Projecting the Benefit of Vericiguat in Populations Simulated from PARADIGM-HF and DAPA-HF: Insights from the VICTORIA Trial

Veraprapas Kittipibul[1,2], Robert J. Mentz[1,2], Rebecca Young[1], Javed Butler[3,4], Justin A. Ezekowitz[5], Carolyn S.P. Lam[6], Piotr Ponikowski[7], Adriaan Voors[8], Stefano Corda[9], Ciaran McMullan[10], Christopher M. O'Connor[11], Kevin J. Anstrom[12], Paul W. Armstrong[5] [1]Duke Clinical Research Institute, Durham, NC, [2]Division of Cardiology, Duke University School of Medicine, Durham, NC, [3]Department of Medicine, University of Mississippi Medical Center, Jackson, MS, [4]Baylor Scott and White Research Institute, Dallas, TX, [5]Canadian VIGOUR Centre, University of Alberta, Edmonton, Alberta, Canada, [6]National Heart Centre Singapore and Duke-National University of Singapore, Singapore, [7]Wroclaw Medical University, Wroclaw, Poland, [8]University of Groningen, University Medical Center of Groningen, Groningen, Netherlands, [9]Bayer Pharma AG, Basel, Switzerland, [10]Merck & Co Inc, Kenilworth, NJ, [11]Inova Heart and Vascular Institute, Falls Church, VA, [12]UNC Gillings School of Global Public Health, Chapel Hill, NC

Background

The VICTORIA trial demonstrated a 10% relative risk reduction and 4.2 events per 100 patient-years absolute risk reduction (ARR) with vericiguat vs placebo in the primary composite outcome (38.5%) of cardiovascular death (CVD) or time to first heart failure hospitalization (HFH) in higher-risk patients with HFrEF.

Objective

To explore vericiguat treatment effects in populations simulated from the PARADIGM-HF and DAPA-HF trials.

Methods

By applying major eligibility criteria to VICTORIA patients (n=5050), we created two sub-populations simulated from the PARADIGM-HF and DAPA-HF trials.

PARADIGM-HF-eligible population: Participants receiving angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) with equivalent dose of lisinopril ≥10 mg/day or sacubitril/valsartan. Excluding LVEF 40-45%, or eGFR <30 mL/min/1.73 m^2. After applying these criteria, we additionally excluded those with the highest 19.8% predicted probability of run-in failure (Desai AS Circ Heart Fail 2016).

DAPA-HF-eligible population: Excluded participants with LVEF 40-45%, or eGFR <30 mL/min/1.73 m^2, or recent (< 30 days) HFH.

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Table 1. Comparison of outcomes between trials and populations simulated from trials.

	VICTORIA		PARADIGM-HF		PARADIGM-HF Eligible		DAPA-HF		DAPA-HF Eligible	
	Vericiguat	C	S/V	C	Vericiguat	C	Dapa	C	Vericiguat	C
Sample size	2,526	2,524	4,187	4,212	**988**	**994**	2,373	2,371	**1,288**	**1,255**
HR (95% CI)										
HFH or CVD	0.90 (0.82–0.98)		0.80 (0.73–0.87)		**0.85 (0.72-0.99)**		0.74 (0.65–0.85)		**0.82 (0.71-0.94)**	
HFH	0.90 (0.81–1.00)		0.79 (0.71–0.89)		**0.86 (0.72-1.03)**		0.70 (0.59–0.83)		**0.81 (0.69-0.94)**	
CVD	0.93 (0.81–1.06)		0.80 (0.71–0.89)		**0.83 (0.64-1.06)**		0.82 (0.69–0.98)		**0.85 (0.70-1.03)**	
Annualized event rate, events per 100 patient-years										
HFH or CVD	33.6	37.8	10.5	13.2	**25.8**	**30.9**	11.6	15.6	**27.2**	**33.8**
ARR	4.2		2.7		**5.1**		4.0		**6.6**	
HFH	25.9	29.1	NA	NA	**20.6**	**24.2**	6.9	9.8	**20.0**	**25.2**
ARR	3.2		1.6		**3.6**		2.9		**5.2**	
CVD	12.9	13.9	6.0	7.5	**8.5**	**10.3**	6.5	7.9	**11.1**	**13.1**
ARR	1.0		1.5		**1.8**		1.4		**2.0**	

ARR: absolute risk reduction, **C:** comparator (i.e., placebo except enalapril in PARADIGM-HF, **S/V:** sacubitril/valsartan

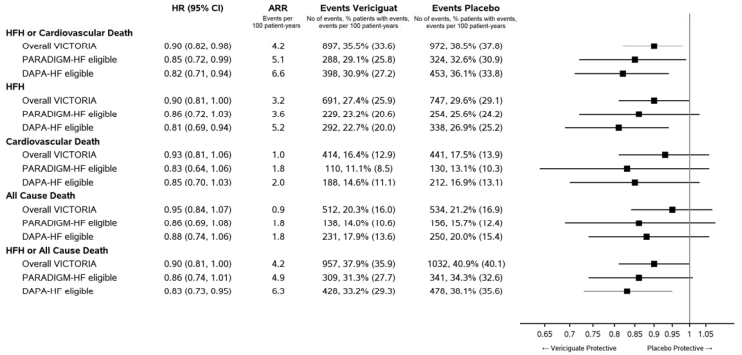
Results

Of 5050 participants, 1982 (39.2%) and 2543 (50.4%) participants were deemed eligible for PARADIGM-HF and DAPA-HF (**Table 1**). This represented less than one-quarter of the original PARADIGM-HF and approximately half of the original DAPA-HF populations.

Vericiguat was associated with significantly lower hazards of the primary outcome of HFH or CVD in these lower-risk populations simulated from PARADIGM-HF (HR 0.85, 95%CI: 0.72-0.99, p=0.04) and DAPA-HF (HR 0.82, 95%CI: 0.71-0.94, p<0.01) compared to overall VICTORIA (**Fig 1**).

ARR in the main clinical outcomes with vericiguat were numerically higher in populations simulated from trials compared to overall VICTORIA (**Table 1**).

Figure 1. Treatment effects in populations simulated from trials.



Conclusions

A trend towards enhanced treatment effects of vericiguat in lower-risk populations simulated from PARADIGM-HF and DAPA-HF was observed.

These findings support further exploration of vericiguat in lower-risk HF populations as is being investigated in the ongoing VICTOR (A Study of Vericiguat in Participants with Chronic Heart Failure With Reduced Ejection Fraction) trial (NCT05093933).

DISCLOSURES

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Correspondence should be addressed to
Email: veraprapas.kittipibul@duke.edu

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