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ORIGINAL ARTICLE

Clinical profile, associated events and safety of vericiguat in a real-world cohort: The VERITA study

Mario Galván Ruiz[1]*, Miguel Fernández de Sanmamed Girón[2], María del Val Groba Marco[2], Lorena Rojo Jorge[3], Claudia Peña Saavedra[2], Elvira Martín Bou[2], Rubén Andrade Guerra[2], Eduardo Caballero Dorta[2] and Antonio García Quintana[2]

[1]*Department of Cardiology, Hospital Universitario de Gran Canaria Doctor Negrín, Universidad de Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain;* [2]*Department of Cardiology, Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas de Gran Canaria, Spain; and* [3]*Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas de Gran Canaria, Spain*

Abstract

Aims The aim of this study was to determine the clinical profile, associated events and safety of vericiguat in a real-world cohort of patients with heart failure with reduced ejection fraction (HFrEF).

Methods This study is a prospective and observational cohort study of patients with HFrEF and recent HF worsening episodes requiring intravenous therapy who initiated vericiguat in an HF outpatient clinic. A subanalysis of patients with ≥6 months' follow-up was performed separately.

Results Out of 103 patients initially included, 52 had a follow-up of at least 6 months (median follow-up of 303 days). At baseline, the mean age was 71.3 ± 9.4 years, 27.2% were women, the median left ventricular ejection fraction was 34% (28%–39%) and 99% were taking beta-blockers, 96.1% sodium-glucose cotransporter-2 (SGLT2) inhibitors, 95.1% sacubitril–valsartan, 90.3% aldosterone antagonists and 93.2% loop diuretics. During follow-up, New York Heart Association (NYHA) functional class improved (from 67.3% and 32.7% in classes III and II, respectively, to 22.4% and 75.5% at study end; $P < 0.001$), as did the EuroQol-5D (EQ-5D) and visual analogue scale (VAS) scores (from 0.83 ± 0.13 to 0.87 ± 0.12, $P = 0.032$, and from 60 to 79, $P = 0.005$, respectively). Vericiguat was well tolerated (13.5% had symptomatic hypotension, and 11.5% had discontinued treatment), and 78.8% of patients achieved the target dose of 10 mg. The number of HF-related hospitalizations/decompensations within the previous 12 months was 2.3 ± 1.4 and decreased with vericiguat to 0.79 ± 1.14 ($P < 0.001$). At study end, 7.7% died (50% for HF).

Conclusions In clinical practice, treatment with vericiguat is associated with substantial improvements in functional class and quality of life and a reduction in hospitalizations for HF, with a low risk of adverse effects.

Keywords heart failure; hospitalization; vericiguat

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**Correspondence to: Mario Galván Ruiz, Department of Cardiology, Hospital Universitario de Gran Canaria Doctor Negrín, Universidad de Las Palmas de Gran Canaria, Calle Plaza Barranco de la Ballena, s/n, 35010 Las Palmas de Gran Canaria, Spain. Email: mariogalvanr@hotmail.com*

Introduction

Heart failure (HF) is a chronic condition that has become epidemic, currently affecting around 2% of the adult population.[1] Furthermore, the prevalence of HF is expected to have increased by 46% in 2030,[2] mainly owing to the aging of the population and the greater prevalence of predisposing factors such as hypertension and diabetes.[2–4]

HF is associated with considerable morbidity and mortality.[2] Unfortunately, mortality rates remain high, and there have been no clear improvements in the last decade.[4] Moreover, HF-related hospitalization rates have increased over time.[2] Of note, rates of rehospitalization and cardiovascular death increase dramatically in patients previously hospitalized for HF.[5,6] This is the consequence not only of the reduced use of HF treatments in clinical practice[1,7,8] but also of the need for new treatment alternatives.[9]

With the aim of reducing the risk of HF-related hospitalizations and death, the 2021 European HF guidelines recommend quadruple therapy with sacubitril–valsartan (better

than angiotensin-converting enzyme inhibitors), beta-blockers, aldosterone antagonists and sodium-glucose cotransporter-2 (SGLT2) inhibitors as the first-line therapeutic approach in patients with HF and reduced left ventricular ejection fraction (HFrEF). Likewise, in patients with a history of worsening HF, guidelines recommend vericiguat to reduce the risk of HF hospitalization and cardiovascular death.[9]

The VICTORIA study was a phase 3 randomized clinical trial in which 5050 symptomatic patients with chronic HF, EF $<$ 45%, elevated natriuretic peptides and evidence of worsening HF received vericiguat (target dose of 10 mg once daily) or placebo in addition to standard therapy. After a median follow-up of 10.8 months, vericiguat significantly reduced the risk of cardiovascular death or first HF hospitalization by 10% (number needed to treat [NNT] = 24), driven primarily by a decrease in HF-related hospitalizations (NNT = 31).[10] Recent studies have shown that many patients with HFrEF could benefit from treatment with vericiguat.[11–13] However, current evidence on the use of vericiguat in clinical practice is very scarce, and more information is warranted.[14–16]

The aim of the VERITA study was to determine the clinical profile, clinical events and safety of patients with HFrEF taking vericiguat in a real-world cohort. We performed a separate subanalysis of patients who had been followed up for at least 6 months.

