VELOCITY HF

Safety and Tolerability of a 5 mg Starting Dose of Vericiguat Among Patients with Heart Failure: The VELOCITY Study

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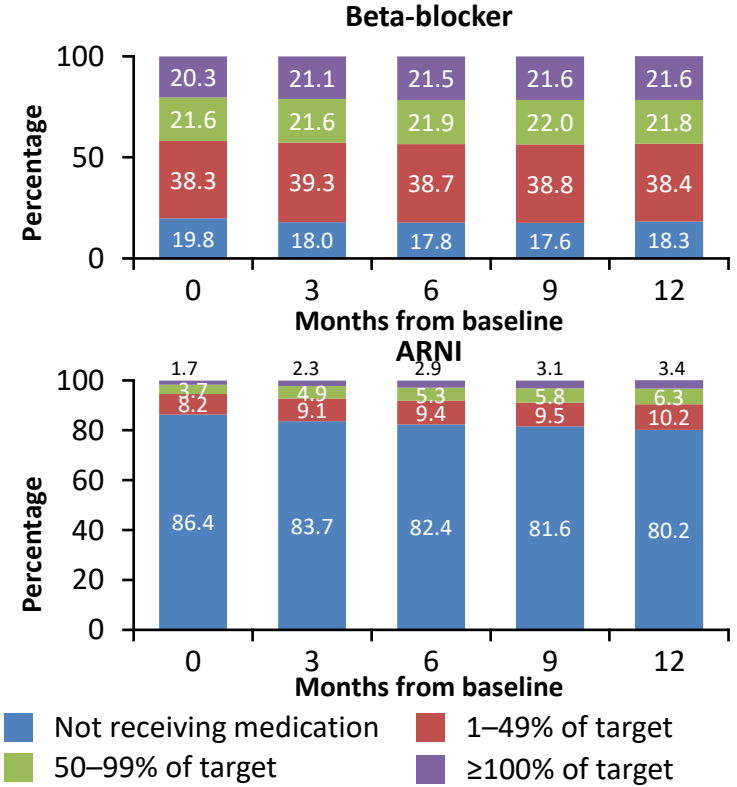
Heart Failure & World Congress on Acute Heart Failure 2025

In routine practice, GDMT for HFrEF is rarely titrated

- In routine practice, the majority of patients with HFrEF do not achieve target doses of GDMT, and few patients have doses increased over time.
- Gaps in GDMT titration exist even among patients with robust blood pressure and kidney function, and with inexpensive medications, suggesting clinical inertia is a dominant barrier to target dosing.

Dose of medication over 3-month follow-up intervals in people with HFrEF in the CHAMP-HF registry.



ARNI, angiotensin receptor-neprilysin inhibitor; CHAMP-HF, Change the Management of Patients with Heart Failure; GDMT, guideline-directed medical therapy; HFrEF, heart failure with reduced ejection fraction.

Greene SJ, et al. *J Am Coll Cardiol*. 2019;73:2365–2383.

VELOCITY examined a simplified vericiguat dose-titration pathway

- Vericiguat, a soluble guanylate cyclase stimulator, is approved for the treatment of WHF with EF <45%.[1,2]
  - The current label recommends initiating vericiguat at 2.5 mg daily, increasing to 5 mg at approximately 2 weeks, and reaching target dose of 10 mg at 4 weeks.

Today, we present the results of the VELOCITY study examining whether bypassing the 2.5 mg step and initiating vericiguat at 5 mg daily would be a well-tolerated approach for people with HF with EF <45%.

EF, ejection fraction; HF, heart failure; OD, once daily; WHF, worsening heart failure.

1. Vericiguat. Summary of product characteristics. 2021. https://www.ema.europa.eu/en/documents/product-information/verquvo-epar-product-information_en.pdf. Accessed 08 May 2025.
2. Vericiguat. Highlights of prescribing information. 2023. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/214377s002lbl.pdf. Accessed 24 April 2025.

VELOCITY was a multinational, prospective, single-arm study

Key eligibility criteria:

- HF with LVEF <45%
- Two subgroups:
  - HF with a recent WHF event†
  - HF with no recent WHF event†
- SBP ≥100 mmHg at baseline and no symptomatic hypotension 4 weeks prior to screening

Primary endpoint – *tolerability of 5 mg starting dose*

- Completion of 2-week period with ≤1 day interruption and without moderate-to-severe symptomatic hypotension.

Secondary endpoints

- Completion of 2-week period without any AE related to study drug.
- Continuous intake of study drug during treatment period, or resumption of study drug after temporary interruption.

