAR?

Cardiovascular effects of NO-sGC-cGMP impairment

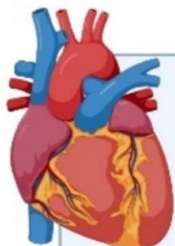


Inflammation
Fibrosis
Hypertrophy
Ventricular remodelling



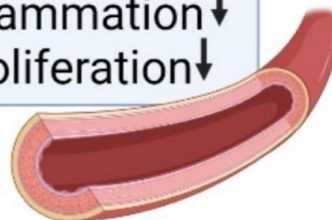
Inflammation
Vascular stiffness
Vascular remodelling

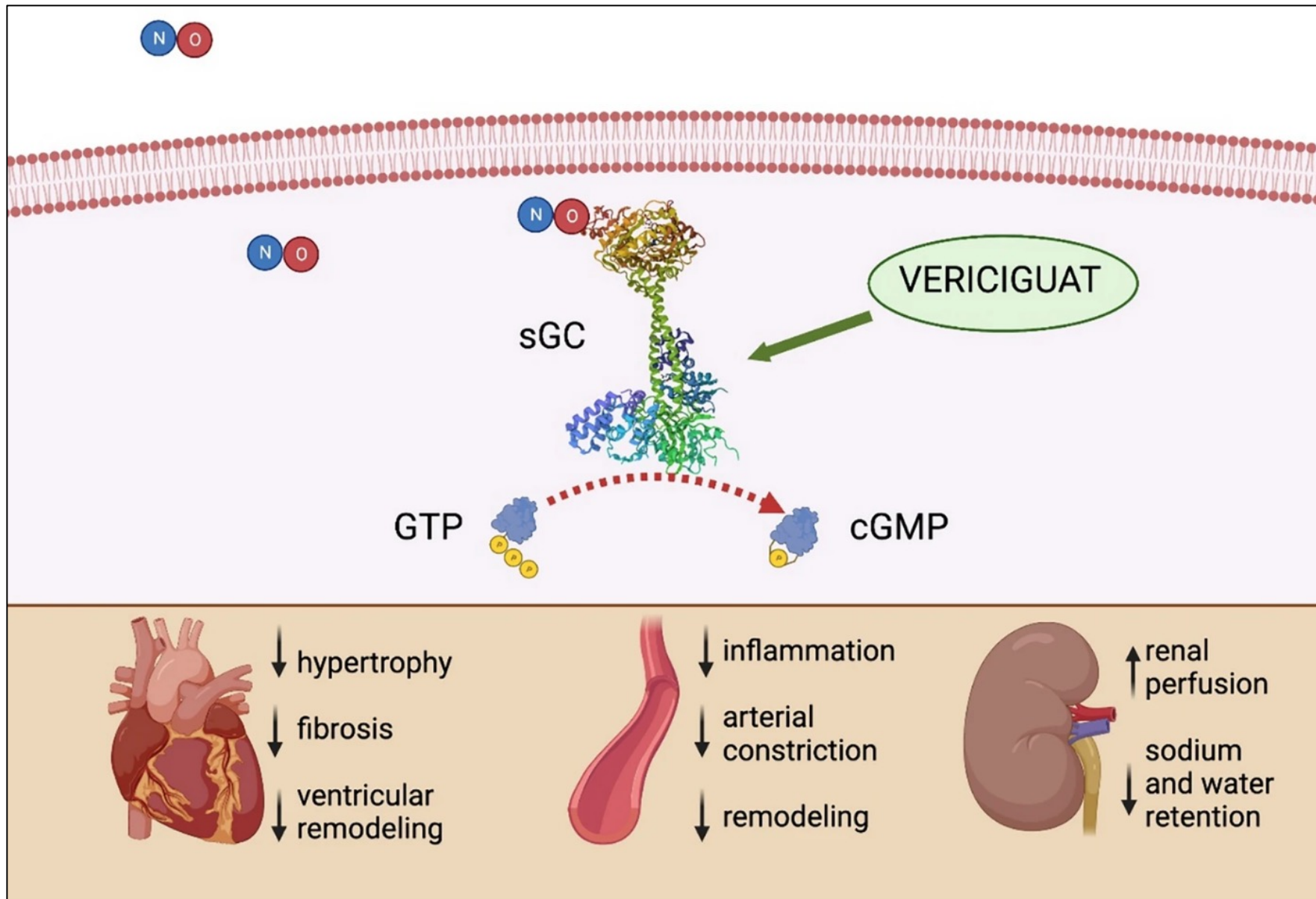
Cardiovascular effects of NO-sGC-cGMP stimulation



Hypertrophy ↓
Fibrosis ↓
Coronary blood flow ↑
LV relaxation/compliance ↑
Afterload/systemic compliance ↑
Ventriculo-arterial coupling ↑

Blood flow ↑
Vasorelaxation ↑
Inflammation ↓
Proliferation ↓





LANDMARK TRIALS ON VERICIGUAT IN HF

- VICTORIA (2020)
- VICTOR (2025)

