XII Meeting. State of the Art in
HEART FAILURE
CLINICAL PRACTICE AND ORGANIZATIONAL MODELS

Venue: Hotel Meliá María Pita, A Coruña

A Coruña 26-27 September 2025

A Coruña Heart Failure Academy

#ACORUÑAHF2025

WHAT'S NEW/COMING IN DRUG THERAPY IN HF?

Mechanism of actions and new therapeutic targets and combinations

Julio Núñez || HCUV

SERVIZO GALEGO DE SAÚDE · ÁREA SANITARIA DA CORUÑA E CEE · inibic · SOCIEDADE GALEGA DE CARDIOLOXÍA · UNIVERSIDADE DA CORUÑA · ciber | CV · UNIÓN EUROPEA Fondo Europeo de Desarrollo Regional · XUNTA DE GALICIA · galicia

VICTOR. Study design

CHRONIC HFrEF

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)
Key secondary powered endpoint : CV death

Other secondary endpoints
First HHF, Total HHF events‡,
All-cause death or HHF, All-cause death

Sample size

- Projected 6000 patients
- Expected ~590 CV deaths and ~1080 events of CV death or hospitalisation
- ~95% power for CV death or HHF
- ~80% power for CV death

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

Butler J, et al. Lancet. 2025 Aug 29:S0140-6736(25)01665-4.

VICTOR. Baseline demographics and medical therapies

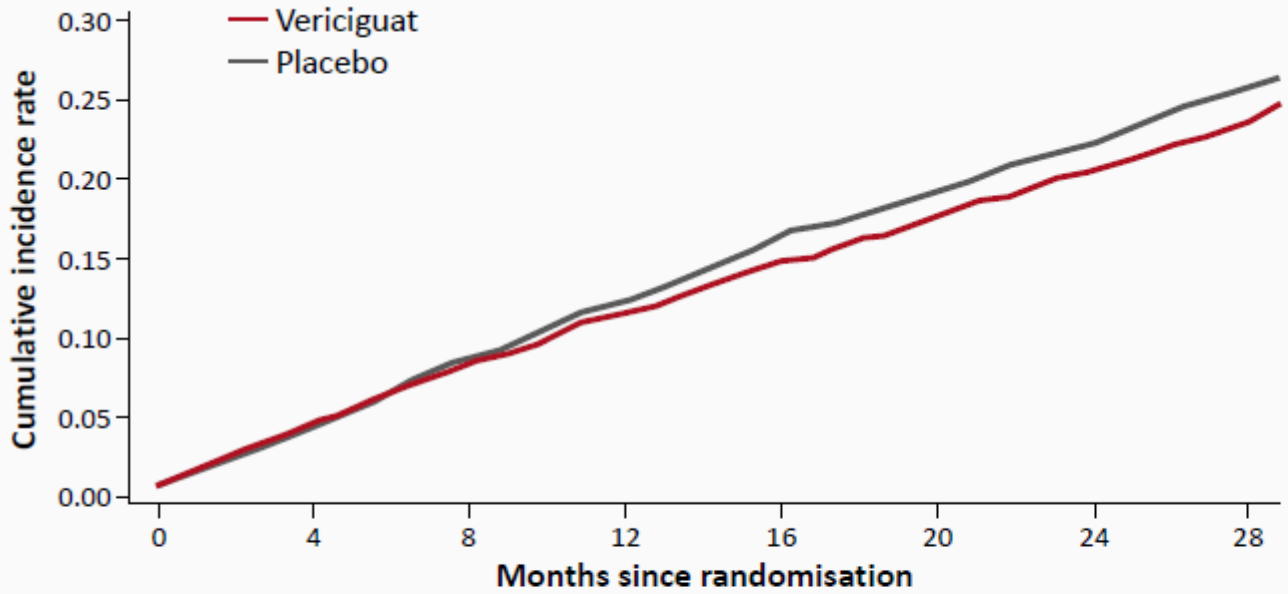
Characteristic	Vericiguat (N=3053)	Placebo (N=3052)
Age, mean, years	67	67
Female sex, n (%)	727 (24)	713 (23)
Race, n (%)		
White	1942 (64)	1992 (65)
Black (expanded)†	343 (11)	313 (10)
American Indian or Alaskan	159 (5)	142 (5)
Native Hawaiian or Pacific Islander	4 (0.1)	7 (0.2)
Asian	383 (13)	363 (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/m²	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 m²	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)

Butler J, et al. Lancet. 2025 Aug 29:S0140-6736(25)01665-4.

Butler J, et al. Lancet. 2025 Aug 29:S0140-6736(25)01665-4.

VICTOR. Primary outcome results: Time to CV death or first HHF



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

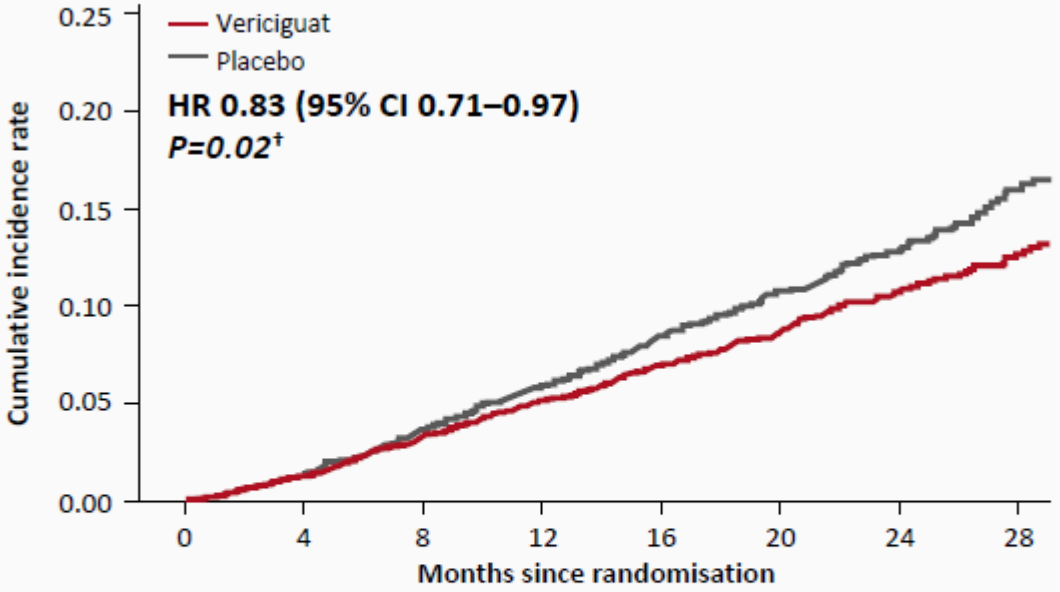
Generally consistent across prespecified subgroups

Butler J, et al. Lancet. 2025 Aug 29:S0140-6736(25)01665-4.

VICTOR. Effects of Vericiguat on mortality

CV death[1,2]

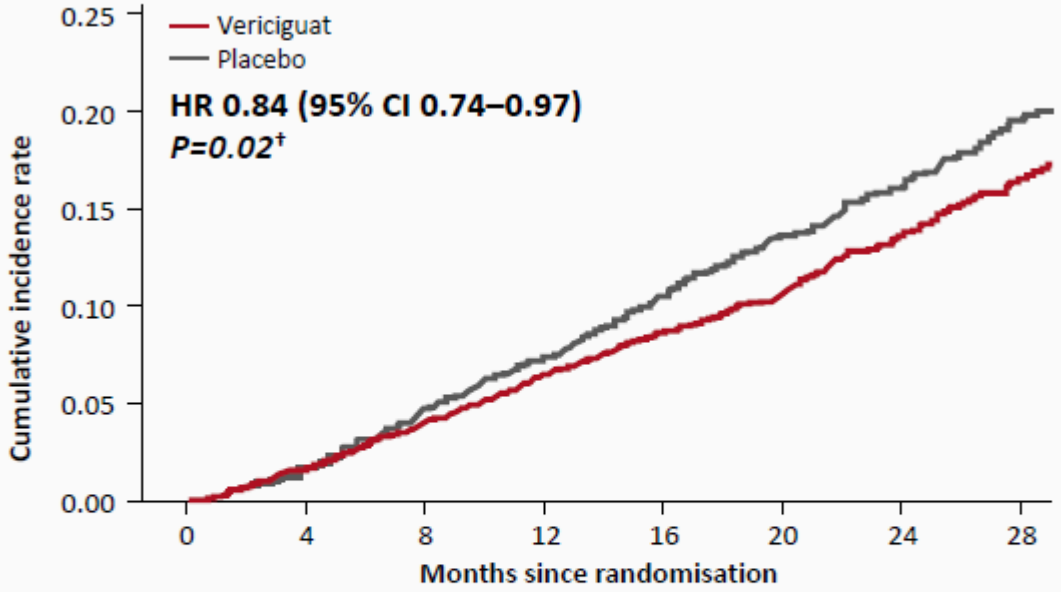
Prespecified powered secondary endpoint



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

†Nominal P value.

