BIELLA CUORE
12-13 SETTEMBRE 2025

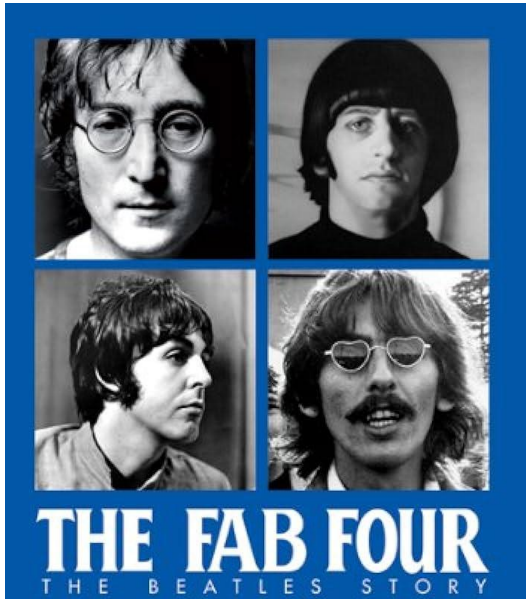
SCOMPENSO CARDIACO
Terapia medica ottimale: “the fabulous four” e oltre?

Alessandra Chinaglia

SCDO Cardiologia

AOU San Luigi Gonzaga

Terapia medica ottimale



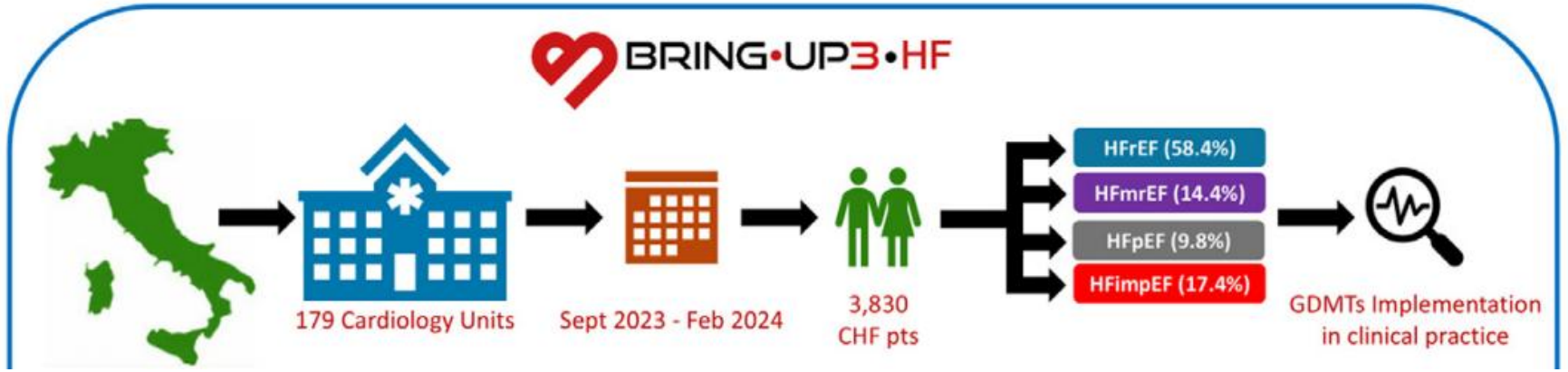
Trattamento dello scompenso a frazione di eiezione ridotta

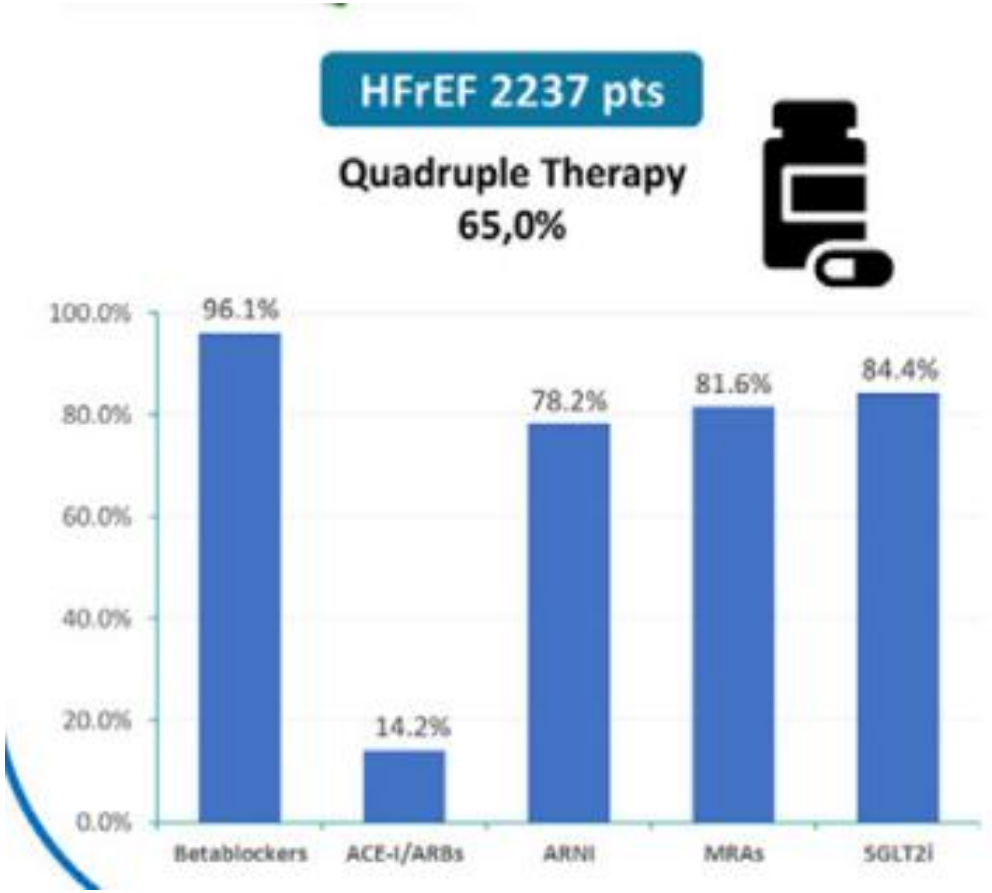
A

Treatment	All-Cause Mortality	HR (95% CI)
ARNI + BB + MRA + SGLT2		0.39 (0.31-0.49)
ARNI + BB + MRA + Vericiguat		0.41 (0.32-0.53)
ARNI + BB + MRA + Omecamtiv		0.44 (0.36-0.55)
ACEI + BB + Dig + H–ISDN		0.46 (0.35-0.61)
ACEI + BB + MRA + IVA		0.48 (0.39-0.58)
ACEI + BB + MRA + Vericiguat		0.49 (0.39-0.62)
ACEI + BB + MRA + Omecamtiv		0.52 (0.43-0.63)
ARNI + ARB + BB + Dig		0.65 (0.55-0.76)
ARNI + BB + MRA		0.44 (0.37-0.54)
ACEI + BB + MRA		0.52 (0.44-0.61)
ACEI + MRA + Dig		0.66 (0.56-0.78)
ACEI + BB + Dig		0.68 (0.59-0.78)
ARB + BB + Dig		0.73 (0.64-0.83)
ACEI + ARB + Dig		0.83 (0.72-0.96)
Dig + H–ISDN		0.67 (0.53-0.86)
ARNI + BB		0.58 (0.50-0.68)
ACEI + BB		0.69 (0.61-0.77)
ARB + BB		0.74 (0.66-0.82)
ACEI + Dig		0.87 (0.78-0.98)
ARB + Dig		0.94 (0.84-1.05)
BB		0.78 (0.72-0.84)
ACEI		0.89 (0.82-0.96)
ARB		0.95 (0.88-1.02)
Dig		0.99 (0.91-1.07)
PLBO		1.00

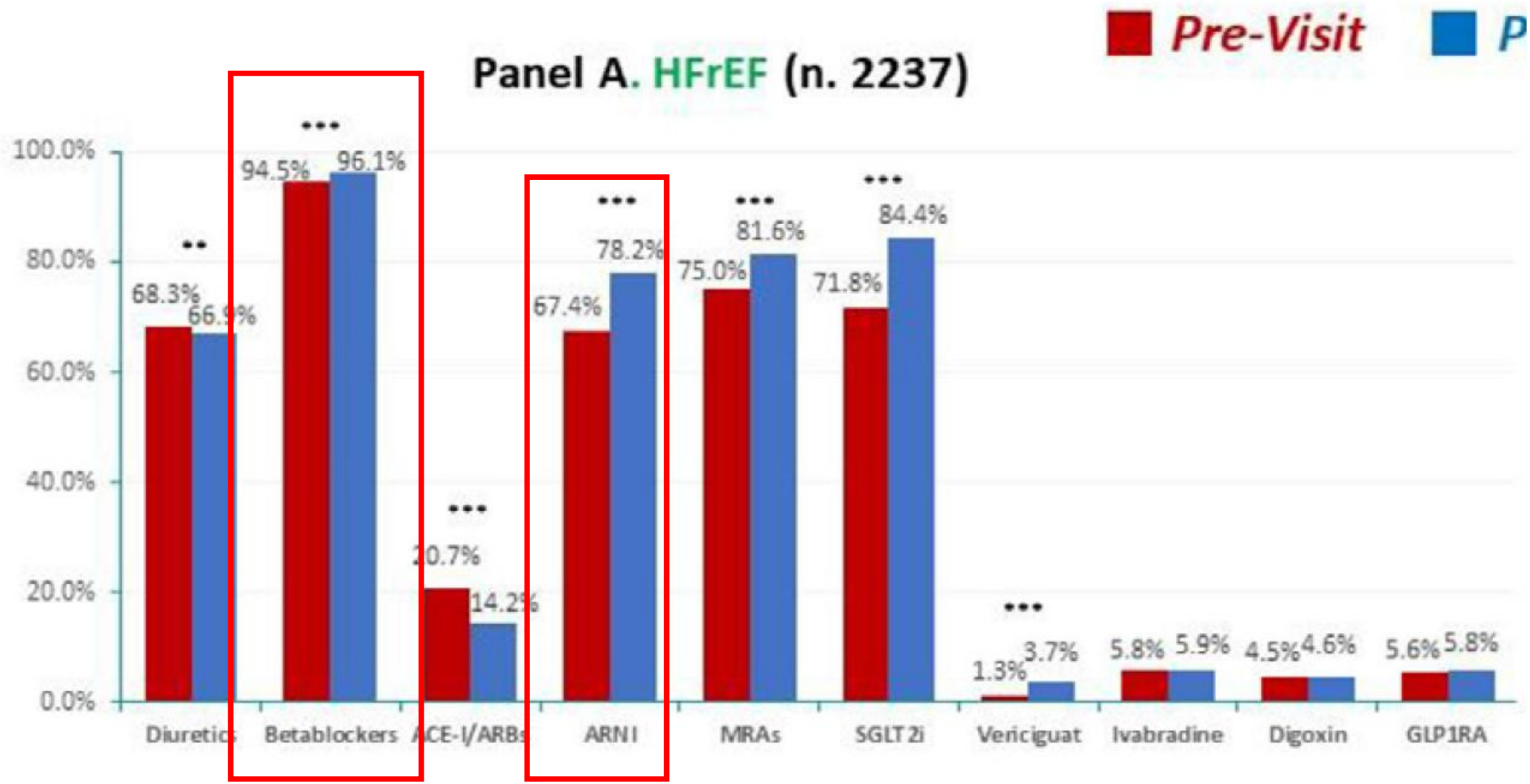
0.25 0.5 1 2

J Am Coll Cardiol HF. 2022 Feb, 10 (2) 73–84


BRING·UP3·HF
179 Cardiology Units
Sept 2023 - Feb 2024
3,830
CHF pts
HFrEF (58.4%)
HFmrEF (14.4%)
HFpEF (9.8%)
HFimpEF (17.4%)
GDMTs Implementation
in clinical practice


HFrEF 2237 pts
Quadruple Therapy
65,0%
100.0%
80.0%
60.0%
40.0%
20.0%
0.0%
96.1%
14.2%
78.2%
81.6%
84.4%
Betablockers
ACE-I/ARBs
ARNI
MRAs
SGLT2i

BRING·UP3·HF



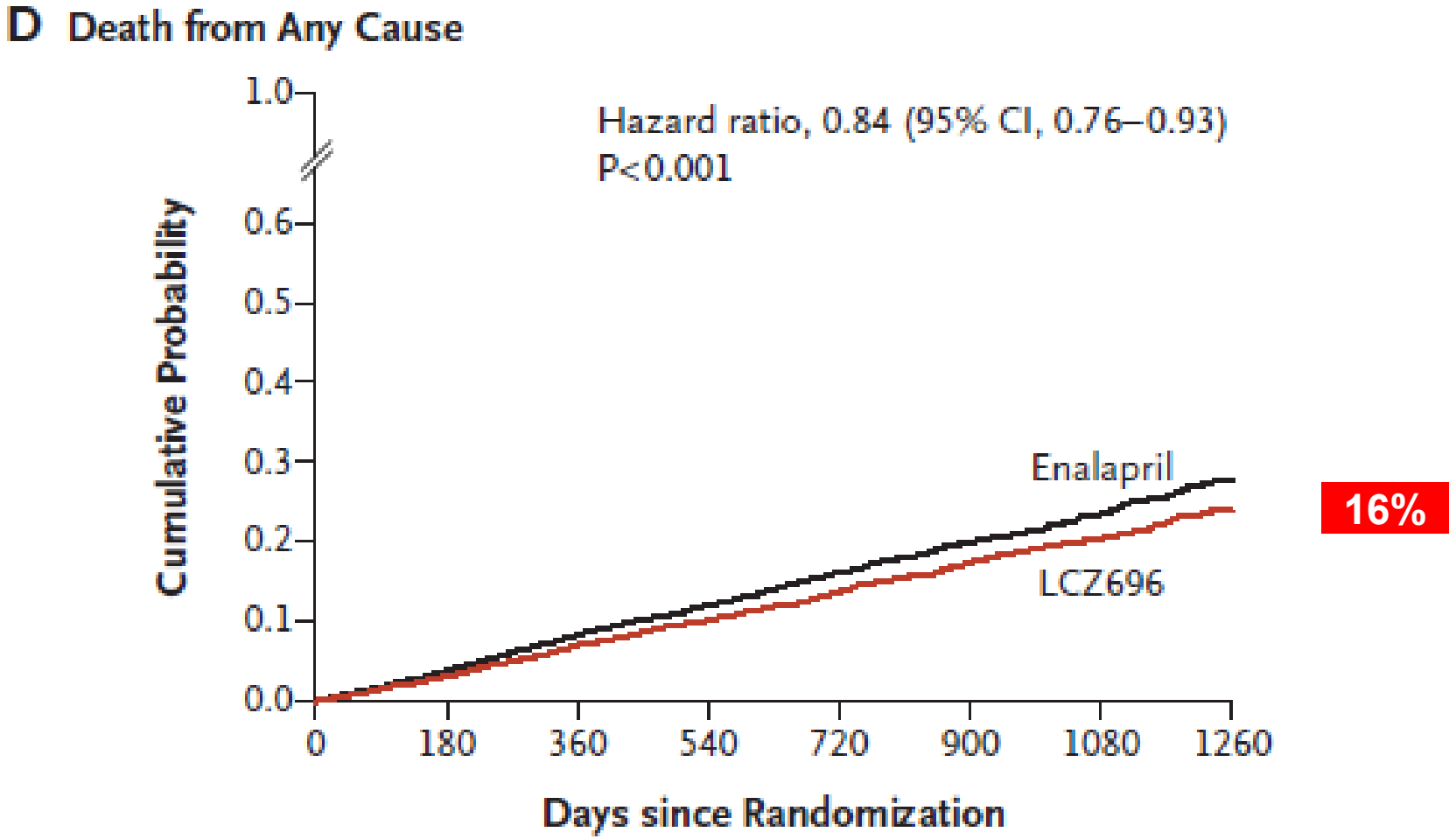
Journal of Cardiac Failure 00 (2025) 111