VICTORIA TRIAL

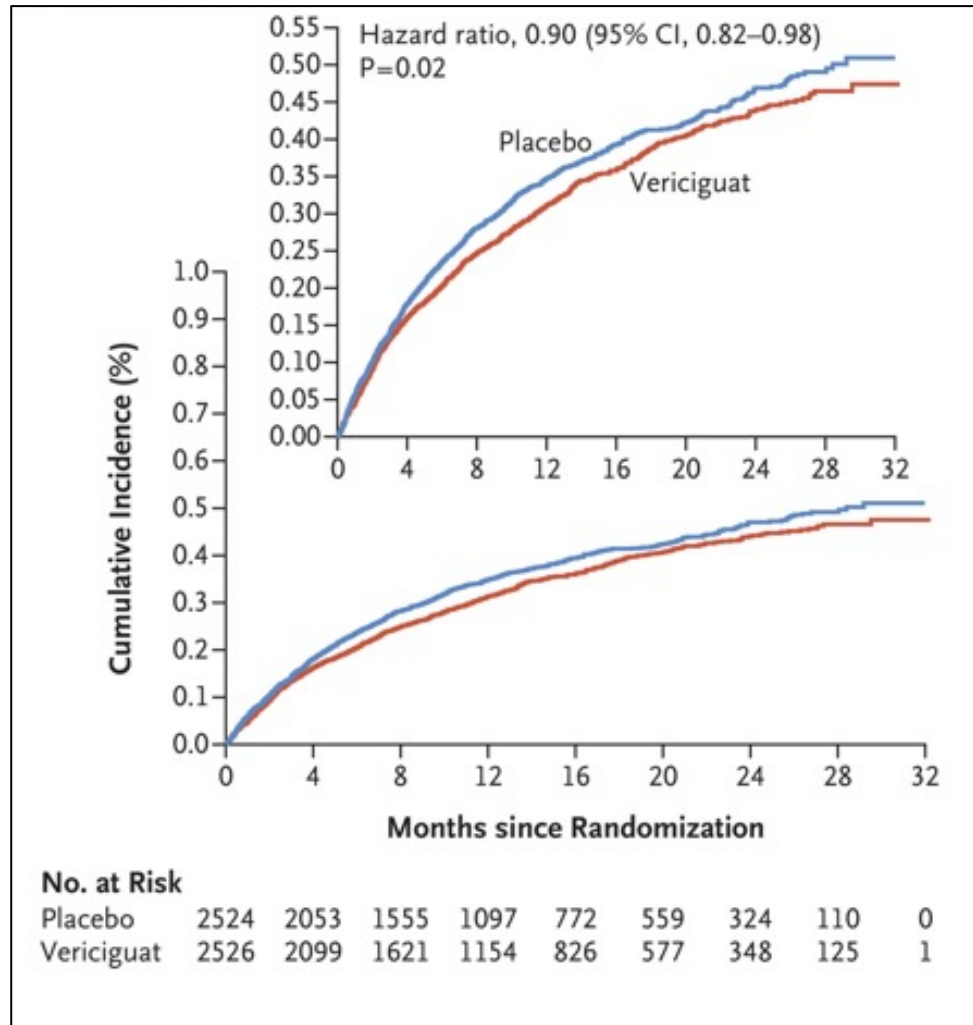
INCLUDED

- EF <45%
- NYHA II-IV
- BNP \geq 300 or NT-proBNP \geq 1,000 (sinus)
or BNP \geq 500 or NT-proBNP \geq 1,600 (AF)
- Recent worsening HF resulting to an admission of IV diuretics

EXCLUDED

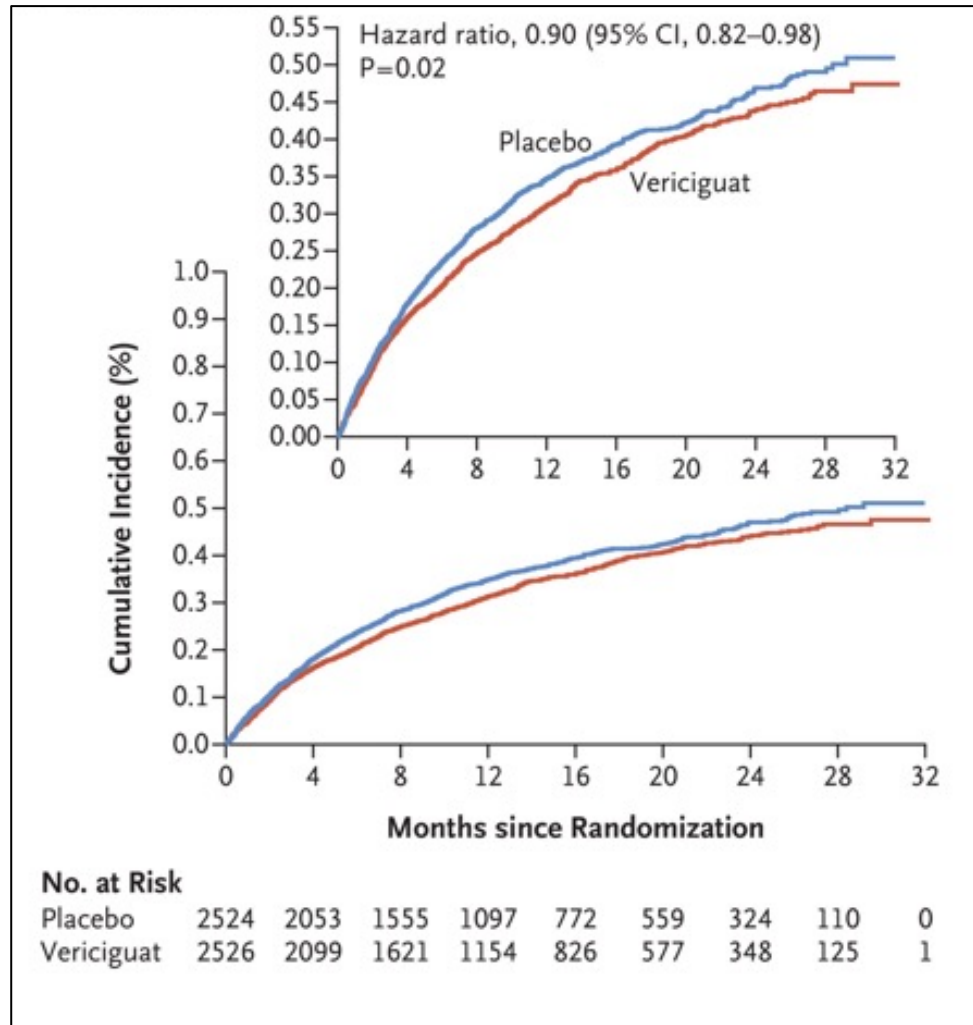
- SBP <100 mmHg
- Use of long- acting nitrates
- Use of PDE5i
- GFR < 15