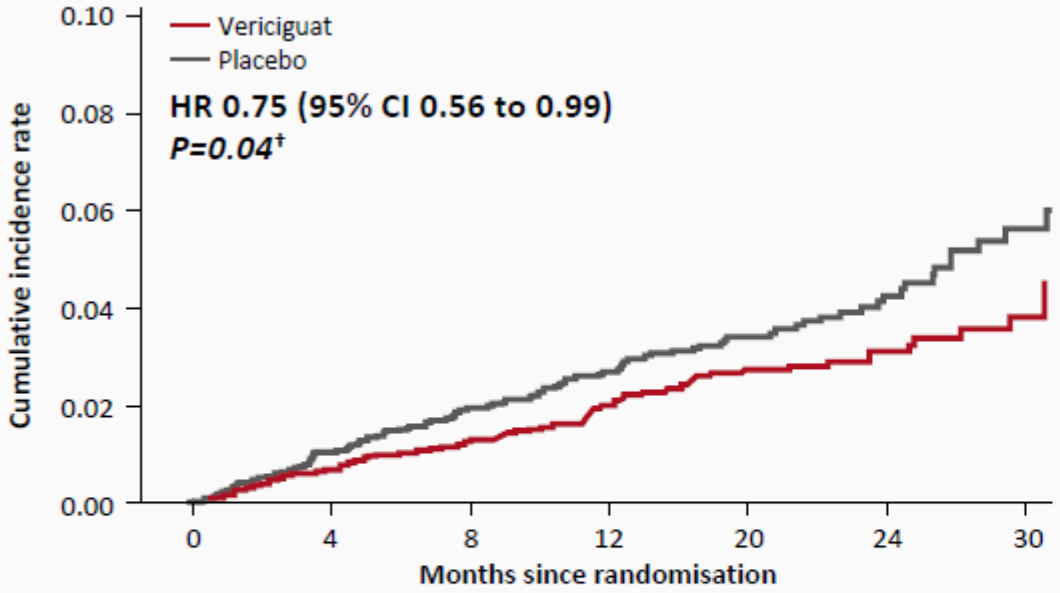
CI, confidence interval; CV, cardiovascular; HHF, hospitalisation for heart failure; HR, hazard ratio.

1. Butler J et al. Impact of vericiguat on mortality in patients with heart failure and reduced ejection fraction: insights from the VICTOR trial. *Eur Heart J* 2025; in press;
2. Butler J et al. Effect of vericiguat on mortality in ambulatory patients with heart failure and reduced ejection fraction: VICTOR trial prespecified analysis. Poster presented at ESC 2025.

Butler J, et al. Lancet. 2025 Aug 29:S0140-6736(25)01665-4.

VICTOR. Mode of death: Exploratory analyses

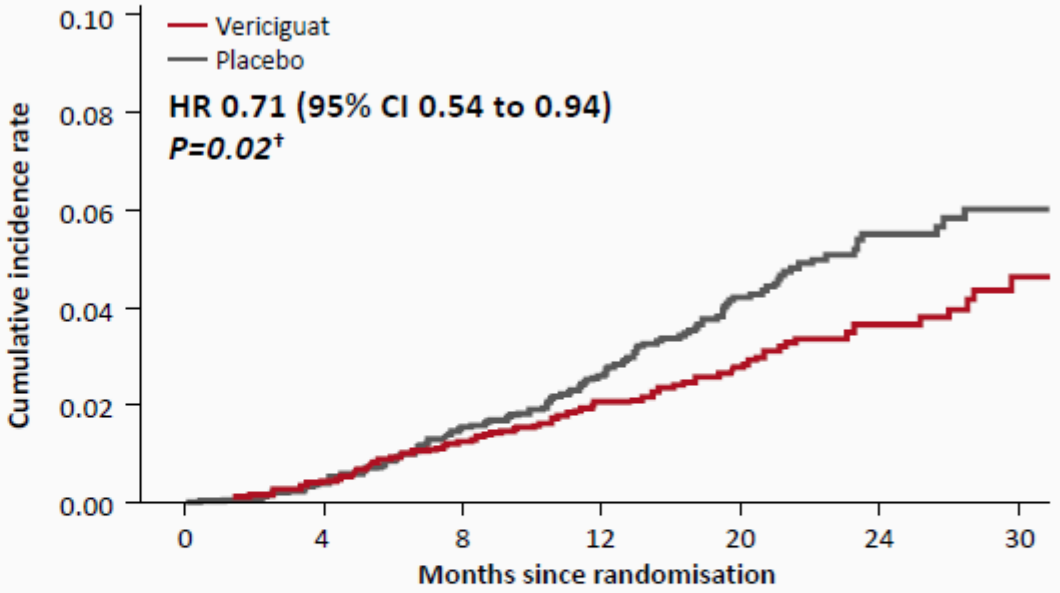
Sudden cardiac death[1,2]



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

†Nominal P value.

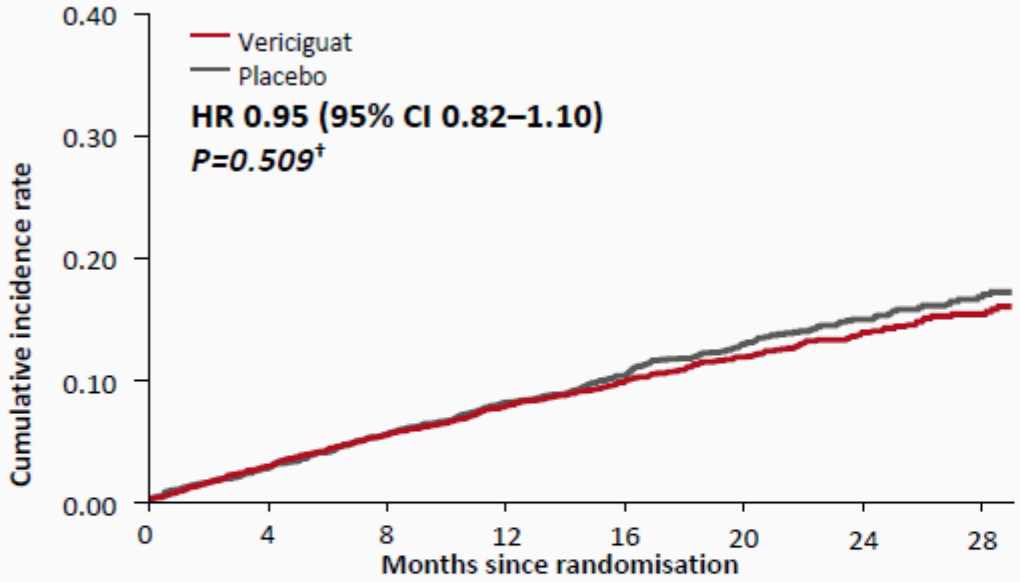
CI, confidence interval; HHF, hospitalisation for heart failure; HR, hazard ratio.

1. Butler J et al. Impact of vericiguat on mortality in patients with heart failure and reduced ejection fraction: insights from the VICTOR trial. *Eur Heart J* 2025; in press.
2. Butler J et al. Effect of vericiguat on mortality in ambulatory patients with heart failure and reduced ejection fraction: VICTOR trial prespecified analysis. Poster presented at ESC 2025.

Butler J, et al. Lancet. 2025 Aug 29:S0140-6736(25)01665-4.

VICTOR. Effect of vericiguat on worsening HF

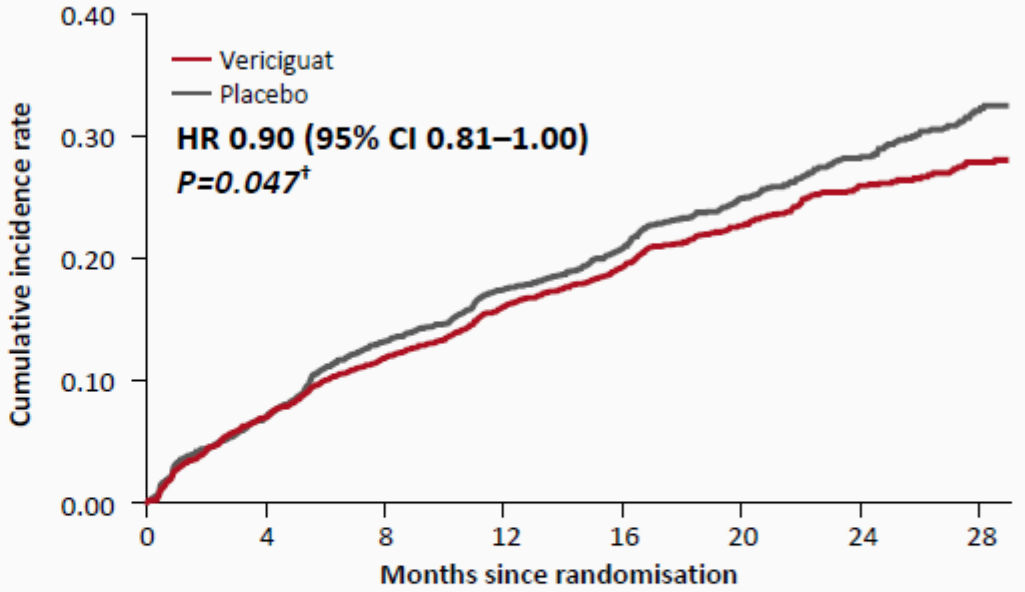
HHF[1,2]
Secondary endpoint



Number of participants at risk								
Vericiguat	3053	2926	2796	2581	1917	1352	849	459
Placebo	3052	2929	2771	2543	1879	1313	822	442

