SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA
68° CONGRESSO NAZIONALE SIGG
Ritorno al futuro
FIRENZE, 13-16 DICEMBRE 2023
PALAZZO DEI CONGRESSI

NUOVE PROSPETTIVE NEL MANAGEMENT DELL'INSUFFICIENZA CARDIACA NELL'ANZIANO

Vericiguat nella terapia delle riacutizzazioni dell'insufficienza cardiaca

Francesco Orso

UNIT Scompenso cardiaco
SOD Geriatria UTIG
AOU Careggi, Firenze

COI

Non to declare

AGENDA

Vericiguat: cosa è? Come funziona? Perché è utile nello scompenso…

Vericiguat: Evidenze di efficacia e sicurezza… Lo studio VICTORIA

Vericiguat: Evidenze di efficacia e sicurezza nel paziente anziano…

Vericiguat: in quali pazienti e quando… Cosa dicono le linee guida

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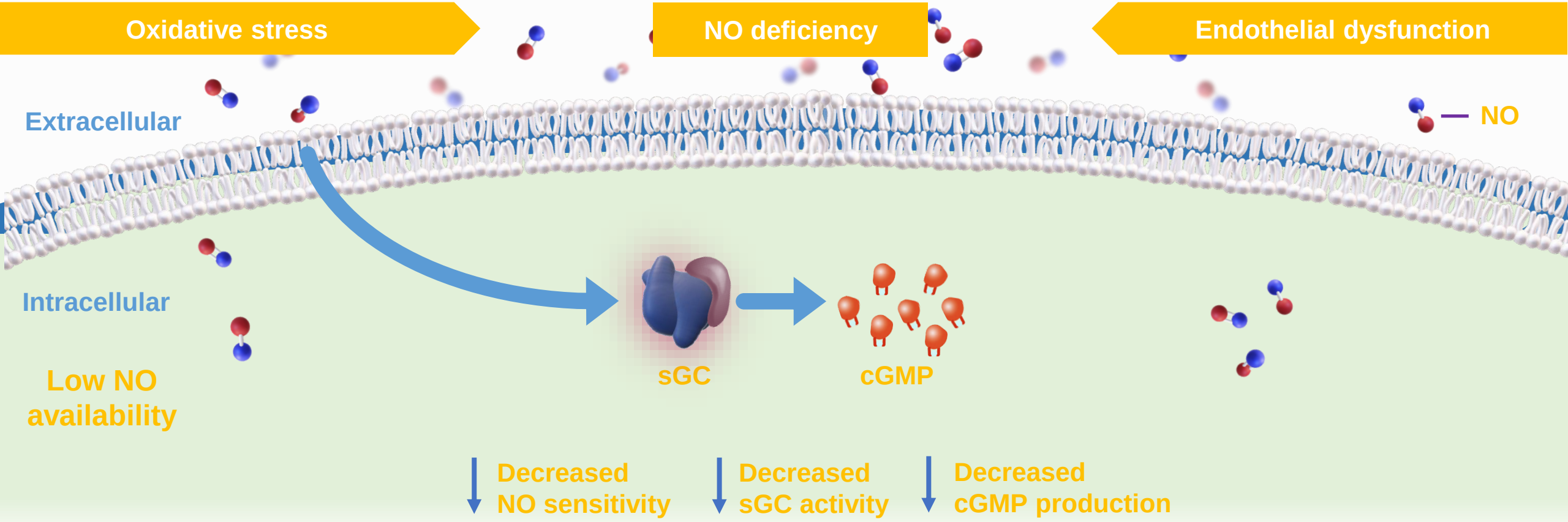
In HF, oxidative stress and endothelial dysfunction lead to decreased activity of the NO–sGC–cGMP pathway[1–5]



cGMP, cyclic guanosine monophosphate; HF, heart failure; NO, nitric oxide; sGC, soluble guanylate cyclase.

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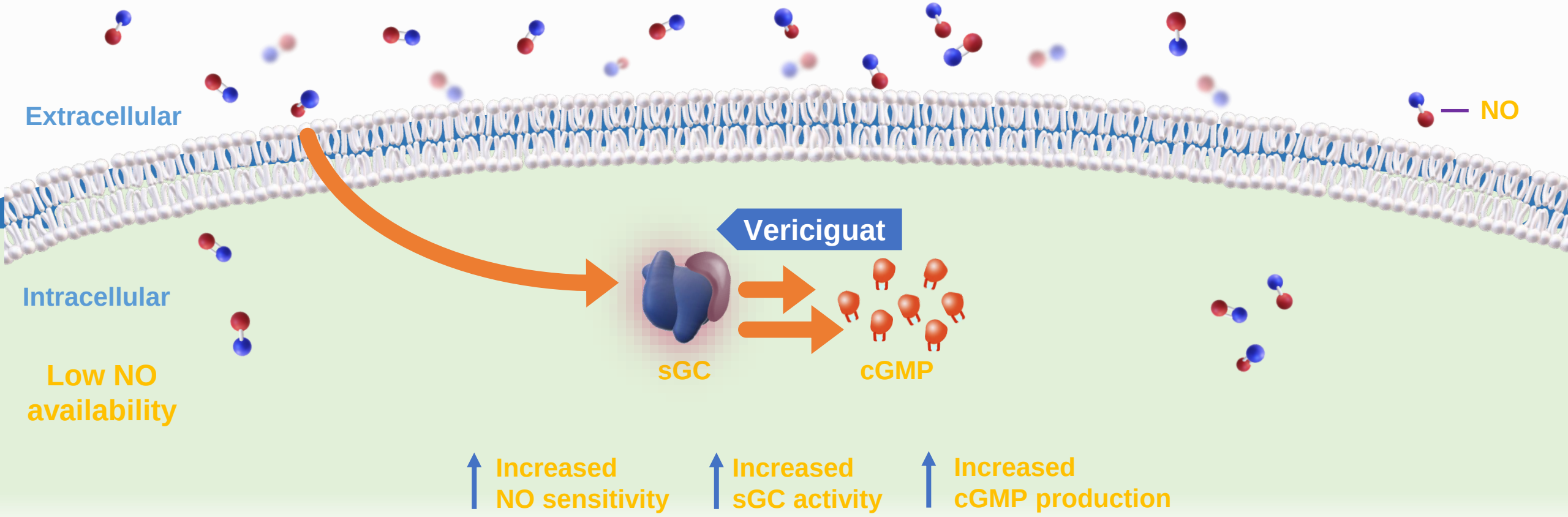
sGC stimulation targets an untapped pathway implicated in the development and progression of HF[1–5]