Methods

We performed a prospective and observational cohort study that included patients with HFrEF and recent worsening of an HF episode who initiated or were already taking vericiguat between December 2022 and February 2024, in addition to standard guideline-directed medical HF therapies. Patients received therapy in the Advanced Heart Failure Clinic of Hospital Universitario de Gran Canaria Dr. Negrín, Spain. Patients with a systolic blood pressure $<$ 100 mmHg could not initiate vericiguat. The total expected follow-up for each patient was 1 year. In the present study, the patients had been followed up for at least 6 months. As this was an observational study, patients did not have to undergo a specific diagnostic or therapeutic procedure to be included. The follow-up visits coincided with routine visits. The research was performed in accordance with the Declaration of Helsinki. The study was approved by the Research Ethics Committee of Hospital Universitario de Gran Canaria Dr. Negrín, Spain (Code 2022-592-1). Patients had to provide their written informed consent before being included in the study.

The data recorded at baseline were biodemographic data (age, sex and body mass index), comorbidities (smoking, hypertension, diabetes, dyslipidaemia, chronic obstructive pulmonary disease and atrial fibrillation), aetiology of HF, criteria met for initiating vericiguat in the VICTORIA trial, New York Heart Association (NYHA) functional class, biochemical parameters, echocardiographic parameters and HF treatments. Baseline clinical characteristics in the subgroup of patients with a follow-up $\geq$ 6 months were analysed, taking into account decompensations during follow-up, age, renal function, sex and the maximum dose of vericiguat reached. In addition, the baseline clinical characteristics of the VERITA study population were compared with those of the VICTORIA trial population.

Patients completed three questionnaires at baseline and at 1.5, 6 and 12 months after initiation of vericiguat, as follows: the Kansas City Cardiomyopathy Questionnaire (KCCQ), the EuroQol-5D (EQ-5D) and a visual analogue scale (VAS). The KCCQ is a 23-item, self-administered disease-specific instrument that quantifies symptoms (frequency, severity and recent change), physical function, quality of life and social function over the previous 2 weeks. The KCCQ scores range from 0 to 100, with higher scores indicating a better health status.[17] The EQ-5D is a standardized, generic questionnaire that assesses health status in terms of five dimensions: mobility, self-care, usual activities, pain and discomfort, and anxiety and depression. Values range from 1 (full health) to 0 (worst health status).[18] The VAS is a 100 mm horizontal line with descriptors at each extreme. It is used as a psychometric measuring instrument to document the characteristics of disease-related symptom severity in individual patients.[19]

During follow-up, changes in HF treatments (including the dosage of sacubitril–valsartan), loop diuretics and NYHA functional class, as well as in the KCCQ, EQ-5D and VAS scores, were evaluated. Adverse effects of vericiguat, discontinuation and uptitration were analysed. Events (HF-related hospitalization/need for intravenous diuretics and death) after the initiation of treatment with vericiguat were also studied. Data were analysed taking into account decompensations during follow-up, age, renal function, sex and the maximum dose of vericiguat achieved.

Statistical analysis

Qualitative data were presented as their absolute (*n*) and relative (%) frequencies. Quantitative data were presented using the mean or median and standard deviation or interquartile range (IQR), as appropriate. The χ^2 test was used to compare categorical variables between the different study cohorts, and the *t* test or its non-parametric equivalent, the Mann–Whitney test, was applied for the continuous variables. All statistical tests were based on a two-tailed alpha of 0.05. All statistical procedures were performed using JAMOVI Version 2.3.21.0.