Cumulative number of events up to the time point								
Vericiguat	0	77	151	218	262	299	323	334
Placebo	0	72	152	223	273	319	343	356

Overall Worsening HF
HHF + urgent HF visit, + oral diuretic intensification or initiation[1,2]
Pre-specified exploratory endpoint



Number of participants at risk								
Vericiguat	3053	2795	2601	2346	1699	1161	702	374
Placebo	3052	2796	2545	2280	1644	1111	682	358

Cumulative number of events up to the time point								
Vericiguat	0	211	356	478	556	621	661	674
Placebo	0	207	395	519	597	673	714	742

†Nominal P value.
CI, confidence interval; HF, heart failure; HHF, hospitalisation for heart failure; HR, hazard ratio.
1. Zannad F et al. Effect of vericiguat on worsening heart failure in compensated outpatients with HFrEF: Insights from VICTOR. *J Am Coll Cardiol* 2025; in press;
2. Zannad F et al. Effect of vericiguat on heart failure hospitalisation events in ambulatory patients with heart failure and reduced ejection fraction: VICTOR trial prespecified analysis. Poster presented at ESC 2025.

Butler J, et al. Lancet. 2025 Aug 29:S0140-6736(25)01665-4.

VICTOR. Safety outcomes

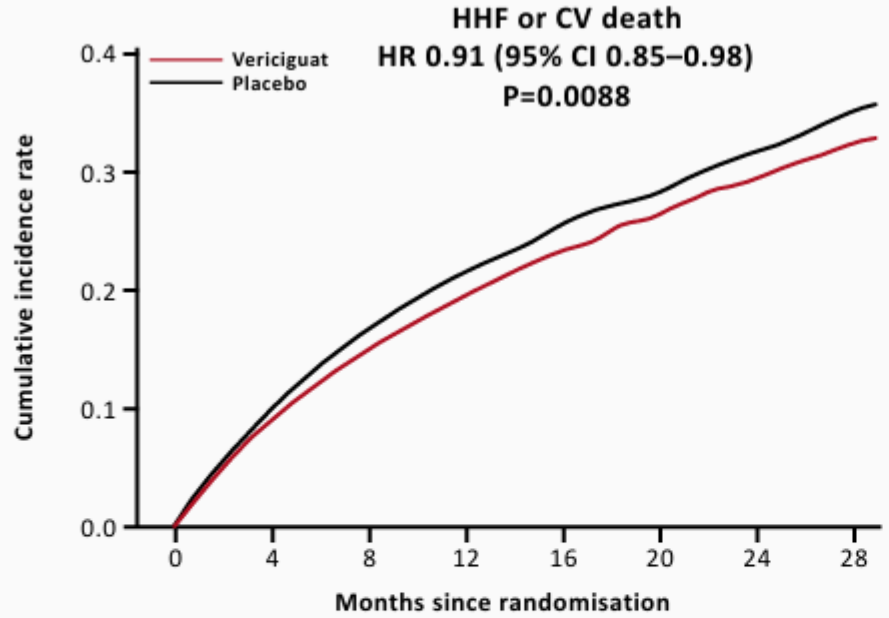
Event	Vericiguat (N=3049)	Placebo (N=3049)
	n (%)	n (%)
Adverse events	1265 (41.5)	1197 (39.3)
Serious adverse events	717 (23.5)	751 (24.6)
Adverse events leading to permanent treatment discontinuation	253 (8.3)	219 (7.2)
Adverse events of clinical interest		
Symptomatic hypotension	345 (11.3)	281 (9.2)
Symptomatic hypotension on background ARNI therapy	230 (7.5)	188 (6.2)
Syncope on background ARNI therapy	4 (0.1)	4 (0.1)
Blood and lymphatic system disorders	234 (7.7)	199 (6.5)
Anaemia	233 (7.6)	193 (6.3)
Hepatic injury	9 (0.3)	12 (0.4)
Cardiac failure	124 (4.1)	123 (4.0)
Renal and urinary disorders	98 (3.2)	110 (3.6)
Acute kidney injury	33 (1.1)	59 (1.9)

ARNI, angiotensin receptor/neprilysin inhibitor.

Butler J, et al. Lancet. 2025 Aug 29:S0140-6736(25)01665-4.

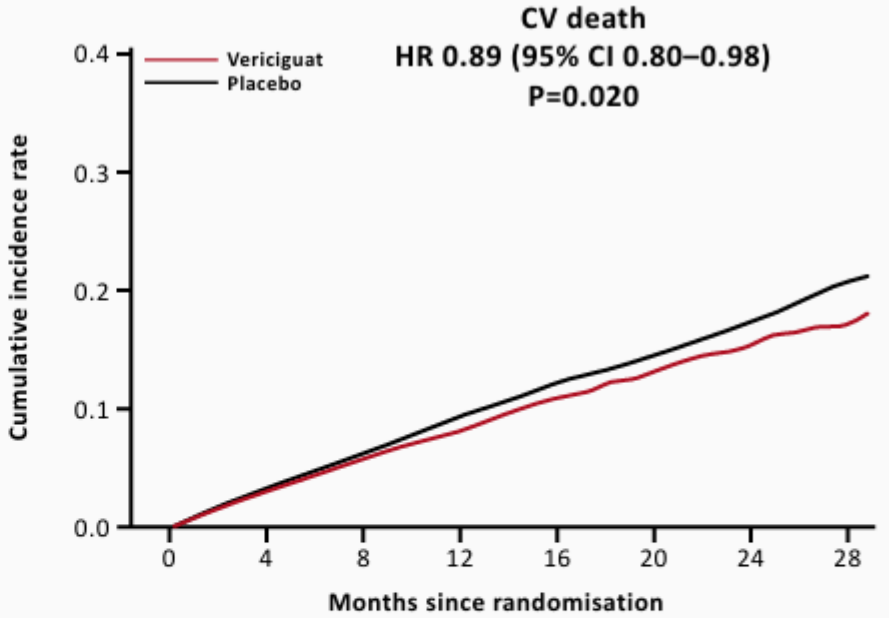
VICTOR & VICTORIA pooled.

Primary composite endpoint and CV death



Number of participants at risk

Vericiguat	5579	5026	4418	3735	2743	1929	1197	584
Placebo	5576	4982	4326	3640	2651	1873	1147	552



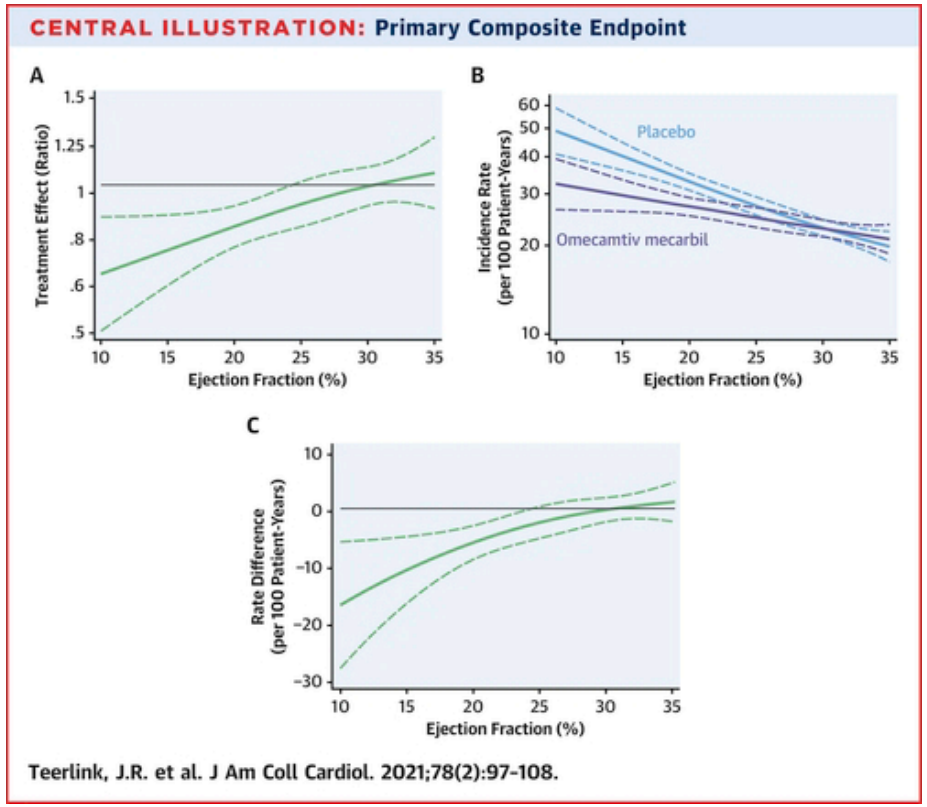
Number of participants at risk

Vericiguat	5579	5376	4896	4220	3162	2295	1455	721
Placebo	5576	5373	4861	4167	3095	2224	1411	671

Vericiguat significantly reduced the risk of the primary composite and the CV death, with treatment effects emerging at around 4 months and around 8 months, respectively

Zannad F, et al. Lancet. 2025 Aug 29:S0140-6736(25)01682-4.