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

PARADIGM- HF

Mortalità

8442 patients
class II, III, IV
FE 29%

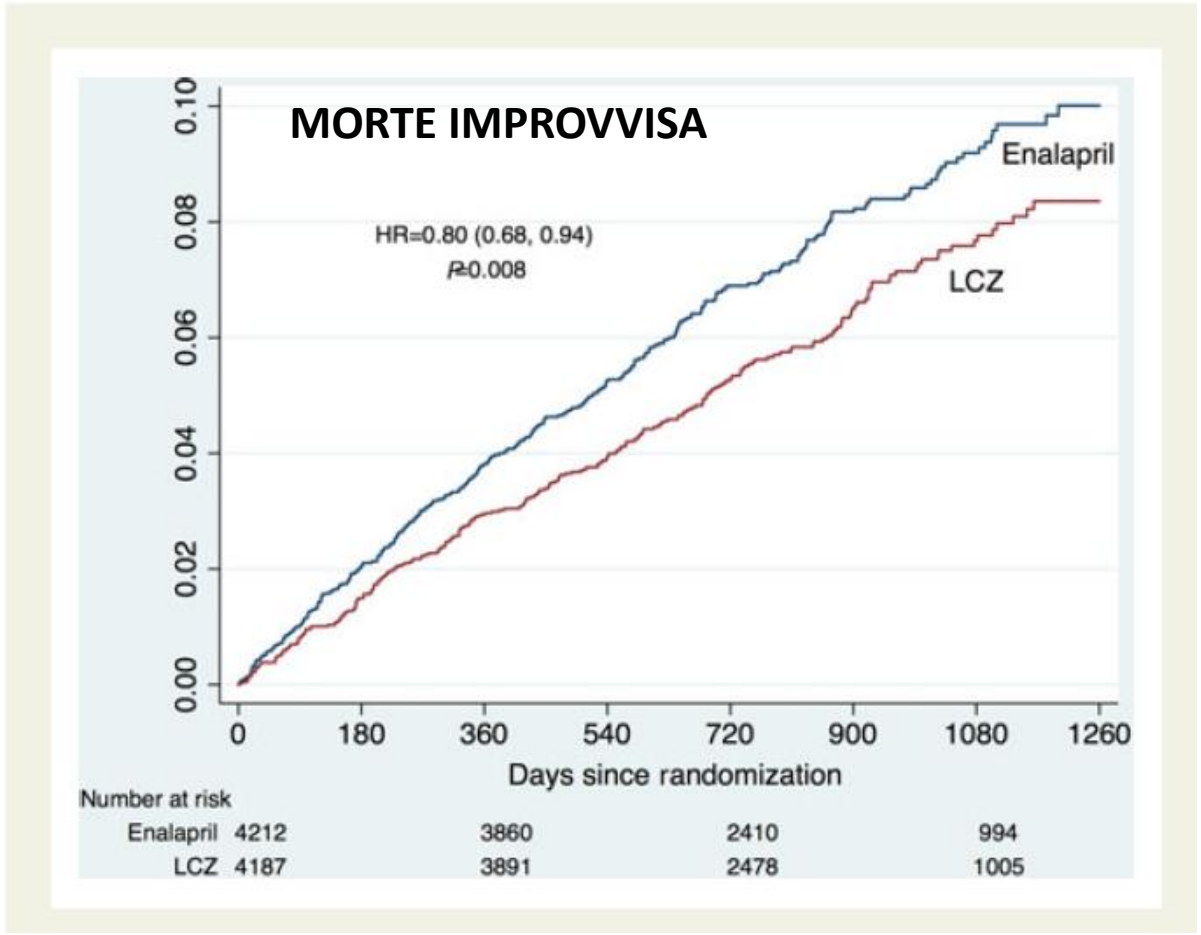


16%

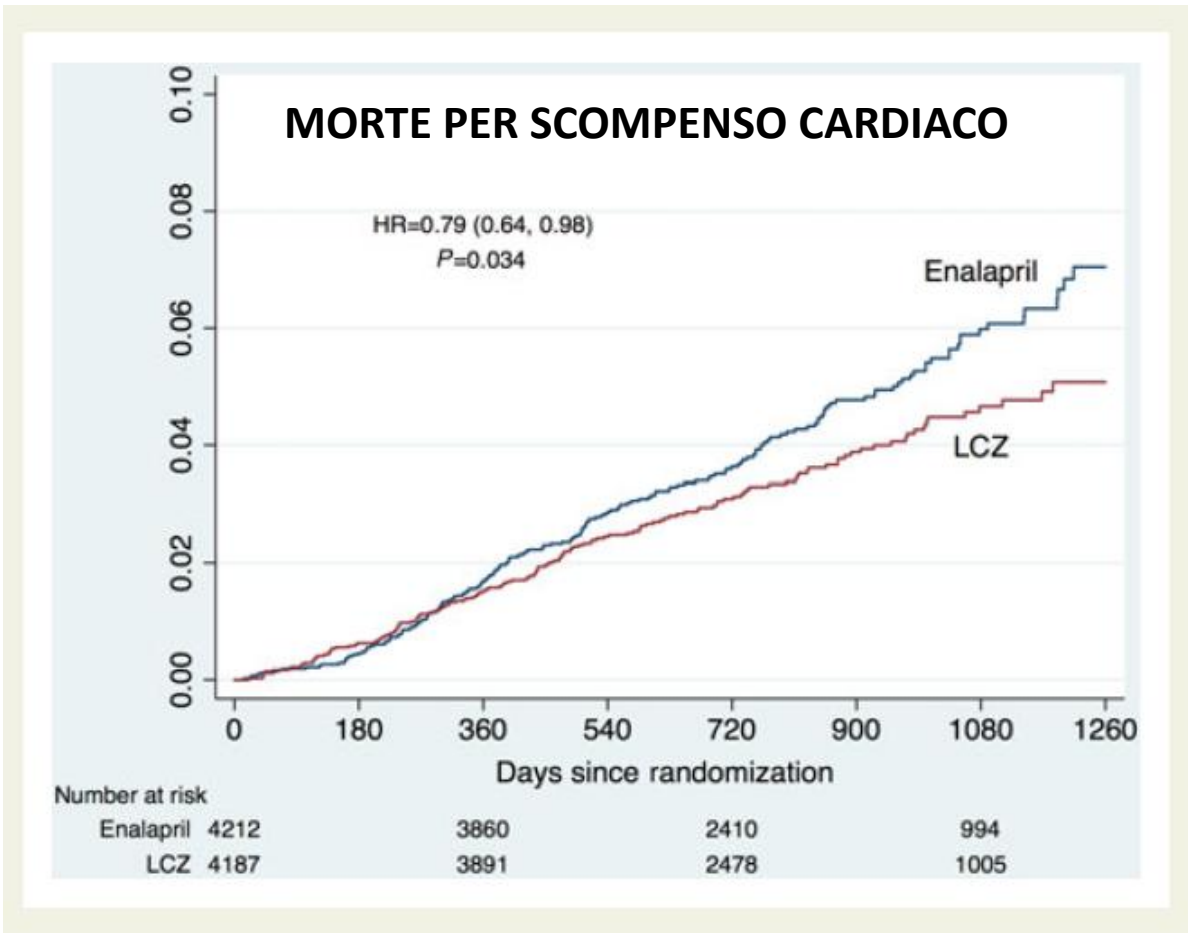
N Engl J Med 2014;371:993-1004

Effect of the angiotensin-receptor-neprilysin inhibitor LCZ696 compared with enalapril on mode of death in heart failure patients

Effetti collaterali: ipotensione, insufficienza renale e iperpotassiemia



36%

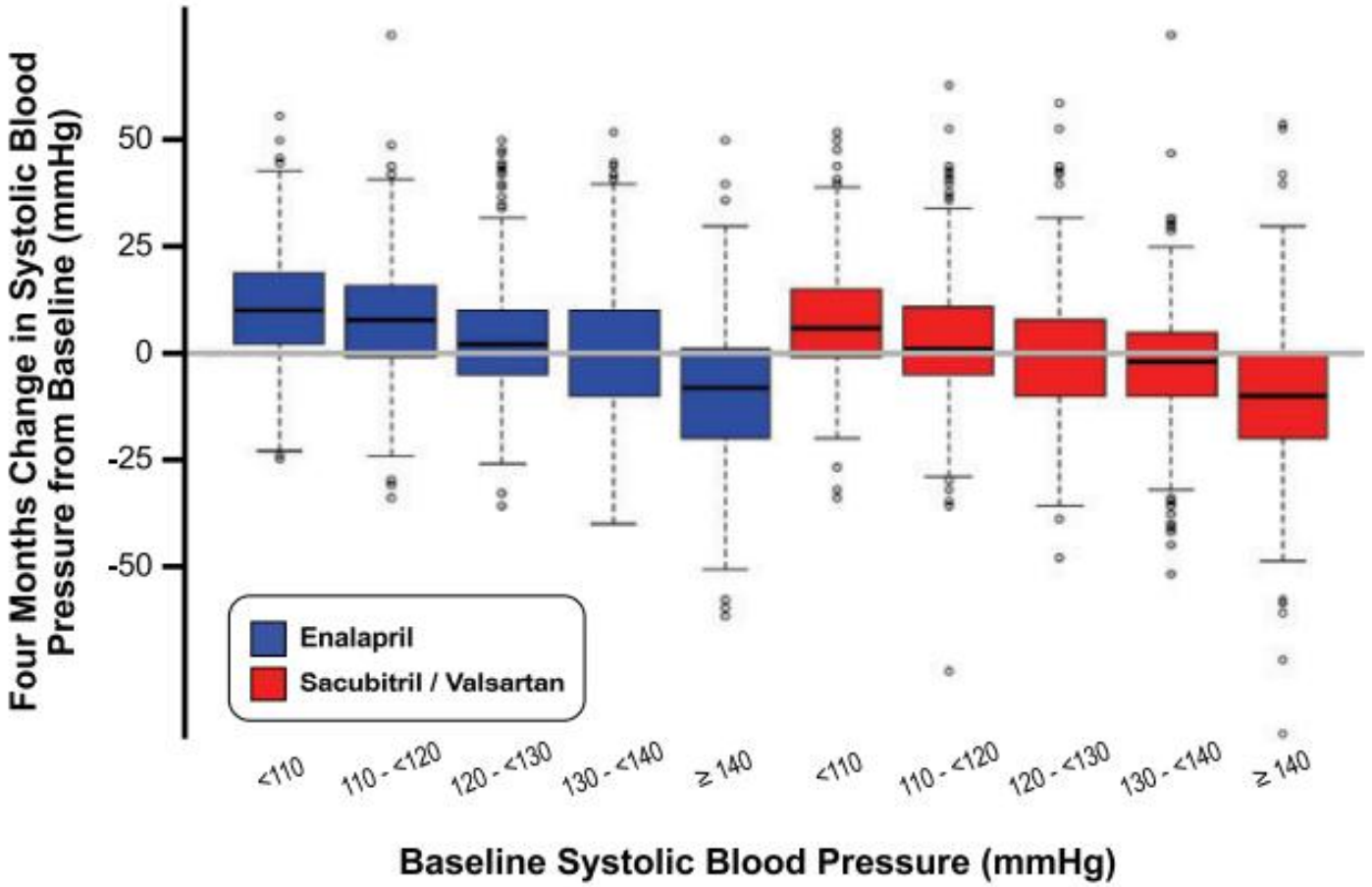


21%

European Heart Journal (2015) 36, 1990–1997

Systolic blood pressure, cardiovascular outcomes and efficacy and safety of sacubitril/valsartan (LCZ696) in patients with chronic heart failure and reduced ejection fraction: results from PARADIGM-HF

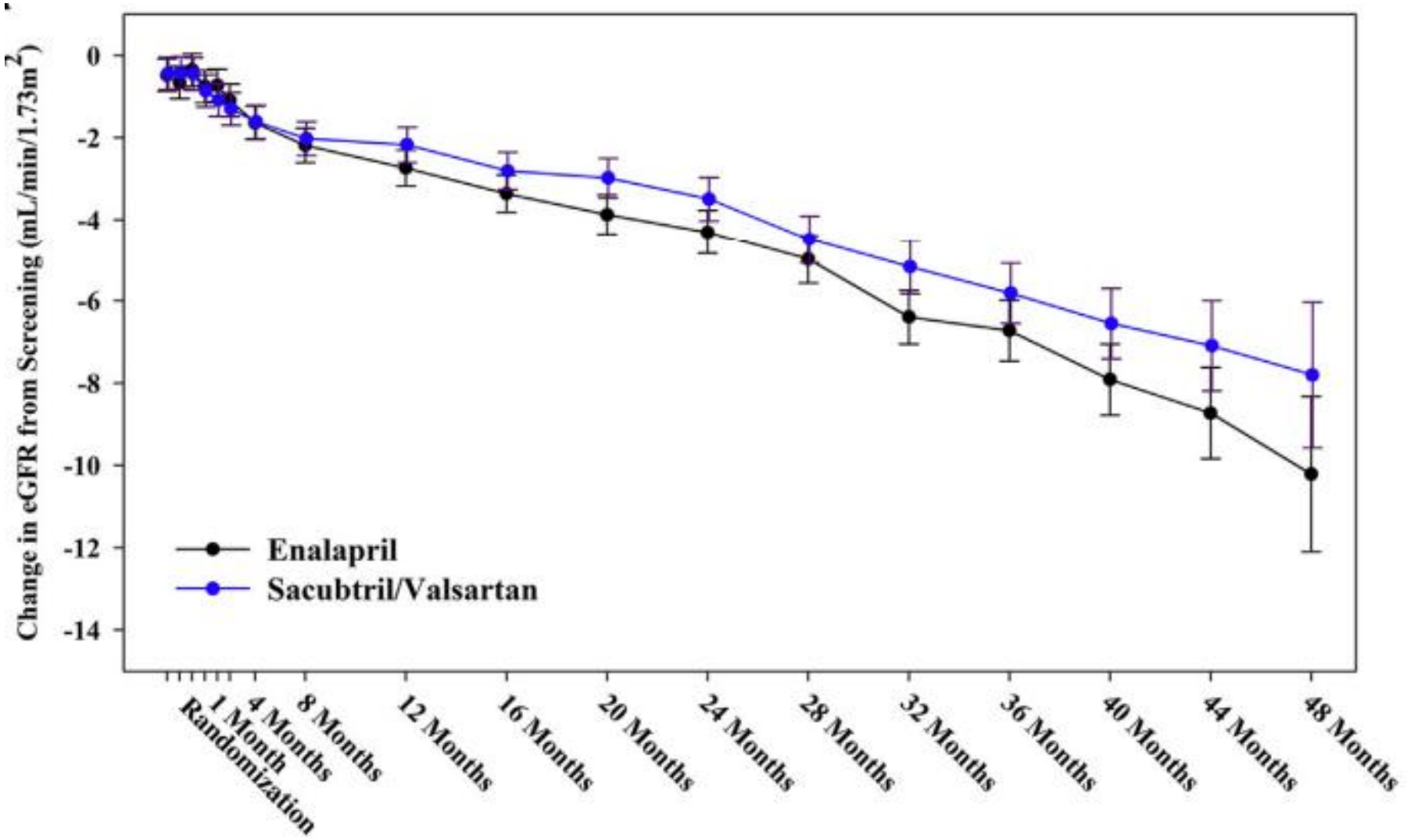
Ipotensione



European Heart Journal (2017) 38, 1132–1143

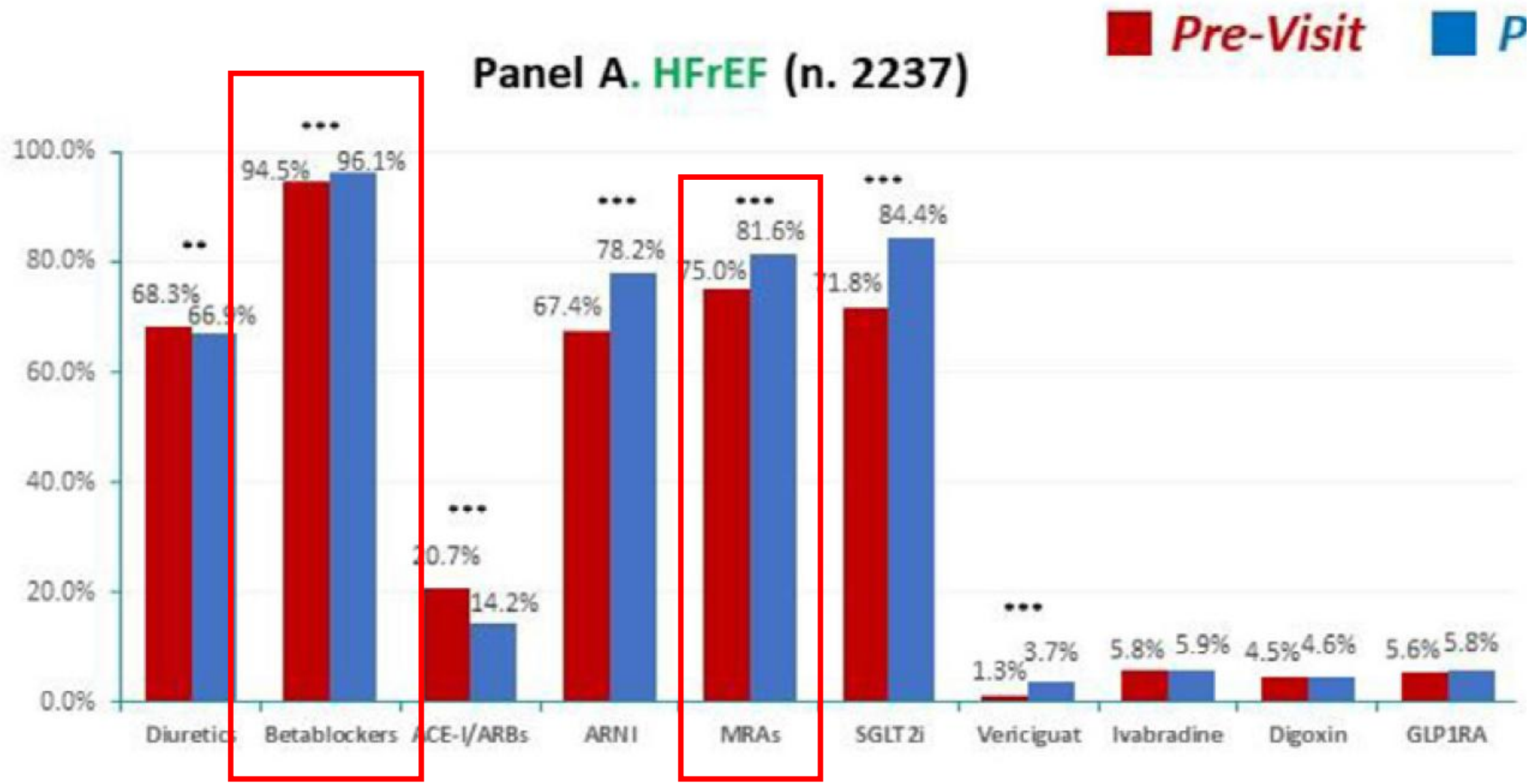
Renal Effects and Associated Outcomes During Angiotensin-Neprilysin Inhibition in Heart Failure