VICTORIA TRIAL



Primary Endpoint: Composite of cardiovascular death and first HF hospitalization

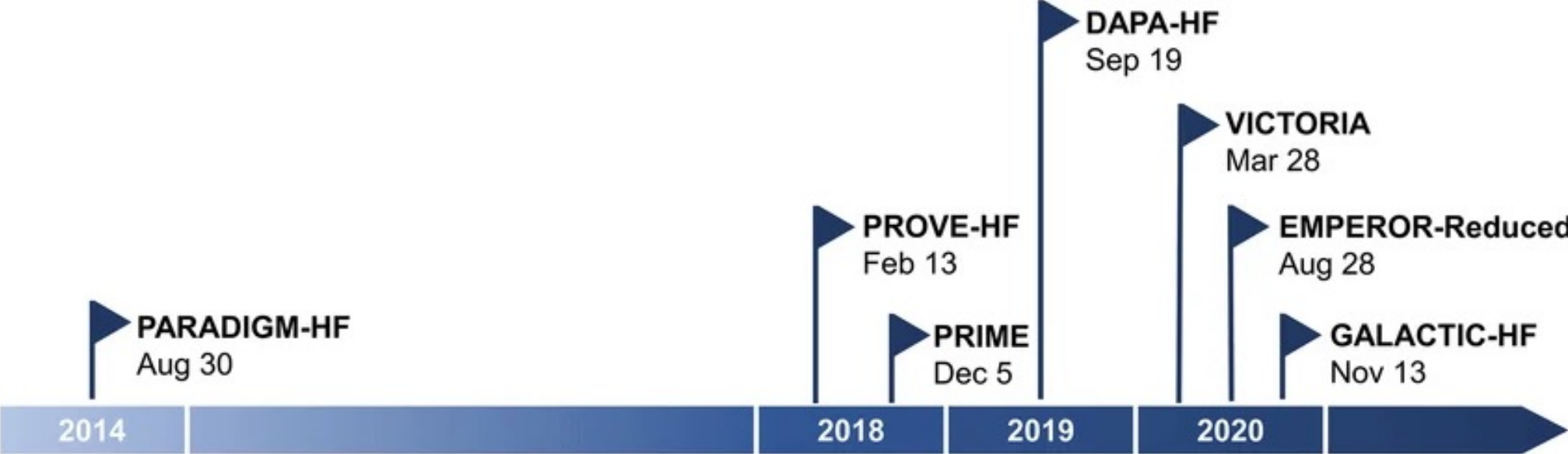
VICTORIA TRIAL



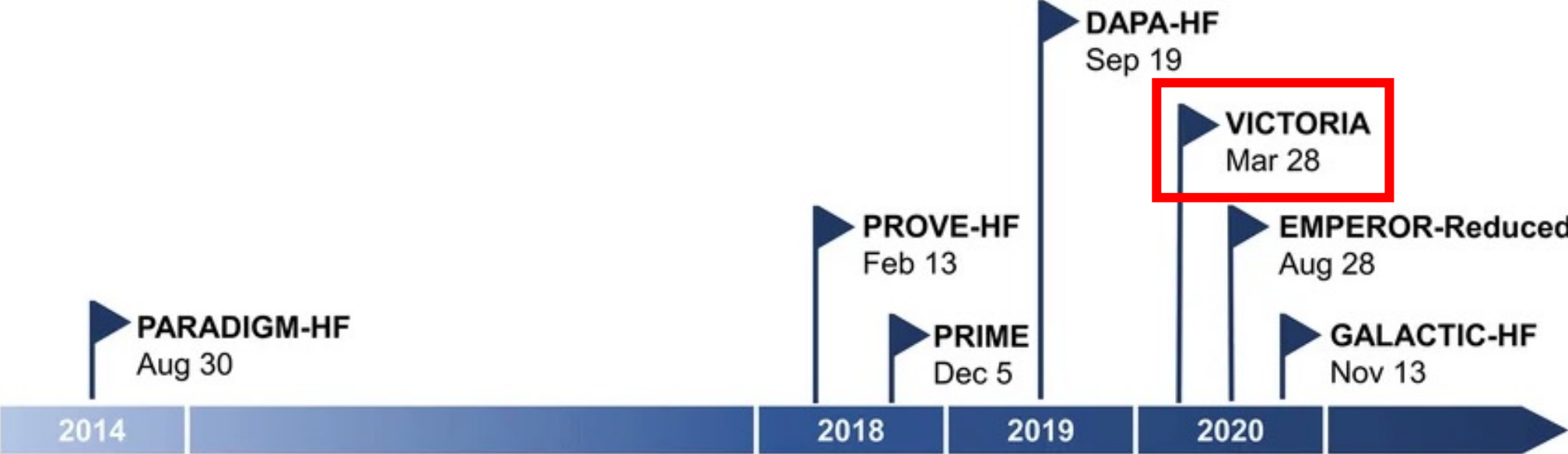
10% Relative Risk Reduction

Primary Endpoint: Composite of cardiovascular death and first HF hospitalization

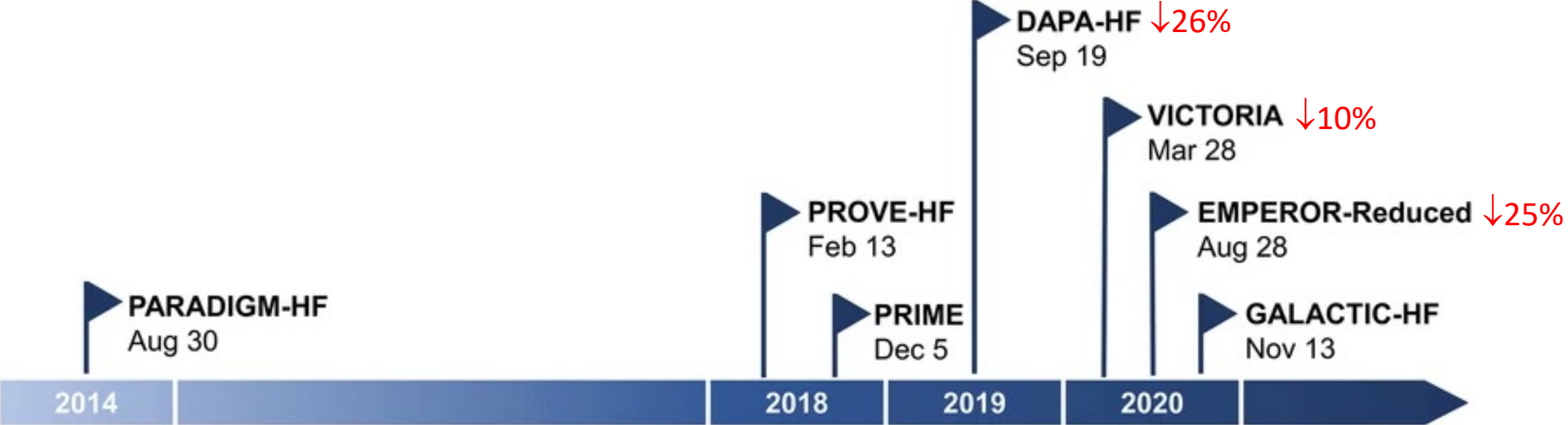
CONTEMPORARY HF TRIALS



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CONTEMPORARY HF TRIALS



2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

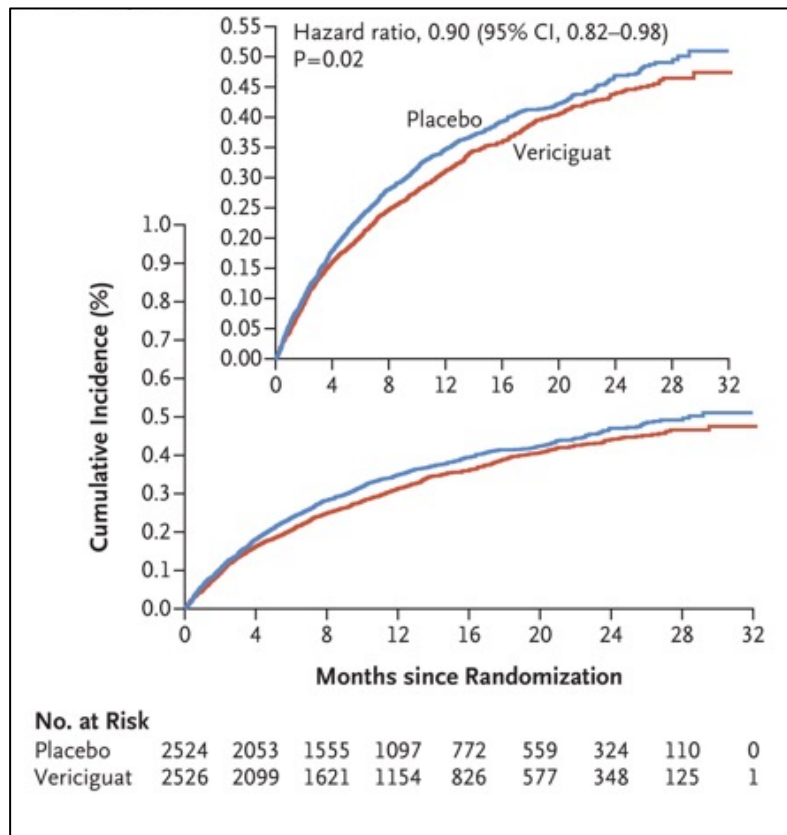
COR	LOE	Recommendation
2b	B-R	1. In selected high-risk patients with HFrEF and recent worsening of HF already on GDMT, an oral soluble guanylate cyclase stimulator (vericiguat) may be considered to reduce HF hospitalization and cardiovascular death. ¹

	PARADIGM HF ¹ (N=8,399) sacubitril/valsartan	DAPA-HF ² (N=4,744) dapagliflozin	EMPEROR-Reduced ³ (N=3,730) empagliflozin	VICTORIA ⁴ (N=5,050) vericiguat
NT-proBNP cutoff, pg/ml	≥600 or ≥400 if HFH <12 months	≥600 or ≥900 (AF) ≥400 if HFH <12 months	Varied with EF	≥1,000 (SR) ≥1,600 (AF)
eGFR cutoff, ml/min/1.73 m ²	≥30	≥30	≥20	≥15
LVEF cutoff	<35%	≤40%	≤40%	<45%
Recent HF decompensation	Not required	Not required	Chronic HF >3 months	HFH <6 months or IV diuretic use <3 months