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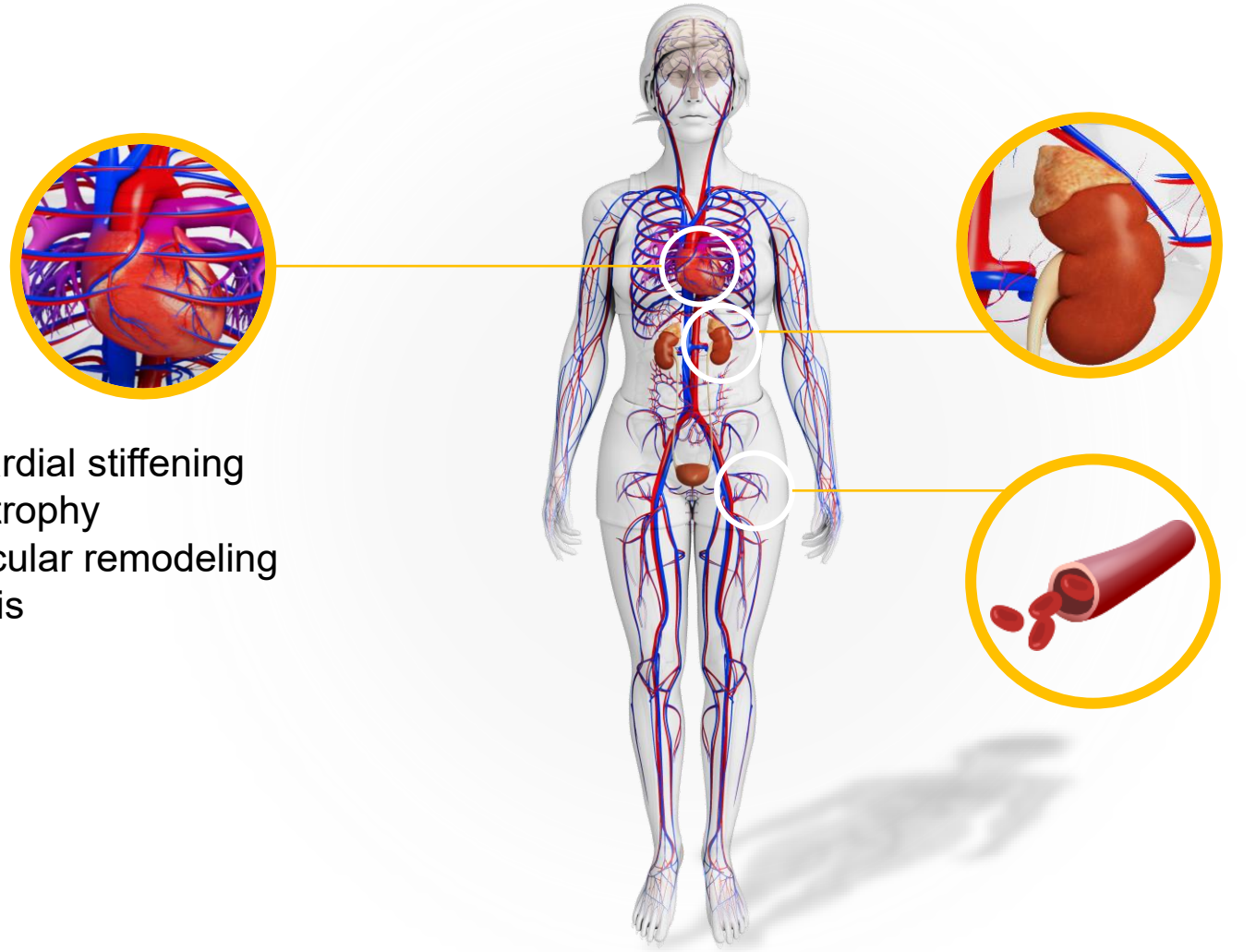
By restoring the NO–sGC–cGMP pathway, vericiguat has the potential to improve HF pathophysiology



↓ Myocardial stiffening
↓ Hypertrophy
↓ Ventricular remodeling
↓ Fibrosis

↓ Renal fibrosis
↑ Renal blood flow

↓ Vasoconstriction
↑ Endothelial function

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This article was published on March 28, 2020, at NEJM.org.

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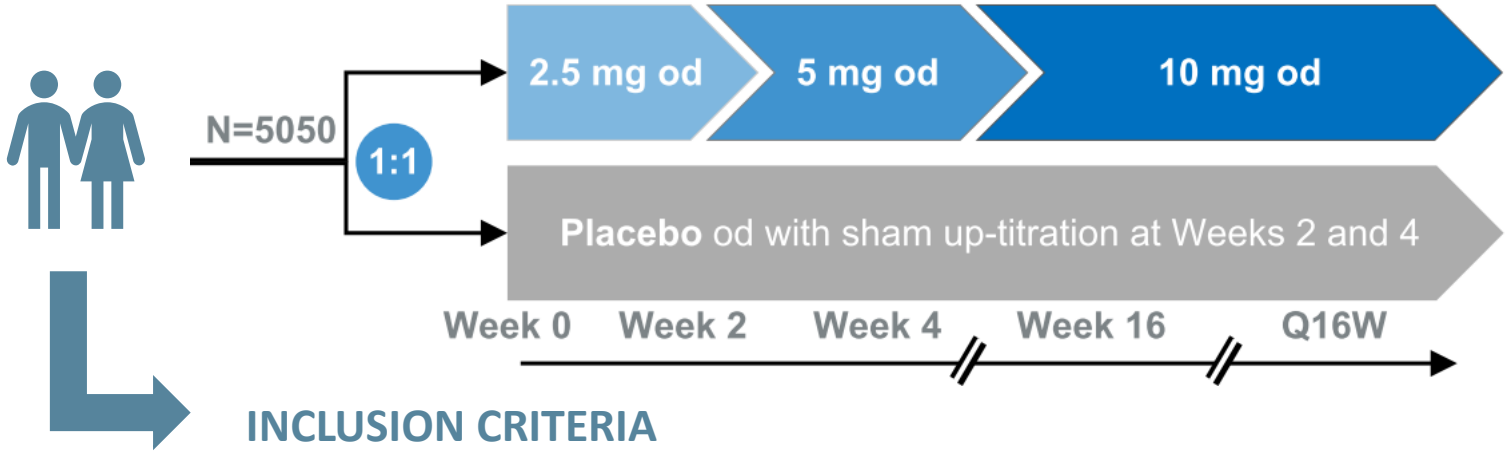
VICTORIA Trial

Multinational, randomized, double-blind, placebo-controlled trial.



INCLUSION CRITERIA

- Chronic heart failure (**NYHA II - IV**),
- **EF < 45%**
- BNP ≥ 300 pg/ml or NT-proBNP ≥ 1000 pg/ml, in SR.
  BNP ≥ 500 pg/ml or NT-proBNP ≥ 1600 pg/ML, AFib.
- eGFR > 15 ml/min /1.73 m2 (cap 15% 15-30 ml/min/1.73 m2)
- **Recent WHF** :
  - HFH < 6 months
  - No HFH but IV diuretic therapy < 3 months

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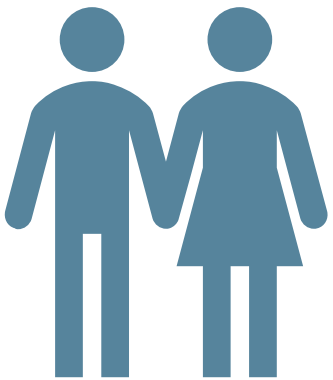
VICTORIA TRIAL

Selected baseline characteristics	Vericiguat (n=2526)	Placebo (n=2524)
Baseline SoC medications, n (%)		
Beta blockers	2349 (93.2)	2342 (93.0)
ACEi/ARB	1847 (73.3)	1853 (73.6)
MRA	1747 (69.3)	1798 (71.4)
3 SoC medications*	1480 (58.7)	1529 (60.7)
Sacubitril/valsartan	360 (14.3)	371 (14.7)
Baseline SoC device, n (%)		
Implantable cardioverter-defibrillator	696 (27.6)	703 (27.9)
Biventricular pacemaker	370 (14.7)	369 (14.6)



Baseline characteristics and endpoints

	PARADIGM HF (N=8,399)[1] sacubitril/valsartan	DAPA-HF (N=4,744)[2] dapagliflozin	EMPEROR-Reduced (N=3,730)[3] empagliflozin	VICTORIA (N=5,050)[5] vericiguat
Median NT-proBNP, pg/ml	1608[6]	1437[2]	1906.5[3]	2816[5]
NYHA class III or IV	25%[1]	32%[2]	25%[3]	41%[5]
HFH <3 months ago	19%[7]	8%[7]	NR	67%[5]
HFH <6 months ago	31%[8]	16%[9]	NA[#,3]	84%[5]
eGFR <60 ml/min/1.73 m^2	37%[9]	41%[2]	48%[3]	53%[§,5]
eGFR inclusion criteria, ml/min/1.73 m^2	≥30[1]	≥30[2]	≥20[3]	≥15[5]
Median follow up (months)	27[1]	18.2[2]	16[3]	10.8[5]

	First HFH or CV death[1]	Worsening HF (unplanned hospitalization/urgent visit resulting in IV therapy for HF) or CV death[2]	First HFH or CV death[3]	First HFH or CV death[5]
Primary endpoint event rate (control arm), events per 100 PY	13.2[10]	15.6[2,10]	21.0[3]	37.8[5,10]