Study registered at clinicaltrials.gov (NCT06195930). †Recent HF event within 6 months of screening or outpatient intravenous/subcutaneous diuretic use within 3 months before screening.
AE, adverse event; HF heart failure; LVEF, left ventricular ejection fraction; OD, once daily; SBP, systolic blood pressure; WHF, worsening heart failure.

Comparing with initiation of vericiguat 2.5 mg in VICTORIA

- To further contextualise results in the current single-arm study, HF patients in the VICTORIA trial initiated on vericiguat 2.5 mg daily were analysed for the VELOCITY study endpoints.

- **Tolerability endpoints for the 2 weeks following initiation of vericiguat 2.5 mg daily (VICTORIA) versus vericiguat 5 mg daily (VELOCITY) were compared.**

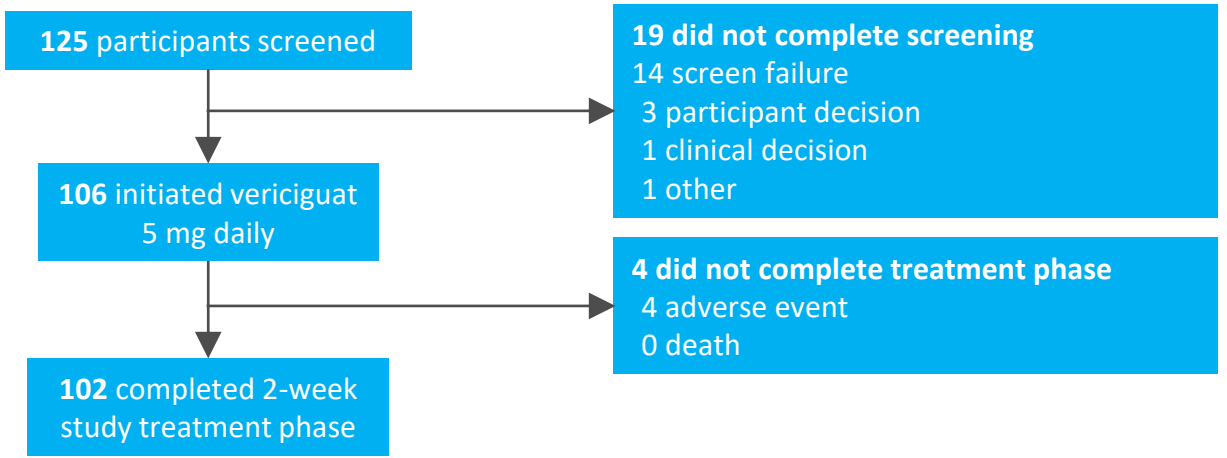
HF, heart failure.

Patient Flow

A total of 125 participants were screened across 28 sites and 7 countries;
106 participants were deemed eligible and initiated on vericiguat 5 mg.

Of the 106 participants, 53 (50.0%) had a recent WHF event.