	PARADIGM HF ¹ sacubitril/valsartan	DAPA HF ² dapagliflozin	EMPEROR-Reduced ³ empagliflozin	VICTORIA ⁴ vericiguat
Median NT-proBNP, pg/ml	1,608	1,437	1,906	2,816
NYHA class III or IV	25%	32%	25%	41%
HFH <6 months ago	31%	16%	NA	84%
eGFR <60 ml/min/1.73 m ²	37%	41%	48%	53%
Median follow up, months	27	18.2	16	10.8
Primary outcome	First HFH or CV death	Worsening HF (unplanned hospitalization/urgent visit resulting in IV therapy for HF) or CV death	First HFH or CV death	First HFH or CV death
Primary endpoint event rate (control arm), events per 100 PY	13.2	15.6	21	37.8

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~38 events per 100 PY

	PARADIGM HF ¹ sacubitril/valsartan	DAPA-HF ² dapagliflozin	EMPEROR-Reduced ³ empagliflozin	VICTORIA ⁴ vericiguat
Hazard Ratio	0.80 (95% CI 0.73-0.87)	0.74 (95% CI 0.65-0.85)	0.78 (95% CI 0.65-0.86)	0.90 (95% CI 0.82-0.92)
Absolute Risk Reduction vs Standard of Care	2.7	4.0	5.2	4.2

SAFETY

Table S4. Patients with adverse events of clinical interest: Symptomatic hypotension and syncope

	Vericiguat		Placebo		Difference in % vs. Placebo	
	No.	(%)	No.	(%)	Estimate (95% CI)*	P-Value
Patients in population	2519		2515			
Symptomatic hypotension	229	(9.1)	198	(7.9)	1.2 (-0.3 to 2.8)	0.121
Syncope	101	(4.0)	87	(3.5)	0.6 (-0.5 to 1.6)	0.303

*Based on the Miettinen & Nurminen method.

Note: Includes events/measurements from the day of first dose of study drug to 14 days after the last dose of study drug. Based on data up to the primary analysis cutoff date (18Jun2019).

CI indicates confidence interval.

FIVE YEARS LATER....VICTOR TRIAL

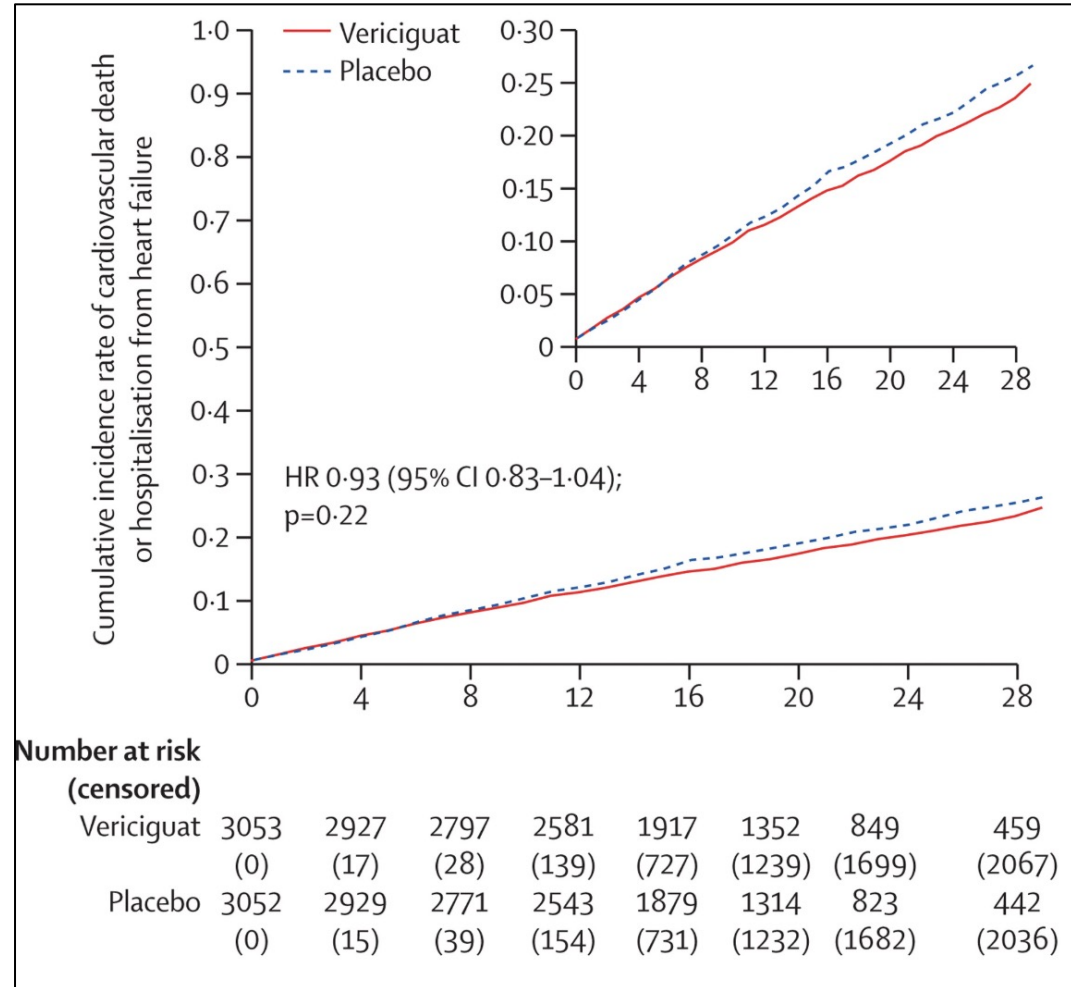
INCLUDED

- EF < 40%
- NYHA class II-IV
- NT-proBNP >600 pg/ml or >900 pg/ml (if AF)
- No hospitalization for HF in the 6 months before randomization
- No outpatient IV diuretic use in the 3 months before randomization