Insufficienza renale



JACC:HEARTFAILUREVOL.6,NO.6,2018

BRING·UP3·HF



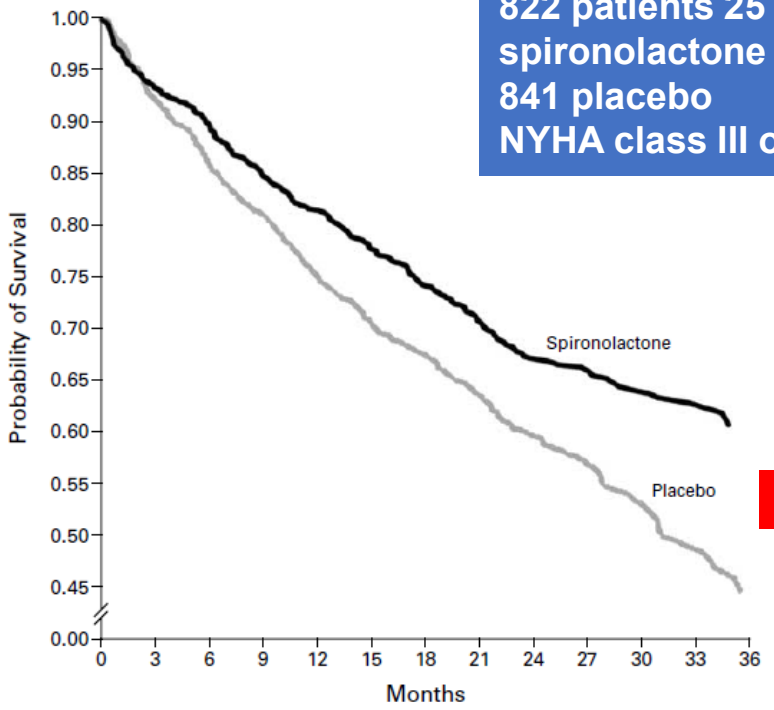
Journal of Cardiac Failure 00 (2025) 111

THE EFFECT OF SPIRONOLACTONE ON MORBIDITY AND MORTALITY IN PATIENTS WITH SEVERE HEART FAILURE

Eplerenone in Patients with Systolic Heart Failure and Mild Symptoms

Effetti collaterali: iperpotassiemia

822 patients 25 mg of spironolactone
841 placebo
NYHA class III or IV



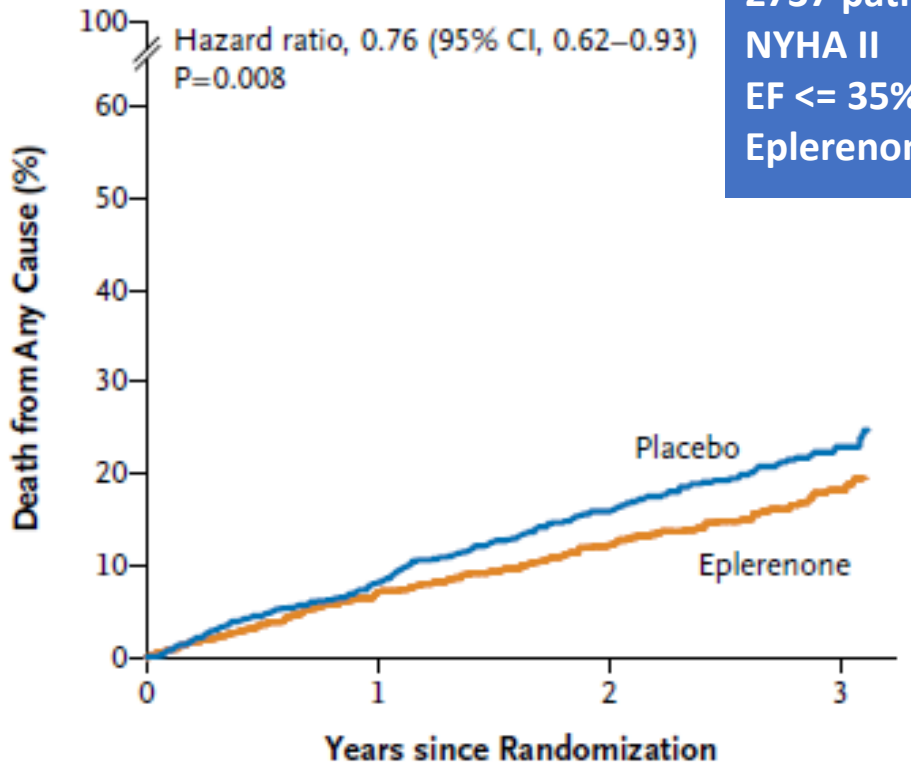
No. at Risk

Placebo	841	775	723	678	628	592	565	483	379	280	179	92	36
Spironolactone	822	766	739	698	669	639	608	526	419	316	193	122	43

30%

B

2737 patients
NYHA II
EF <= 35%
Eplerenone 25 mg-50 mg



24%

No. at Risk

Placebo	1373	947	587	242
Eplerenone	1364	972	625	269

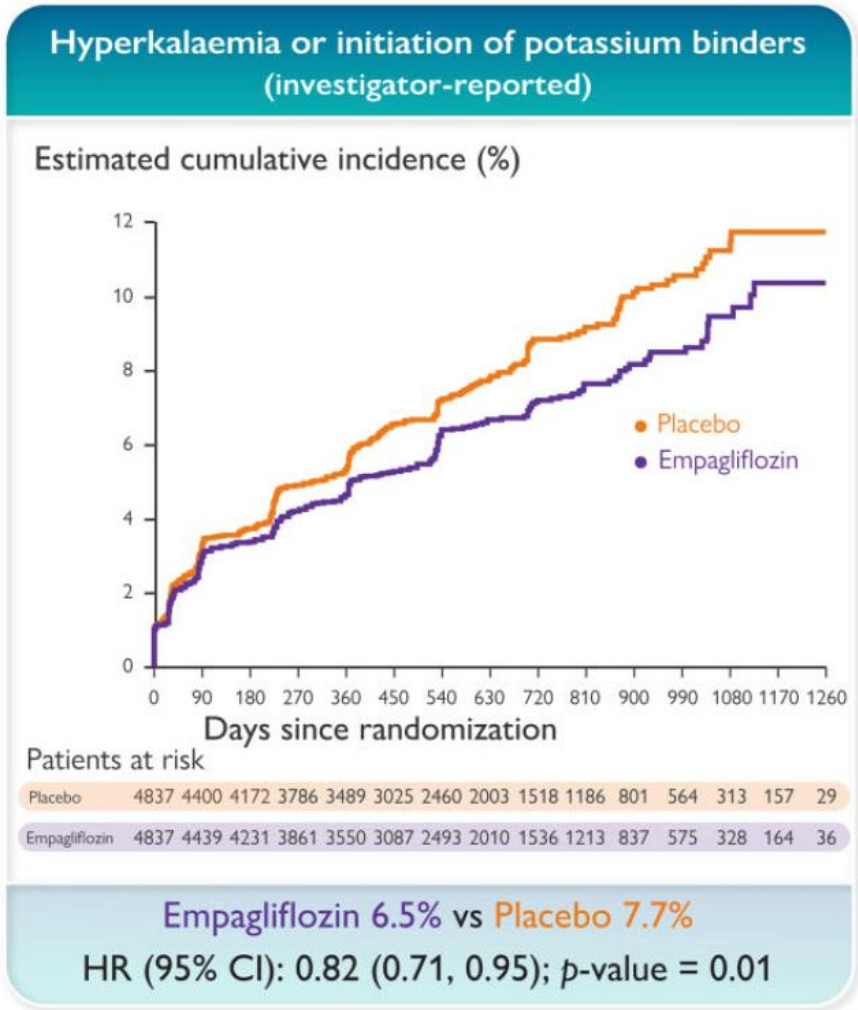
Pitt B et al. N Engl J Med. 1999;341:709-17

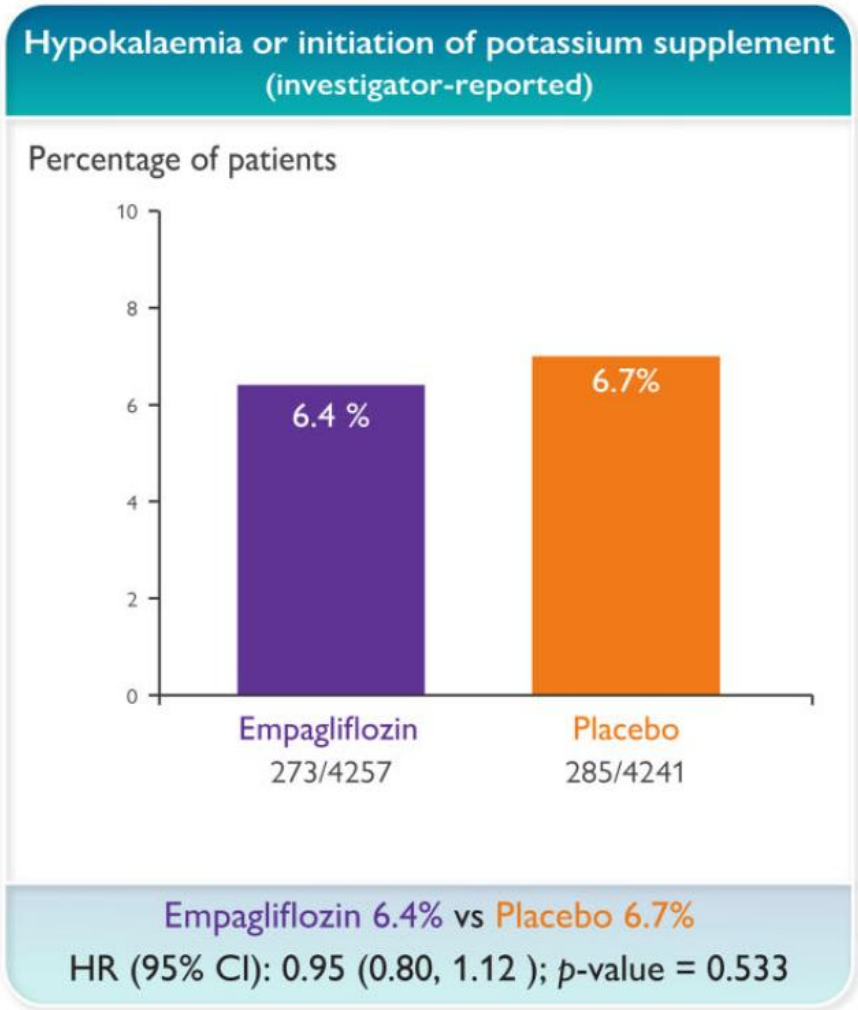
Zannad, N Engl J Med 2011;364:11-21.

Empagliflozin and serum potassium in heart failure: an analysis from EMPEROR-Pooled

EMPEROR-Pooled

EMPEROR-Pooled (EMPEROR-Reduced and EMPEROR-Preserved combined) included 9583 patients

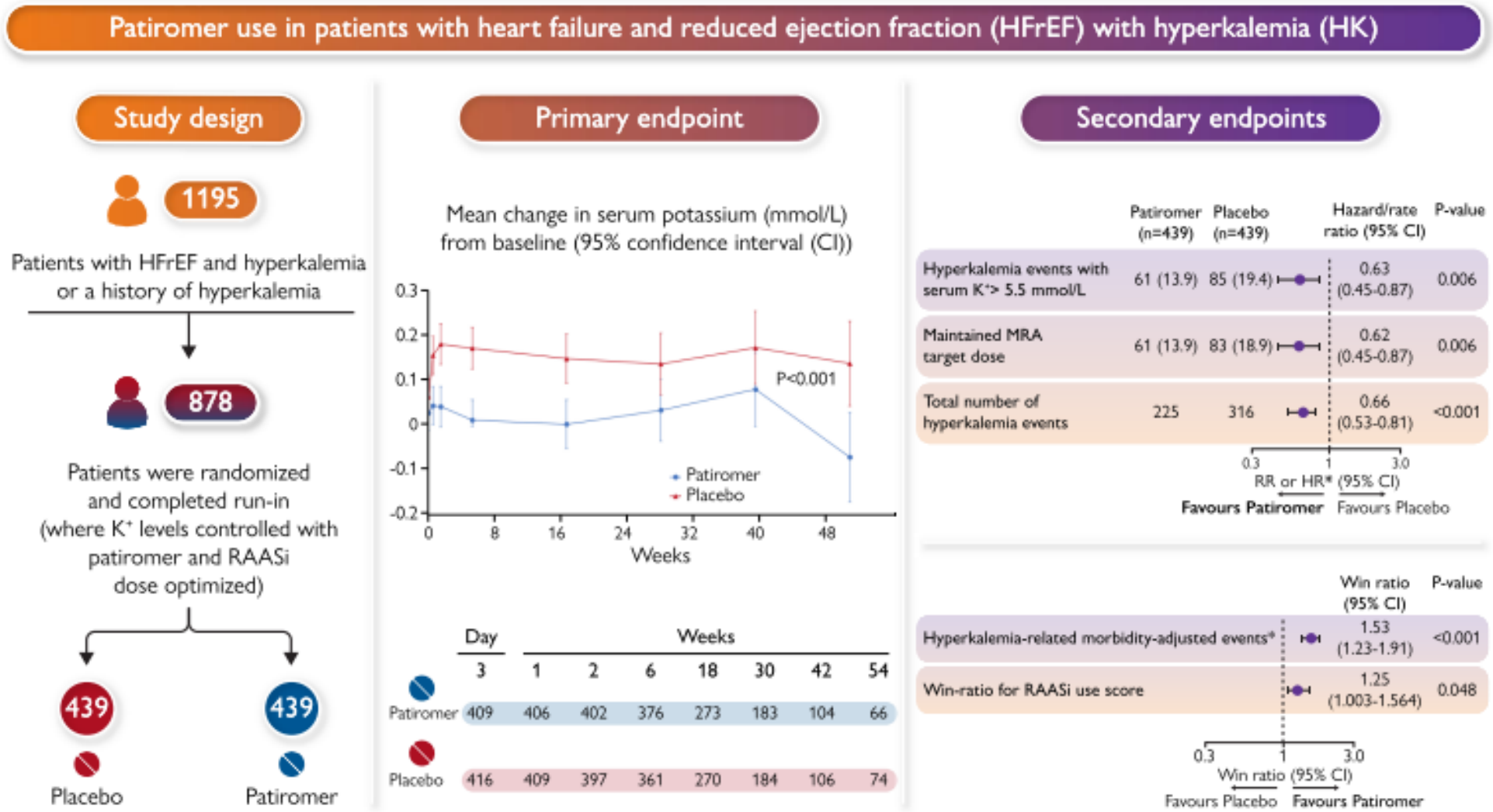




European Heart Journal (2022) 00, 1–10

Patiromer for the management of hyperkalemia in heart failure with reduced ejection fraction: the DIAMOND trial