Study disposition



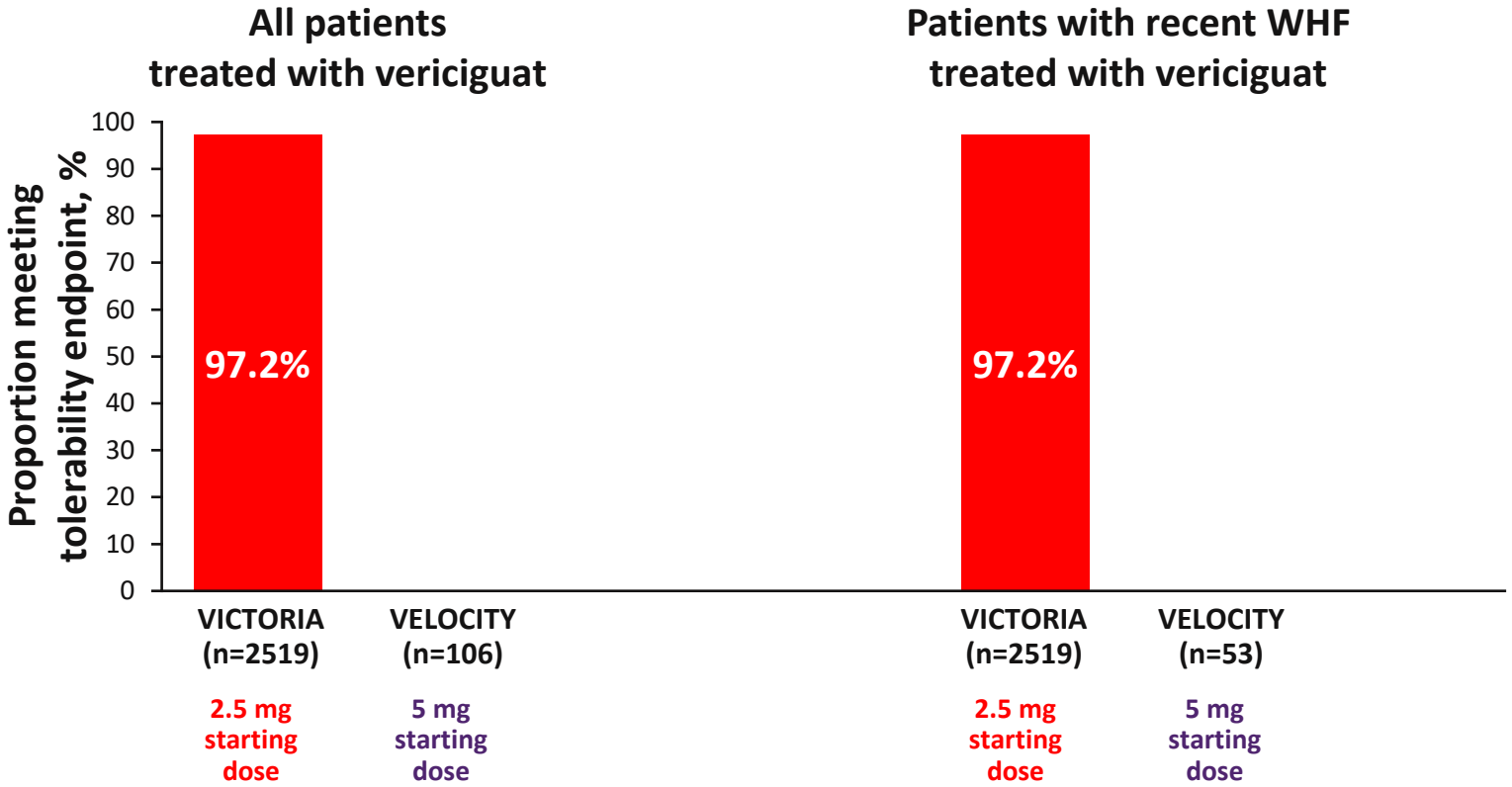
WHF, worsening heart failure.

Baseline Characteristics

	Overall (N=106)	Recent WHF (n=53)	No recent WHF (n=53)
Mean age, years ±SD	67±11	67±11	67±11
Female, %	28%	30%	26%
White race, %	96%	96%	96%
Systolic blood pressure, mmHg ±SD	126±17	126±16	125±17
eGFR, mL/min/1.73 m^2 ±SD	65±23	58±22	72±22
Past medical history, %			
Chronic kidney disease	25%	36%	15%
Type 2 diabetes	37%	40%	34%
Background medications, %			
Loop diuretic	68%	85%	51%
ACEI/ARB/ARNI	93%	89%	98%
ARNI	54%	45%	62%
β-blocker	94%	94%	94%
MRA	82%	87%	77%
SGLT2i	81%	81%	81%