Results

A total of 103 patients were initially included in the study; 52 patients had been followed up for at least 6 months. At baseline, the mean age was 71.3 ± 9.4 years, and 27.2% were women. Comorbidities were common in this population (86.4% had hypertension, 66% had atrial fibrillation, 61.2% had chronic kidney disease and 56.3% had diabetes). The most frequent aetiologies of HF were ischaemic (56.3%) and dilated non-ischaemic (33%). All patients were in NYHA functional class II (40.8%) or III (59.2%). At baseline, the median (IQR) left end-diastolic ventricular diameter was 62 mm (55–67), and the left ventricular ejection fraction was 34% (28–39). In addition, 36.9% had mild mitral regurgitation (I/IV), 15.5% had moderate mitral regurgitation (II/IV), 28.2% had moderate–severe mitral regurgitation (III/IV), 11.7% had severe mitral regurgitation (IV/IV) and 7.8% had no mitral regurgitation. Regarding baseline HF treatments, 99% of patients were taking beta-blockers, 96.1% SGLT2 inhibitors, 95.1% sacubitril–valsartan, 90.3% aldosterone antagonists and 93.2% loop diuretics. Additionally, 29.1% received cardiac resynchronization therapy, 22.3% an implantable cardioverter defibrillator and 17.5% levosimendan (continuous infusion, without loading dose and in most cases, periodically). The baseline clinical characteristics of patients with a follow-up $>$ 6 months were similar to those of the overall study population (Table 1). Compared with the baseline clinical characteristics of the VICTORIA trial (Table S1), patients in the VERITA study were older (71.3 ± 9.4 vs. 67.5 ± 12.2 years; P = 0.002), more frequently had atrial fibrillation (66% vs. 43.5%; $P < 0.001$), were more frequently in NYHA functional class III (59.2% vs. 40%; P = 0.007), had lower N-terminal pro-brain natriuretic peptide (NT-proBNP) levels (2034 vs. 2803 pg/mL; $P < 0.001$) and were taking more guideline-directed medical therapies (beta-blockers, sacubitril–valsartan and aldosterone antagonists). In patients who had been followed up for at least 6 months, baseline clinical characteristics were similar regardless of the development of decompensation during follow-up, age, renal function, sex and the maximum dose of vericiguat achieved (Table S2).

After initiation of treatment with vericiguat, NYHA functional class improved from 67.3% and 32.7% in classes III and II, respectively, to 22.4% and 75.5% at study end. In addition, 2.1% of patients achieved NYHA class I (Figure 1). With regard to questionnaires, there were significant improvements in the scores of the EQ-5D and VAS, with a trend in the KCCQ (Figure 2 and Table S3). Furthermore, the dosage of sacubitril–valsartan increased significantly after the introduction of vericiguat (Figure S1), and although there was a trend towards a reduction in mean dosage of furosemide during follow-up (from 41.5 ± 23.5 to 38.5 ± 23.7 mg; P = 0.455), a lower proportion of patients required high doses of furosemide at study end (Figure S2). Patients who reduced the dose of sacubitril–valsartan had lower doses of vericiguat, including the five patients who discontinued the drug. In contrast, patients who titrated the sacubitril–valsartan dose also received higher doses of vericiguat.

Adverse effects of vericiguat during the study period were uncommon, with asymptomatic and symptomatic hypotension [11 (21.2%) and 7 (13.5%), respectively] being the most frequent, although only five patients (9.6%) discontinued their treatment because of these effects. Most patients (78.8%) achieved the target dose of 10 mg of vericiguat (Table 2).

The median (IQR) follow-up period of the study was 303 days (256–365). During the study period, 38.5% of patients were hospitalized for HF or required intravenous diuretics. Before the initiation of vericiguat, the mean number of HF-related hospitalizations/decompensations within the previous 12 months was 2.3 ± 1.4; after the initiation of vericiguat (median follow-up of 303 days), this number decreased to 0.79 ± 1.14 ($P < 0.001$). At study end, 7.7% of patients had died, half of them because of HF (Table 3). NYHA functional class and the questionnaire scores improved with vericiguat, regardless of age, sex or renal function. Furthermore, the risk of adverse effects, HF-related hospitalizations and death was also independent of age, sex and renal function (Table S4).

Discussion

Our study reports the first and broadest experience recorded in a large sample of patients with HFrEF treated with vericiguat in an HF clinic in Spain. The addition of vericiguat to standard guideline-directed medical HF therapies translated into reduced worsening of HF episodes (HF-related hospitalizations or need for intravenous diuretics) and improvements in functional class and quality of life. Vericiguat was well tolerated, and most patients achieved the target dose.

