Factors Influencing the Up-Titration to 10 mg Target Dose of Vericiguat: Data from a Large Observational Cohort Study in the United States

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Background and purpose

- Vericiguat, a soluble guanylate cyclase stimulator available in the US since 2021, is recommended by ESC guidelines for patients with chronic HFrEF, NYHA class II–IV, who had a worsening HF event despite guideline-directed medical therapy (GDMT) to reduce the risk of cardio-vascular mortality or heart failure hospitalization (HFH). 10 mg/day was the effective target dose tested in the VICTORIA trial (**N Engl J Med 2020;382:1883-93).**
- However, data are limited regarding the characteristics of vericiguat users in contemporary clinical practice, including factors associated with up-titration to the 10 mg/day target dose. Purpose of this analysis was, to evaluate if a 5 mg starting dose may facilitate up-titration.

Methods

- Using two large closed claims data sources from Health Verity in the US, linked with electronic health data from Veradigm, we identified patients with a first ambulatory prescription for vericiguat (the index date) from 1 January 2021 to 1 April 2023.
- Patients were required to have ≥6 months' continuous enrollment before the index date. Vericiguat prescriptions and dosages were captured at the index date and during 3 months' follow-up.
- Factors associated with reaching 10 mg/day at any time during follow-up among patients with a 2.5 mg (recommended) or 5 mg first dose were identified using Cox regression. For this model, all patients with 10 mg as the first recorded dose were excluded. Because in-hospital initiation of medications is not routinely captured in the database, patients with a HFH within 4 weeks of first outpatient vericiguat claim were excluded as well.

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Results

- Of 1361 new users of vericiguat in total, 2.5 mg/day was recorded in 57% of patients , 5 mg/day in 24% , and 10 mg/day in 19% as first dose. (Table).
- Among the 935 initiators on 2.5 mg or 5 mg included in the Cox model, 73 (8%) had a record of a 10 mg prescription during the 3 months` follow-up after index date..

Table. Baseline characteristics at index date.

	Vericiguat dose at index date		
	2.5 mg	**5 mg**	**10 mg**
n (%)	770 (57)	330 (24)	261 (19)
Mean (SD) age, yrs	61.7 (14.3)	61.4 (14.1)	62.4 (14.4)
Males	66%	62%	66%
HFH in 6 months pre-index date	36%	39%	37%

- Beta-blockers were the most common GDMT (Fig 1); hypertension was the most prevalent comorbidity (Fig 2).

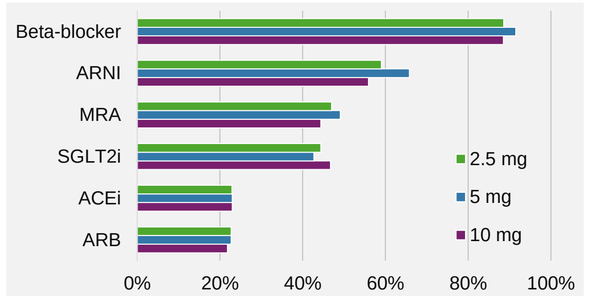

Fig 1. GDMT treatment prescribed in 6 months pre-index date.