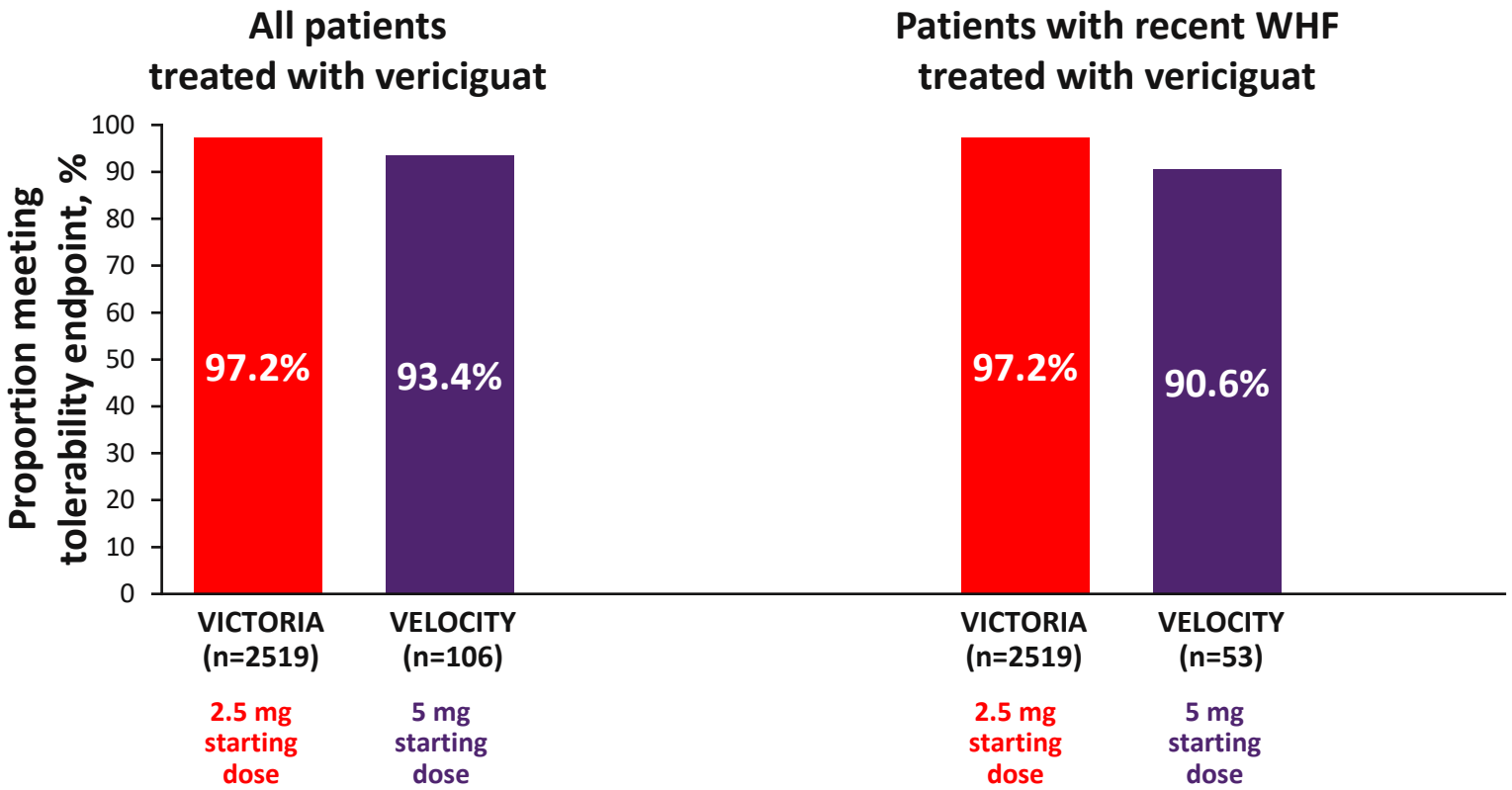
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor/neprilysin inhibitor; eGFR, estimated glomerular filtration rate; MRA, mineralocorticoid receptor antagonist; SD, standard deviation; SGLT2i, sodium–glucose cotransporter 2 inhibitor; WHF, worsening heart failure.