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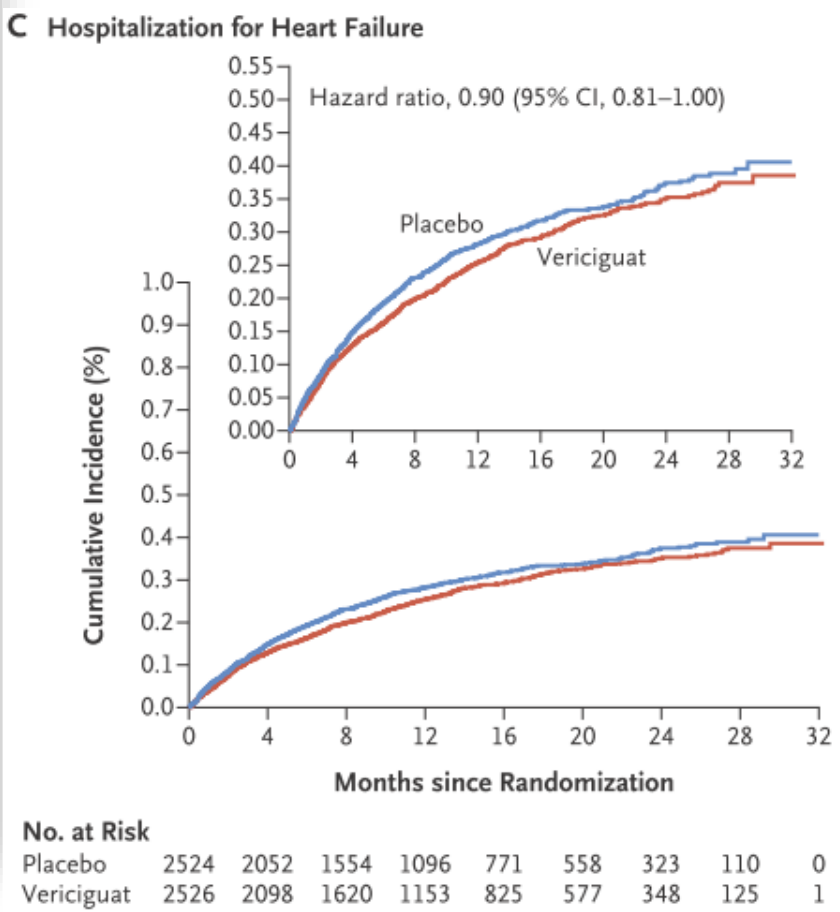
VICTORIA Trial

PRIMARY OUTCOME

CV death or first HFH



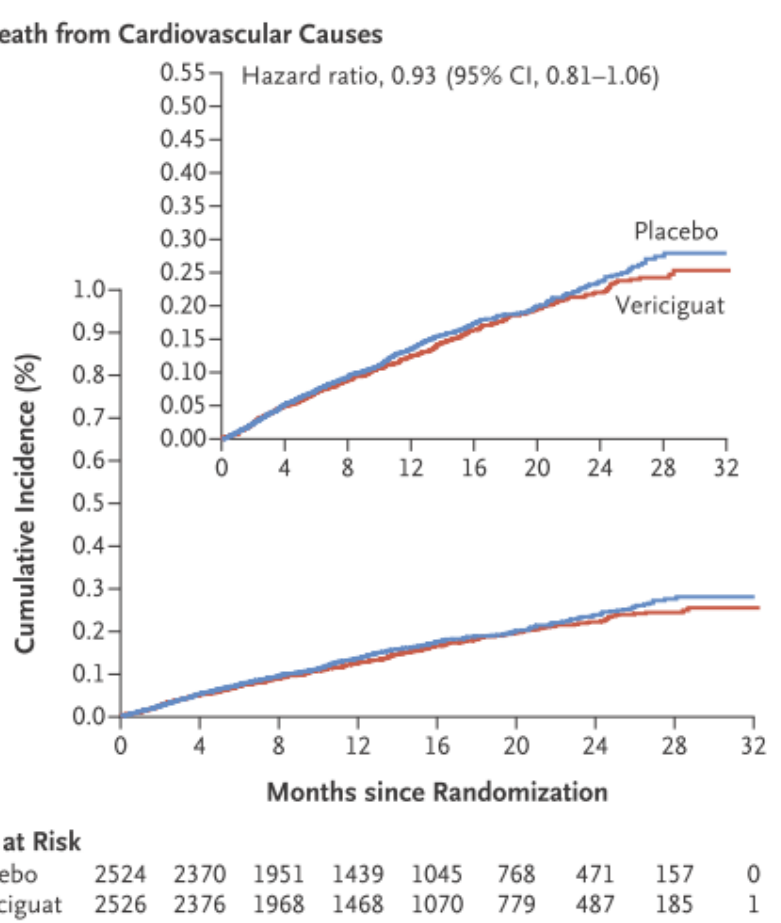


Table 1 Comparison of contemporary clinical trials in heart failure with reduced ejection fraction

	PARADIGM-HF		DAPA-HF		VICTORIA		EMPEROR-Reduced	
	Comparator	Sacubitril/valsartan	Comparator	Dapagliflozin	Comparator	Vericiguat	Comparator	Empagliflozin
Hazard ratios (95% CI) for key outcomes								
Primary endpoint	0.80 (0.73–0.87)		0.74 (0.65–0.85)		0.90 (0.82–0.98)		0.75 (0.65–0.86)	
Cardiovascular death	0.80 (0.71–0.89)		0.82 (0.69–0.98)		0.93 (0.81–1.06)		0.92 (0.75–1.12)	
First HF hospitalization	0.79 (0.71–0.89)		0.70 (0.59–0.83)		0.90 (0.81–1.00)		0.69 (0.59–0.81)	
Annualized event rate (events per 100 patient-years at risk)								
Primary endpoint	13.2	10.5	15.6	11.6	37.8	33.6	21.0	15.8
Absolute rate reduction	2.7		4.0		4.2		5.2	
Cardiovascular death	7.5	6.0	7.9	6.5	13.9	12.9	8.1	7.6
Absolute rate reduction	1.5		1.4		1.0		0.6	
First HF hospitalization	NA	NA	9.8	6.9	29.1	25.9	15.5	10.7
Absolute rate reduction	1.6		2.9		3.2		4.8	

CI, confidence interval; eGFR, estimated glomerular filtration rate; HF, heart failure; NA, not available; NT-proBNP, N-terminal pro B-type antriuretic peptide.

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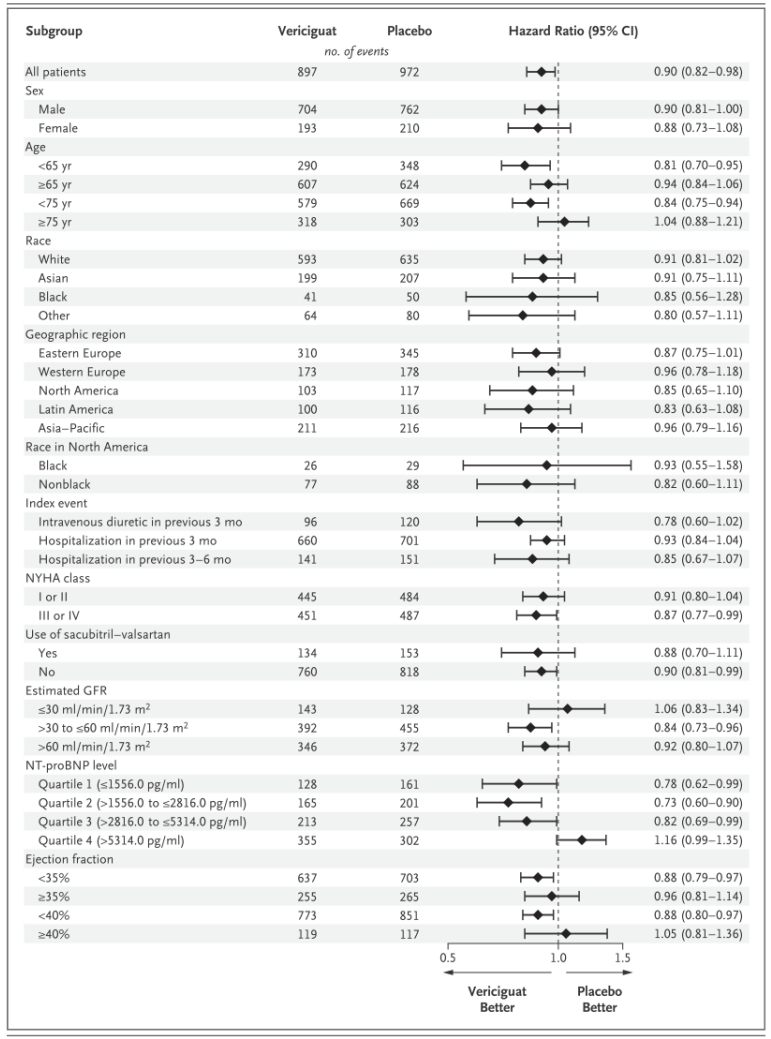
This article was published on March 28, 2020, at NEJM.org.