	VICTORIA (2020) ¹	VICTOR (2025) ²
Included patients	Recent hospitalization (within 6 months) or outpatient IV diuretic use (within 3 months)	Stable, ambulatory patients without a recent heart failure hospitalization 47.5% had no previous hospitalization
Median NT-proBNP, pg/ml	3,377	1,476
NYHA Class	II - 59% III - 40%	II - 79% III - 21%
GDMT	ARNI – 14.5% ACEI/ARB – 73% SGLT2i – 3.1%	ARNI – 56.0% ACEI/ARB – 38.3% SGLT2i – 59.1%

VICTOR TRIAL

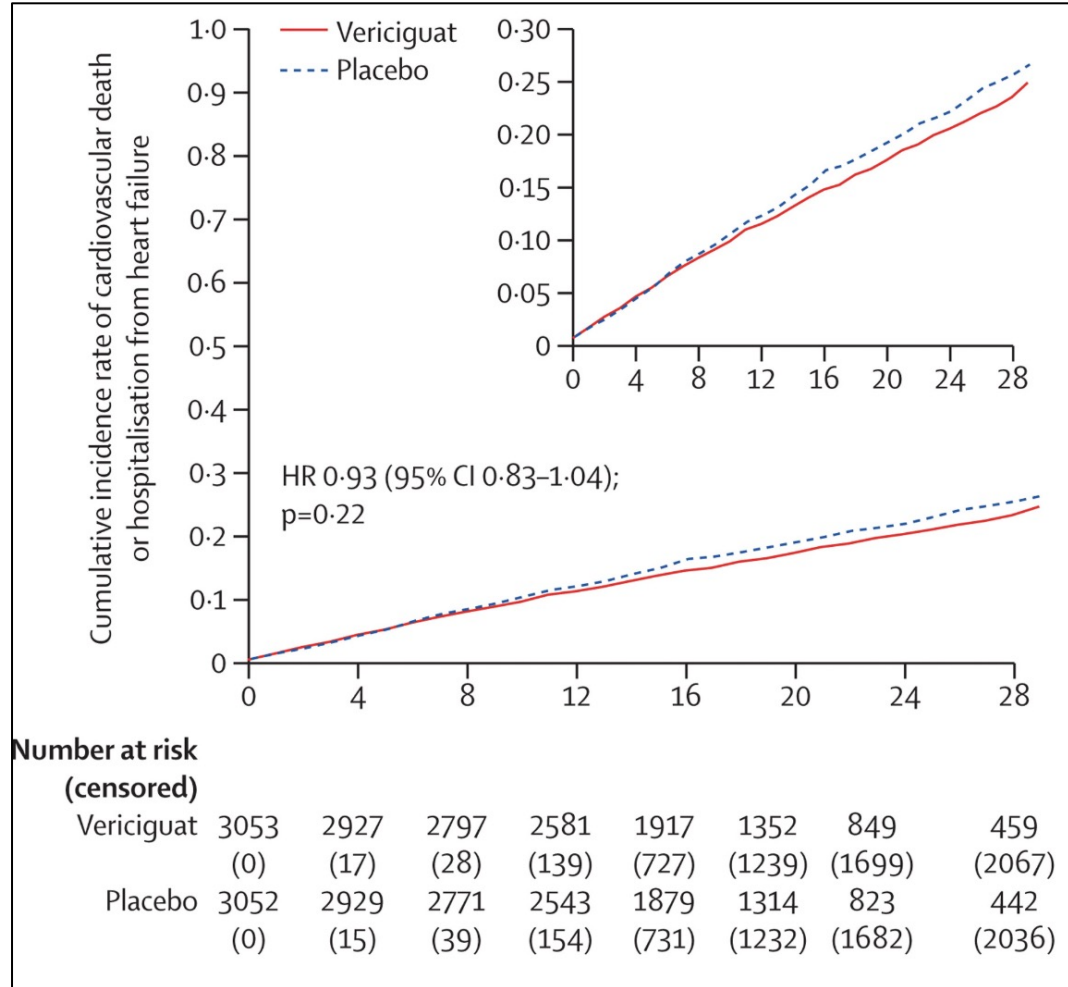
Primary Endpoint



Composite of time to cardiovascular death or first HF hospitalization

VICTOR TRIAL

Primary Endpoint

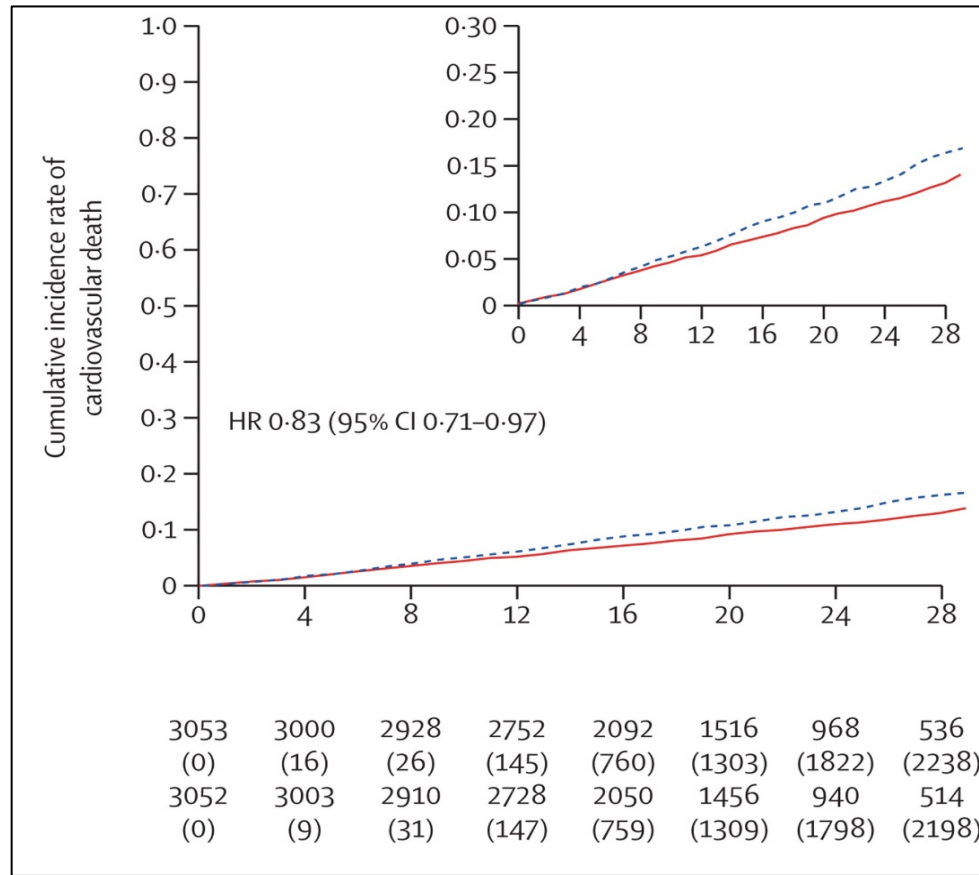


**No benefit
over placebo**

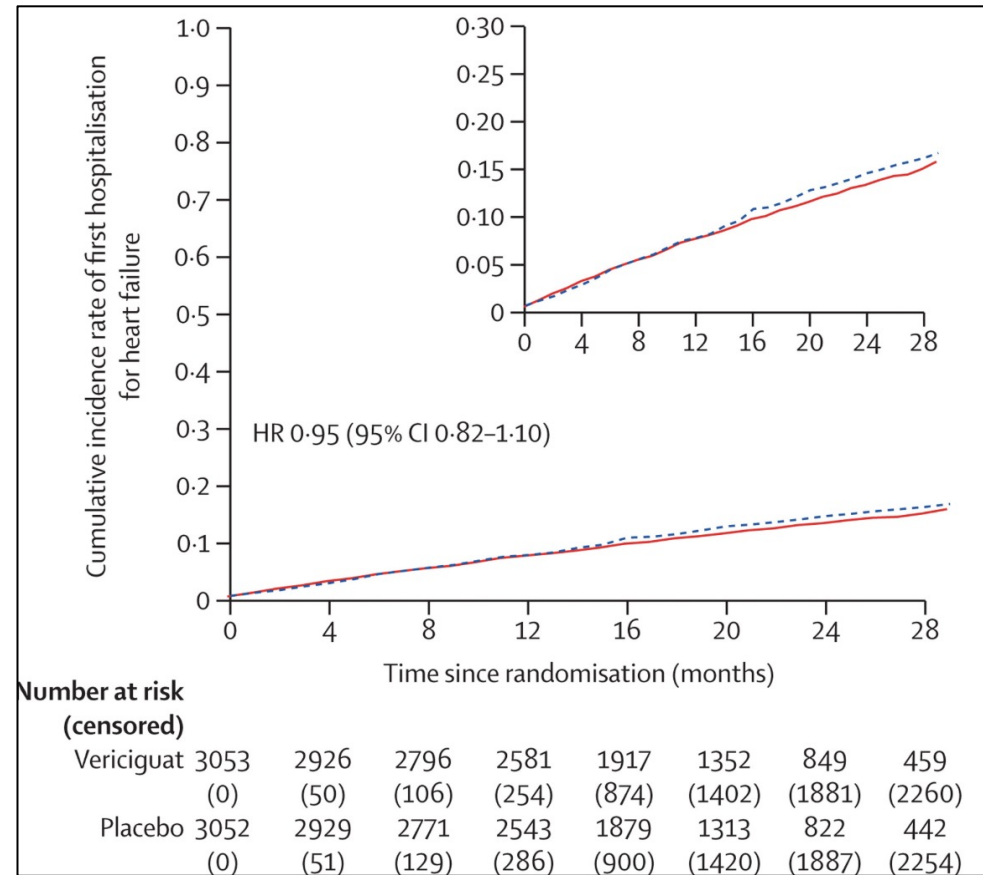
Composite of time to cardiovascular death or first HF hospitalization