Primary Tolerability Endpoint



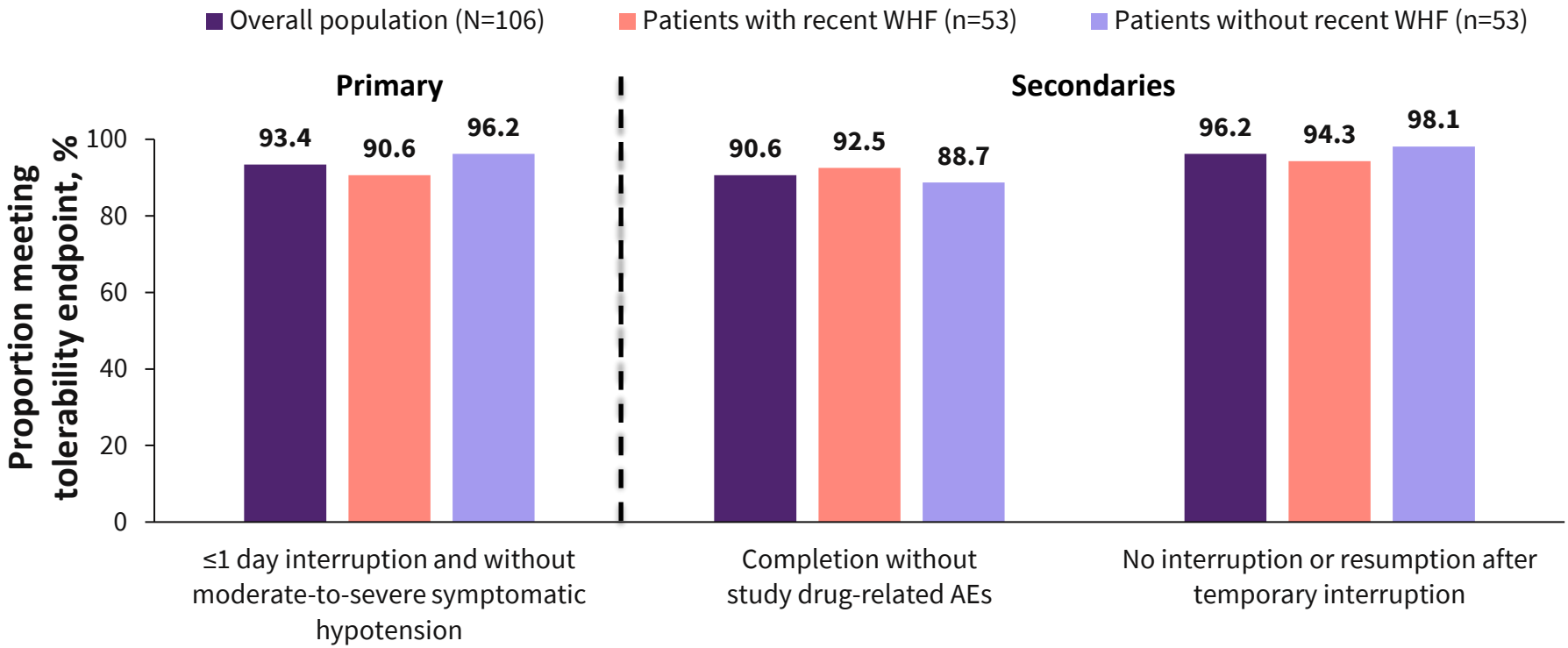
VICTORIA is registered at clinicaltrials.gov (NCT02861534).
WHF, worsening heart failure.

Primary Tolerability Endpoint



VICTORIA is registered at clinicaltrials.gov (NCT02861534).
WHF, worsening heart failure.

Safety and tolerability endpoints among VELOCITY patients



AE, adverse event; WHF, worsening heart failure.

Treatment-Emergent Adverse Events†

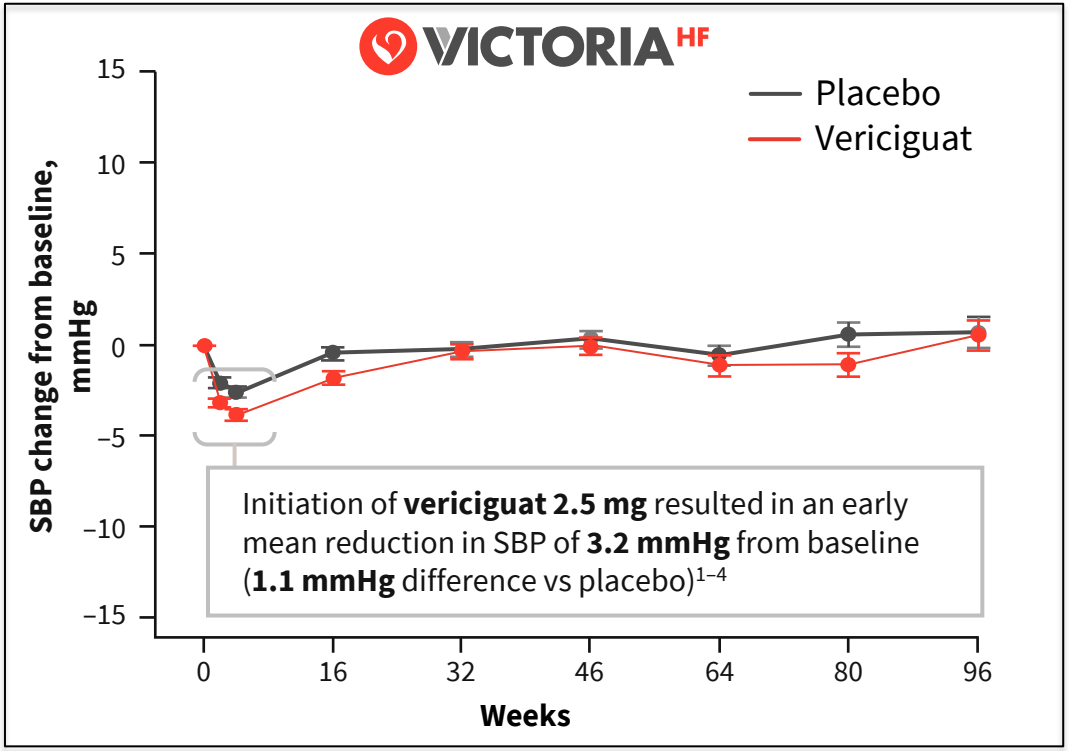
n (%)	Participants with TEAEs initiated on vericiguat 5 mg†
Any TEAE	14 (13.2)
Maximum intensity for any TEAE	
Mild	9 (8.5)
Moderate	4 (3.8)
Severe	1 (0.9)
Any TEAE leading to discontinuation of intervention	4 (3.8)

