Abstract: 61083

Regional variation in heart failure treatment: an analysis of the VICTOR trial background therapy

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Introduction

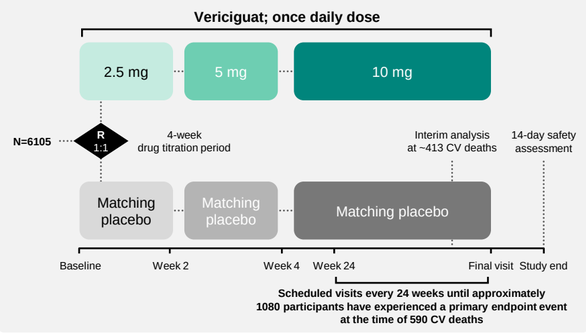
- Heart failure (HF) is associated with a high risk of morbidity and mortality, and poor functionality and health status, necessitating the need for novel interventions.[1–4]
- Vericiguat is a soluble guanylate cyclase stimulator approved for the treatment of people with ejection fraction (EF) <45% following a worsening HF event, characterised by hospitalisation for HF (HHF) or need for an urgent outpatient visit requiring intravenous (IV) diuretic therapy.[5]
  - The VICTORIA study (NCT02861534) demonstrated that vericiguat was associated with risk reduction for the composite of cardiovascular (CV) death and HHF in people with EF <45% and recent HF worsening.[6]
- The ongoing VICTOR study (NCT05093933) was designed to investigate the outcomes of participants with HF with reduced EF (HFrEF; EF ≤40%) *without* a recent worsening HF event who are receiving contemporary background treatment; the study will determine the additive value of vericiguat in the treatment course of these participants.[7,8]
- Due to developments in the HFrEF treatment landscape, it is important to investigate the benefit of novel therapies when administered with optimal background therapies, including angiotensin receptor/neprilysin inhibitors (ARNIs) or sodium–glucose cotransporter 2 inhibitors (SGLT2is).
- Baseline demographics and the disease characteristics of the overall VICTOR study population have been previously described.[9]
- Using data from the VICTOR study, we investigated baseline therapy use by region.

Methods

Design

- VICTOR is a double-blind, placebo-controlled, parallel-group, 1:1 randomised, event-driven trial investigating the effects of oral vericiguat (target dose 10 mg) versus placebo in ambulatory participants with HFrEF and no recent worsening HF event.[8,9]
- The study rationale and design have previously been described.[8]
  - The study design is shown in **Figure 1**.[8,9]
  - The inclusion and exclusion criteria are outlined in **Table 1**.[9]

Figure 1. Design of the VICTOR study[8,9]



Primary endpoint
- Time to CV death or HHF

Hierarchical secondary endpoints

Time to:
- CV death
- First HHF
- Total HHF events (first and recurrent events)
- All-cause mortality/HHF
- All-cause mortality

CV, cardiovascular; HF, heart failure; HHF, hospitalisation for heart failure; R, randomised.

Table 1. VICTOR study: key inclusion and exclusion criteria[9]

Inclusion	Exclusion
HF with LVEF ≤40%	HHF within the 6 months prior to randomisation or IV diuretic treatment within 3 months prior to randomisation
NYHA class II–IV symptoms on optimally tolerated GDMT	eGFR <15 mL/min/1.73 m^2 based on the CKD-EPI criteria
NT-proBNP level (600–6000 pg/mL for history of sinus rhythm; 900–6000 pg/mL for history of AF)	–

AF, atrial fibrillation; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; GDMT, guideline-directed medical therapy; HF, heart failure; HHF, hospitalisation for heart failure; IV, intravenous; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro B-type natriuretic peptide; NYHA, New York Heart Association.

Statistical analysis

- Concomitant medications available at baseline are presented as counts (percentages) and age is presented as mean ± standard deviation (SD).
- All analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC, USA).
- The analysis of VICTOR was based on data available on 22 May 2024.

Results

Participants

- A total of 10,923 participants were screened and 6105 participants were randomised and evaluated for baseline characteristics (**Table 2**).

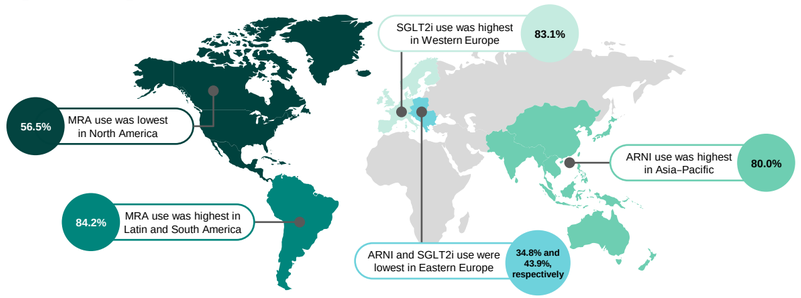
Table 2. Baseline participant GDMT and use of devices in regional populations