Eficacy and Safety of **Omecamtiv Mecarbil** in Patients with Symptomatic Heart Failure With Severely Reduced Ejection Fraction



John R. Teerlink et al. *JACC* 2021; 78:97-108.

Eficacy and Safety of **Omecamtiv Mecarbil** in Patients with Symptomatic Heart Failure With Severely Reduced Ejection Fraction

About the Study

Currently Recruiting: Participants and Sites

Study Drug/Intervention: Omecamtiv Mecarbil

Anticipated Sample Size: 1,800 patients

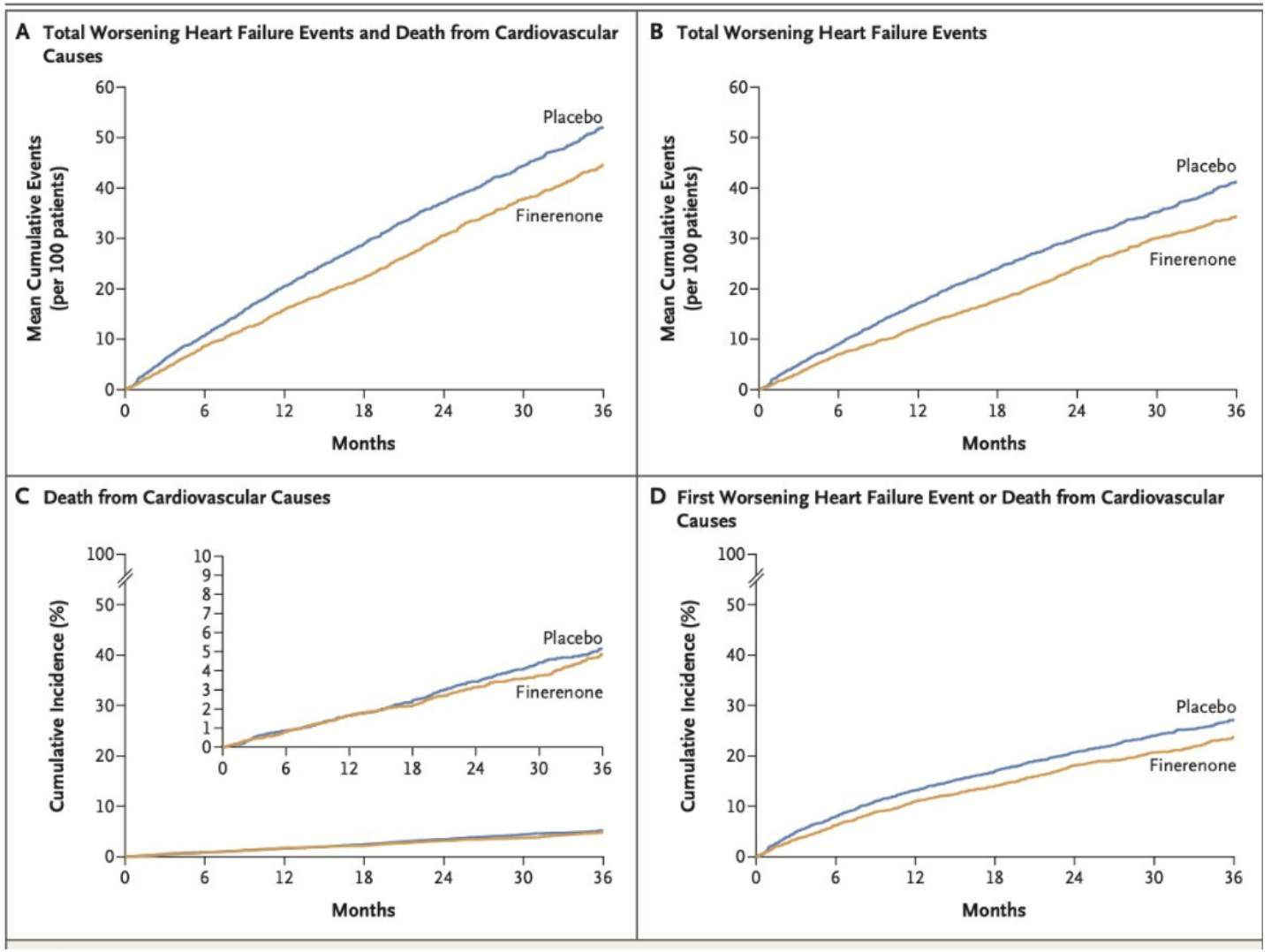
Study Timeline: This study is expected to conclude in April 2028.

Inclusion criteria

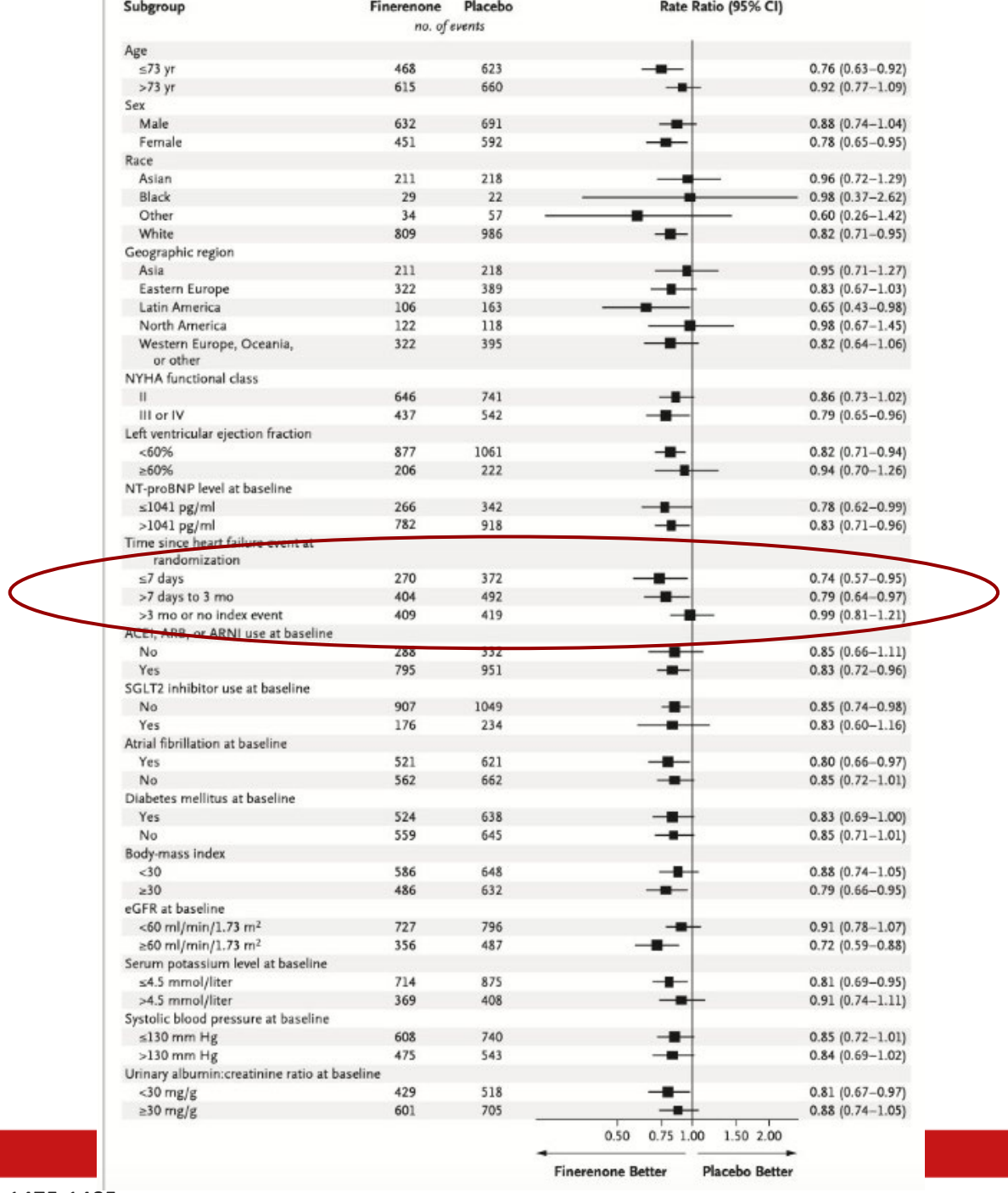
1. History of chronic HFrEF, defined as requiring treatment for HF for a minimum of 3 months prior to screening
2. Receiving oral loop diuretics
3. LVEF < 30%
    1. Patients with AFF must have an LVEF < 25%
    2. Hospitalized for HF or had an HF event within 6 months prior to screening.
4. Standard-of-care HF therapies for at least 30 days prior to screening.
    1. Patients enrolled either during HF hospitalization or soon after discharge can be reinitiating or titrating chronic HF therapies
5. SBP ≤ 130 mmHg and DBP ≤ 90 mmHg.
6. Elevated natriuretic peptide at screening:
    1. Patients without AFF: BNP ≥ 300 pg/mL or NT-proBNP ≥ 1,000 pg/mL
    2. Patients with AFF: BNP ≥ 900 pg/mL or NT-proBNP ≥ 3,000 pg/mL