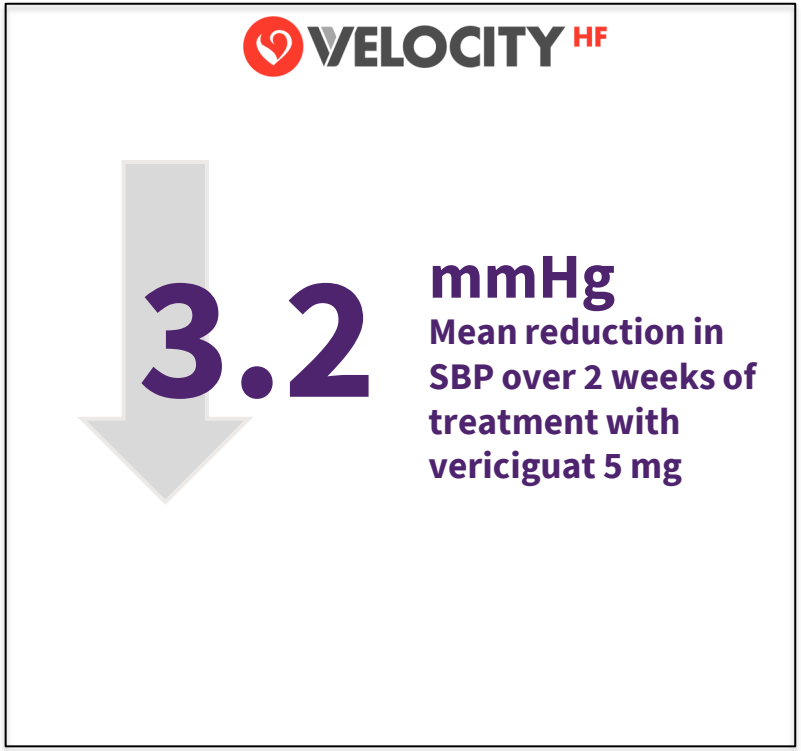
There were no deaths during the study.

†There were 106 participants in total.
TEAE, treatment-emergent adverse event.

Systolic BP & initiation of vericiguat 2.5 mg vs 5 mg

Descriptive comparison with VICTORIA





BP, blood pressure. 1. Lam CSP et al. *J Am Heart Assoc* 2021;10:e021094; 2. Armstrong PW et al. *N Engl J Med* 2020;382:1883–1893; 3. Bayer AG. [Data on file];
4. Vericiguat. Summary of product characteristics. 2021. https://www.ema.europa.eu/en/documents/product-information/verquvo-epar-product-information_en.pdf. Accessed 08 May 2025.

Limitations

- This was a single-arm study without a control group.
- Comparison of VELOCITY and VICTORIA was not randomised.
- VELOCITY (and VICTORIA) required participants with SBP ≥100 mmHg for eligibility.
  - The safety and tolerability of initiating vericiguat among people with HFrEF with lower SBP is unclear.

HFrEF, heart failure with reduced ejection fraction; SBP, systolic blood pressure.

Conclusions

- In this prospective, multinational study of patients with chronic HF with EF <45% who were well treated with background GDMT, >9 of 10 patients safely tolerated initiation of vericiguat at a starting dose of 5 mg daily.

- Findings were generally consistent regardless of history of recent WHF.

- In the context of safety and tolerability data from prior vericiguat studies, the current data support a potential update in clinical guidance towards routine initiation of vericiguat at a starting dose of 5 mg, rather than 2.5 mg, among patients without recent hypotension.

EF, ejection fraction; GDMT, guideline-directed medical therapy; HF, heart failure; WHF, worsening heart failure.

Full Details Available Online

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European Journal of Heart Failure

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