Region	Global	Asia–Pacific	Eastern Europe	Latin and South America	North America	Western Europe
ITT participants, n	6105	854	1700	1775	649	1127
Age, years (mean±SD)	67±11	64±12	66±11	66±11	69±10	71±9
Baseline therapy, n (%)						
β-blocker	5762 (94.4)	783 (91.7)	1619 (95.2)	1666 (93.9)	616 (94.9)	1078 (95.7)
ACEI or ARB	2336 (38.3)	136 (15.9)	1007 (59.2)	847 (47.7)	145 (22.3)	201 (17.8)
ARNI	3417 (56.0)	683 (80.0)	591 (34.8)	816 (46.0)	455 (70.1)	872 (77.4)
MRA	4743 (77.7)	641 (75.1)	1381 (81.2)	1494 (84.2)	367 (56.5)	860 (76.3)
SGLT2i	3608 (59.1)	507 (59.4)	747 (43.9)	1052 (59.3)	366 (56.4)	936 (83.1)
ARNI or SGLT2i	4562 (74.7)	766 (89.7)	954 (56.1)	1261 (71.0)	533 (82.1)	1048 (93.0)
Nitrate plus hydralazine	25 (0.4)	1 (0.1)	4 (0.2)	7 (0.4)	11 (1.7)	2 (0.2)
Ivabradine	355 (5.8)	76 (8.9)	109 (6.4)	64 (3.6)	19 (2.9)	87 (7.7)
ICD	2009 (32.9)	172 (20.1)	571 (33.6)	233 (13.1)	394 (60.7)	639 (56.7)
CRT	902 (14.8)	79 (9.3)	240 (14.1)	128 (7.2)	193 (29.7)	262 (23.2)

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor/neprilysin inhibitor; CRT, cardiac resynchronisation therapy; GDMT, guideline-directed medical therapy; ICD, implantable cardiac defibrillator; ITT, intention to treat; MRA, mineralocorticoid receptor antagonist; SD, standard deviation; SGLT2i, sodium–glucose cotransporter 2 inhibitor.

- The mean age±SD was 67±11 years, 23.6% were women, mean EF±SD was 30.4±7.0, and 79.0% had New York Heart Association class II symptoms.[9]
- In the overall study population, the use of evidence-based medical therapy was high at baseline:
  - β-blockers were used by 94.4%.
  - Renin–angiotensin system inhibitors were used by 93.9%, including 56.0% on an ARNI.
  - Mineralocorticoid receptor antagonists (MRA) were used by 77.7%.
  - SGLT2is were used by 59.1%.
- Globally, an implantable cardiac defibrillator (ICD) was present in 32.9% of participants and 14.8% had undergone cardiac resynchronisation therapy (CRT).
- Global and regional medication and device use are presented in **Table 2** and **Figure 2**.
  - At baseline, the use of an ARNI was highest in the Asia-Pacific region (80.0%) and lowest in Eastern Europe (34.8%).
  - SGLT2i use was highest in Western Europe (83.1%) and lowest in Eastern Europe (43.9%), and MRA use was highest in Latin and South America (84.2%) and lowest in North America (56.5%).
  - The highest use of ICD and CRT was seen in North America (60.7% and 29.7%, respectively) and was lowest in the Latin and South America region (13.1 % and 7.2%, respectively).
  - The use of β-blockers was similar across regions.

Figure 2. Regional use of GDMT and devices



ARNI, angiotensin receptor/neprilysin inhibitor; GDMT, guideline-directed medical therapies; MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium–glucose cotransporter 2 inhibitor.

Conclusion

- The VICTOR trial recruited a contemporary HFrEF population with high use of GDMT and device therapy at baseline.
- There were considerable regional variations in HFrEF treatment.
- Further studies are needed to assess the determinants of global disparities in HFrEF care.

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Conflicts of interest / Disclosures

C.I.S reports consulting fees from Bayer, Merck, and NovoNordisk; payment/honoraria from Novartis, AstraZeneca, Boehringer Ingelheim, Bayer, Merck, Servier, Sanofi, Pfizer, NovoNordisk, Eli Lilly, Viatris, and Medtronic; and travel support for attending meetings from Bayer, Servier, Pfizer, Novartis, and Boehringer Ingelheim. **J.B.** received consulting fees from Abbott, American Regent, Amgen, Applied Therapeutic, AskBio, Astellas, AstraZeneca, Bayer, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, Cardiac Dimension, Cardiocell, Cardior, Cardiorem, CSL Behring, CVRx, Cytokinetics, Daxor, Edwards, Element Science, Faraday, Foundry, G3P, Innolife, Impulse Dynamics, Imbria, Inventiva, Ionis, Lexicon, Lilly, LivaNova, Janssen, Medtronics, Merck, Occlutech, Owkin, Novartis, NovoNordisk, Pfizer, Pharmacosmos, Pharmain, Prolaio, Regeneron, Renibus, Roche, Salamandra, Sanofi, SC Pharma, Secretome, Sequana, SQ Innovation, Tenex, Tricog, Ultromics, Vifor, and Zoll; payment/honoraria from Novartis, Boehringer Ingelheim-Lilly, AstraZeneca, Impulse Dynamics, and Vifor. **C.J.M.** is an employee of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, and may own stock and/or stock options. **S.C.** is an employee of Bayer AG. **F.Z.** reports fees from 89bio, Applied Therapeutics, Bayer, Betagenon, Biopeutics, Boehringer Ingelheim, Bristol Myers Squibb, CVRx, Cardior, Cambrian, Cereno Pharmaceutical, Cellprothera, CEVA, Merck, Northsea, Novartis, NovoNordisk, Otsuka, Owkin, and Salubri; payment/honoraria from Bayer, Boehringer Ingelheim, CVRx, Cellprothera, CEVA, and Merck; participates on a data safety monitoring board/advisory board for Merck/Acceleron; equities at G3Pharmaceutical, Cereno, Cardiorenal, Eshmoun Clinical Research; and is founder of The Global CardioVascular Clinical Trialists (CVCT).

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