DOI: 10.1056/NEJMoa1915928

Armstrong PW et al. N Engl J Med. 2020

VICTORIA Trial



VICTORIA Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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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In this phase 3, randomized, double-blind, placebo-controlled trial, we assigned 5050 patients with chronic heart failure (New York Heart Association class II, III, or IV) and an ejection fraction of less than 45% to receive vericiguat (target dose, 10 mg once daily) or placebo, in addition to guideline-based medical therapy. The primary outcome was a composite of death from cardiovascular causes or first hospitalization for heart failure.

RESULTS
Over a median of 10.8 months, a primary-outcome event occurred in 897 of 2526 patients (35.5%) in the vericiguat group and in 972 of 2524 patients (38.5%) in the placebo group (hazard ratio, 0.90; 95% confidence interval [CI], 0.82 to 0.98; P=0.02). A total of 691 patients (27.4%) in the vericiguat group and 747 patients (29.6%) in the placebo group were hospitalized for heart failure (hazard ratio, 0.90; 95% CI, 0.81 to 1.00). Death from cardiovascular causes occurred in 414 patients (16.4%) in the vericiguat group and in 441 patients (17.5%) in the placebo group (hazard ratio, 0.93; 95% CI, 0.81 to 1.06). The composite of death from any cause or hospitalization for heart failure occurred in 957 patients (37.9%) in the vericiguat group and in 1032 patients (40.9%) in the placebo group (hazard ratio, 0.90; 95% CI, 0.83 to 0.98; P=0.02). Symptomatic hypotension occurred in 9.1% of the patients in the vericiguat group and in 7.9% of the patients in the placebo group (P=0.12), and syncope occurred in 4.0% of the patients in the vericiguat group and in 3.5% of the patients in the placebo group (P=0.30).

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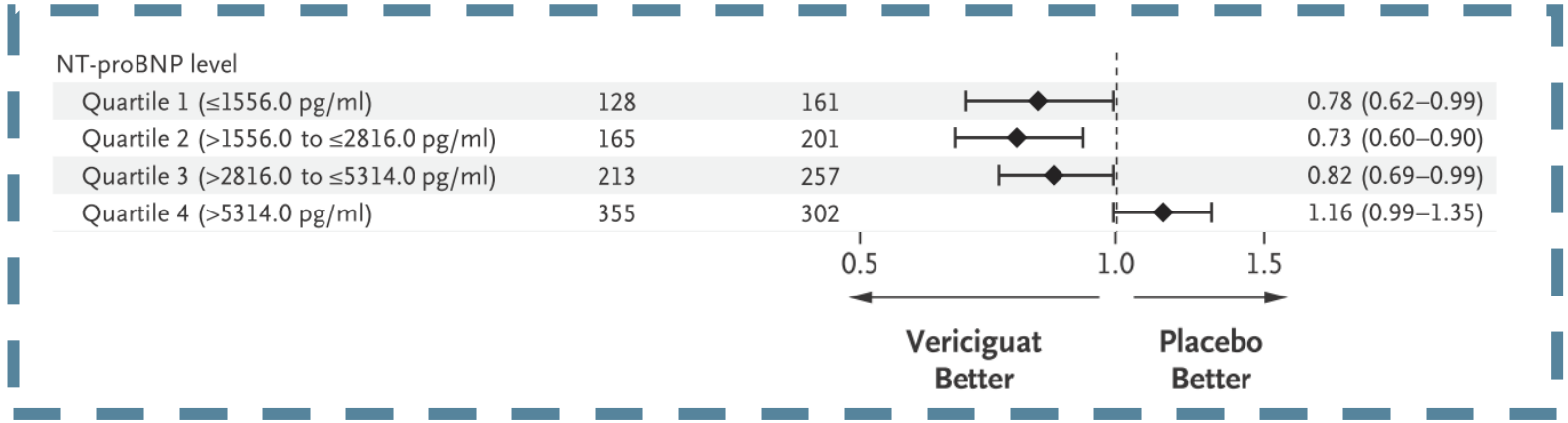
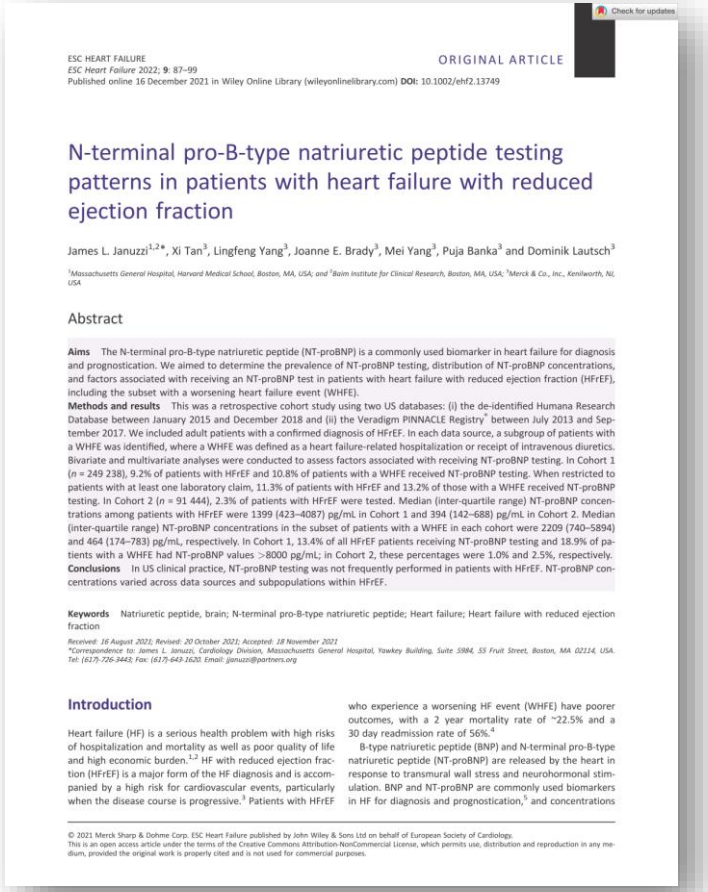


Armstrong PW et al. N Engl J Med. 2020

Qual è la percentuale di pazienti con WHF e NT-proBNP ≤5.000 pg/ml?



ESC HEART FAILURE
ESC Heart Failure 2022; **9**: 87–99
Published online 16 December 2021 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.13749

ORIGINAL ARTICLE

N-terminal pro-B-type natriuretic peptide testing patterns in patients with heart failure with reduced ejection fraction

James L. Januzzi[1,2]*, Xi Tan[3], Lingfeng Yang[3], Joanne E. Brady[3], Mei Yang[3], Puja Banka[3] and Dominik Lautsch[3]

[1]Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; and [2]Baim Institute for Clinical Research, Boston, MA, USA; [3]Merck & Co., Inc., Kenilworth, NJ, USA

Abstract

Aims The N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a commonly used biomarker in heart failure for diagnosis and prognostication. We aimed to determine the prevalence of NT-proBNP testing, distribution of NT-proBNP concentrations, and factors associated with receiving an NT-proBNP test in patients with heart failure with reduced ejection fraction (HFrEF), including the subset with a worsening heart failure event (WHFE).

Methods and results This was a retrospective cohort study using two US databases: (i) the de-identified Humana Research Database between January 2015 and December 2018 and (ii) the Veradigm PINNACLE Registry® between July 2013 and September 2017. We included adult patients with a confirmed diagnosis of HFrEF. In each data source, a subgroup of patients with a WHFE was identified, where a WHFE was defined as a heart failure-related hospitalization or receipt of intravenous diuretics. Bivariate and multivariate analyses were conducted to assess factors associated with receiving NT-proBNP testing. In Cohort 1 (n = 249 238), 9.2% of patients with HFrEF and 10.8% of patients with a WHFE received NT-proBNP testing. When restricted to patients with at least one laboratory claim, 11.3% of patients with HFrEF and 13.2% of those with a WHFE received NT-proBNP testing. In Cohort 2 (n = 91 444), 2.3% of patients with HFrEF were tested. Median (inter-quartile range) NT-proBNP concentrations among patients with HFrEF were 1399 (423–4087) pg/mL in Cohort 1 and 394 (142–688) pg/mL in Cohort 2. Median (inter-quartile range) NT-proBNP concentrations in the subset of patients with a WHFE in each cohort were 2209 (740–5894) and 464 (174–783) pg/mL, respectively. In Cohort 1, 13.4% of all HFrEF patients receiving NT-proBNP testing and 18.9% of patients with a WHFE had NT-proBNP values >8000 pg/mL; in Cohort 2, these percentages were 1.0% and 2.5%, respectively.

