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ORIGINAL RESEARCH

Vericiguat in patients with heart failure and implantable cardioverter-defibrillator

Carlos Escobar[1], Jesús Saldaña[1], José Luis Merino[1], Rafael Peinado[1]

[1]Cardiology Department, Arrhythmia Unit, University Hospital La Paz, Madrid, Spain

Abstract

Background: This analysis assesses the effectiveness and tolerability profile of vericiguat in patients with heart failure with reduced ejection fraction (HFrEF) and implantable cardioverter-defibrillator, with an emphasis on the emergence of ventricular arrhythmias.

Methods: Retrospective analysis of patients with HFrEF and implantable cardioverter-defibrillator who started treatment with vericiguat in daily clinical practice in a tertiary university hospital in Spain.

Results: The study population comprised 14 patients treated since January 2023. At baseline, mean age was 77.0±7.0 years, 71.4% of patients were men and mean left ventricular ejection fraction was 32.1±5.4%. Regarding heart failure treatments, 13 (92.3%) patients were prescribed renin–angiotensin–aldosterone system inhibitors, mainly sacubitril-valsartan (61.5%), they were all prescribed aldosterone antagonists, 10 (71.4%) were prescribed β-blockers and 10 (71.4%) were prescribed sodium–glucose cotransporter-2 (SGLT2) inhibitors. After a mean duration of treatment with vericiguat of 12.4±5.3 months, two (14.3%) patients presented to the emergency department, one with hypotension and the other with impaired kidney function, and a further two (14.3%) patients were hospitalised, one of whom had decompensated heart failure. At baseline, four (28.6%) patients presented non-sustained/sustained ventricular tachycardia; at study end, this decreased to two patients (50% of patients with ventricular arrhythmias at baseline). Additionally, in one patient (25% of patients with ventricular arrhythmias at baseline), there was a substantial reduction in the number of episodes of ventricular arrhythmia. At study end, seven patients achieved the target dose of 10 mg daily and one patient discontinued vericiguat owing to hypotension.

Conclusions: Amongst patients with HFrEF and implantable cardioverter-defibrillator, vericiguat showed a good safety profile in addition to standard heart failure therapy, with low rates of adverse events. Moreover, a potential reduction in the risk of ventricular arrhythmias could also be obtained with vericiguat.

Keywords: arrythmia, heart failure, vericiguat.

Citation

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Introduction

Heart failure (HF) is becoming epidemic, with a current prevalence in the adult population of about 2%.[1] Despite the availability of treatment, the mortality and morbidity of HF remain unacceptably high,[2] not only because of insufficient use of guided HF therapies in clinical practice[3,4] but also owing to the need for new HF drugs with different and complementary targets.[5] Thus, to reduce the burden of HF, it is necessary to target the various neurohormonal systems that play a role in the pathogenesis of HF such as the renin–angiotensin system and the sympathetic nervous system.[6] Of note, in patients with HF and reduced left ventricular ejection fraction (HFrEF), the nitric oxide–soluble guanylate cyclase (sGC)-cyclic guanosine monophosphate (cGMP) pathway is impaired, leading to cardiac, vascular and renal disorders.[7] Vericiguat directly stimulates sGC and effectively restores this system.[8,9]

The VICTORIA trial showed that, compared with placebo, the addition of vericiguat to standard therapy translated into a significant 10% risk reduction in the composite end point of cardiovascular death or hospitalisation because of HF.[10] Remarkably, this benefit was independent of the background HF therapy. However, whilst nearly 28% of

patients in the VICTORIA trial had an implantable cardioverter-defibrillator (ICD) and 15% had a biventricular pacemaker, no specific analysis was performed in this population.[10] On the other hand, though many patients with HFrEF would benefit from treatment with vericiguat, few data on the use of vericiguat in clinical practice have been reported to date.[11]

Therefore, analysing data from patients with HFrEF and an ICD receiving vericiguat in a real-world setting would be of great interest because it would enable the determination of the effectiveness and tolerability profile of vericiguat in this population and assessment of the possible effects of vericiguat on cardiac arrhythmias.