DIAMOND

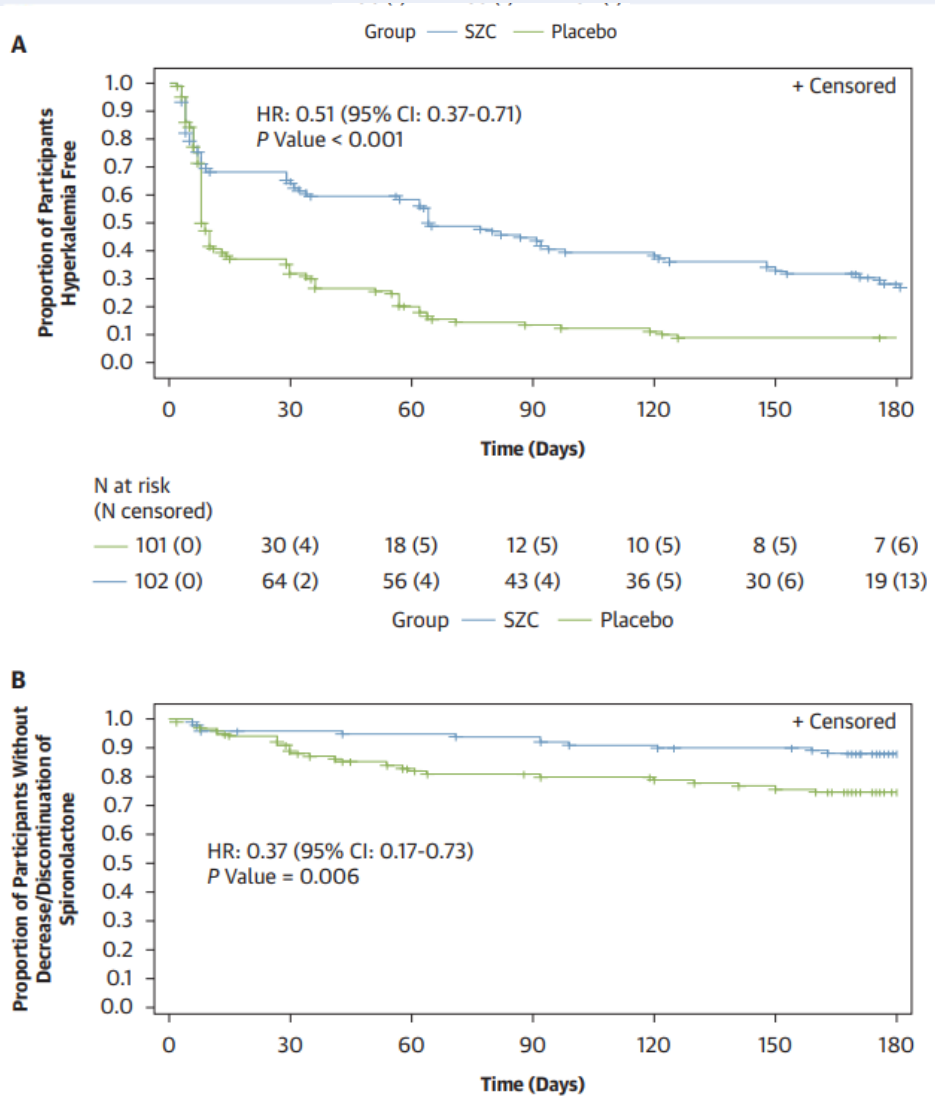


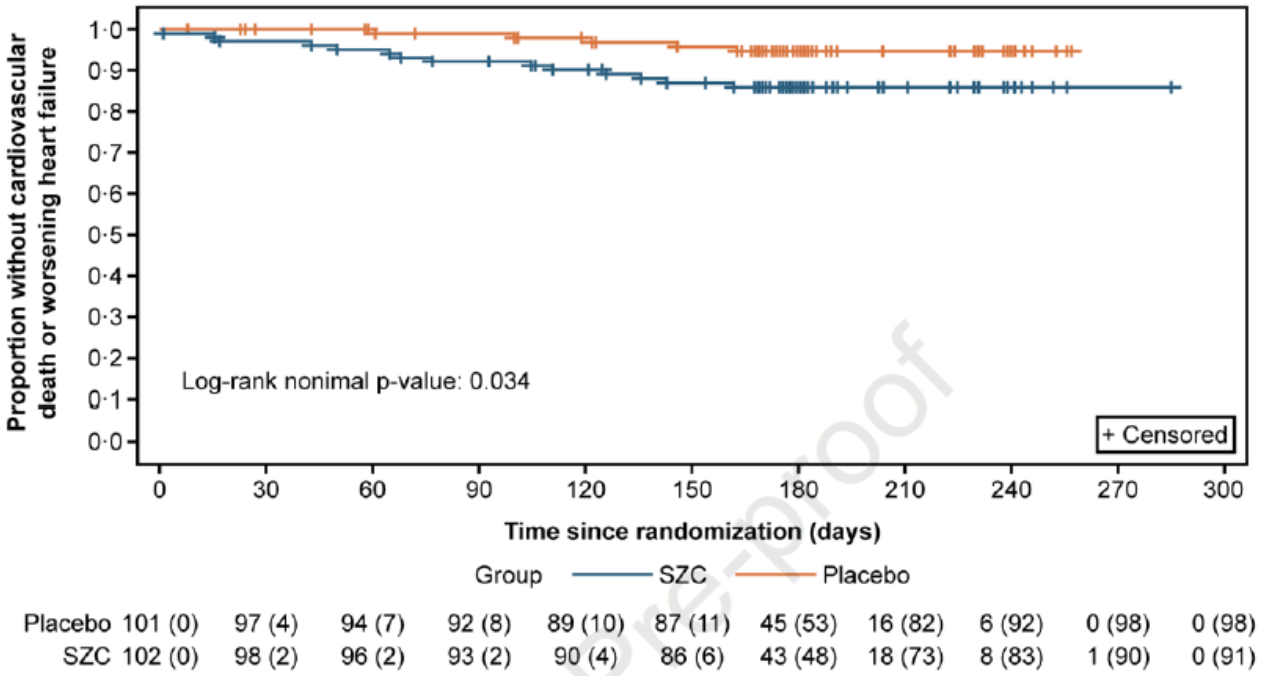
Butler, European Heart Journal (2022) 43, 4362–4373

Sodium Zirconium Cyclosilicate for Management of Hyperkalemia During Spironolactone Optimization in Patients With Heart Failure

REALIZE-K

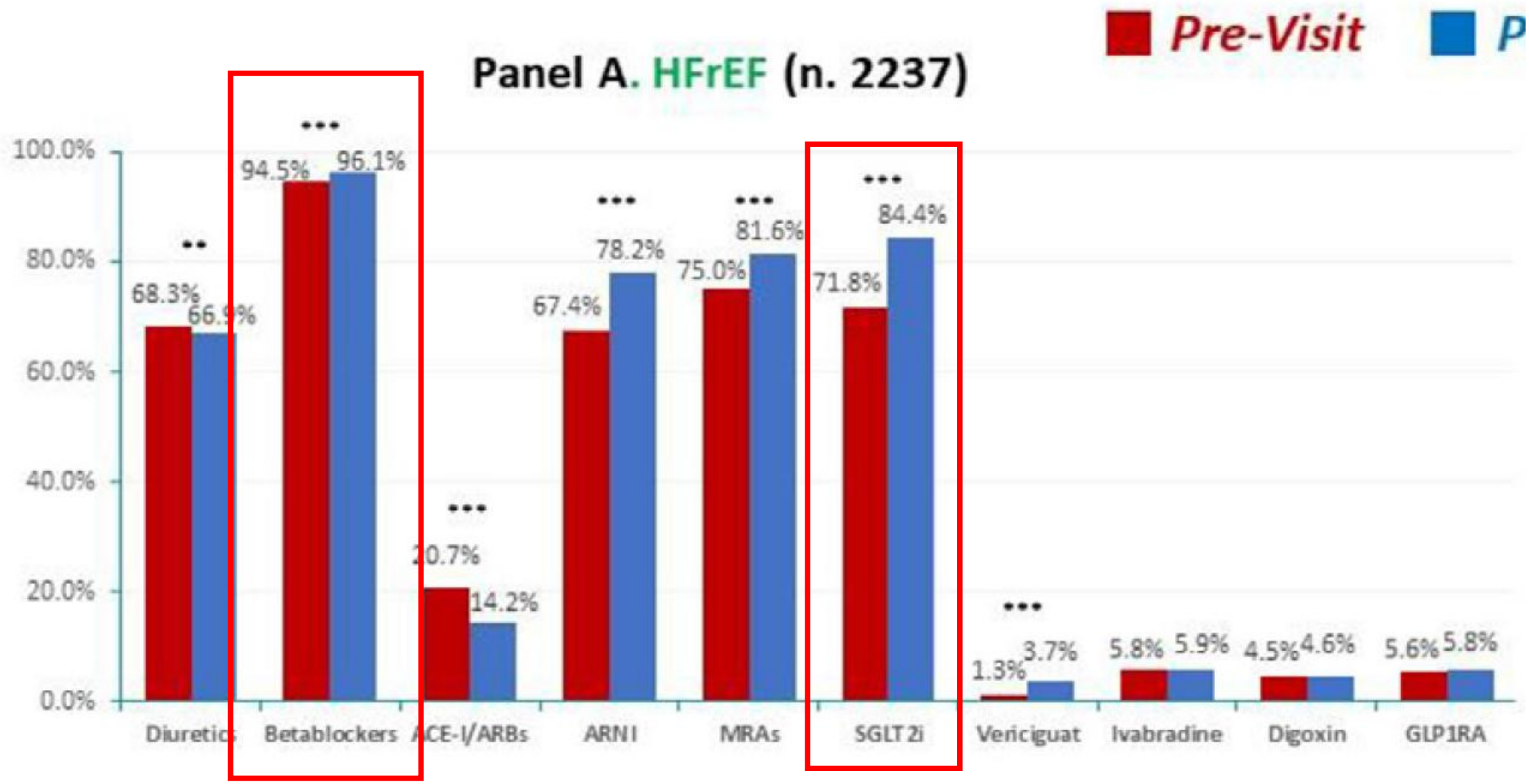
Time to first A) hyperkalemia and B) spironolactone decrease/discontinuation due to hyperkalemia





Kosiborod, JACC. Mar 2025

BRING·UP3·HF

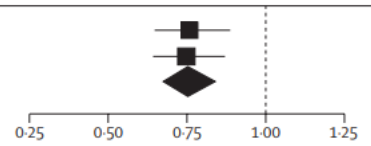


Journal of Cardiac Failure 00 (2025) 111

SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials

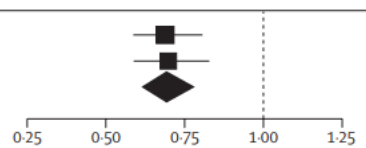
F All (first and recurrent) hospitalisation for heart failure or cardiovascular death

	Number with event/number of patients (%)		RR (95% CI)
	SGLT2 inhibitor	Placebo	
EMPEROR-Reduced	575/1863 (30·9%)	753/1867 (40·3%)	0·76 (0·65–0·89)
DAPA-HF	567/2373 (23·9%)	742/2371 (31·3%)	0·75 (0·65–0·88)
Total			**0·75 (0·68–0·84)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·91			



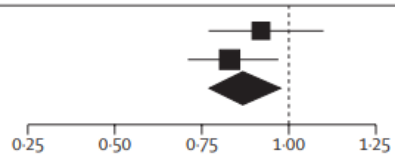
D First hospitalisation for heart failure

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
EMPEROR-Reduced	246/1863 (13·2%)	342/1867 (18·3%)	0·69 (0·59–0·81)
DAPA-HF	231/2373 (9·7%)	318/2371 (13·4%)	0·70 (0·59–0·83)
Total			**0·69 (0·62–0·78)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·90			



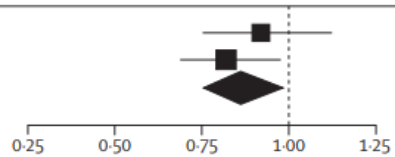
A All-cause mortality

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
EMPEROR-Reduced	249/1863 (13·4%)	266/1867 (14·2%)	0·92 (0·77–1·10)
DAPA-HF	276/2373 (11·6%)	329/2371 (13·9%)	0·83 (0·71–0·97)
Total			**0·87 (0·77–0·98)**
Test for overall treatment effect p=0·018			
Test for heterogeneity of effect p=0·39			



B Cardiovascular death

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
EMPEROR-Reduced	187/1863 (10·0%)	202/1867 (10·8%)	0·92 (0·75–1·12)
DAPA-HF	227/2373 (9·6%)	273/2371 (11·5%)	0·82 (0·69–0·98)
Total			**0·86 (0·76–0·98)**
Test for overall treatment effect p=0·027			
Test for heterogeneity of effect p=0·40			



Lancet, 2020 Sep 19;396(10254):819-829

Main clinical concerns in initiating SGLT2i

Starting in the acute setting

- **EMPULSE (11)**: win ratio of clinical benefit[a] favours SGLT2i
- **EMPA-RESPONSE-AHF (10)** : composite endpoint favours SGLT2i[b]
- **DICTATE-AHF (12)**: evidence for enhanced diuresis[c]

NO difference in AEs between SGLT2i and placebo

Risk of volume depletion

- **DICTATE-AHF (12)**: no ≠ in weight-based diuretic efficiency
- **EMPAG-HF (14)** (25 mg): 25% ↑ UO, no effect on eGFR slope nor on AEs
- **DELIVER (3)**: 32% ↓ new initiation of loop diuretics
- **EMPEROR-preserved (4)**: ↓ diuretic initiation or dose escalation, ↑ de-escalation / discontinuation

Hyperkalemia

EMPEROR-pooled (15): significant ↓ incidence of hyperkalemia, no ↑ of hypokalemia

SGLT2i mitigates the occurrence of hyperkalaemia & **may maximize long-term tolerance** of the quadruple therapy regimen (**GDMT**)

Deterioration of renal function

Mean ≠ in eGFR change:

- **EMPEROR-reduced (1)**: −2.5 mL/min/1.73m2; no ≠ risk of CV and renal outcomes if early eGFR ↓
- **DAPA-HF (2)**: −3.1 mL/min/1.73m2; similar early ↓ in eGFR after initiation across the range of eGFR

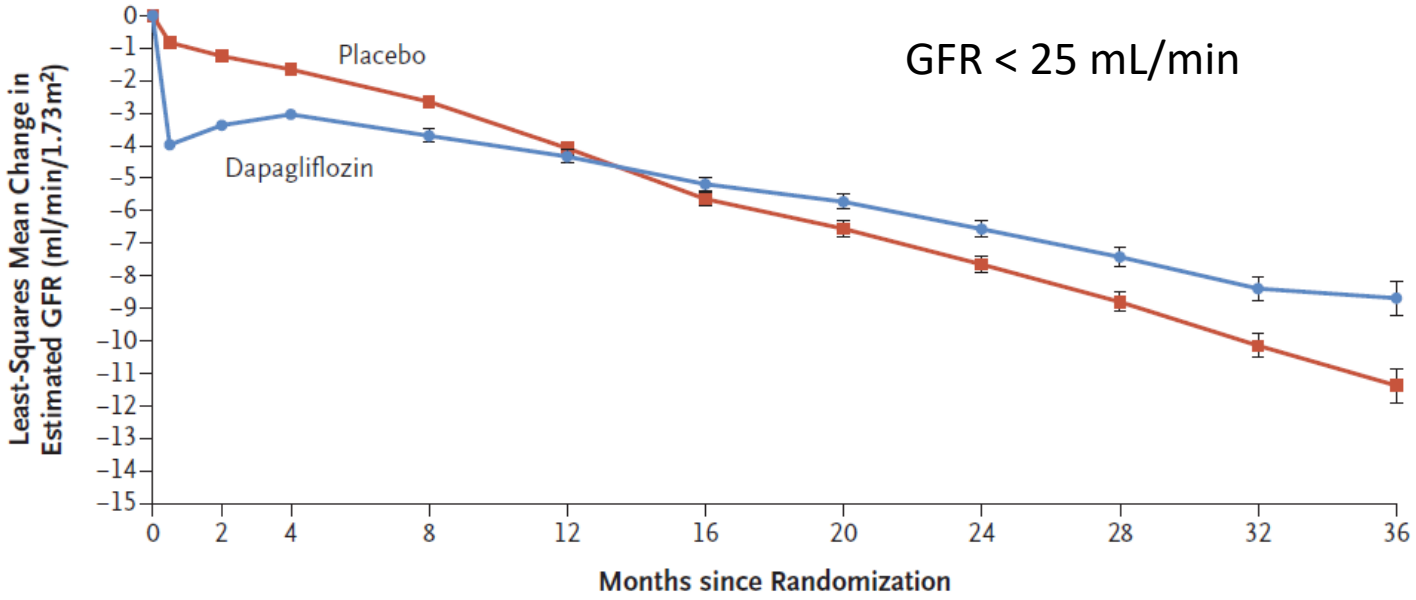
If eGFR fall below initiation thresholds: ↑ CV outcomes risk. SGLT2i still beneficial on CV outcomes, w/out ↑ in safety outcomes

European Heart Journal Supplements (2025) 27 (Supplement 1), i137–i140

DAPA CKD

Dapagliflozin in Patients with Chronic Kidney Disease

4304 participants
eGFR 25 - 75 ml/min/1.73 m_2
Urinary albumin-to-creatinine ratio 200 - 5000