Conclusions In US clinical practice, NT-proBNP testing was not frequently performed in patients with HFrEF. NT-proBNP concentrations varied across data sources and subpopulations within HFrEF.

Keywords Natriuretic peptide, brain; N-terminal pro-B-type natriuretic peptide; Heart failure; Heart failure with reduced ejection fraction

Received: 16 August 2021; Revised: 20 October 2021; Accepted: 18 November 2021
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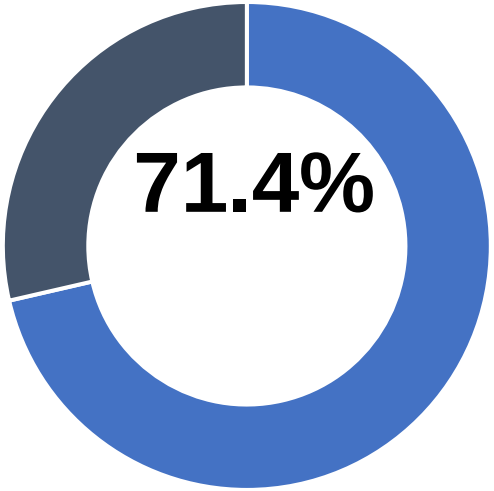
Introduction

Heart failure (HF) is a serious health problem with high risks of hospitalization and mortality as well as poor quality of life and high economic burden.[1,2] HF with reduced ejection fraction (HFrEF) is a major form of the HF diagnosis and is accompanied by a high risk for cardiovascular events, particularly when the disease course is progressive.[3] Patients with HFrEF who experience a worsening HF event (WHFE) have poorer outcomes, with a 2 year mortality rate of ~22.5% and a 30 day readmission rate of 56%.[4]

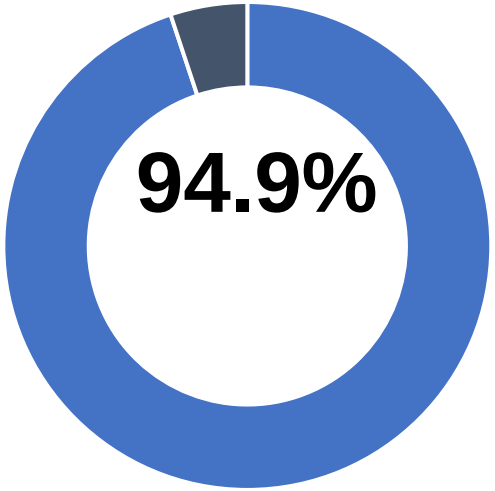
B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) are released by the heart in response to transmural wall stress and neurohormonal stimulation. BNP and NT-proBNP are commonly used biomarkers in HF for diagnosis and prognostication,[5] and concentrations

Humana Research Database



of **patients hospitalized with a worsening HF event** have **NT-proBNP ≤5,000 pg/ml at discharge**

PINNACLE Registry



of **outpatients with a previous worsening HF** event have **NT-proBNP ≤5,000 pg/ml**[#1]

Januzzi JL *et al. ESC Heart Fail* 2021;9:87–99

JACC: HEART FAILURE VOL. 8, NO. 11, 2020

N-Terminal Pro-B-Type Natriuretic Peptide and Clinical Outcomes

Vericiguat Heart Failure With Reduced Ejection Fraction Study

Justin A. Ezekowitz, MBBCH, MSc,[a] Christopher M. O'Connor, MD,[b,c] Richard W. Troughton, MD,[d] Wendimagegn G. Alemayehu, PhD,[b] Cynthia M. Westerhout, PhD,[e] Adriaan A. Voors, MD, PhD,[f] Javed Butler, MD, MPH, MBA,[g] Carolyn S.P. Lam, MBBS, PhD,[f,d] Piotr Ponikowski, MD,[h] Michele Emdin, MD, PhD,[i] Mahesh J. Patel, MD,[j] Burkert Pieske, MD,[k] Lothar Roessig, MD,[l] Adrian F. Hernandez, MD, MHS,[b] Paul W. Armstrong, MD[e]

ABSTRACT

OBJECTIVES The purpose of this study was to examine the treatment effect of vericiguat in relation to N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels at randomization.

BACKGROUND Vericiguat compared with placebo reduced the primary outcome of cardiovascular death (CVD) or heart failure hospitalization (HFH) in patients with HF with reduced ejection fraction (HFrEF) in the VICTORIA (A Study of Vericiguat in Participants With Heart Failure With Reduced Ejection Fraction) trial. Because an interaction existed between treatment and the primary outcome according to pre-specified quartiles of NT-proBNP at randomization, we examined this further.

METHODS This study evaluated the NT-proBNP relationship with the primary outcome in 4,805 of 5,050 patients as a risk-adjusted, log-transformed continuous variable. Hazard ratios (HRs) and 95% confidence intervals (CIs) are presented.

RESULTS Median NT-proBNP was 2,816 pg/ml (25th to 75th percentile: 1,556 to 5,314 pg/ml). The study treatment effect varied across the spectrum of NT-proBNP at randomization (with $\log^2$ transformation, p for interaction = 0.002). A significant association between treatment effects existed in patients with levels <4,000 pg/ml and remained evident up to 8,000 pg/ml. A 23% relative risk reduction occurred in the primary endpoint with NT-proBNP ≤4,000 pg/ml (HR: 0.77; 95% CI: 0.68 to 0.88). For NT-proBNP values ≤4,000 pg/ml (n = 3,100), the HR was 0.78 (95% CI: 0.67 to 0.90) for HFH and 0.75 (95% CI: 0.60 to 0.94) for CVD. For NT-proBNP ≤8,000 pg/ml (n = 4,133), the HR was 0.85 (95% CI: 0.76 to 0.95) for the primary outcome, 0.84 (95% CI: 0.75 to 0.95) for HFH, and 0.84 (95% CI: 0.71 to 0.99) for CVD. For NT-proBNP >8,000 pg/ml (n = 672), the HR was 1.16 (95% CI: 0.94 to 1.41) for the primary outcome.

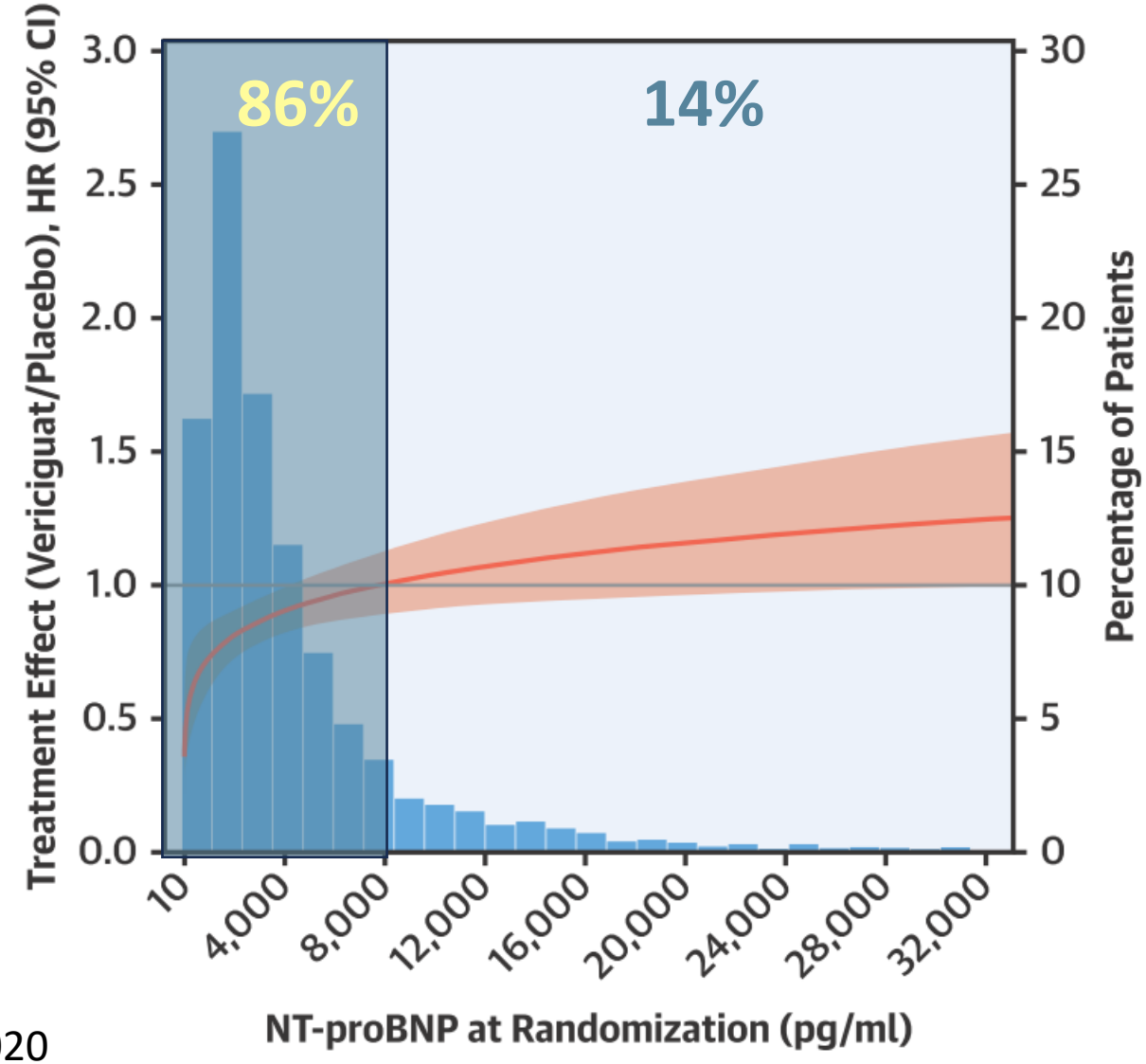
CONCLUSIONS A reduction in the primary composite endpoint and its CVD and HFH components was observed in patients on vericiguat compared with subjects on placebo with NT-proBNP levels up to 8,000 pg/ml. This provided new insight into the benefit observed in high-risk patients with worsening HFrEF. (A Study of Vericiguat in Participants With Heart Failure With Reduced Ejection Fraction [HFrEF] [MK-1242-001] [VICTORIA]; NCT02861534)