HFrEF is a complex process involving various neurohormonal systems, all of which must be targeted if we are to reduce the burden of HF. The nitric oxide–soluble guanylate cyclase–cGMP pathway is impaired in this population, with the result that it must be restored to decrease the risk of HF-related hospitalization and death.[20] In this context, the VICTORIA trial demonstrated the benefits of adding vericiguat to standard therapy among patients with HFrEF.[10] In fact, early initiation of vericiguat would reduce the risk of adverse events in this population.[16] Various studies have shown that in clinical practice, a substantial number of patients with HFrEF would benefit from vericiguat,[11–13,21,22] although current data on vericiguat in a real-life population are limited to a low number of studies or studies with a very small sample.[14,15] As a result, our data provide relevant information on the use of vericiguat in clinical practice.

Table 1 Baseline clinical characteristics of the study population overall and of patients followed up for >6 months.

	Baseline (n = 103)	Follow-up > 6 months (n = 52)	P
Biodemographic data			
Sex, female	28 (27.2%)	11 (21.2%)	0.414
Age, years (mean ± SD)	71.3 ± 9.4	72.0 ± 10.4	0.673
BMI, kg/m^2 (mean ± SD)	28.1 ± 5.8	28.2 ± 5.7	0.919
Follow-up (months), median (IQR)	-	303 (256–365)	-
Comorbidities			
Current smoker	12 (11.7%)	5 (9.6%)	0.702
Former smoker	47 (45.6%)	29 (55.8%)	0.233
Hypertension	89 (86.4%)	50 (96.2%)	0.060
Diabetes	58 (56.3%)	31 (59.6%)	0.694
Dyslipidaemia	86 (83.5%)	48 (92.3%)	0.130
COPD	15 (14.6%)	9 (17.3%)	0.656
Atrial fibrillation	68 (66%)	38 (73.1%)	0.372
Chronic kidney disease	63 (61.2%)	37 (71.2%)	0.220
Aetiology of HF			
Ischaemic	58 (56.3%)	28 (53.8%)	0.771
Dilated non-ischaemic	34 (33%)	20 (38.5%)	0.501
Restrictive	1 (1%)	0	0.620
Toxicity	2 (1.9%)	2 (3.8%)	0.480
Valvular	5 (6.4%)	2 (3.8%)	0.775
Criteria for initiating vericiguat in the VICTORIA trial			
Infusion of levosimendan	8 (7.8%)	6 (11.5%)	0.439
HF-related hospitalization in the previous 3 months	37 (35.9%)	17 (32.7%)	0.690
HF-related hospitalization in the previous 3–6 months	29 (28.2%)	12 (23.1%)	0.499
Intravenous diuretics for HF (without hospitalization) in the previous 3 months	29 (28.2%)	17 (32.7%)	0.559
Number of previous HF hospitalizations/ED visits in the previous 12 months	1.9 ± 1.3	2.3 ± 1.4	0.080
NYHA functional class			
NYHA I	0	1 (2.1%)	
NYHA II	42 (40.8%)	17 (32.7%)	<0.001
NYHA III	61 (59.2%)	35 (67.3%)	
Echocardiogram parameters			
LVEF, % (mean ± SD)	34 ± 7.5	31.8 ± 7.2	0.083
LVDd, mm (mean ± SD)	61.9 ± 11.8	63.6 ± 8.9	0.362
TAPSE, mm (mean ± SD)	18 ± 3.3	17.4 ± 3.3	0.287
PASP (mean ± SD)	37.5 ± 12.2	37.6 ± 12.3	0.962
Grade III–IV mitral regurgitation	41 (39.9%)	22 (42.3%)	0.765
Grade III–IV tricuspid regurgitation	18 (17.5%)	9 (17.3%)	0.979
Biochemical parameters			
Haemoglobin, g/dL (mean ± SD)	13.8 ± 1.7	13.7 ± 2.0	0.745
N/L ratio, median (IQR)	2.84 (2.0–3.9)	3.04 (2.2–4.37)	0.144
Creatinine (mg/dL), median (IQR)	1.3 (1.1–1.7)	1.43 (1.09–1.75)	0.002
eGFR (mL/min/1.73 m^2), median (IQR)	51 (36–65)	47 (35–60)	0.097
Hb1Ac, % (mean ± SD)	6.6 ± 1.3	-	-
Sodium, mmol/L (mean ± SD)	140 ± 3	139 ± 3.6	0.069
Chlorine, mmol/L (mean ± SD)	101 ± 4.2	100 ± 4	0.157
Potassium, mmol/L (mean ± SD)	4.7 ± 0.6	4.58 ± 0.52	0.221
NT-proBNP (pg/mL), median (IQR)	2034 (910–3372)	2116 (1019–4469)	0.630
CA 125, U/mL median (IQR)	18 (12–29)	16 (11–25)	0.04
Systolic blood pressure (mmHg), median (IQR)	117 (103–128)		
HF treatments			
Beta-blockers	102 (99%)	52 (100%)	0.999
Sacubitril–valsartan	98 (95.1%)	49 (94.2%)	0.808
Dose of sacubitril–valsartan			
No	4 (3.9%)	3 (5.8%)	
12/13 mg	19 (18.4%)	4 (7.7%)	0.023
24/26 mg	41 (39.8%)	11 (21.2%)	
49/51 mg	16 (15.5%)	22 (42.3%)	
97/103 mg	23 (22.3%)	12 (23.1%)	
Aldosterone antagonists	93 (90.3%)	47 (90.4%)	0.985
Dose of aldosterone antagonists			
No	5 (9.6%)	6 (11.8%)	
12.5 mg	13 (25%)	6 (11.8%)	0.372
25 mg	24 (46.2%)	29 (56.9%)	
50 mg	10 (19.2%)	10 (19.6%)	