VICTOR TRIAL

Secondary Endpoints



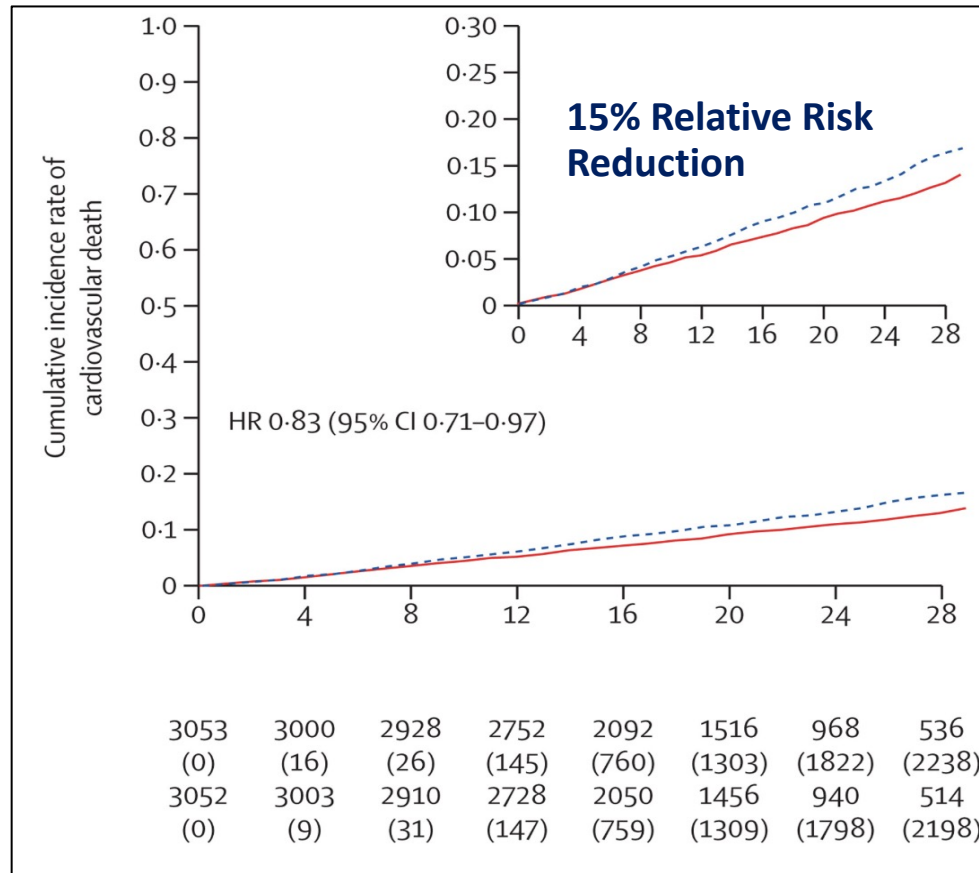
Time to cardiovascular death



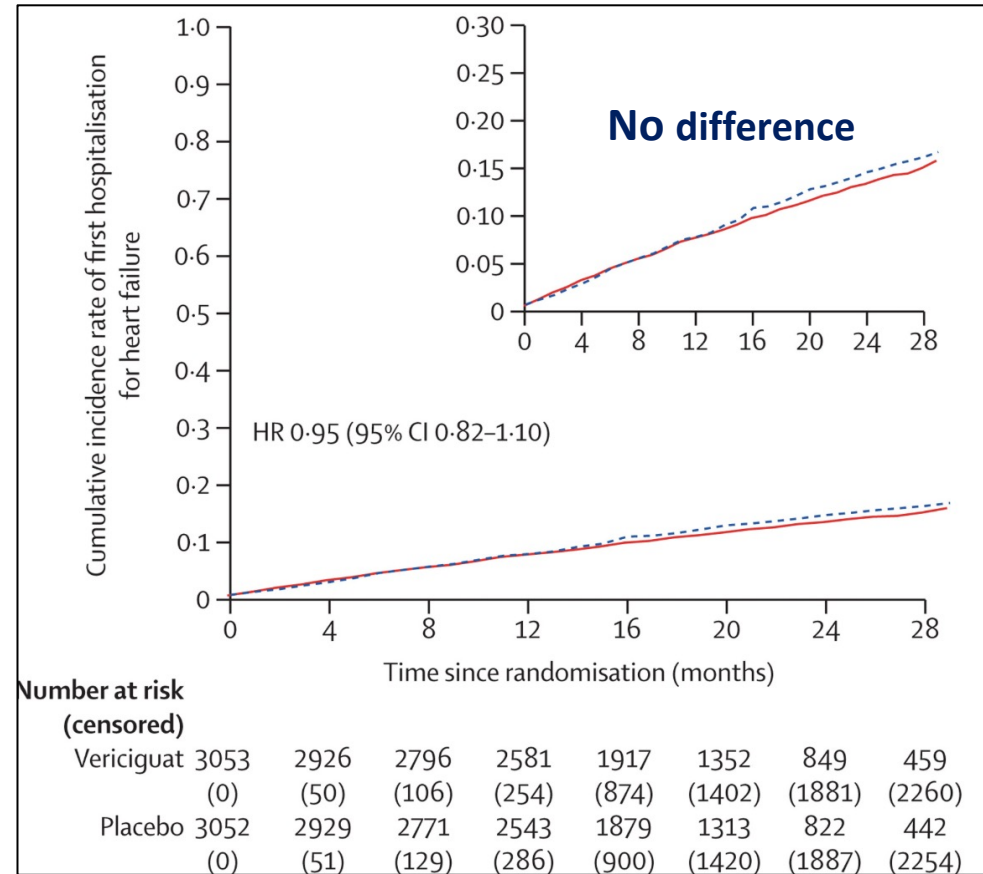
Time to first HF hospitalization

VICTOR TRIAL

Secondary Endpoints



Time to cardiovascular death



Time to first HF hospitalization

VICTORIA + VICTOR

- 11,155 patients: 5,050 in VICTORIA and 6,105 in the VICTOR
- No evidence of intertrial heterogeneity of treatment effect
- Primary endpoint of cardiovascular death or hospitalization for heart failure

25.9% (vericiguat) vs 27.9% (placebo)

HR 0.91 [95% CI 0.85–0.98]; p=0.0088

VERICIGUAT

- Stimulates sGC directly and enhances its sensitivity to endogenous NO
- Well-tolerated with minimal effect to blood pressure
- Can be used in the setting of significant renal dysfunction
- Improves cardiovascular outcomes across the HFrEF spectrum



Thank You