From the [a]Division of Cardiology, Department of Medicine, Canadian VIGOUR Centre, University of Alberta, Edmonton, Canada; [b]Division of Cardiology, Department of Medicine, Duke Clinical Research Institute, Duke University, Durham, North Carolina; [c]Inova Heart and Vascular Institute, Falls Church, Virginia; [d]Department of Medicine, University of Otago, Christchurch, New Zealand; [e]Department of Cardiology and Thorax Surgery, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands; [f]Department of Medicine, University of Mississippi Medical Center, Jackson, Mississippi; [g]Department of Cardiology, National Heart Centre Singapore and Duke-National University of Singapore; [h]Wroclaw Medical University, Department of Heart Disease, Wroclaw, Poland; [i]Cardiothoracic Department, Fondazione Toscana Gabriele Monasterio, Pisa, Italy; and Institute of Life Sciences, Scuola Superiore Sant'Anna, Pisa, Italy; [j]Merck & Co. Inc., Kenilworth, New Jersey; [k]Department of Internal Medicine-Cardiology, Charité University Medicine, German Heart Center, Berlin, Germany; and [l]Bayer AG, Wuppertal, Germany. Scott Solomon, MD, served as Guest Editor for this paper.

ISSN 2213-1779 https://doi.org/10.1016/j.jchf.2020.08.008

PRIMARY OUTCOME

CV death or first HFH



NTproBNP <4,000
(n 3.100)

RRR 23%

ARR 6.8%

NTproBNP <8,000
(n 4.133)

RRR 15%

ARR 5.4%

Ezekowitz JA et al, J Am Coll Cardiol HF 2020

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Armstrong PW et al. N Engl J Med. 2020

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.

AGENDA

Vericiguat: cosa è? Come funziona? Perché è utile nello scompenso…

Vericiguat: Evidenze di efficacia e sicurezza… Lo studio VICTORIA

Vericiguat: Evidenze di efficacia e sicurezza nel paziente anziano…

ARTICLE IN PRESS

Journal of Cardiac Failure Vol. 00 No. 00 2021

New Drugs for Heart Failure: What is the Evidence in Older Patients?

FRANCESCO ORSO, MD,[1] ANDREA HERBST, MD,[1] ALESSANDRA PRATESI, MD, PhD,[2] FRANCESCO FATTIROLLI, MD,[2,3] ANDREA UNGAR, MD, PhD,[1] NICCOLÒ MARCHIONNI, MD,[2,3] AND SAMUELE BALDASSERONI, MD, PhD[1]

Italy

ABSTRACT

Heart failure (HF) is a major public health concern, with a high prevalence in the older population. The majority of randomized clinical trials evaluating new emerging pharmacologic agents for HF (eg, angiotensin receptor−neprilysin inhibitors, sodium-glucose cotransporter 2 inhibitors, intravenous iron for deficiency treatment, transthyretin stabilizers, soluble guanylate cyclase stimulators, cardiac myosin activators, and new potassium binders) have found positive results on various clinical outcomes, particularly in patients with reduced ejection fraction. These treatments might have an important role in the management of older patients as well. Nevertheless, trials demonstrating benefit of these drugs have involved patients significantly younger (on average, approximately 10 years) and fewer comorbidities than those commonly encountered in clinical practice. We describe the recent evidence regarding the newest HF drugs and their applicability to older individuals in terms of efficacy and safety, and we discuss their effects on outcomes particularly valuable to older patients, such as preservation of cognitive function, functional status, independence, and quality of life. Although available subgroup analyses seem to confirm efficacy and safety across the age spectrum for some of these drugs, their effects on older patients centered outcomes often have been neglected. Future HF trials should be designed to include older patients more representative of the real clinical practice, to overcome generalizability biases. (*J Cardiac Fail 2021;00:1–13*)

Key Words: heart failure, older adults, treatments, new drugs.

Owing to associated high hospitalization rate, mortality and costs to healthcare system, heart failure (HF) is a major concern to public health.[1] In patients with HF, the goals of treatment are to improve clinical status, functional capacity, and quality of life (QoL), to prevent hospital admission and to decrease disease-specific and all-cause mortality.[2–3] Despite substantial improvements obtained with drugs and devices validated in randomized clinical trials (RCTs) over the past 30 years, particularly in the subset of patients with HF with reduced ejection fraction (HFrEF), HF-specific morbidity and mortality remain high.[2,3] For patients with HF with preserved ejection fraction (HFpEF) or HF with mid-range ejection fraction, the situation is even worse, because to date no treatment has definitively improved hard outcomes in these subsets of patients.[3,4]

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Manuscript received April 2, 2021; revised manuscript received July 9, 2021; revised manuscript accepted July 19, 2021.

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1071-9164/$ - see front matter

https://doi.org/10.1016/j.cardfail.2021.07.011

In general, RCTs designed to assess the efficacy and safety of treatments for HF selectively have enrolled patients of young to middle age and with few chronic comorbidities.[4–6] In fact, patients with HF in administrative databases or real-world clinical registries are close to 80 years of age, whereas those in RCTs are most frequently approximately 65–70 years of age.[5,7] This issue raises concerns about the generalizability of RCTs results to older (≥75 years) patients with HF, often characterized by greater clinical complexity, polypharmacy, and consequent increased likelihood of drug interactions and nonadherence.[5–7] Furthermore, as recently recommended by an American Heart Association statement, other outcomes beyond the traditional ones of cardiovascular (CV) or all-cause morbidity and mortality, should be prioritized in older patients with cardiac disease.[8] These outcomes are represented, for example, by assessment of QoL and of progression of disability or cognitive impairment. Conversely, as shown in Table 1, most recent HF trials failed to assess these outcomes, or adopted exclusion criteria that, by definition, limited such analyses by impeding the enrollment of older individuals with more complex disease.

Seven therapeutic novelties are of potential interest in older patients with HF: angiotensin receptor and neprilysin inhibitors (ARNIs), sodium-glucose cotransporter 2 inhibitors (SGLT2is), correction of iron deficiency, tafamidis for

New Drugs for Heart Failure: What is the Evidence in Older Patients?