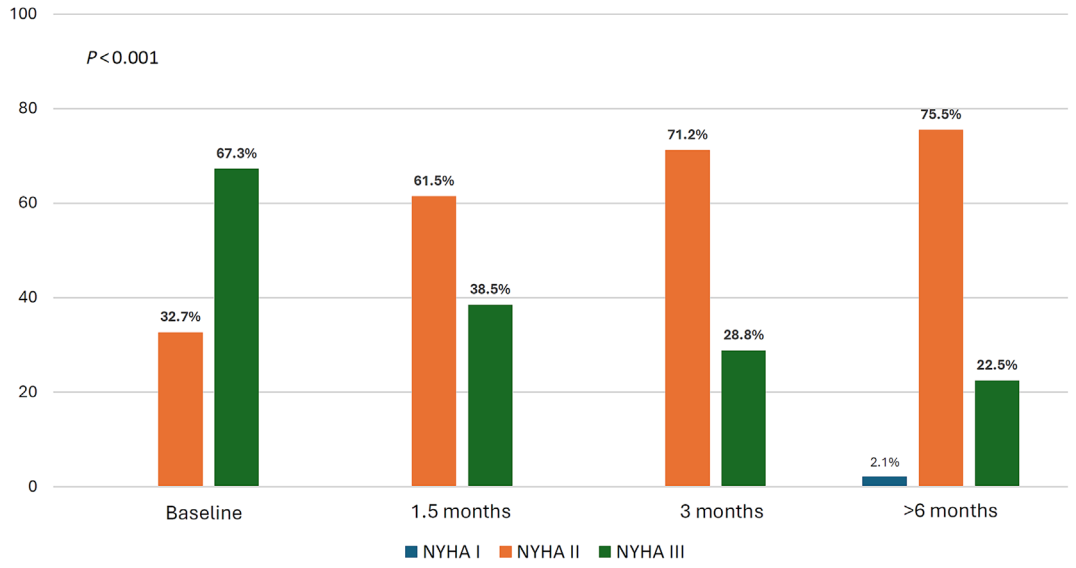
(*Continues*)

Table 1 (continued)

	Baseline (n = 103)	Follow-up > 6 months (n = 52)	P
SGLT2i	99 (96.1%)	52 (100%)	0.700
Loop diuretics	96 (93.2%)	49 (94.2%)	0.806
Dose of loop diuretics, mg (mean ± SD)	41.5 ± 23.5	38.5 ± 23.7	0.455
Levosimendan	18 (17.5%)	11 (21.2%)	0.579
Devices			
ICD	23 (22.3%)	15 (28.8%)	0.373
Resynchronization therapy	30 (29.1%)	24 (46.2%)	0.036
MitraClip	8 (7.8%)	6 (11.5%)	0.439

Note: Qualitative variables are presented as absolute (n) and relative (%) frequencies; quantitative variables are presented as mean and standard deviation (SD) or median and interquartile range (IQR) when indicated.
Abbreviations: BMI, body mass index; CA 125, cancer antigen 125; COPD, chronic obstructive pulmonary disease; ED, emergency department; eGFR, estimated glomerular filtration rate; Hb1Ac, glycated haemoglobin; HF, heart failure; ICD, implantable cardioverter-defibrillator; LVDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; SGLT2i, sodium-glucose cotransporter-2 inhibitor; TAPSE, tricuspid annular plane systolic excursion.

Figure 1 Changes in NYHA functional class after initiation of treatment with vericiguat (n = 52). NYHA, New York Heart Association.