Aldosterone receptor antagonists: Finerenone

CHRONIC HFmr/pEF



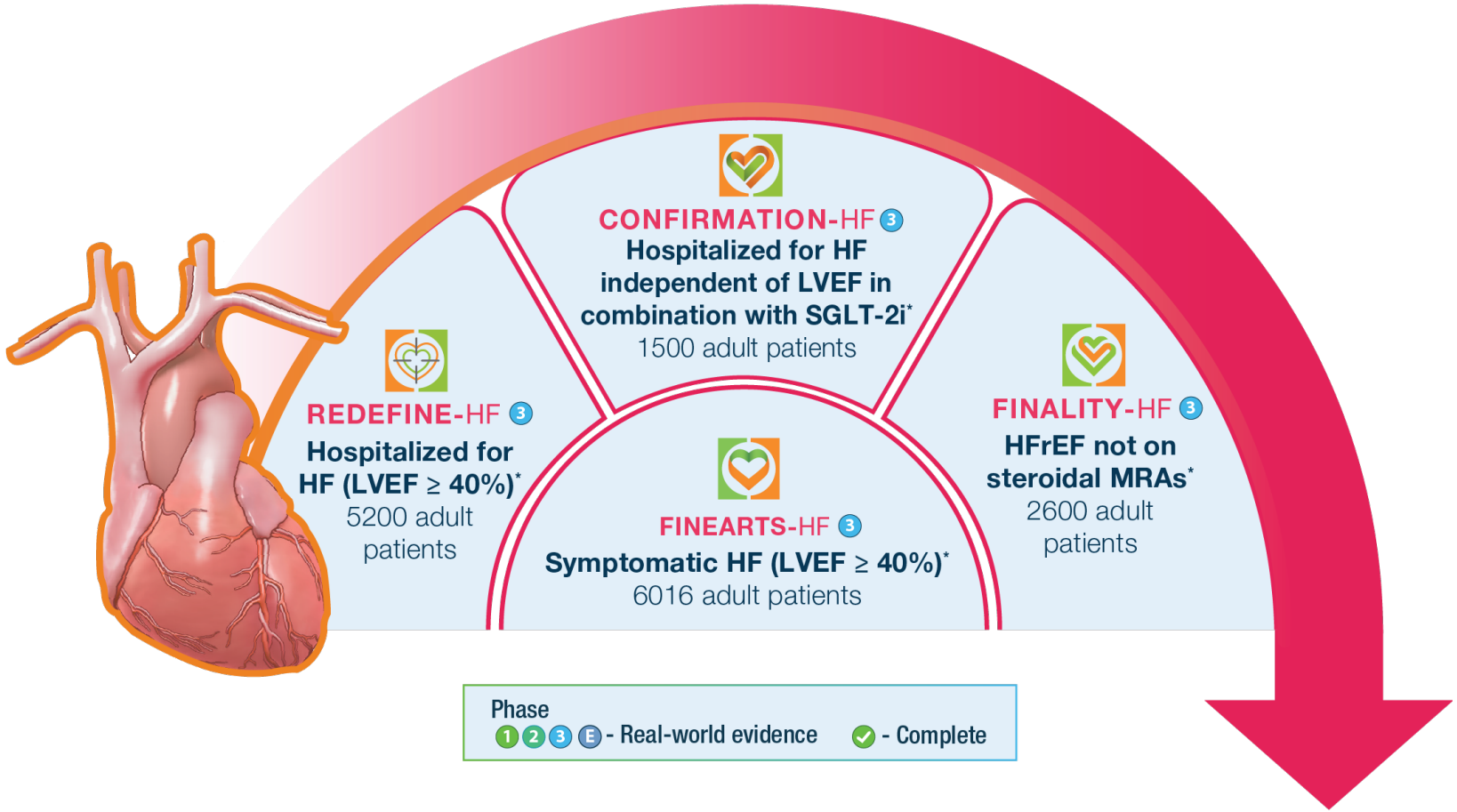
Solomon SD, N Engl J Med. 2024 Oct 24;391(16):1475-1485.



Subgroup	Finerenone (no. of events)	Placebo (no. of events)	Rate Ratio (95% CI)
Age			
≤73 yr	468	623	0.76 (0.63–0.92)
>73 yr	615	660	0.92 (0.77–1.09)
Sex			
Male	632	691	0.88 (0.74–1.04)
Female	451	592	0.78 (0.65–0.95)
Race			
Asian	211	218	0.96 (0.72–1.29)
Black	29	22	0.98 (0.37–2.62)
Other	34	57	0.60 (0.26–1.42)
White	809	986	0.82 (0.71–0.95)
Geographic region			
Asia	211	218	0.95 (0.71–1.27)
Eastern Europe	322	389	0.83 (0.67–1.03)
Latin America	106	163	0.65 (0.43–0.98)
North America	122	118	0.98 (0.67–1.45)
Western Europe, Oceania, or other	322	395	0.82 (0.64–1.06)
NYHA functional class			
II	646	741	0.86 (0.73–1.02)
III or IV	437	542	0.79 (0.65–0.96)
Left ventricular ejection fraction			
<60%	877	1061	0.82 (0.71–0.94)
≥60%	206	222	0.94 (0.70–1.26)
NT-proBNP level at baseline			
≤1041 pg/ml	266	342	0.78 (0.62–0.99)
>1041 pg/ml	782	918	0.83 (0.71–0.96)
Time since heart failure event at randomization			
≤7 days	270	372	0.74 (0.57–0.95)
>7 days to 3 mo	404	492	0.79 (0.64–0.97)
>3 mo or no index event	409	419	0.99 (0.81–1.21)
ACEI, ARB, or ARNI use at baseline			
No	288	332	0.85 (0.66–1.11)
Yes	795	951	0.83 (0.72–0.96)
SGLT2 inhibitor use at baseline			
No	907	1049	0.85 (0.74–0.98)
Yes	176	234	0.83 (0.60–1.16)
Atrial fibrillation at baseline			
Yes	521	621	0.80 (0.66–0.97)
No	562	662	0.85 (0.72–1.01)
Diabetes mellitus at baseline			
Yes	524	638	0.83 (0.69–1.00)
No	559	645	0.85 (0.71–1.01)
Body-mass index			
<30	586	648	0.88 (0.74–1.05)
≥30	486	632	0.79 (0.66–0.95)
eGFR at baseline			
<60 ml/min/1.73 m²	727	796	0.91 (0.78–1.07)
≥60 ml/min/1.73 m²	356	487	0.72 (0.59–0.88)
Serum potassium level at baseline			
≤4.5 mmol/liter	714	875	0.81 (0.69–0.95)
>4.5 mmol/liter	369	408	0.91 (0.74–1.11)
Systolic blood pressure at baseline			
≤130 mm Hg	608	740	0.85 (0.72–1.01)
>130 mm Hg	475	543	0.84 (0.69–1.02)
Urinary albumin:creatinine ratio at baseline			
<30 mg/g	429	518	0.81 (0.67–0.97)
≥30 mg/g	601	705	0.88 (0.74–1.05)

Solomon SD, N Engl J Med. 2024 Oct 24;391(16):1475-1485.

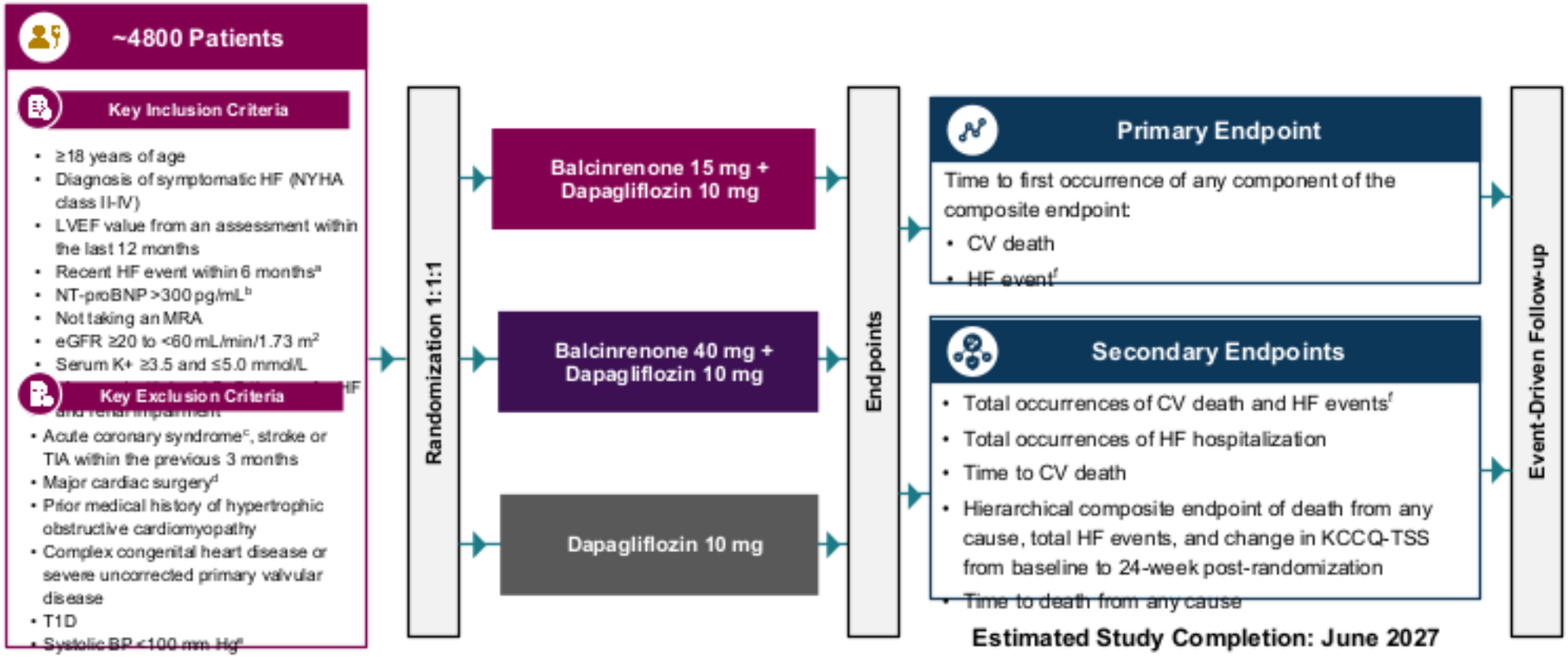
Aldosterone receptor antagonists: Finerenone MOONRAKER program