This article assesses the effectiveness and tolerability profile of vericiguat in clinical practice in patients with HFrEF and an ICD, with an emphasis on the emergence of ventricular arrhythmias.

Methods

We performed a retrospective analysis of patients with HFrEF and an ICD (with or without resynchronisation therapy) who started treatment with vericiguat as part of daily clinical practice in a tertiary university hospital (Hospital Universitario La Paz, Madrid, Spain). The study was approved by the local ethics committee (Ethics Committee of Hospital Universitario La Paz, Madrid, Spain; approval number code HULP: PI-6173), and all patients provided written informed consent before being enrolled. All data were collected from the electronic medical history and the patient interview at a routine visit. At baseline, biodemographic data, medical history and HF treatments were recorded. During follow-up, data regarding the use of vericiguat (duration of treatment, target dose, discontinuation rates) were collected, as were visits to the emergency department and hospitalisations and the presence of ventricular arrhythmias detected by the ICD.

Quantitative variables were described by mean and standard deviation and qualitative variables by their absolute and relative frequency distribution. Differences in the proportion distribution of qualitative variables were analysed using Fisher's exact test and differences in means were assessed with the non-parametric Mann–Whitney test. Differences were considered significant at p values <0.05. All analyses were performed using IBM SPSS Statistics, Version 26.0 (IBM Corp., Armonk, New York, USA).

Results

A total of 14 patients with HFrEF and an ICD had started treatment with vericiguat since January 2023. Mean age at baseline was 77.0±7.0 years, 71.4% of patients were men and mean left ventricular ejection fraction was 32.1±5.4%. Ischaemic heart disease was the cause of HF in almost two-thirds of cases. Regarding HF treatments, 92.9% (13/14) were prescribed renin–angiotensin–aldosterone system (RAAS) inhibitors, mainly sacubitril-valsartan (64.3%), 100% were prescribed aldosterone antagonists, 71.4% (10/14) were prescribed β-blockers and 71.4% (10/14) were prescribed SGLT2 inhibitors (Table 1).

Mean duration of treatment with vericiguat was 12.4±5.3 months, and 50.0% (7/14) achieved the target dose of 10 mg daily. Only one (7.1%) patient discontinued vericiguat owing to hypotension. During this period, two (14.3%) patients had to visit the emergency department, one with hypotension and the other with impaired kidney function. A further two (14.3%) patients were hospitalised, one with decompensated HF and the other with sepsis, which proved fatal (Table 1).

At baseline, four (28.6%) patients presented non-sustained/sustained ventricular arrhythmias (5–6 episodes per month). Mean age of these four patients was 81.0±1.4 years, all were men and mean left ventricular ejection fraction was 32.7±6.3%. All patients were prescribed RAAS inhibitors, aldosterone antagonists and SGLT2 inhibitors, and three were administered β-blockers. Mean duration of treatment with vericiguat was 12.0±4.5 months, and two (50%) patients achieved the target dose of 10 mg daily. No significant differences were observed in the clinical characteristics and HF therapies of these patients compared with those patients without non-sustained/sustained ventricular arrhythmias at baseline. At study end, the number of patients with non-sustained/sustained ventricular arrhythmias decreased to two (14.3% of the total population; 50% amongst those with ventricular arrhythmias at baseline). Additionally, one patient (7.1% of the total population; 25% amongst those with ventricular arrhythmias at baseline), exhibited a substantial reduction in the number of episodes of ventricular arrhythmia (from 6 to 2 episodes per month). Left ventricular ejection fraction remained stable and no substantial change in natriuretic peptide levels was observed during this period in the sub-group of patients with non-sustained/sustained ventricular arrhythmias at baseline. No antiarrhythmic drugs were added during the study period (Table 1 and Figure 1).