In our study, the mean age was 71 years, around three quarters of patients were men, comorbidities were common, the median left ventricular ejection fraction was 34%, all patients were in NYHA functional class II (41%) or III (59%) and the median NT-proBNP levels were 2034 pg/mL. Compared with the baseline clinical characteristics of the VICTORIA trial, patients in the VERITA study were older, were more frequently in NYHA functional class III but had lower NT-proBNP levels. In a retrospective nationwide longitudinal cohort study in Germany, vericiguat was initiated in patients with a mean age of 73 years, of whom 28% were women. Likewise, the number of comorbidities was high.[14] Therefore, it seems that in clinical practice, vericiguat is being prescribed to patients with a worse risk profile but also with a higher use of HF therapies than those included in the VICTORIA trial. Of note, this better optimization of HF therapy could explain the lower levels of NT-proBNP shown in our study. As a result, our data extend the information provided by the pivotal phase 3 clinical trial to the whole spectrum of patients with HFrEF and a worsening HF event.

Relevant differences regarding the baseline HF treatments at initiation of vericiguat were recorded. Thus, whereas in the VICTORIA study,[10] 93% were taking beta-blockers, 69% aldosterone antagonists and 14% sacubitril–valsartan, and in the German retrospective nationwide longitudinal cohort study, the proportion of patients receiving the four pillars of guideline-recommended therapy at baseline was 29%,[14] we found that 99% of patients were taking beta-blockers, 96% SGLT2 inhibitors, 95% sacubitril–valsartan and 90% aldosterone antagonists. Moreover, in contrast to the VICTORIA trial, nearly 18% of patients were taking levosimendan. This observation is important, as it could explain differences in the risk

Figure 2 Changes in KCCQ, EQ-5D and VAS scores after initiation of treatment with vericiguat (n = 52). EQ-5D, EuroQol-5D; KCCQ, Kansas City Cardiomyopathy Questionnaire; VAS, visual analogue scale.