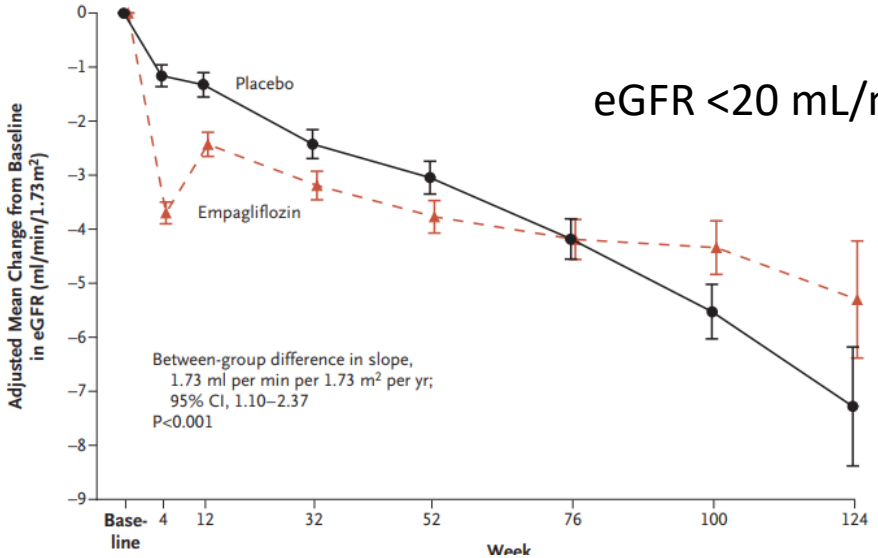


GFR < 25 mL/min

EMPEROR-R

Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure

3730 patients
NYHA II, III, IV
EF<= 40%
Diabete 49.8%



eGFR <20 mL/min/1,73 m

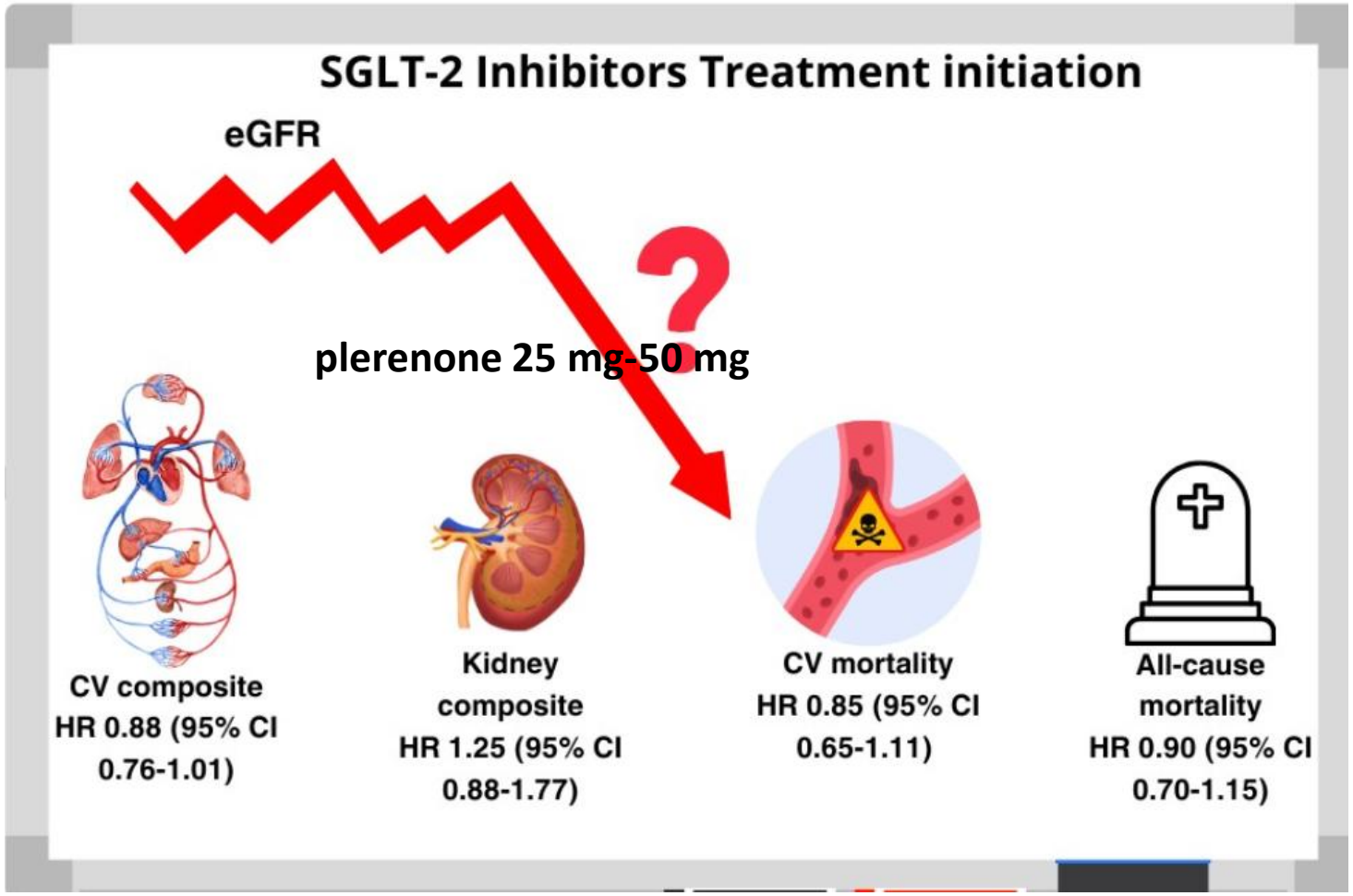
NEJM.org, September 24, 2020

N Engl J Med August 2020

A placebo-correcetd effect of the initial eGFR decline following SGLT-2 inhibitor initiation: a systematic review and meta-analysis

23890 patients, the dip occurring in 13575 (56.82%)
8245(34.51%) in the intervention arm
5330 (22.31%) in the placebo arm

5 papers



Heart Failure 2025

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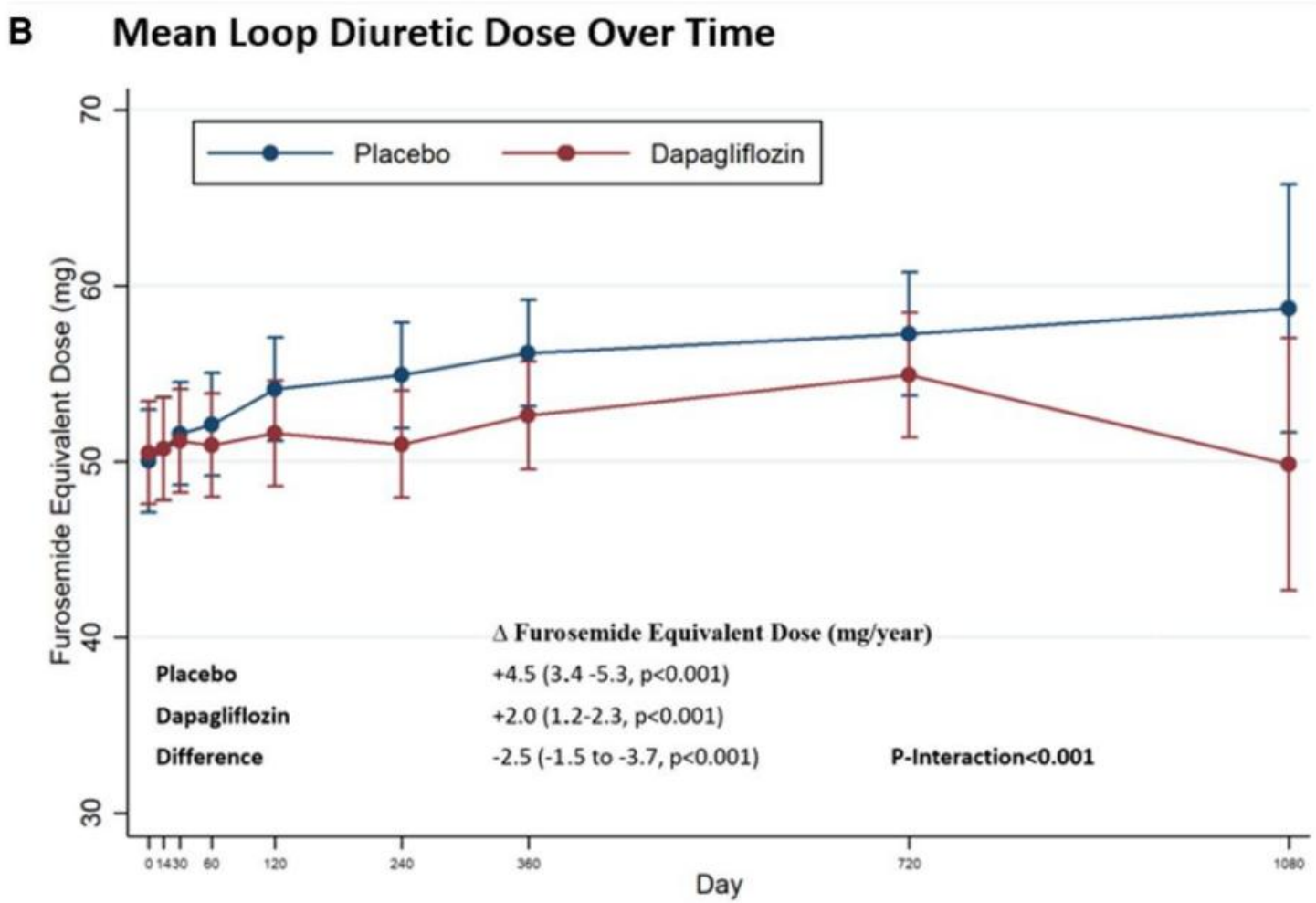
European Heart Journal Supplements (2025) 27 (Supplement 1), i137–i140

Dapagliflozin and diuretic utilization in heart failure with mildly reduced or preserved ejection fraction: the DELIVER trial



European Heart Journal (2023) 00, 1–14

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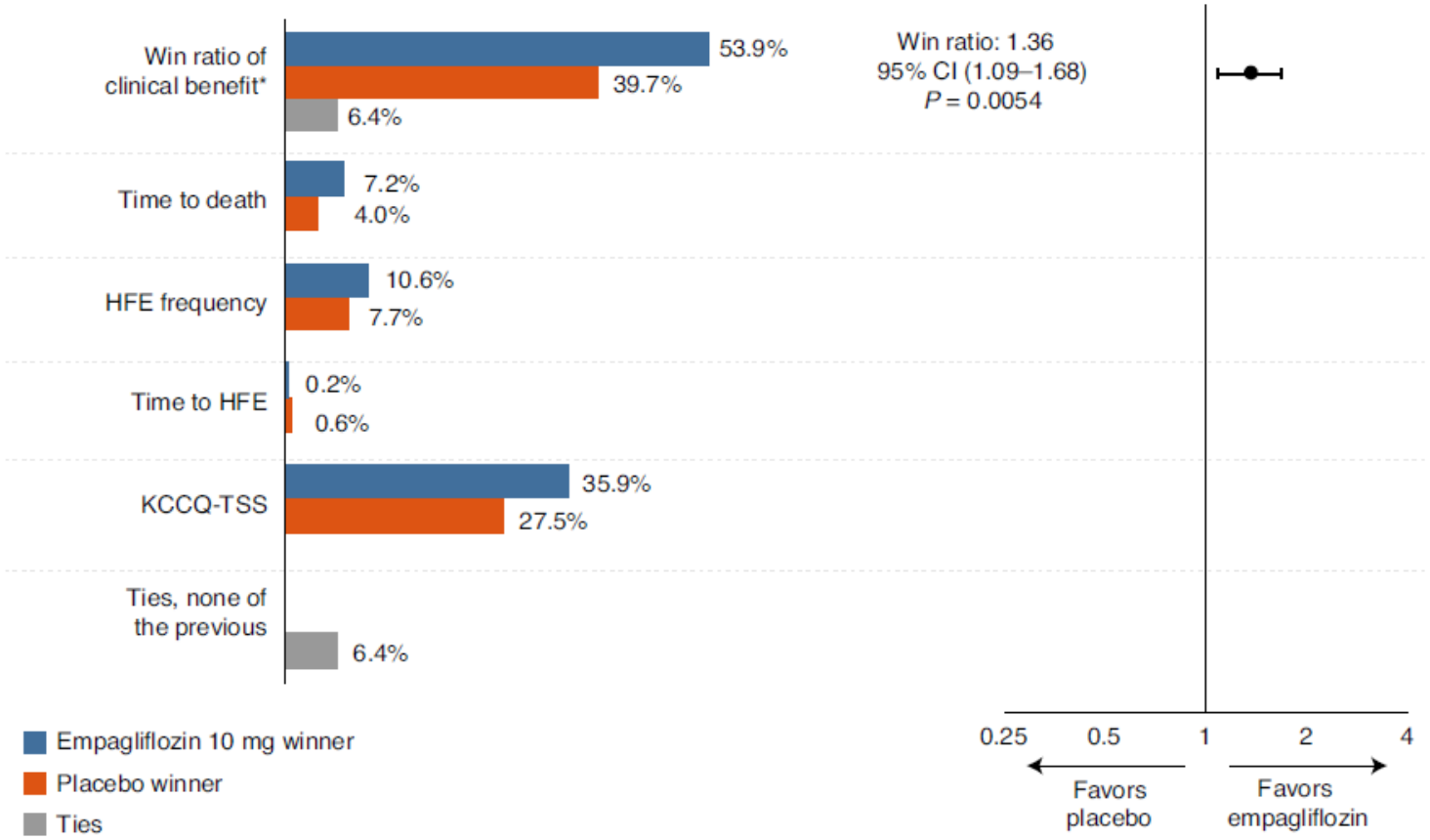
European Heart Journal Supplements (2025) 27 (Supplement 1), i137–i140

The SGLT2 inhibitor empagliflozin in patients hospitalized for acute heart failure: a multinational randomized trial

EMPULSE

clinical benefit: composite of death from any cause, number of HF events, and time to first HF event, or a ≥5 point difference in change from baseline in the KCCQ total symptom score at 90 days,

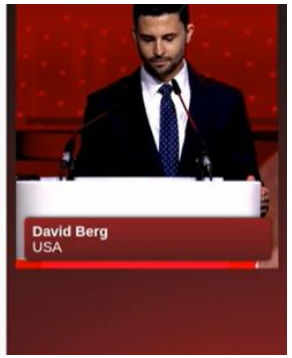


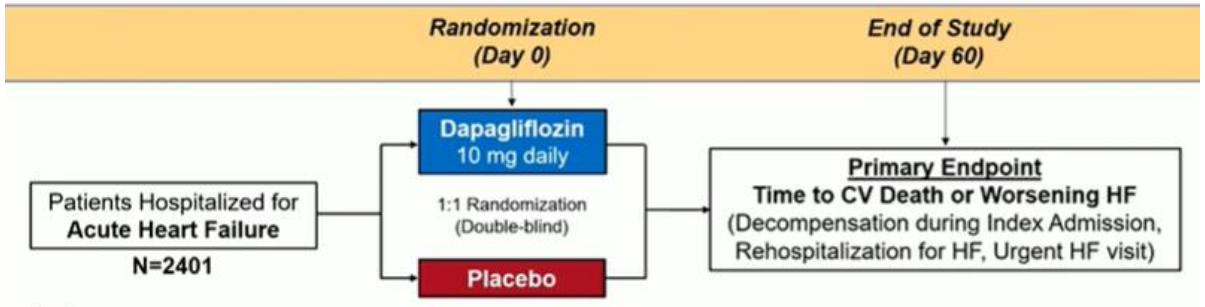
Nat Med 2022;28:568–74

DAPA ACT HF – TIMI 68

Dapagliflozin in Patients Hospitalized for Heart Failure

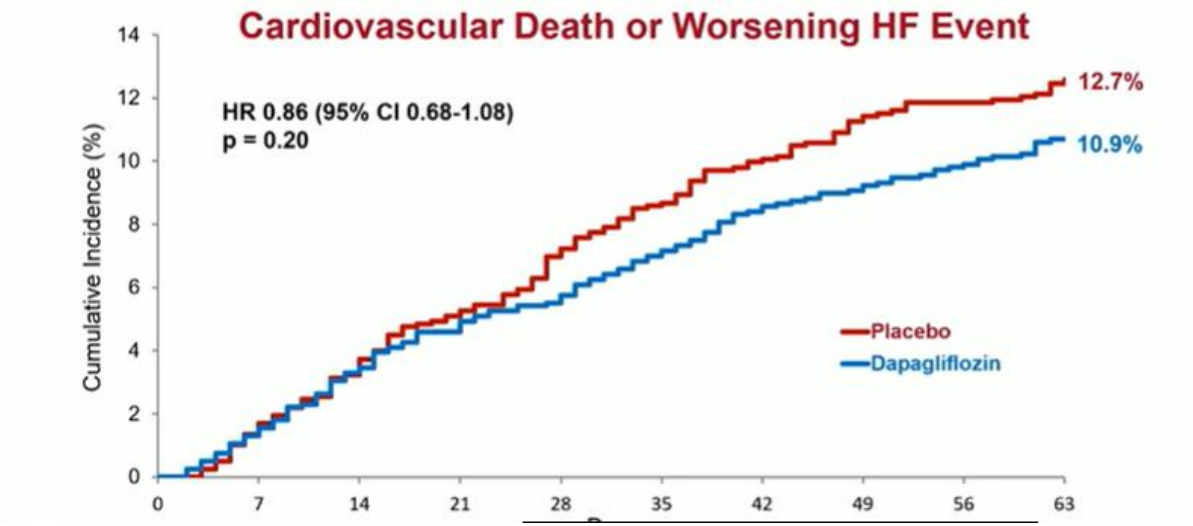
David D. Berg, MD, MPH
for the DAPA ACT HF – TIMI 68 Investigators





Primary Endpoint

DAPA ACT HF
TIMI 68



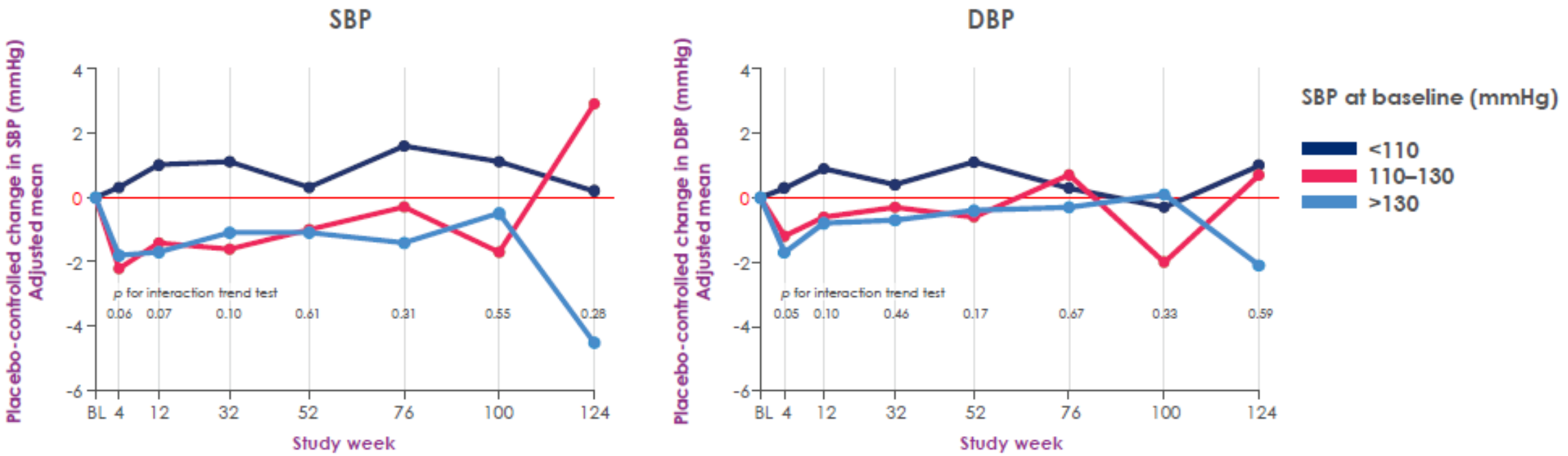
Safety Endpoints

DAPA ACT HF
TIMI 68

	Dapagliflozin (N=1218)	Placebo (N=1183)
Symptomatic hypotension	43 (3.6%)	26 (2.2%)
Worsening kidney function	71 (5.9%)	55 (4.7%)
Major hypoglycemia	3 (0.2%)	3 (0.3%)
Diabetic ketoacidosis	0 (0.0%)	0 (0.0%)
AE leading to IP discontinuation	58 (4.8%)	56 (4.7%)

