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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

VICTOR Prespecified Analysis Results: Vericiguat Effects on Mortality in Ambulatory Patients With HFrEF

Dr. Greene:
Hello from HFSA 2025 here in Minneapolis. I'm Dr. Stephen Greene, and today I'll be reviewing data that were just presented from a prespecified analysis of the VICTOR trial regarding the effect of vericiguat on mortality in ambulatory patients with HFrEF.

So VICTOR was a large phase 3 outcome trial of more than 6,100 patients randomized to vericiguat versus placebo. All patients had chronic heart failure with reduced ejection fraction of 40% or less.

Notably, patients were excluded if they had a recent worsening heart failure event, so excluded if they had a heart failure hospitalization in the prior 6 months or outpatient IV diuretic in the last 3 months. And the rationale for this exclusion criteria is because patients with recent worsening heart failure events had already been studied in the prior VICTORIA trial.

Another key thing to mention about the VICTOR eligibility criteria is that all patients were required to have an NT-proBNP of less than or equal to 6,000 at baseline.

And the rationale for this criteria was that in a prior post hoc analysis of the VICTORIA study, we saw this patient group of lower NT-proBNP in the bottom 3 quartiles had a magnified clinical benefit with vericiguat, including reductions on all-cause death and cardiovascular death. So VICTOR was really trying to validate that mortality hypothesis that was generated from VICTORIA.

Well, what did the VICTOR trial show? Well, for the primary endpoint of CV death or heart failure hospitalization, there is actually a neutral primary endpoint. However, for key secondary endpoints, including cardiovascular death, we saw a 17% relative risk reduction. For all-cause death, a 16% relative risk reduction. For sudden death, a 25% relative risk reduction, and for heart failure death, a 29% relative risk reduction.

So given these striking mortality findings, we wanted to dig deeper and to establish the consistency of these mortality findings across many prespecified subgroups in the trial. Most notably, to look at the effect of heart failure death in patients with varying use of background GDMTs. And likewise, to look at sudden death benefit with or without an implantable cardioverter defibrillator.

So to keep going with the results we saw, for example, in sudden death across the whole spectrum of prespecified subsets in VICTOR, we saw consistent benefit with vericiguat versus placebo on sudden death prevention. That includes a fully additive incremental benefit among patients who already had an ICD.

Now looking at the heart failure death benefit, we likewise also saw striking consistency in this heart failure death benefit with vericiguat across prespecified subgroups. Notably, included among patients with quadruple medical therapy as their background or even lesser degrees of background medical therapy.

Likewise consistency with patients with different demographics, vital signs, and laboratories regarding eGFR and blood pressure, for example, comorbidities, again, consistency being the key term.

Now when you think about what are the clinical application of these findings for heart failure death and sudden death, it's notable from real-world data in the United States that heart failure death has increased over the last several years.

Heart failure death is a huge burden, and having a therapy that reduces heart failure death is something that we should appreciate.

Likewise, when we're looking at real-world evidence, we're seeing that place of death is changing for our heart failure patients. Now we're seeing that the actual most commonplace of death for patients with heart failure is actually at home. And that's why a therapy that reduces sudden death is increasingly relevant to our clinical practice.

So the take-home point, VICTOR trial showed that there was benefits on cardiovascular death, all-cause death, heart failure death, and sudden death with vericiguat versus placebo. And again, it showed consistency in these benefits across a spectrum of background medicines, devices, comorbidities, and laboratory findings.

From HFSA 2025, I'm Dr. Stephen Greene, and thank you very much for listening.