Phase III

BalanceD-HF

Balcinrenone/Dapagliflozin vs Dapagliflozin in Patients With HF and Impaired Kidney Function



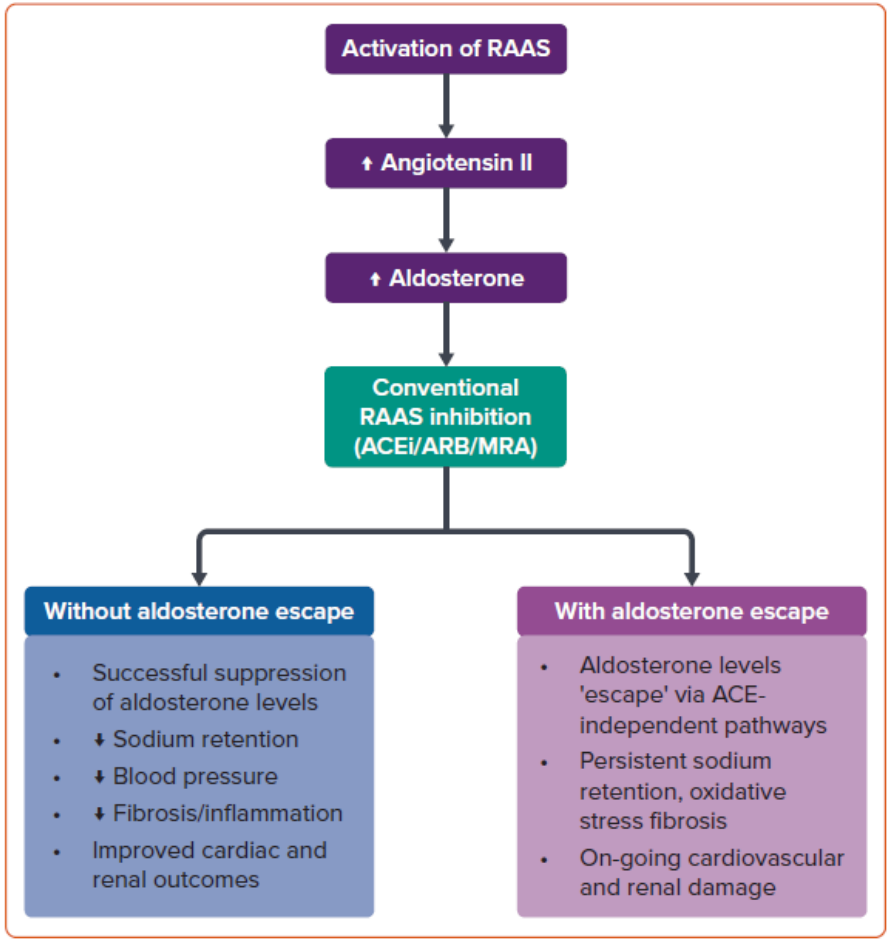
Note: For the complete inclusion/exclusion criteria, please visit https://www.clinicaltrials.gov/study/NCT05093933

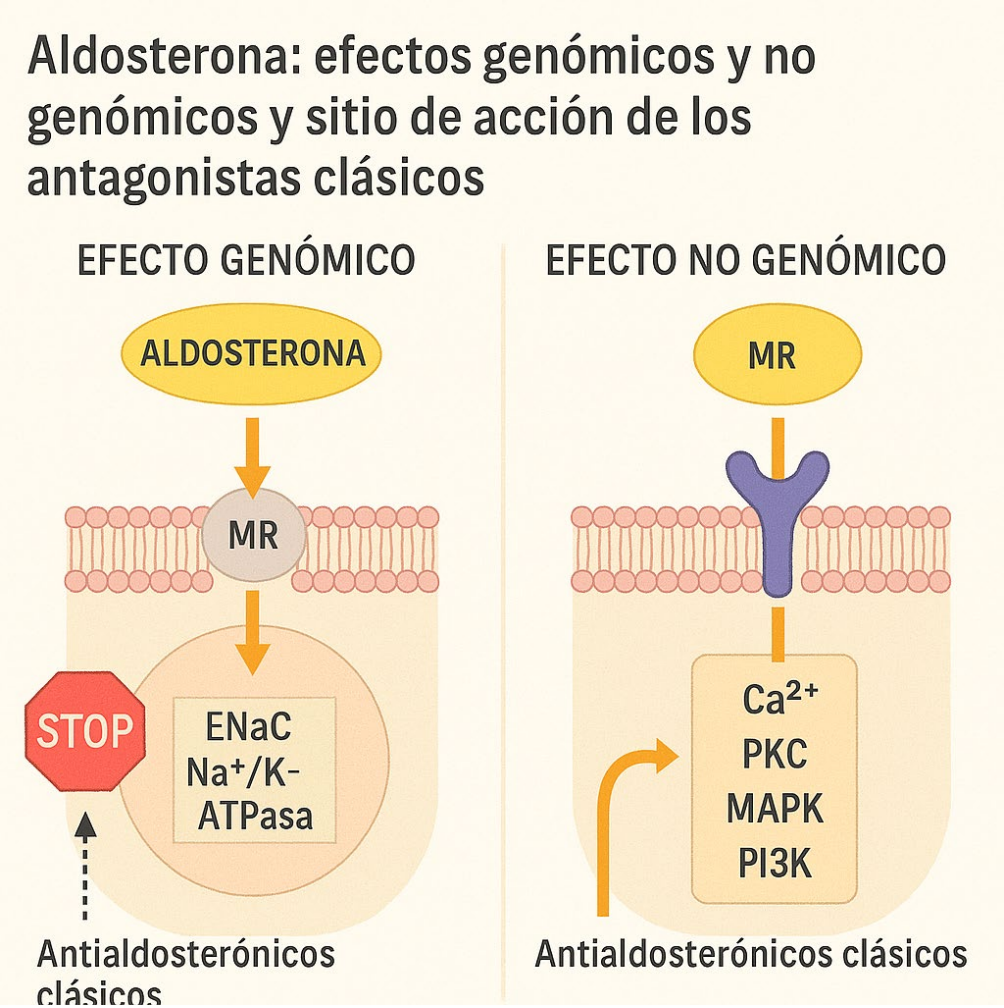
[a]Hospitalization for HF or urgent HF visit; [b]>600 pg/mL if concomitant AF or atrial flutter; [c]Unstable angina or MI; [d]Planned or previously in the last 3 months, including coronary resynchronisation or valvular repair or replacement, or implantation of a cardiac resynchronisation therapy device; [e]or symptomatic hypotension within the past 24 hours; [f]HF hospitalization or HF event without hospitalization.

AF = atrial fibrillation; BP = blood pressure; CV = cardiovascular; eGFR = estimated glomerular filtration rate; HF = heart failure; K+ = potassium; KCCQ-TSS = Kansas City Cardiomyopathy Questionnaire total symptom score; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MRA = mineralocorticoid receptor antagonist; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association; SoC = standard of care; T1D = type 1 diabetes; TIA = transient ischemic attack.