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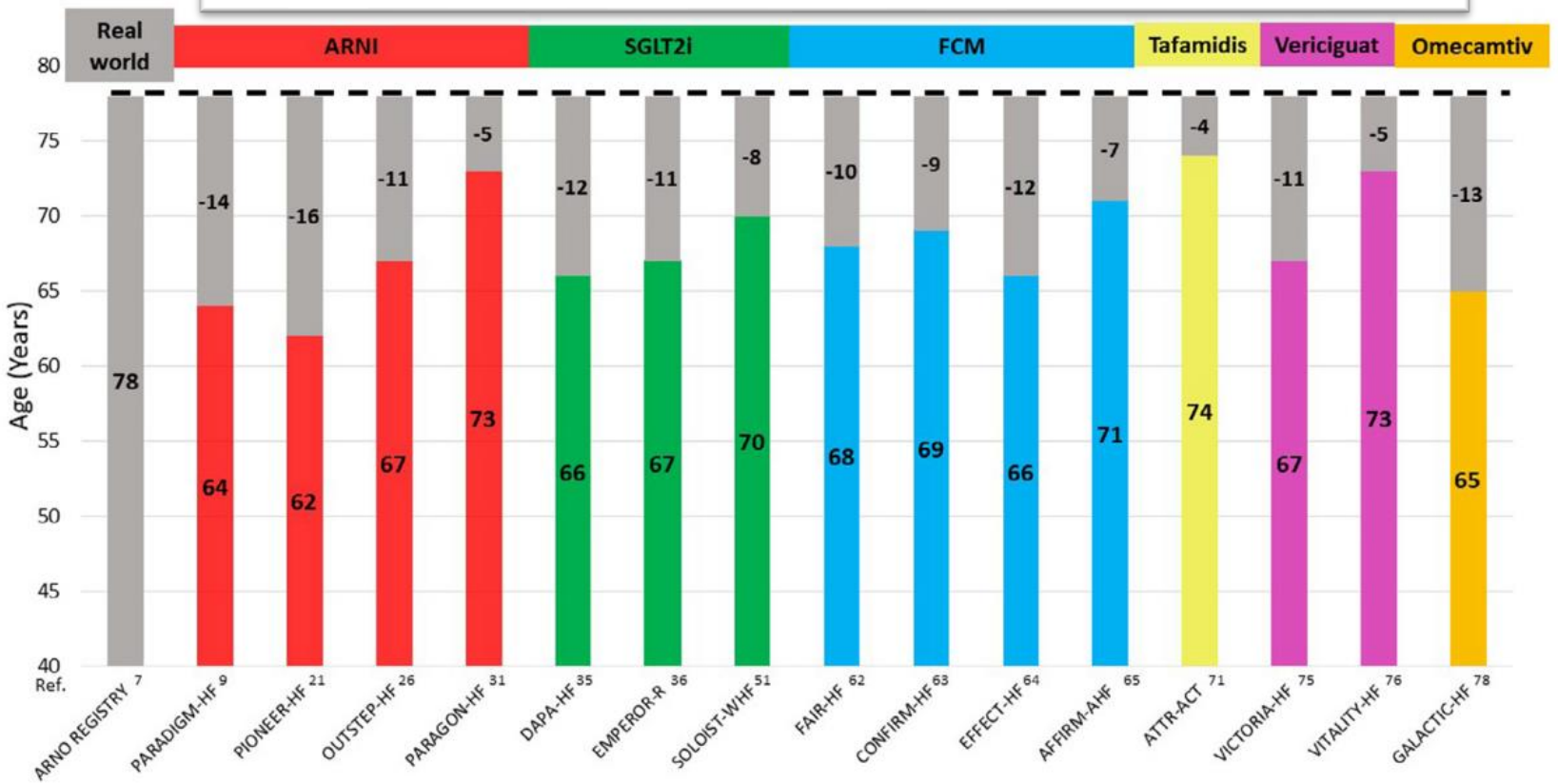

Fig. 1. Mean age of patients enrolled in the real world (grey column) and in trials testing new HF drugs (colored columns). The gray columns show the difference (in years of age) between the two settings. ARNI, angiotensin receptor−neprilisin inhibitor; FCM, ferric carboxymaltose; SGLT2i, sodium-glucose cotransporter 2 inhibitor.

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ABSTRACT

BACKGROUND
The effect of vericiguat, a novel oral soluble guanylate cyclase stimulator, in patients with heart failure and reduced ejection fraction who had recently been hospitalized or had received intravenous diuretic therapy is unclear.

METHODS
In this phase 3, randomized, double-blind, placebo-controlled trial, we assigned 5050 patients with chronic heart failure (New York Heart Association class II, III, or IV) and an ejection fraction of less than 45% to receive vericiguat (target dose, 10 mg once daily) or placebo, in addition to guideline-based medical therapy. The primary outcome was a composite of death from cardiovascular causes or first hospitalization for heart failure.

RESULTS
Over a median of 10.8 months, a primary-outcome event occurred in 897 of 2526 patients (35.5%) in the vericiguat group and in 972 of 2524 patients (38.5%) in the placebo group (hazard ratio, 0.90; 95% confidence interval [CI], 0.82 to 0.98; P=0.02). A total of 691 patients (27.4%) in the vericiguat group and 747 patients (29.6%) in the placebo group were hospitalized for heart failure (hazard ratio, 0.90; 95% CI, 0.81 to 1.00). Death from cardiovascular causes occurred in 414 patients (16.4%) in the vericiguat group and in 441 patients (17.5%) in the placebo group (hazard ratio, 0.93; 95% CI, 0.81 to 1.06). The composite of death from any cause or hospitalization for heart failure occurred in 957 patients (37.9%) in the vericiguat group and in 1032 patients (40.9%) in the placebo group (hazard ratio, 0.90; 95% CI, 0.83 to 0.98; P=0.02). Symptomatic hypotension occurred in 9.1% of the patients in the vericiguat group and in 7.9% of the patients in the placebo group (P=0.12), and syncope occurred in 4.0% of the patients in the vericiguat group and in 3.5% of the patients in the placebo group (P=0.30).

CONCLUSIONS
Among patients with high-risk heart failure, the incidence of death from cardiovascular causes or hospitalization for heart failure was lower among those who received vericiguat than among those who received placebo. (Funded by Merck Sharp & Dohme [a subsidiary of Merck] and Bayer; VICTORIA ClinicalTrials.gov number, NCT02861534.)

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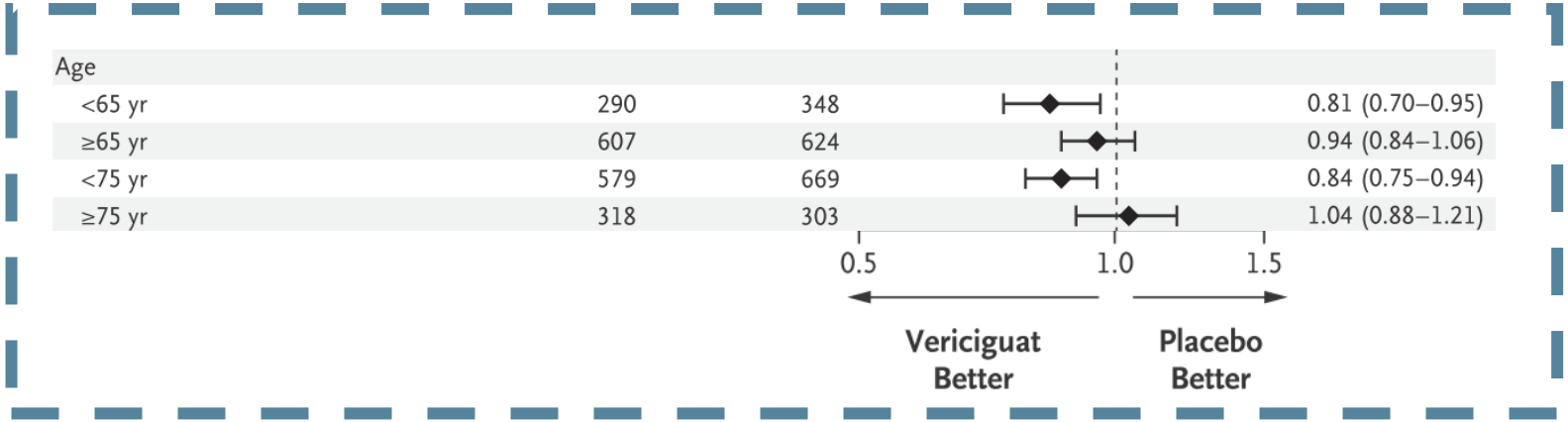
*A full list of VICTORIA Study Group members is provided in the Supplementary Appendix, available at NEJM.org.