Empagliflozin Improves Cardiovascular and Renal Outcomes in Heart Failure Irrespective of Systolic Blood Pressure

Placebo-corrected change in blood pressure from baseline in patients treated with empagliflozin



Between-group differences were of borderline significance after 4 and 12 weeks, but were not significant at later time points

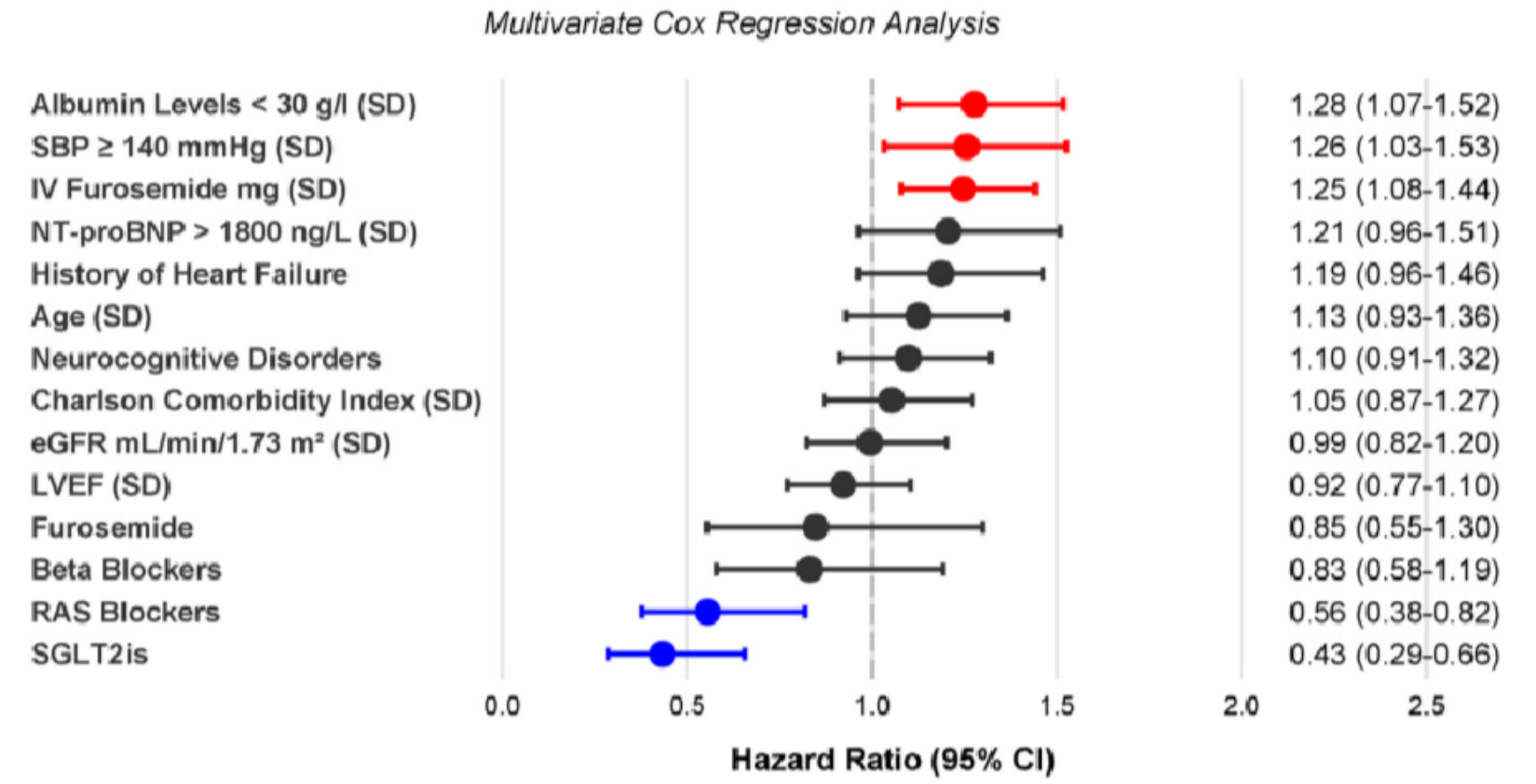
Böhm M et al. J Am Coll Cardiol. 2021;78:1337.

Real-World Outcomes of SGLT2 Inhibitors in Very Elderly Patients With Heart Failure With Preserved Ejection Fraction

Patients >80 years admitted to 3 geriatric units in Paris
298 patients
mean age 90 years (59% >90 and 7% >100 years of age)

The 1-year mortality was 28.1% and the rate of HF rehospitalization was 22.8% .

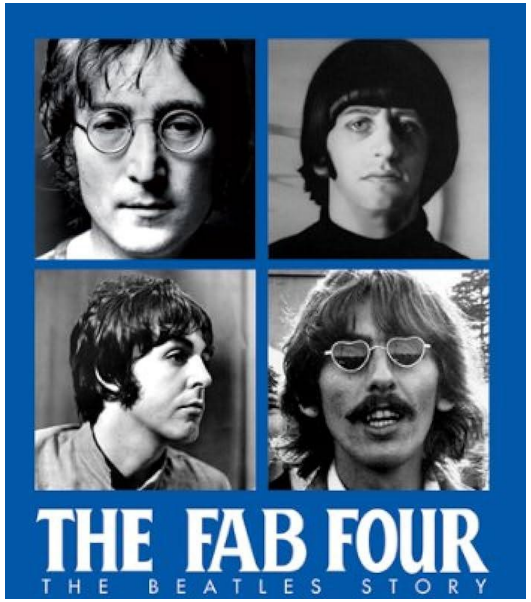
FIGURE 1 Factors Associated With Mortality or HF Rehospitalization in Very Elderly Patients With HFpEF



JACC: HEART FAILURE 2025

Terapia medica ottimale

Trattamento dello scompenso a frazione di eiezione ridotta



A

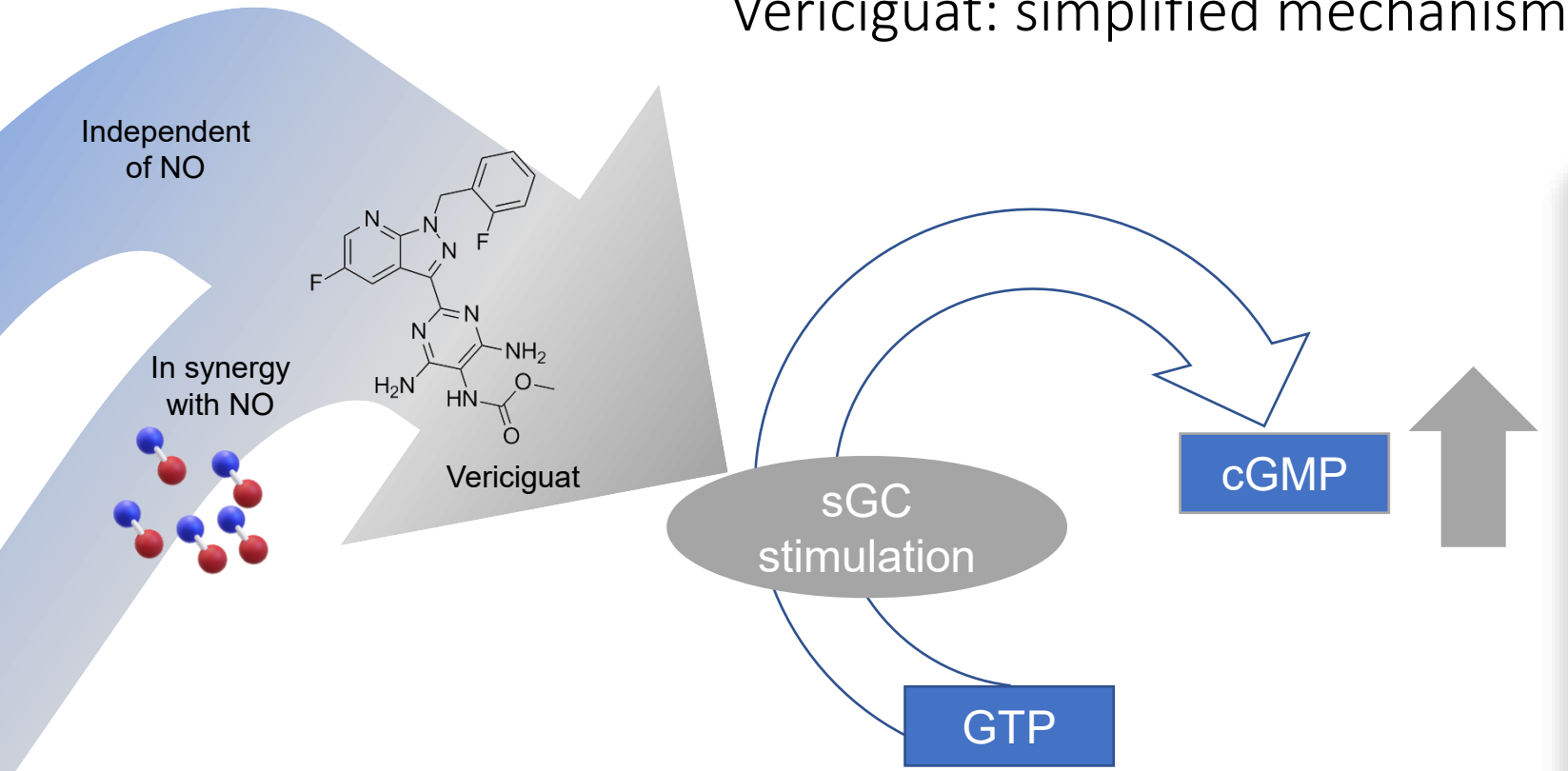
Treatment	All-Cause Mortality	HR (95% CI)
ARNI + BB + MRA + SGLT2		0.39 (0.31-0.49)
ARNI + BB + MRA + Vericiguat		0.41 (0.32-0.53)
ARNI + BB + MRA + Omecamtiv		0.44 (0.36-0.55)
ACEI + BB + Dig + H–ISDN		0.46 (0.35-0.61)
ACEI + BB + MRA + IVA		0.48 (0.39-0.58)
ACEI + BB + MRA + Vericiguat		0.49 (0.39-0.62)
ACEI + BB + MRA + Omecamtiv		0.52 (0.43-0.63)
ARNI + ARB + BB + Dig		0.65 (0.55-0.76)
ARNI + BB + MRA		0.44 (0.37-0.54)
ACEI + BB + MRA		0.52 (0.44-0.61)
ACEI + MRA + Dig		0.66 (0.56-0.78)
ACEI + BB + Dig		0.68 (0.59-0.78)
ARB + BB + Dig		0.73 (0.64-0.83)
ACEI + ARB + Dig		0.83 (0.72-0.96)
Dig + H–ISDN		0.67 (0.53-0.86)
ARNI + BB		0.58 (0.50-0.68)
ACEI + BB		0.69 (0.61-0.77)
ARB + BB		0.74 (0.66-0.82)
ACEI + Dig		0.87 (0.78-0.98)
ARB + Dig		0.94 (0.84-1.05)
BB		0.78 (0.72-0.84)
ACEI		0.89 (0.82-0.96)
ARB		0.95 (0.88-1.02)
Dig		0.99 (0.91-1.07)
PLBO		1.00

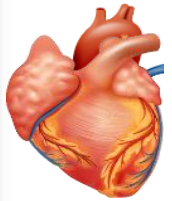
0.25 0.5 1 2

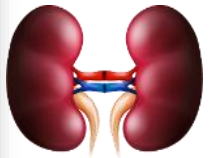
J Am Coll Cardiol HF. 2022 Feb, 10 (2) 73–84

E oltre ???? Fab Five ???

Vericiguat: simplified mechanism of action





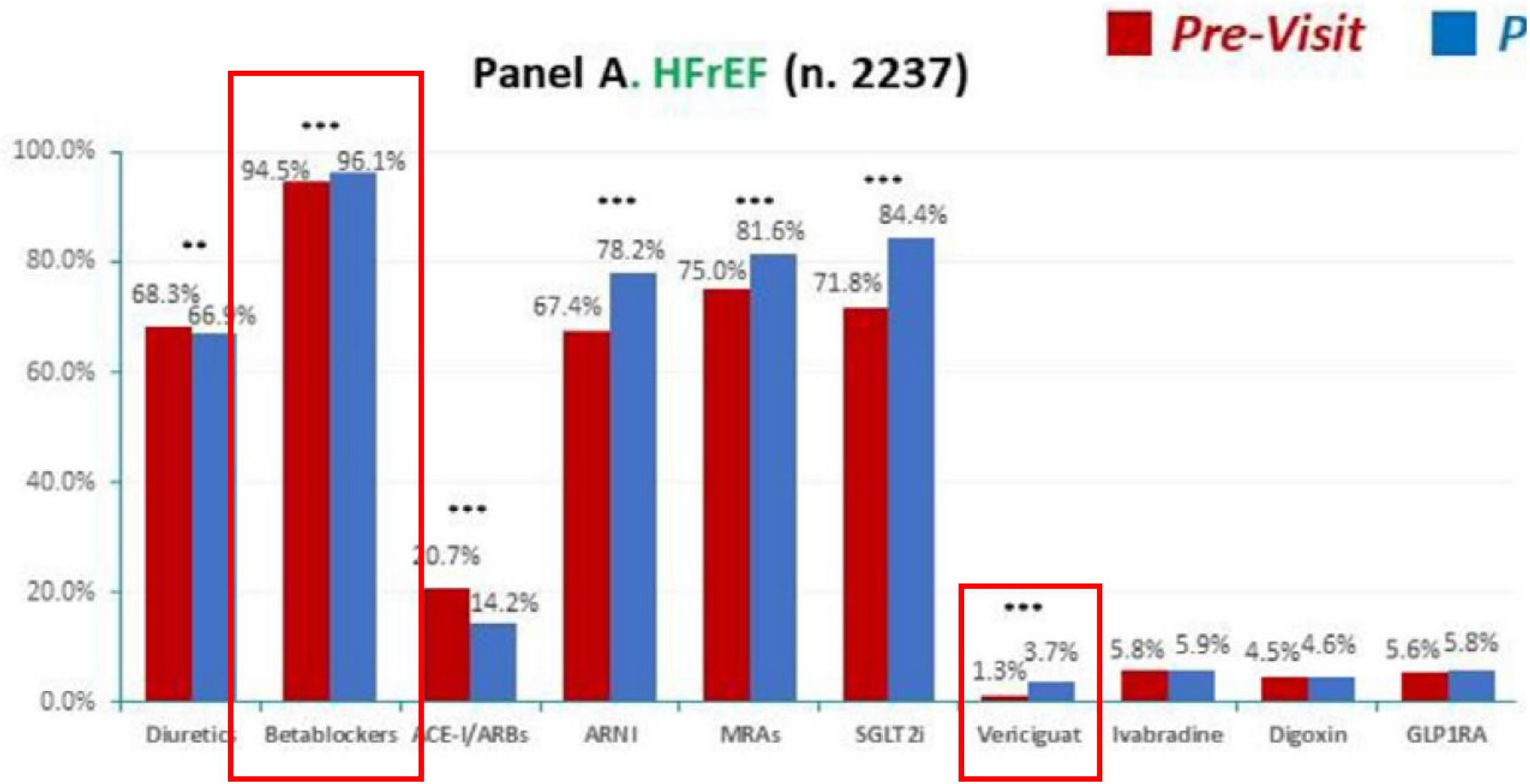


- Improved myocardial function
- Reduced left ventricular remodeling
- Improved vascular function
- Decreased fibrosis
- Decreased inflammation

cGMP, cyclic guanosine monophosphate; GTP, guanosine triphosphate; NO, nitric oxide; sGC, soluble guanylate cyclase.

1. Armstrong PW et al. *JACC Heart Fail.* 2018;6:96–104; 2.Gheorghiade M et al. *Heart Fail Rev*. 2013;18:123–134; 3. Sandner P et al. *Handb Exp Pharmacol*. 2021;264:355–394.