Discussion

Our data showed that treatment with vericiguat in patients with HFrEF and an ICD was effective and showed a favourable safety profile. Thus, after a mean follow-up of

Table 1. Baseline clinical characteristics and patient progress during treatment with vericiguat.

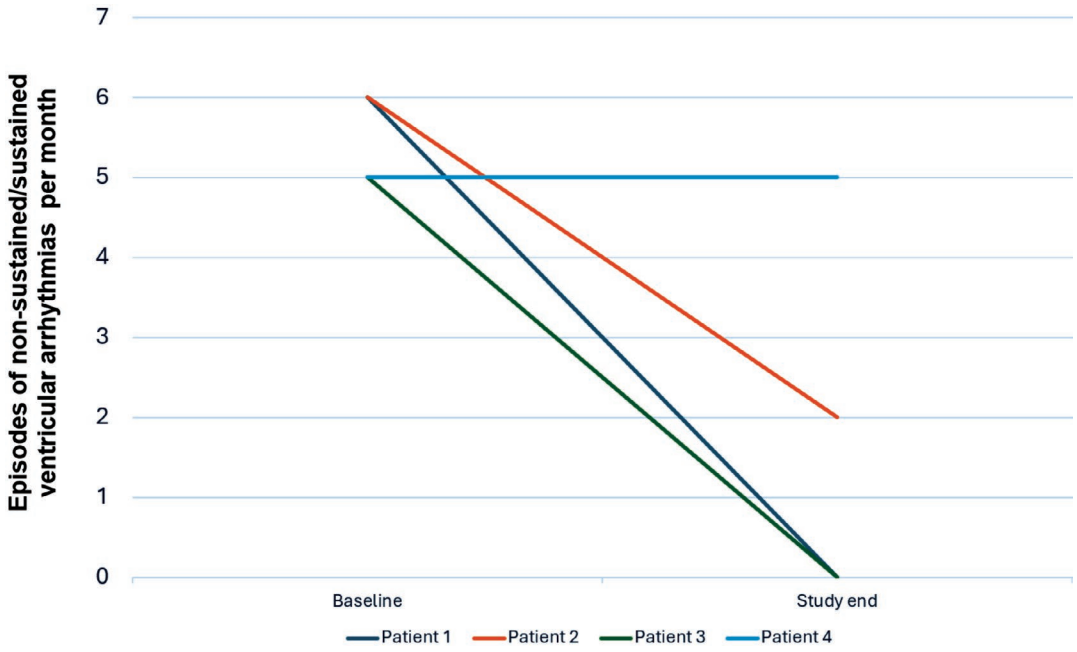
	Total population (*n*=14)	Patients with VA at baseline (*n*=4)	Patients without VA at baseline (*n*=10)	*p*
Age, years	77.0±7.0	81.0±1.4	78.4±5.0	0.34
Sex (male), *n* (%)	10 (71.4)	4 (100)	6 (60.0)	0.10
LVEF, %	32.1±5.4	32.7±6.3	32.0±5.4	0.84
Atrial fibrillation, *n* (%)	11 (78.6)	3 (75.0)	8 (80.0)	0.84
Hypertension, *n* (%)	11 (78.6)	3 (75.0)	8 (80.0)	0.84
Ischaemic heart disease, *n* (%)	9 (64.3)	3 (75.0)	6 (60.0)	0.60
Diabetes, *n* (%)	6 (42.9)	1 (25.0)	5 (50.0)	0.39
ICD, *n* (%)	14 (100)	4 (100)	10 (100)	0.99
CRT, *n* (%)	4 (28.6)	2 (50.0)	2 (20.0)	0.26
HF treatments, *n* (%)				
Loop diuretics	7 (50.0)	1 (25.0)	6 (60.0)	0.24
RAAS inhibitors	13 (92.9)	4 (100)	9 (90.0)	0.85
ACEi/ARB	4 (28.6)	2 (50.0)	2 (20.0)	0.26
Sacubitril-valsartan	9 (64.3)	2 (50.0)	7 (70.0)	0.48
Beta blockers	10 (71.4)	3 (75.0)	7 (70.0)	0.85
Aldosterone antagonists	14 (100)	4 (100)	10 (100)	0.99
SGLT2 inhibitors	10 (71.4)	4 (100)	6 (60.0)	0.60
Follow-up				
Visits to the emergency department, *n* (%)	2 (14.3)	1 (25.0)	1 (10.0)	0.47
Cardiovascular	2 (100)	1 (100)	1 (100)	0.47
Hospitalizations, *n* (%)	2 (14.3)	0	2 (20.0)	0.64
Cardiovascular	1 (50.0)	0	1 (50.0)	0.84
Non-sustained/sustained VA, *n* (%)				
Baseline	4 (28.6)	4 (100)	0	0.01
End of follow-up	2 (14.3)	2 (50.0)	0	0.09
Vericiguat, *n* (%)				
Duration of treatment, months	12.4±5.3	12.0±4.5	12.5±5.0	0.87
Target dose				
10 mg	7 (50.0)	2 (50.0)	5 (50.0)	
5 mg	1 (7.1)	0	1 (10.0)	0.85
2.5 mg	6 (42.9)	2 (50.0)	4 (40.0)	
Discontinuation	1 (7.1)	0	1 (10.0)	0.90

ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CRT, cardiac resynchronisation therapy; HF, heart failure; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; RAAS, renin–angiotensin–aldosterone system; SGLT2, sodium–glucose cotransporter-2; VA, ventricular arrhythmias.

12.4 months, only two (14.3%) patients were treated in the emergency department and one (7.1%) was hospitalised with HF. In the VICTORIA trial, over a median follow-up of 10.8 months, 27.4% of patients were hospitalised with HF and 20.3% of patients died (any cause) (10.5% when patients hospitalised with HF were excluded).[10] Despite differences in the clinical profile between our study and the VICTORIA trial (mean age 77.0 *vs* 67.3 years; left ventricular ejection fraction 32.1% *vs* 28.9%, respectively), our findings suggest that vericiguat could prove even more successful in clinical practice than those reported in the VICTORIA trial. Moreover, in our study, only one (7.1%) patient discontinued treatment with vericiguat owing to hypotension (in the VICTORIA trial, 9.1% of patients treated with vericiguat had symptomatic hypotension).[10]

Experimental studies have suggested a potential antiarrhythmic effect of vericiguat in HF that has not been demonstrated to date in human studies.[12,13] This potential effect could be associated with a reduction in electrical and structural remodelling of cardiac structures and with a decrease in the inducibility of ventricular

Figure 1. Evolution of episodes of non-sustained/sustained ventricular arrhythmias per month during the study period in those patients with ventricular arrhythmias at baseline.



tachyarrhythmias.[12,13] As a result, the exact mechanism through which vericiguat could potentially have a positive effect on ventricular arrhythmias remains unknown, because no specific study has been developed in humans and the mechanisms shown in animals do not necessarily have to be the same. However, as the left ventricular ejection fraction remained stable and no substantial change in natriuretic peptide levels was observed, it is likely that this effect may be independent of improvements in haemodynamics or ventricular function. This is the first study to indicate that vericiguat could be helpful in reducing the frequency of ventricular tachyarrhythmias in patients with HFrEF, thus potentially translating into a decrease in the risk of sudden death.

Conclusions

Amongst patients with HFrEF and an ICD, vericiguat showed a good safety profile in addition to standard HF therapy, with low rates of adverse events in clinical practice. Moreover, a potential reduction in the risk of ventricular arrhythmias could also be obtained with vericiguat, providing additional benefits in the treatment of affected patients.

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Correspondence: Carlos Escobar, Cardiology Department, Arrhythmia Unit, University Hospital La Paz, P.º de la Castellana, 261, Fuencarral-El Pardo, 28046 Madrid, Spain. Email: escobar_cervantes_carlos@hotmail.com

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