Aldosterone synthase inhibitors

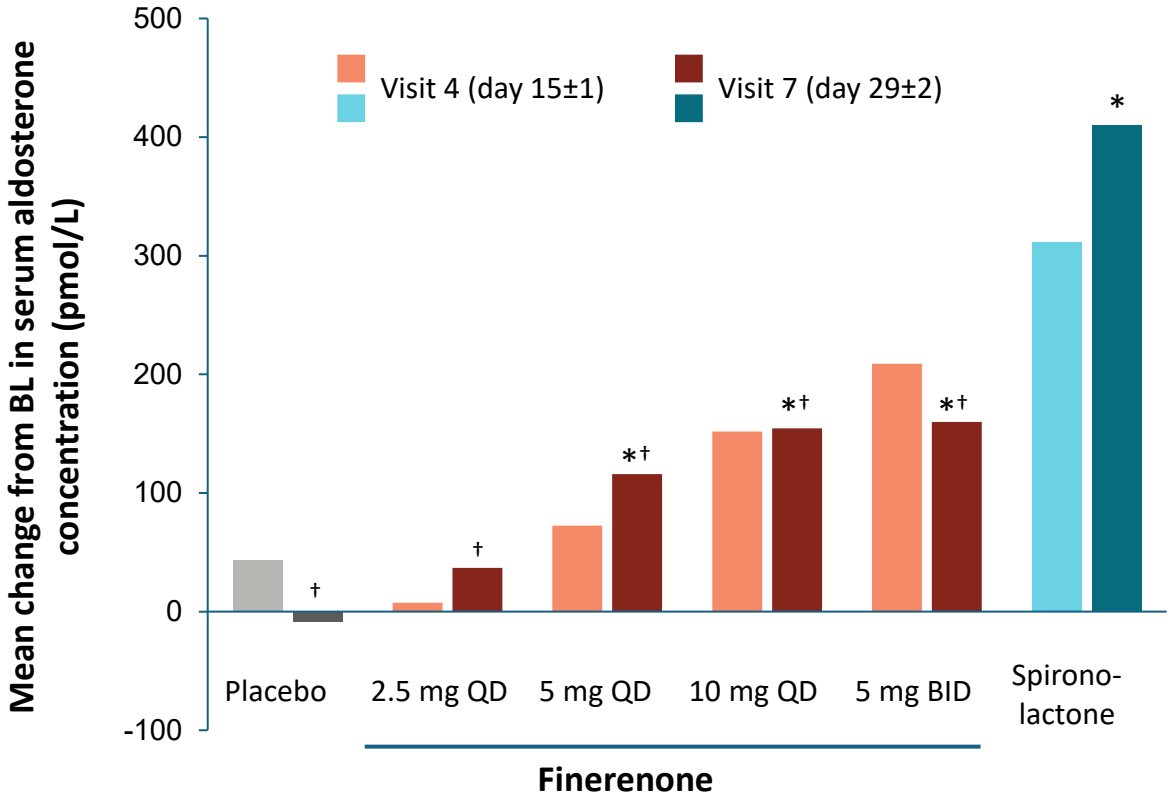
Figure 3: Mechanistic Overview of the Aldosterone Escape Phenomenon





MRAs have been shown to increase aldosterone levels, in contrast to aldosterone synthase inhibitors

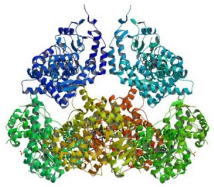
458 Patients with HFrEF and mild or moderate CKD



Compared with placebo, finerenone and spironolactone were associated with **significant increases** in serum aldosterone from baseline to visit 7

Inhibition of mineralocorticoid receptors by MRAs promotes **counter-regulatory processes** that lead to **aldosterone production**

Vicadrostat is a potent and selective inhibitor of aldosterone synthase that may mitigate the deleterious cardiorenal effects of aldosterone



Aldosterone synthase (CYB11B2) is **93% homologous in amino acid sequence** to cortisol synthase (CYP11B1)[3]

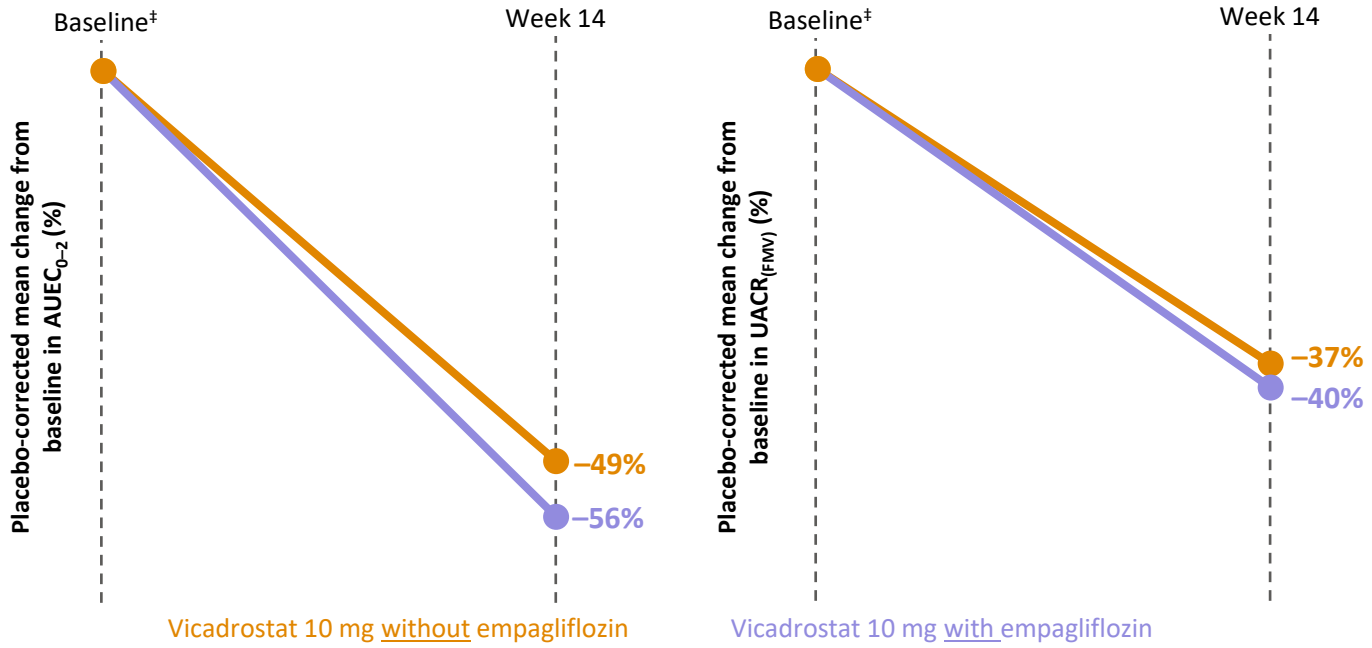
Vicadrostat potency and selectivity for aldosterone synthase[1]

IC_{50} (CYP11B2): 19 nM
Selectivity vs CYP11B1: 250-fold

Vicadrostat is potent and selective for AS[1,2]

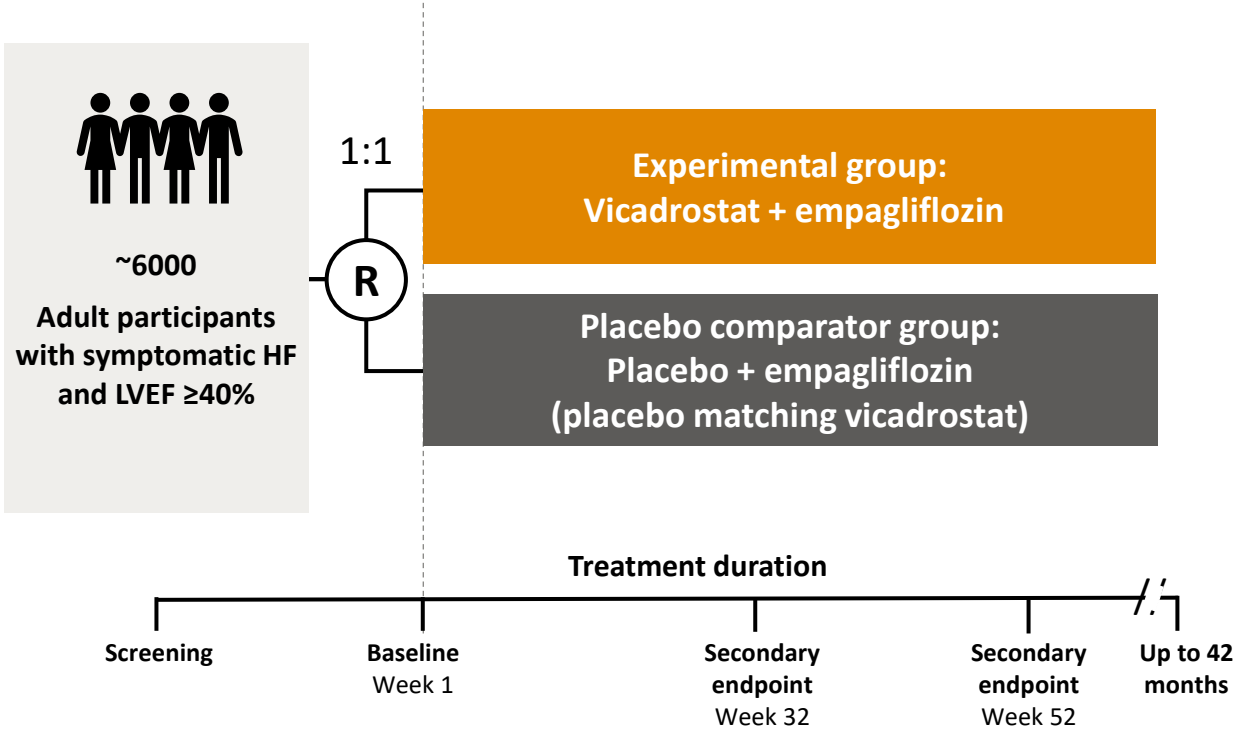
Inhibition of aldosterone synthase has potential to address cardiovascular risk and kidney disease progression

