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ATTR-CM Care: Impact of Vutrisiran on Survival and Cardiovascular Events

Ryan Quigley:
You're listening to *Heart Matters* on ReachMD, and this is an *AudioAbstract.* I'm Ryan Quigley, and today, I'll be discussing the HELIOS-B trial, which evaluated the impact of vutrisiran in patients with transthyretin amyloid cardiomyopathy, or ATTR-CM.

For context, ATTR-CM is a progressive and life-limiting disease that leads to heart failure, arrhythmias, and early death. Despite advances with TTR stabilizers such as tafamidis and acoramidis, patients still face substantial morbidity and mortality.

Enter vutrisiran, a subcutaneous RNA interference therapy that silences hepatic production of transthyretin. Mechanistically, vutrisiran acts upstream by silencing transthyretin mRNA in the liver, reducing circulating amyloidogenic protein and potentially slowing further cardiac amyloid deposition. This targeted approach offers disease modification earlier in the amyloid pathway—an important distinction from downstream therapies that primarily address heart failure symptoms.

To further explore the potential benefit of vutrisiran, the HELIOS-B trial, published in the *Journal of the American College of Cardiology* in May 2025, set out to determine whether this therapy could improve survival and reduce cardiovascular events in patients with ATTR-CM.

This phase 3, randomized, double-blind study enrolled 655 adults with either hereditary or wild-type ATTR-CM across multiple global sites. Participants received vutrisiran 25 milligrams or placebo by subcutaneous injection every three months for up to three years, with an open-label extension for continued follow-up. Approximately 60 percent weren't taking tafamidis at baseline, allowing for separate monotherapy and combination analyses.

With that background in mind, let's take a look at the results. After a median of 39 to 42 months of follow-up, vutrisiran reduced the risk of all-cause mortality by 36 percent compared with placebo in the overall population. Cardiovascular mortality fell by 33 percent. When the investigators combined cardiovascular death and cardiovascular events—including hospitalizations and urgent heart failure visits—vutrisiran reduced risk by 28 percent.

The benefits also extended across key event types. Compared with placebo, vutrisiran lowered the rate of cardiovascular hospitalizations by 25 percent, heart failure hospitalizations by 33 percent, and urgent heart failure visits by nearly half. These effects were consistent whether or not patients were receiving tafamidis.

Still, the study has limitations. Although randomized and placebo-controlled, it wasn't designed to assess the comparative benefit of combining vutrisiran with tafamidis. The subgroup analyses in patients already taking tafamidis were underpowered, so any potential additive effect of dual therapy remains speculative. Additionally, as with most amyloid trials, improvements in survival take time to manifest, underscoring the value of early diagnosis and intervention.

The takeaway? For patients with ATTR-CM— whether hereditary or wild-type—vutrisiran offers a meaningful reduction in death and major cardiovascular events. These data support its role as an effective, disease-modifying therapy that can extend and improve life in a population long underserved by traditional heart failure management.

This has been an *AudioAbstract* for *Heart Matters*, and I'm Ryan Quigley. To access this and other episodes in our series, visit ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!

Reference:
Witteles RM, Garcia-Pavia P, Damy T, et al. Vutrisiran improves survival and reduces cardiovascular events in ATTR amyloid cardiomyopathy: HELIOS-B. *J Am Coll Cardiol.* 2025;85(20):1959–1970. doi:10.1016/j.jacc.2025.04.008

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