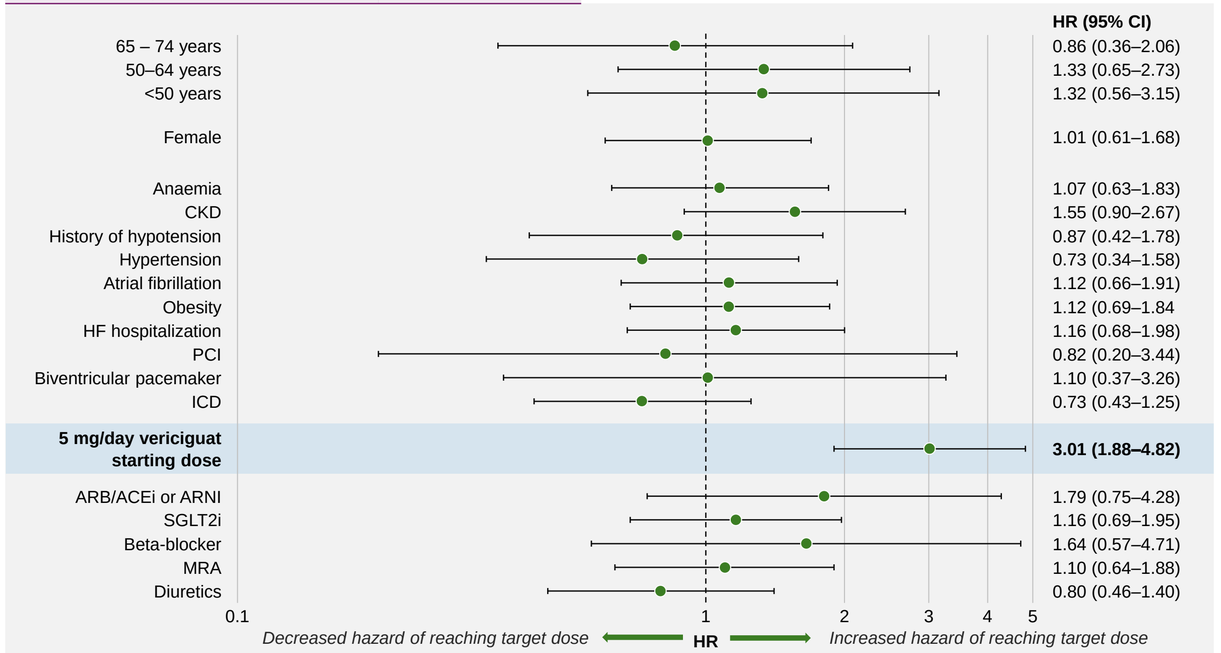

Fig 3. Multivariable adjusted hazard ratios (95% CI)* for reaching the 10 mg target dose during 3 months' follow-up (92% of patients had the full 3 months of follow-up available). *Adjusted for all other variables in the model. Reference group for 5 mg/day was 2.5 mg/day. HR = hazard ratio.

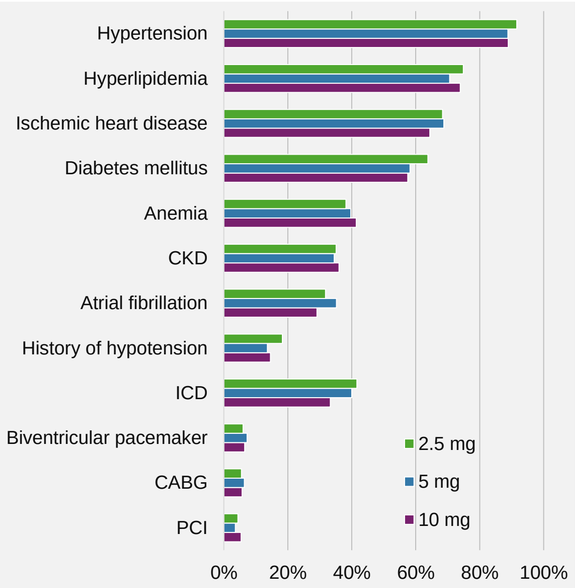

Fig 2. Comorbidities and procedures in the 6 months before index date. ICD = implantable cardioverter defibrillator.

- A vericiguat starting dose of 5 mg/day was the strongest predictor for reaching the 10 mg target dose during follow-up (Fig 3). Factors often associated with underdosing / lack of up-titration (e.g. older age, CKD, anaemia, history of hypotension) did not appear to limit up-titration of vericiguat (Fig 3).

Conclusions

- Compared with patients initiated on the recommended 2.5 mg/day dose, patients with 5 mg/day as first recorded dose were 3 times more likely to reach the target dose of 10 mg during follow-up.
- A prospective study examining the safety of a 5 mg vericiguat starting dose is needed and could ultimately lead to more patients reaching the 10 mg target dose.