BRING·UP3·HF



Journal of Cardiac Failure 00 (2025) 111

Vericiguat in Patients with Heart Failure and Reduced Ejection Fraction

VICTORIA

5050 patients

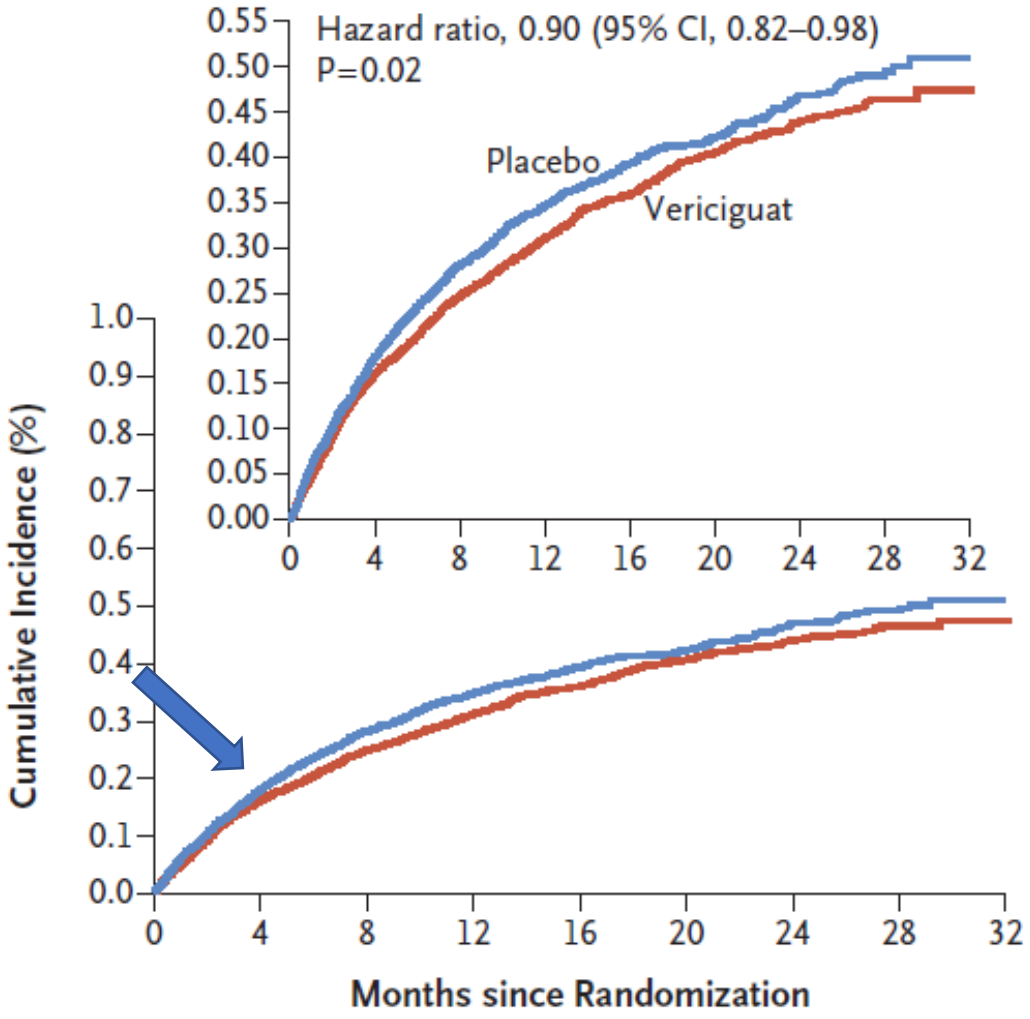
- **chronic heart failure (NYHA II-IV)**
- **EF < 45%**
- **BNP > 300 in SR or > 500 in AF**
- **Worsening HF**

- 93.1% BB
- 73.4% ACEi/ARB
- 14.5% ARNi
- 70.3% MRA

Median follow-up: 10.8 months

Annual NNT: 24

Death from cardiovascular causes or first hospitalization for heart failure

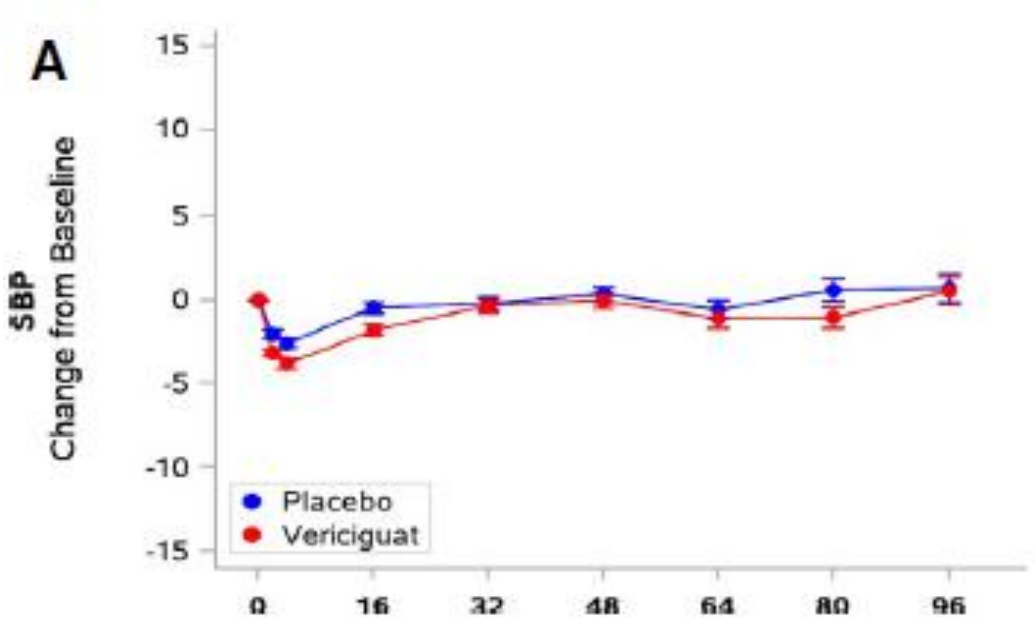


N Engl J Med 2020;382:1883-93

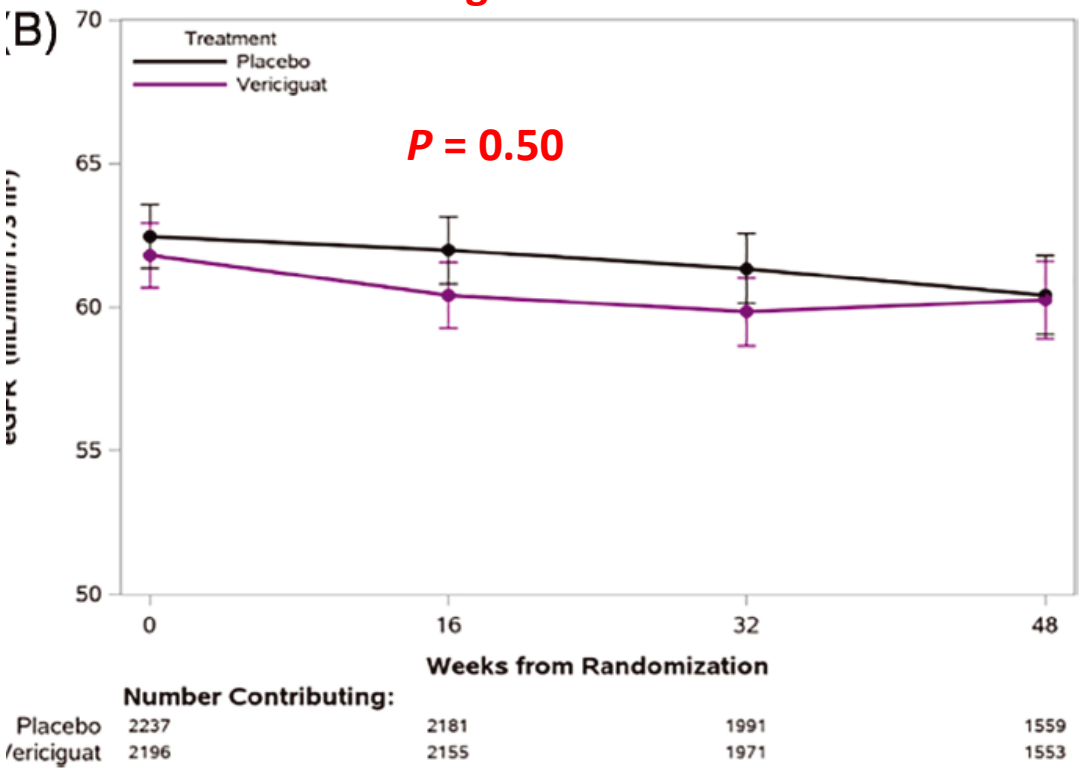
Blood Pressure and Safety Events With Vericiguat in the VICTORIA Trial

Renal function and the effects of vericiguat in patients with worsening heart failure with reduced ejection fraction: insights from the VICTORIA (Vericiguat Global Study in Subjects with HFrEF) trial

Change in Blood Pressure



Change in GFR



Exclusion criteria : systolic blood pressure <100 mm Hg.

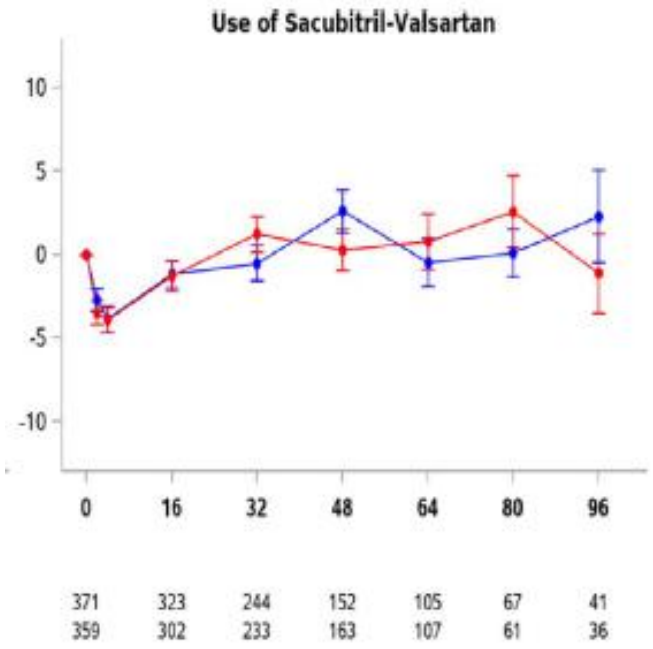
Exclusion criteria : GFR < 15

J Am Heart Assoc. 2021;10:e021094

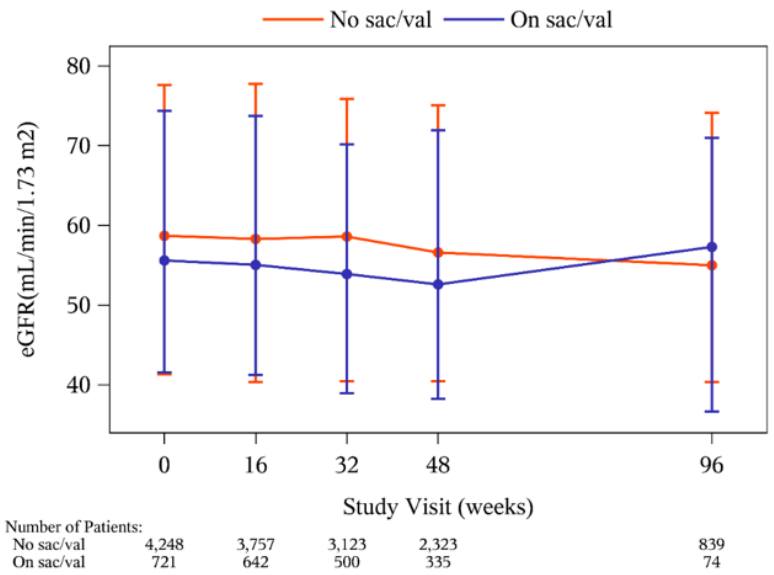
European Journal of Heart Failure (2021) 23, 1313–1321

Efficacy and safety of vericiguat in patients with heart failure with reduced ejection fraction treated with sacubitril/valsartan: insights from the VICTORIA trial