Vicadrostat reduced aldosterone exposure* and UACR† [2]



There were no observed decreases in mean serum cortisol by week 14 with vicadrostat 10 mg compared with placebo[2]

EASi-HF™ Phase III trial
Study plan



- ***The study will continue until there are sufficient data to confirm efficacy***
- ***Doctors regularly check participants' health and note any side effects***
- ***Participants can stay in the study as long as they benefit from and tolerate treatment***

Primary outcome measure:

Time to first event of CV death or HHF

Key secondary endpoints:

- Time to first event of CV death, HHF or urgent heart failure visit
- Occurrence of HHFs (first and recurrent)
- Absolute change from baseline in KCCQ-TTS at Week 32
- Time to CV death, all-cause mortality and first HHF
- Time to first occurrence of death from kidney failure, chronic dialysis, renal transplant, or sustained eGFR reduction*
- Absolute change from baseline in KCCQ Clinical Summary Score (KCCQ-CSS) at Week 32
- Absolute change from baseline in KCCQ-TSS at Week 52

Inhibidores de la aldosterona sintasa **Baxdrostat**

Phase III Study Investigating Heart Failure and Cardiovascular Death with Baxdrostat in combination with Dapagliflozin - Prevent-HF

Study identifier:
D6973C00001

ClinicalTrials.gov identifier:
NCT06677060

EudraCT identifier:
N/A

CTIS identifier:
2024-514506-32-00

Official Title

A Phase III, Randomised, Placebo-controlled, Event-driven Study to Evaluate the Effect of Baxdrostat in Combination with Dapagliflozin Compared with Dapagliflozin Alone on the Risk of Incident Heart Failure and Cardiovascular Death

Medical condition heart failure	Phase Phase 3	Healthy volunteers No
Study drug Baxdrostat and dapagliflozin	Sex All	Estimated Enrollment 11300
Study type Interventional	Age 40 Years - n/a	Date **Study Start Date:** 14 Mar 2025 **Estimated Primary Completion Date:** 17 Dec 2029 **Estimated Study Completion Date:** 17 Dec 2029

Agonistas GLP-1: agonistas duales y triples

The MARITIME-HF Study

MariTide is a bispecific glucagon-like peptide 1 (GLP-1) receptor agonist and glucose-dependent insulinotropic polypeptide receptor (GIPR) antagonist

Study Overview

Brief Summary

This study will examine if maridebart cafraglutide as an adjunct to standard of care will lead to a reduction in heart failure (HF) events such as HF hospitalizations and urgent HF visits, cardiovascular (CV) deaths and improvement in HF symptoms in participants with HF with preserved ejection fraction (HFpEF) and HF with mildly reduced ejection fraction (HFmrEF) who are obese. This is a phase 3, global, multicenter, 2-part study with a double-blind period and an open-label extension (OLE). The study is event-driven, and Part 1 will conclude when approximately 850 primary endpoint events have occurred.

Official Title

A Phase 3 Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Maridebart Cafraglutide on Mortality and Morbidity in Participants Living With Heart Failure With Preserved or Mildly Reduced Ejection Fraction and Obesity (MARITIME-HF)

Study Start (Actual)
2025-06-25

Primary Completion (Estimated)
2028-06-30

Study Completion (Estimated)
2030-09-29

Enrollment (Estimated)
5056

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Time to First Occurrence of a Composite Endpoint Consisting of: CV Death or HF Events	Heart Failure events include: hospitalization for HF or urgent HF visits.	Up to approximately 35 months

Inflammation. **Ziltivekimab**

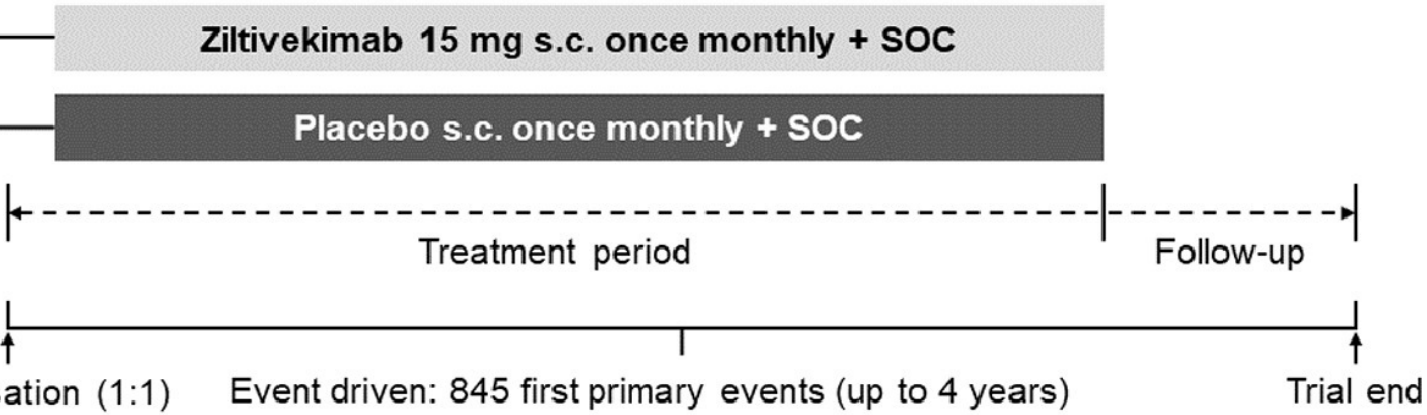
"These data suggest that ziltivekimab may be unique among currently available IL-6 inhibitors and strongly support its use in future cardiovascular outcome trials."

Paul M. Ridker, MD, MPH

Healio

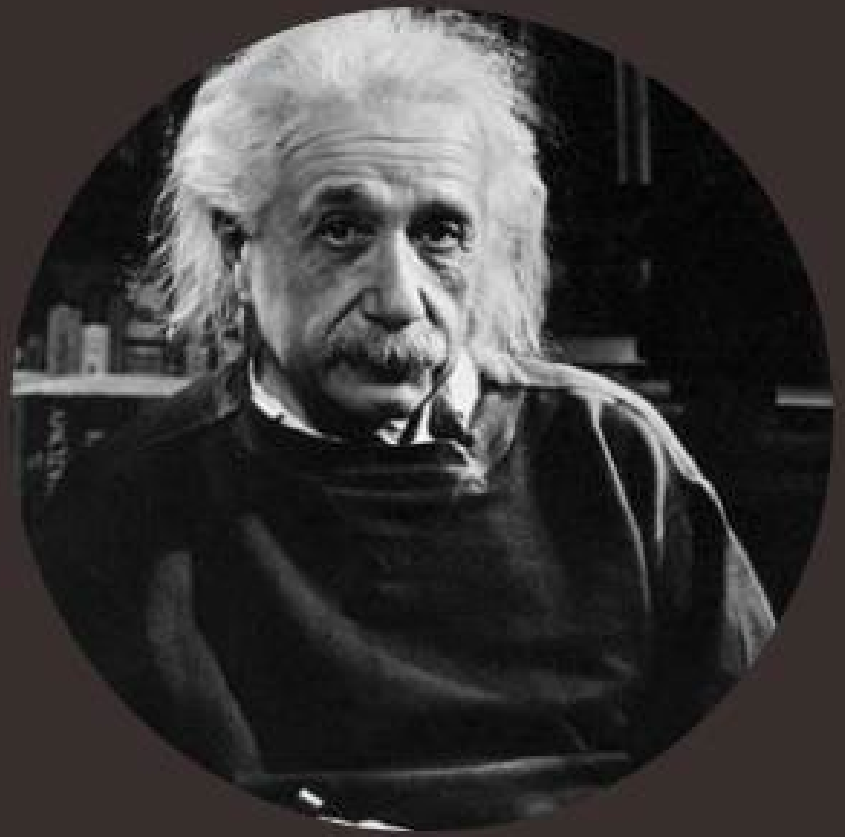
HERMES CVOT

5,600 patients
- Elevated hsCRP ≥2 mg/L
- NYHA II–IV
- LVEF >40%
- Elevated NT-proBNP levels
- Echocardiographic signs of HFpEF/HFmrEF



Primary endpoint:
Time to the first occurrence of
- CV death
- Hospitalisation for HF
- Urgent HF visit

Confirmatory secondary endpoints (hierarchy):
- Time to the first occurrence of CV death, hospitalisation for HF or urgent HF visit, non-fatal myocardial infarction, or non-fatal stroke
- Number of CV death, hospitalisation for HF, or urgent HF visits
- Time to occurrence of CV death
- Time to occurrence of all-cause death



Si buscas resultados distintos, no hagas siempre lo mismo.

— Albert Einstein —