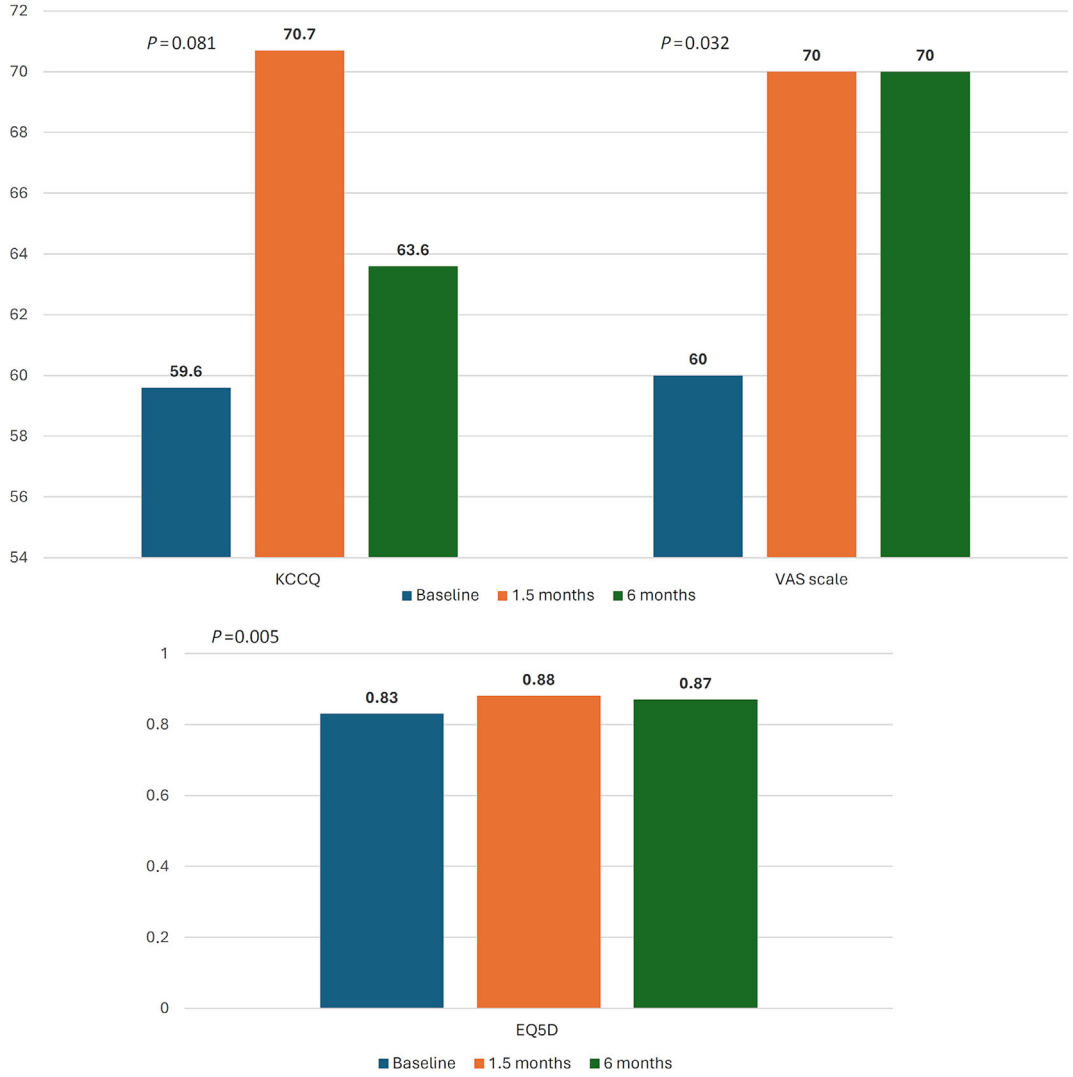


Table 2 Adverse effects and uptitration of vericiguat during follow-up (n = 52).

Adverse effect	
Gastrointestinal symptoms	1 (1.9%)
Asymptomatic hypotension	11 (21.2%)
Symptomatic hypotension	7 (13.5%)
Uptitration of vericiguat	
Discontinuation	6 (11.5%)
2.5 mg	2 (3.8%)
5 mg	3 (5.8%)
10 mg	41 (78.8%)
Reasons for discontinuation	
Hypotension	5 (9.6%)
Other	1 (1.9%)

Note: Qualitative variables are presented as absolute (n) and relative (%) frequencies.

Table 3 Events after initiation of treatment with vericiguat (n = 52).

Median follow-up, days (IQR)	303 (256–365)
HF-related hospitalizations/need for i.v. diuretics	20 (38.5%)
Number of HF hospitalizations/need for i.v. diuretics	0.79 ± 1.14
Heart transplant	1 (1.9%)
Death	4 (7.7%)
HF	2 (3.8%)
Non-cardiovascular	2 (3.8%)

Note: Qualitative variables are presented as absolute (n) and relative (%) frequencies; quantitative variables are presented as mean and standard deviation (SD) or median and interquartile range (IQR) when indicated.
Abbreviations: HF, heart failure; i.v., intravenous.

of developing events during follow-up, according to background HF therapy. Of note, a substudy of the VICTORIA trial showed that the efficacy of vericiguat was consistent across background medical therapy for HF,[23] suggesting that before starting treatment with vericiguat, patients need not already be taking the four pillars of treatment.

In the VERITA study, the dosage of sacubitril–valsartan increased significantly after the introduction of vericiguat, and the proportion of patients requiring high doses of furosemide at study end was lower. Moreover, the uptitration of sacubitril–valsartan was not associated with a higher risk of hypotensive episodes. In the VICTORIA trial, the relative efficacy of vericiguat was consistent, regardless of the use of sacubitril–valsartan or the range of loop diuretic doses.[24,25] Interestingly, in the VICTORIA trial, more patients in the placebo group had sacubitril/valsartan added compared with those on vericiguat.[24] This difference between the VICTORIA trial and the VERITA study could be explained by the timing of these studies, as nowadays the use of sacubitril/valsartan is clearly preferred over angiotensin-converting enzyme inhibitors.[9] In the German retrospective nationwide longitudinal cohort study, the percentage of patients receiving the four pillars of guideline-recommended therapy increased from 29% to 44% after the introduction of vericiguat.[14] Consequently, based on these data, the introduction of vericiguat may facilitate the optimization of concomitant HF therapies, particularly sacubitril–valsartan, as a relationship additive. Additionally, by reducing decompensations, it could allow greater titration of modifying drugs.

In our study, treatment with vericiguat was associated with significant improvements in NYHA functional class as well as in quality of life and health status, assessed based on various questionnaires. In addition, this improvement remained unchanged over time. Surprisingly, in the VICTORIA trial, despite improvements in outcomes, vericiguat did not significantly improve KCCQ scores compared with placebo.[26] In our study, analysis of KCCQ scores only revealed a trend, although statistically significant results were recorded for the EQ-5D and VAS scores. Therefore, this could only be the consequence of the questionnaires used. However, as in our cohort of patients, vericiguat was prescribed on top of quadruple HF therapy, this strongly suggests that the improvements reported in the questionnaires could be related to the treatment with vericiguat rather than an effect that differed depending on the patients' clinical profile (i.e., clinical trial vs. real-life population).