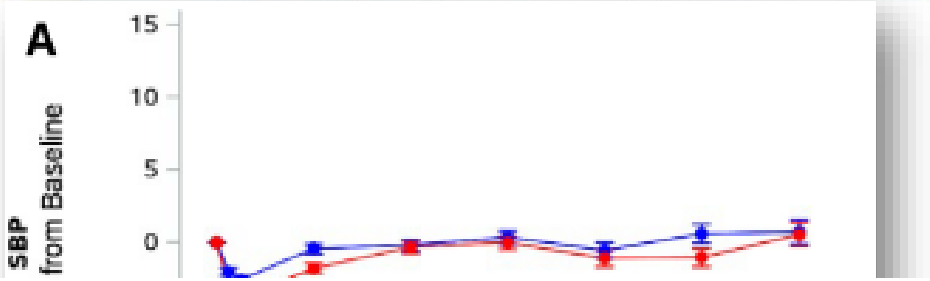
This article was published on March 28, 2020, at NEJM.org.

DOI: 10.1056/NEJMoa1915928

VICTORIA Trial



Armstrong PW et al. N Engl J Med. 2020



Journal of the American Heart Association

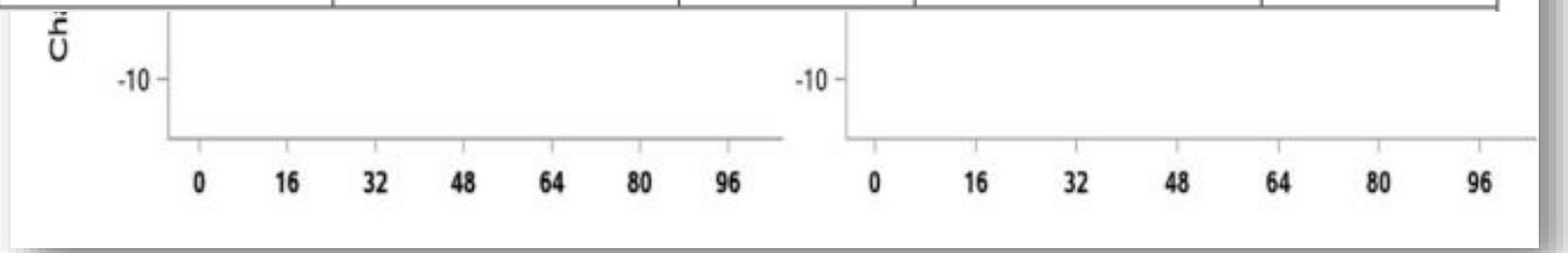
ORIGINAL RESEARCH

Blood Pressure and Safety Events With

Table 2. Treatment Effect on Time to Symptomatic Hypotension or Syncope by Vulnerable Subgroups

	Vericiguat Rate (Events)*	Placebo Rate (Events)*	Unadjusted		Adjusted	
			HR (95% CI)	*P* value	HR (95% CI)	*P* value
Symptomatic hypotension or syncope						
Age ≤75 y	12.03 (222)	9.61 (179)	1.26 (1.03–1.53)	0.28	1.23 (1.01–1.51)	0.42
Age >75 y	13.35 (90)	12.99 (88)	1.03 (0.77–1.39)		1.06 (0.78–1.44)	
SBP ≥110 mm Hg	10.08 (193)	9.13 (178)	1.11 (0.91–1.36)	0.36	1.11 (0.90–1.37)	0.33
SBP <110 mm Hg	19.66 (119)	15.05 (89)	1.30 (0.99–1.71)		1.32 (0.99–1.75)	
No use of ARNI	11.61 (258)	9.55 (212)	1.22 (1.02–1.46)	0.48	1.23 (1.02–1.49)	0.24
Use of ARNI	18.09 (54)	17.23 (55)	1.05 (0.72–1.53)		0.95 (0.64–1.41)	

J Am Heart Assoc. 2021;10:e021094. DOI: 10.1161/JAHA.121.021094



J Am Heart Assoc. 2021

AGENDA

Vericiguat: cosa è? Come funziona? Perché è utile nello scompenso…

Vericiguat: Evidenze di efficacia e sicurezza… Lo studio VICTORIA

Vericiguat: Evidenze di efficacia e sicurezza nel paziente anziano…

Vericiguat: in quali pazienti e quando… Le linee guida

ESC European Society of Cardiology
European Heart Journal (2021) **00**, 1–128
doi:10.1093/eurheartj/ehab368

ESC GUIDELINES

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

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ESC Clinical Practice Guidelines Committee (CPG): listed in the Appendix.

ESC subspecialty communities having participated in the development of this document:

Associations: Association for Acute CardioVascular Care (ACVC), Association of Cardiovascular Nursing & Allied Professions (ACNAP), European Association of Cardiovascular Imaging (EACVI), European Association of Preventive Cardiology (EAPC), European Association of Percutaneous Cardiovascular Interventions (EAPCI), European Heart Rhythm Association (EHRA), Heart Failure Association (HFA).

Councils: Council of Cardio-Oncology, Council on Basic Cardiovascular Science, Council on Valvular Heart Disease.

Working Groups: Adult Congenital Heart Disease, Cardiovascular Pharmacotherapy, Cardiovascular Regenerative and Reparative Medicine, Cardiovascular Surgery, e-Cardiology, Myocardial and Pericardial Diseases, Myocardial Function.

Patient Forum

New recommendations

Recommendations for treatment of chronic HF	
HFrEF	
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I
Vericiguat may be considered in patients in NYHA class II–IV who have had worsening HF despite treatment with an ACE-I (or ARNI), a beta-blocker and an MRA to reduce the risk of CV mortality or HF hospitalization.	IIb

Circulation

AHA/ACC/HFSA CLINICAL PRACTICE GUIDELINE

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

Writing Committee Members*

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AIM: The "2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure" replaces the "2013 ACCF/AHA Guideline for the Management of Heart Failure" and the "2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure." The 2022 guideline is intended to provide patient-centric recommendations for clinicians to prevent, diagnose, and manage patients with heart failure.

METHODS: A comprehensive literature search was conducted from May 2020 to December 2020, encompassing studies, reviews, and other evidence conducted on human subjects that were published in English from MEDLINE (PubMed), EMBASE, the Cochrane Collaboration, the Agency for Healthcare Research and Quality, and other relevant databases. Additional relevant clinical trials and research studies, published through September 2021, were also considered. This guideline was harmonized with other American Heart Association/American College of Cardiology guidelines published through December 2021.

STRUCTURE: Heart failure remains a leading cause of morbidity and mortality globally. The 2022 heart failure guideline provides recommendations based on contemporary evidence for the treatment of these patients. The recommendations present an evidence-based approach to managing patients with heart failure, with the intent to improve quality of care and align with patients' interests. Many recommendations from the earlier heart failure guidelines have been updated with new evidence, and new recommendations have been created when supported by published data. Value statements are provided for certain treatments with high-quality published economic analyses.

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry may apply; see Appendix 1 for detailed information. †ACC/AHA Representative. ‡ACC/AHA Joint Committee on Clinical Practice Guidelines Liaison. §ACC/AHA Task Force on Performance Measures Representative. ‖HFSA Representative.

ACC/AHA Joint Committee on Clinical Practice Guidelines Members, see page e986.

The American Heart Association requests that this document be cited as follows: Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, Deswal A, Drazner MH, Dunlay SM, Evers LR, Fang JC, Fedson SE, Fonarow GC, Hayek SS, Hernandez AF, Khazanie P, Kittleson MM, Lee CS, Link MS, Milano CA, Nnacheta LC, Sandhu AT, Stevenson LW, Vardeny O, Vest AR, Yancy CW. 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. *Circulation.* 2022;145:e895–e1032. doi: 10.1161/CIR.0000000000001063

Circulation is available at www.ahajournals.org/journal/circ

7.3.9.3. Pharmacological Treatment for Stage C HFrEF: Soluble Guanylyl Cyclase Stimulators

Recommendation for Pharmacological Treatment for Stage C HFrEF: Soluble Guanylyl Cyclase Stimulators
Referenced studies that support the recommendation are summarized in the Online Data Supplements.

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]

Conclusioni

Con **Vericiguat** abbiamo una nuova strategia terapeutica in grado di **migliorare la prognosi in pazienti ad alto rischio con recente episodio di WHF**, che troviamo **frequentemente nella pratica clinica**, e per i quali al momento attuale non sembrano esserci molti altri trattamenti.

Questa strategia…

- Si basa su un **forte razionale fisiopatologico**.
- È verosimilmente **sicura e ben tollerata**, anche se abbiamo bisogno di ***real world evidence***.
- Sembra essere efficace e ben tollerata anche nel paziente anziano anche se soprattutto in questi pazienti sarà importante selezionare i migliori candidati.