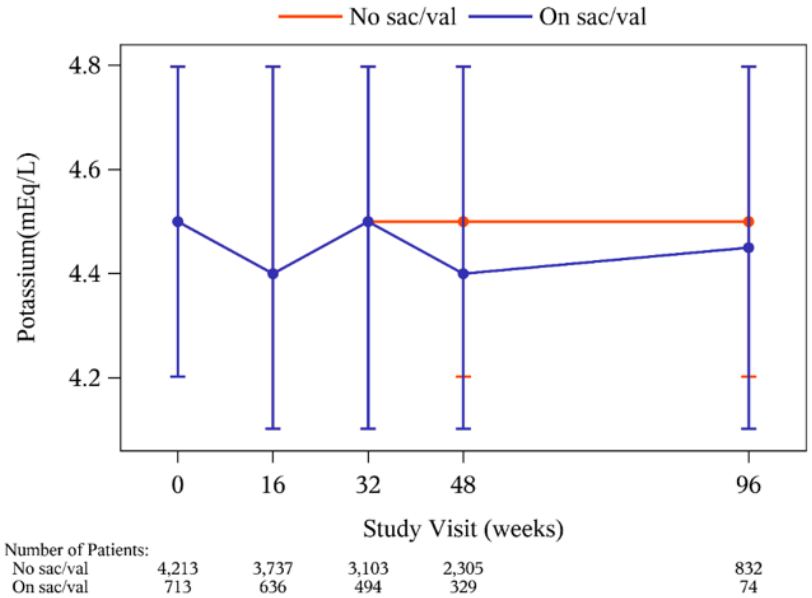
Blood pressure



GFR



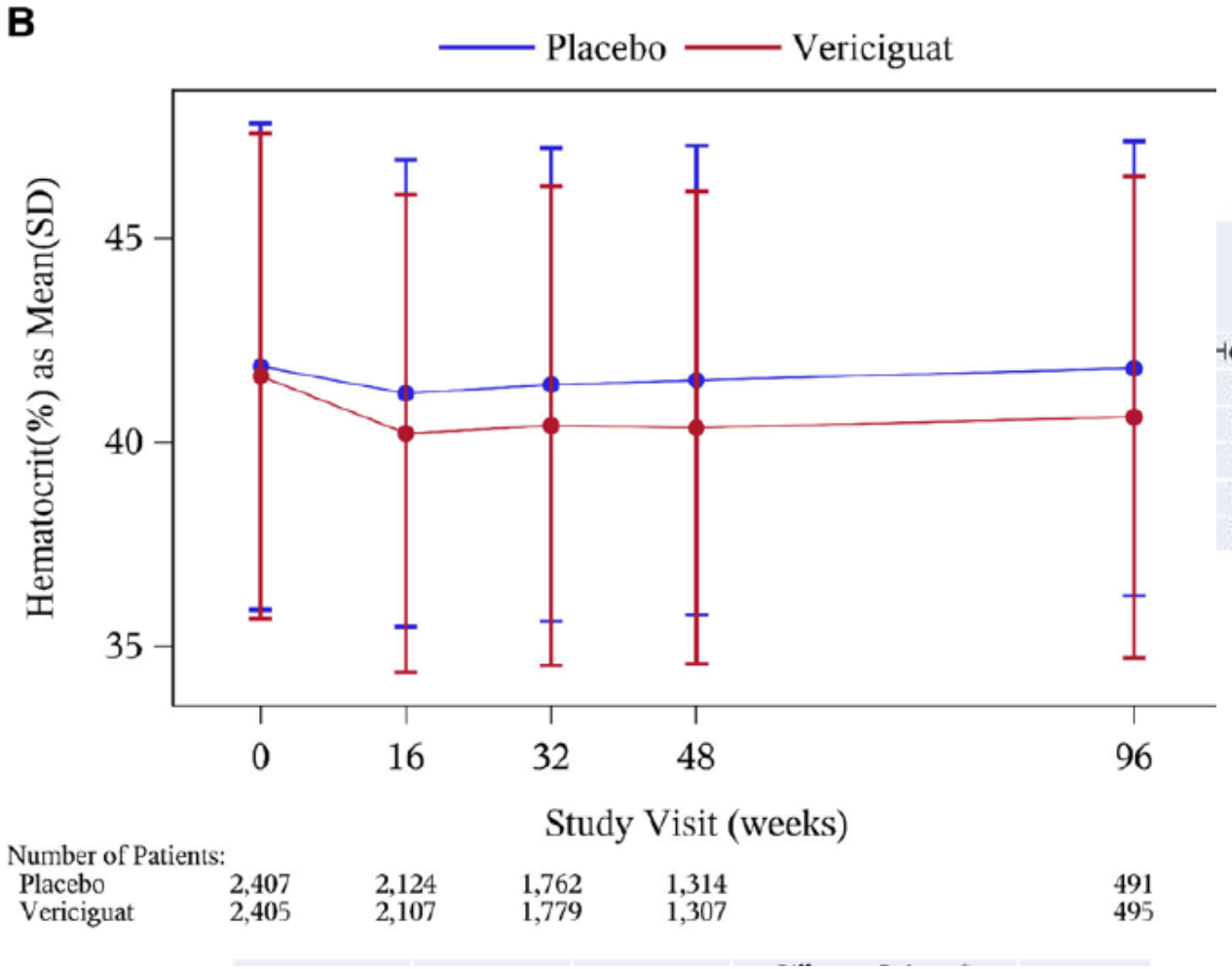
Potassium



European Journal of Heart Failure (2022) **24**, 1614–1622

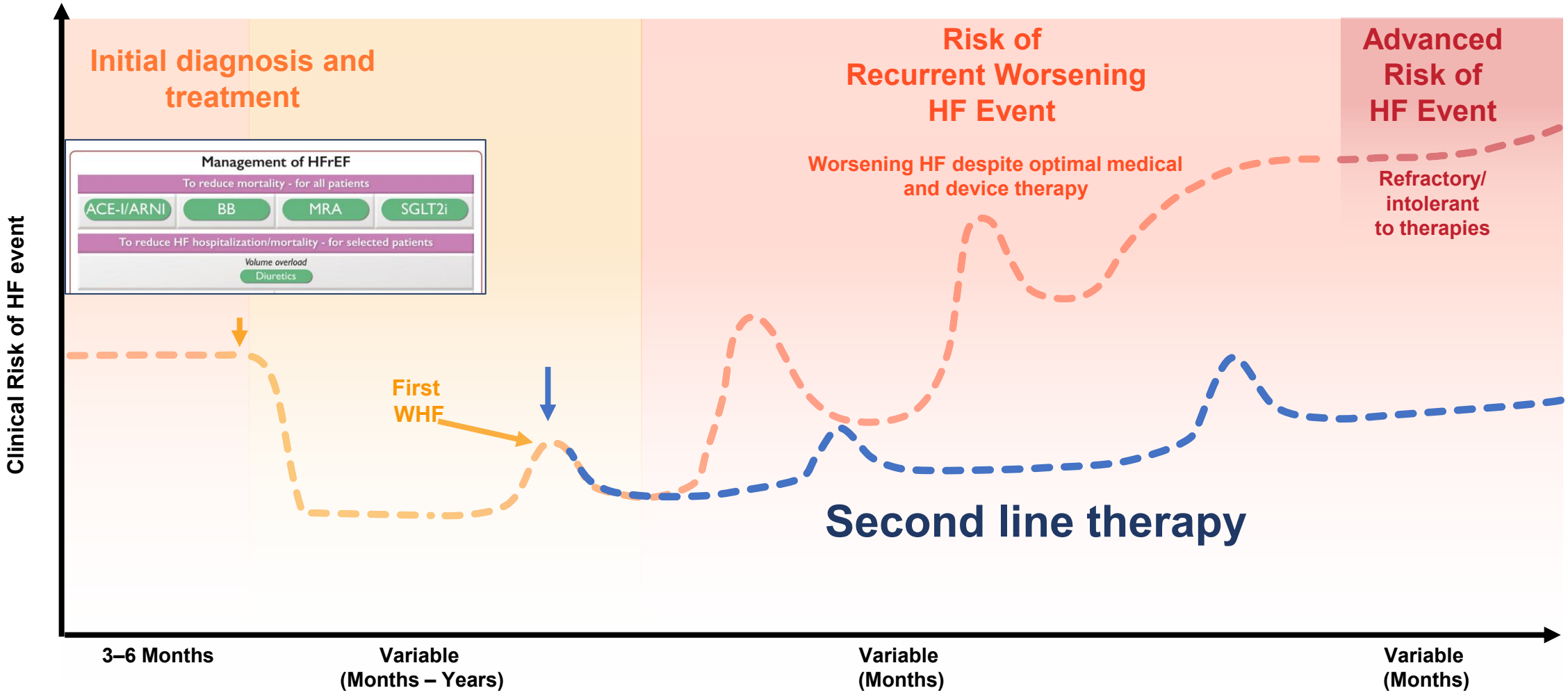
Hemoglobin and Clinical Outcomes in the Vericiguat Global Study in Patients With Heart Failure and Reduced Ejection Fraction (VICTORIA)

Hematocrit



	Vericiguat Mean (SE)*	Placebo Mean (SE)*	Difference Estimate* (V-P) (95% CI)	P-value†
Hematocrit				
Baseline	41.62 (0.122)	41.85 (0.122)	-0.039 (-0.102, 0.023)	0.220
Week 16	40.19 (0.130)	41.20 (0.126)	-0.882 (-1.121, -0.642)	<.001
Week 32	40.41 (0.143)	41.45 (0.141)	-0.857 (-1.132, -0.581)	<.001
Week 48	40.42 (0.165)	41.59 (0.162)	-0.898 (-1.213, -0.582)	<.001
Week 96	40.74 (0.288)	41.93 (0.269)	-1.013 (-1.554, -0.472)	<.001

Circulation. 2021;144:1489–1499


Initial diagnosis and treatment
Management of HFrEF
To reduce mortality - for all patients
ACE-I/ARNI
BB
MRA
SGLT2i
To reduce HF hospitalization/mortality - for selected patients
Volume overload
Diuretics
Risk of Recurrent Worsening HF Event
Worsening HF despite optimal medical and device therapy
Advanced Risk of HF Event
Refractory/ intolerant to therapies
First WHF
Second line therapy
Clinical Risk of HF event
3–6 Months
Variable (Months – Years)
Variable (Months)
Variable (Months)

Vericiguat in ambulatory patients with chronic heart failure with reduced ejection fraction: Results of the VICTOR trial

Faiez Zannad, MD, PhD, on behalf of Javed Butler (co-PI) and the VICTOR Executive Committee
Global CardioVascular Clinical Trialists Forum (CVCT) and Université de Lorraine, Nancy, France

VICTOR: study design (NCT05093933)

Phase 3, double-blind, placebo-controlled study in people with HFrEF [1,2]

Key inclusion criteria

- HFrEF (LVEF ≤40%)
- No recent HF events (no HHF for 6 months, no IV diuretics for 3 months)
- NT-proBNP levels of 600–6000 pg/mL†
- No recent changes in doses of GDMT

Primary endpoints
CV death or first HHF

Secondary endpoints (Hierarchical)

6105 participants , **482** sites, **36** countries

Median follow-up time:
- 18.5 months

Study drug discontinuation due to adverse events (excluding discontinuation due to death)
- **8.4%** of participants in the vericiguat group
- **7.3%** of participants in the placebo group

Mean dose:
- **8.2 mg** in the vericiguat group
- **8.5 mg** in the placebo group

Vericiguat in ambulatory patients with chronic heart failure with reduced ejection fraction: Results of the VICTOR trial

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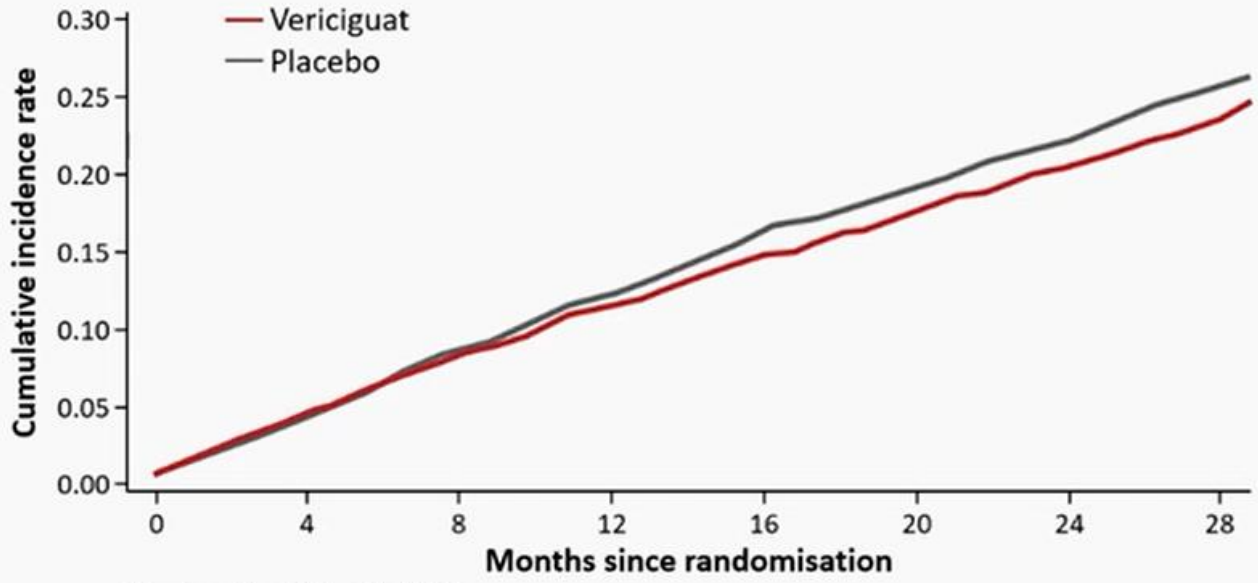


	Number of participants at risk							
Vericiguat	3053	2927	2797	2581	1917	1352	849	459
Placebo	3052	2929	2771	2543	1879	1314	823	442
	Cumulative number of events up to the time point							
Vericiguat	0	109	228	333	409	462	505	527
Placebo	0	108	242	355	442	506	547	574

Vericiguat: 549 (**18.0%**)
Placebo: 584 (**19.1%**)
HR **0.93** (95% CI 0.83–1.04); P=0.22

Generally consistent across prespecified subgroups

Vericiguat in ambulatory patients with chronic heart failure with reduced ejection fraction: Results of the VICTOR trial

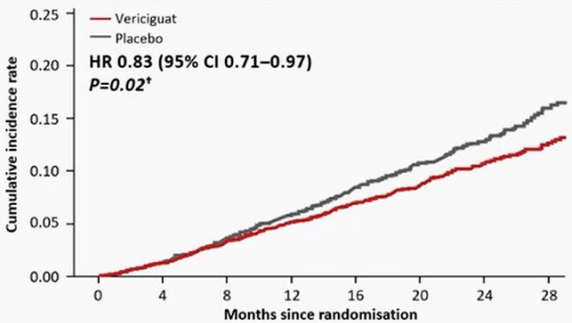
Faiez Zannad, MD, PhD, on behalf of Javed Butler (co-PI) and the VICTOR Executive Committee

Global CardioVascular Clinical Trialists Forum (CVCT) and Université de Lorraine, Nancy, France

Effects of vericiguat on mortality

CV death[1,2]

Prespecified powered secondary endpoint



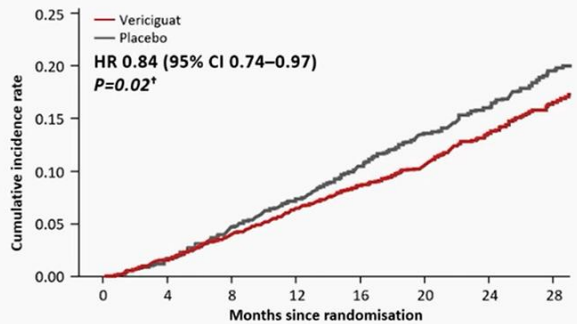
Number of participants at risk

Vericiguat	3053	3000	2928	2752	2092	1516	968	536
Placebo	3052	3003	2910	2728	2050	1456	940	514

Cumulative number of events up to the time point

Vericiguat	0	37	99	156	201	234	263	279
Placebo	0	40	111	177	243	287	314	340

All-cause death[1,2]



Number of participants at risk

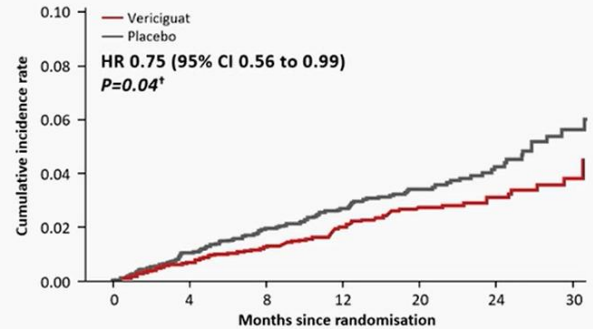
Vericiguat	3053	3000	2928	2752	2092	1516	968	536
Placebo	3052	3003	2910	2728	2050	1456	940	514

Cumulative number of events up to the time point

Vericiguat	0	51	123	197	254	292	335	361
Placebo	0	47	140	223	307	368	402	432

Mode of death: Exploratory analyses

Sudden cardiac death[1,2]



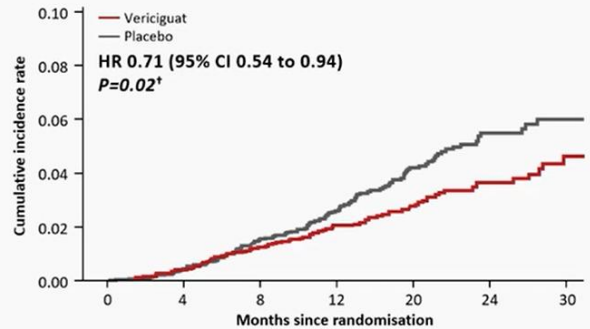
Number of participants at risk

Vericiguat	3053	2984	2894	2241	1516	838	340
Placebo	3052	2978	2862	2208	1456	816	326

Cumulative number of events up to the time point

Vericiguat	0	20	37	57	70	75	79
Placebo	0	32	58	77	92	100	109

HF-related death[1,2]



Number of participants at risk

Vericiguat	3053	2982	2887	2229	1505	827	333
Placebo	3052	2970	2850	2189	1438	798	312

Cumulative number of events up to the time point

Vericiguat	0	13	38	59	73	83	88
Placebo	0	12	46	73	103	118	121

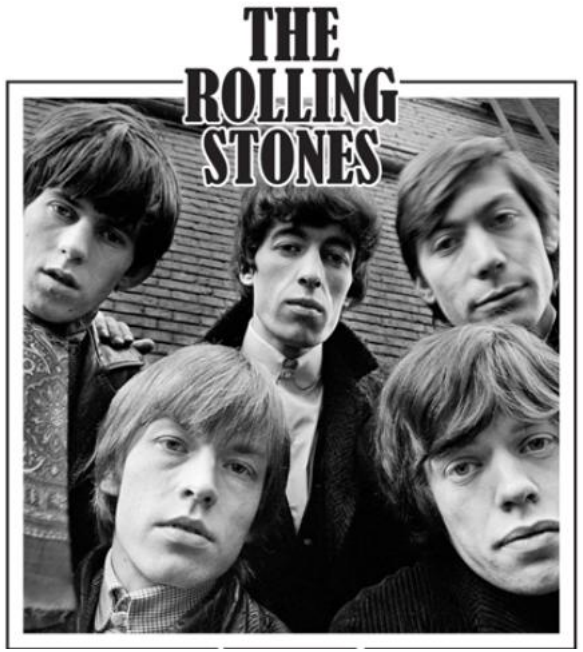
Baseline demographics and medical therapies

Characteristic	Vericiguat (N=3053)	Placebo (N=3052)
Age, mean, years	67	67
Female sex, n (%)	727 (24)	713 (23)
Race, n (%)		
White	1942 (64)	1992 (65)
Black (expanded)†	343 (11)	313 (10)
American Indian or Alaskan	159 (5)	142 (5)
Native Hawaiian or Pacific Islander	4 (0.1)	7 (0.2)
Asian	383 (13)	363 (12)
Multiracial	313 (10)	330 (11)
Comorbidities, n (%)		
Diabetes	1274 (42)	1311 (43)
Atrial fibrillation	1135 (37)	1182 (39)
Hypertension	2153 (71)	2176 (71)
Coronary artery disease	1861 (61)	1883 (62)
Systolic blood pressure, mean ± SD, mmHg	121 ± 16	122 ± 16
Haemoglobin, mean ± SD, g/dL	14 ± 3	14 ± 2
Body mass index, mean, kg/m^2	28	29
NT-proBNP, median, pg/mL	1370	1381
No prior HHF, n (%)	1426 (47)	1473 (48)
LVEF, mean, %	31	30
Estimated glomerular filtration rate, mean, mL/min/1.73 m^2	71	71

Medical therapy, n (%)	Vericiguat (N=3053)	Placebo (N=3052)
Loop diuretics	2131 (70)	2129 (70)
Beta-blockers	2886 (95)	2880 (94)
Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker	1150 (38)	1188 (39)
ARNI	1734 (57)	1682 (55)
Mineralocorticoid receptor antagonist	2358 (77)	2390 (78)
SGLT2i	1812 (59)	1798 (59)
Implantable cardioverter-defibrillator	993 (33)	1016 (33)
Cardiac resynchronisation therapy	464 (15)	440 (14)

†Expanded Black includes participants who identify as Black, or Multi-racial and Black.

Fab Five



JACC Preprint

A	Treatment	All–Cause Mortality	HR	95%–CI
	ARNI + BB + MRA + SGLT2 + Vericiguat*		0.35	[0.27; 0.45]
	ARNI + BB + MRA + SGLT2		0.39	[0.32; 0.49]
	ARNI + BB + MRA + Vericiguat		0.40	[0.32; 0.49]
	ARNI + BB + MRA		0.45	[0.37; 0.54]
	ARNI + BB + MRA + Omecamtiv		0.45	[0.37; 0.55]
	ACEI + BB + MRA + SGLT2		0.46	[0.38; 0.56]
	ACEI + BB + MRA + Vericiguat		0.46	[0.38; 0.56]
	ACEI + BB + Dig + H–ISDN		0.47	[0.36; 0.61]
	ACEI + BB + MRA + IVA		0.48	[0.39; 0.58]
	ARNI + BB + SGLT2		0.52	[0.43; 0.63]
	ACEI + BB + MRA		0.52	[0.44; 0.62]
	ACEI + BB + MRA + Omecamtiv		0.52	[0.44; 0.63]
	ARB + BB + MRA		0.56	[0.47; 0.65]
	ARNI + BB		0.59	[0.51; 0.69]
	ACEI + ARB + BB + Dig		0.65	[0.55; 0.76]
	ACEI + MRA + Dig		0.66	[0.56; 0.78]
	Dig + H–ISDN		0.68	[0.53; 0.86]
	ACEI + BB + Dig		0.68	[0.59; 0.78]
	ACEI + BB		0.69	[0.62; 0.77]
	ARB + BB + Dig		0.73	[0.63; 0.83]
	ARB + BB		0.74	[0.66; 0.82]
	BB		0.78	[0.72; 0.84]
	ACEI + ARB + Dig		0.83	[0.72; 0.96]
	ACEI + Dig		0.88	[0.78; 0.98]
	ACEI		0.89	[0.82; 0.96]
	ARB + Dig		0.94	[0.84; 1.04]
	ARB		0.95	[0.88; 1.02]
	Dig		0.99	[0.91; 1.07]

0.2 0.5 1 1.5

Hazard Ratio [95% CI]