Vericiguat was well tolerated during the study period, with hypotension being the most frequent adverse effect reported. Only 11.5% discontinued treatment with vericiguat owing to adverse effects after a median follow-up of 303 days. In the VICTORIA trial, symptomatic hypotension was recorded in 9.1% of patients in the vericiguat group (vs. 13.5% in our study).[10] A substudy of the VICTORIA trial showed that the benefit of vericiguat was similar across the spectrum of baseline systolic blood pressure, even among patients predisposed to hypotension.[27] Interestingly, in the VICTORIA trial,[10] patients on SGLT2 inhibitors (2.4% of the cohort) at baseline appeared to have lower systolic blood pressures compared with those who were not. In our study, even though nearly all patients received SGLT2 inhibitors (and sacubitril/valsartan), the rate of hypotension remained low. In fact, other authors have also shown that vericiguat is well tolerated in clinical practice, with high rates of adherence and with most patients reaching the target dose of 10 mg of vericiguat.[14]

We recorded a mean of 2.3 HF-related hospitalizations/decompensations within the 12 months before the initiation of vericiguat, although this figure decreased significantly to 0.79 (median follow-up of 303 days) after the introduction of vericiguat. In the VICTORIA trial, vericiguat significantly reduced HF-related hospitalizations (first and recurrent episodes).[10,28] At study end, 7.7% of patients had died, half of them from HF (vs. 20% in the VICTORIA trial, with a median follow-up of 10.8 months).[10] However, it should be taken into account that in our study, approximately 36% of patients were hospitalized in the previous 3 months, 28% between 3 and 6 months and the remaining 28% received intravenous diuretics for HF without hospitalization in the previous 3 months. In the VICTORIA trial, these figures were 66%, 18% and 16%, respectively.[10] As patients early after a worsening event usually have higher rates of primary outcome events, this could have had an impact on the events' results. In addition, differences in the background HF therapies between both studies could have also played a role. In summary, regarding the risk of events, our data are consistent with or even better than those reported in the VICTORIA trial, suggesting that vericiguat could also substantially reduce the HF burden in clinical practice.

Remarkably, improvements in NYHA functional class and questionnaire scores, as well as events and the risk of adverse effects with vericiguat, were generally independent of the development of decompensations during follow-up, age, renal function, sex and the maximum dose of vericiguat achieved. This indicates that vericiguat can be used in clinical practice for a broad spectrum of patients with HFrEF after a worsening HF event. In fact, this observation is in line with different substudies of the VICTORIA trial. Thus, it has been reported that the relative efficacy and safety of vericiguat remain unchanged regardless of the index HF event (<3 months after HF hospitalization, 3–6 months after HF hospitalization or requiring outpatient intravenous diuretic therapy for worsening HF, with no HF-related hospitalization in the previous 3 months),[29] age and sex,[30] and baseline renal function or worsening renal function during the study.[31]

Our study is subject to limitations. As there is no control group, we cannot determine the relative benefit of adding vericiguat to standard therapy compared with patients not receiving vericiguat. On the other hand, the results of our

study can be extended only to patients with a similar clinical profile (advanced HF unit), background HF therapy and health care system, considering also the study's small sample size and the single-centre design.

In conclusion, vericiguat is prescribed to older patients with many comorbidities in clinical practice. Treatment with vericiguat is associated with substantial improvements in functional class and in quality of life, fewer frequent HF-related hospitalizations and a low risk of adverse effects.

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Conflict of interest statement

M. Galván Ruiz reports consulting fees from Bayer. M. Fernández de Sanmamed Girón, M. del Val Groba Marco, L. Rojo Jorge, C. Peña Saavedra, E. Martín Bou and R. Andrade Guerra report no conflicts of interest for this publication. E. Caballero Dorta reports consulting fees from Abbot. A. García Quintana reports consulting fees from Bayer, Novartis and Novo Nordisk.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Baseline clinical characteristics of the VICTORIA and VERITA studies (n = 103).
Table S2. Differences in baseline clinical characteristics according to the development of decompensations during follow-up, age, renal function, sex, and maximum dose of vericiguat achieved (n = 52).
Table S3. Change in the KCCQ, EQ-5D, and VAS scores compared with baseline (n = 52).
Table S4. Change in NYHA functional class, KCCQ, EQ-5D, and VAS scores, adverse effects and events according to age, renal function, sex, and maximum dose of vericiguat achieved during follow-up (n = 52).
Figure S1. Change in the dose of sacubitril-valsartan after initiation of treatment with vericiguat (n = 52).
Figure S2. Change in the dose of loop diuretics after initiation of treatment with vericiguat (n = 52).

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