

Long-Term Vutrisiran Reduces Cardiovascular Events and Hospitalizations in Patients with Transthyretin Cardiac Amyloidosis in the HELIOS-B One-Year Open Label Extension

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Introduction

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- ATTR-CM is a progressive and debilitating disease caused by the accumulation of misfolded TTR protein as amyloid deposits in the heart, resulting in frequent CV events, hospitalizations, and increased mortality^{1,2}
- Vutrisiran is an RNAi silencer approved for hATTR-PN and ATTR-CM that inhibits the production of hepatic TTR, leading to rapid knockdown of the pathogenic TTR protein³
- The phase 3 HELIOS-B study evaluated vutrisiran in adults with ATTR-CM over a 33–36-month double-blind period⁴, followed by a 2-year open label extension
- During the double-blind period, vutrisiran significantly reduced the risk of mortality and CV events, CV hospitalizations, HF hospitalizations, and urgent HF visits relative to placebo⁵

Objective

- To compare hospitalizations and urgent HF visits through Month 48 (i.e., through the 1-year OLE) between patients originally randomized to vutrisiran (continuous vutrisiran) and those who initiated vutrisiran after 3 years on placebo (delayed vutrisiran)

Methods

- We assessed all-cause hospitalizations, CV hospitalizations, HF hospitalizations, non-CV hospitalizations, and urgent HF visits from the 1-year OLE data cut
- Outcomes were assessed in the overall population, the monotherapy population (patients not receiving tafamidis at baseline), and the prespecified baseline tafamidis subgroup (patients receiving tafamidis at baseline)

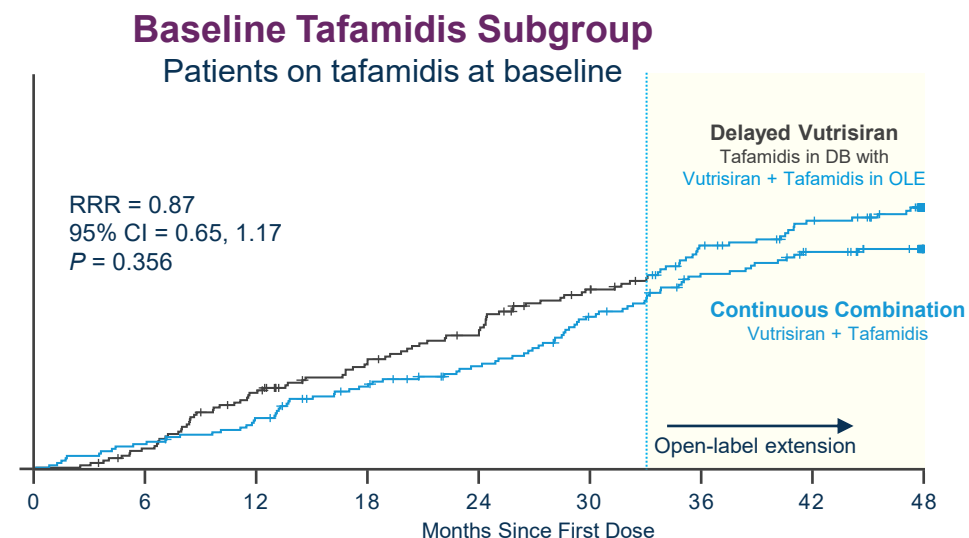
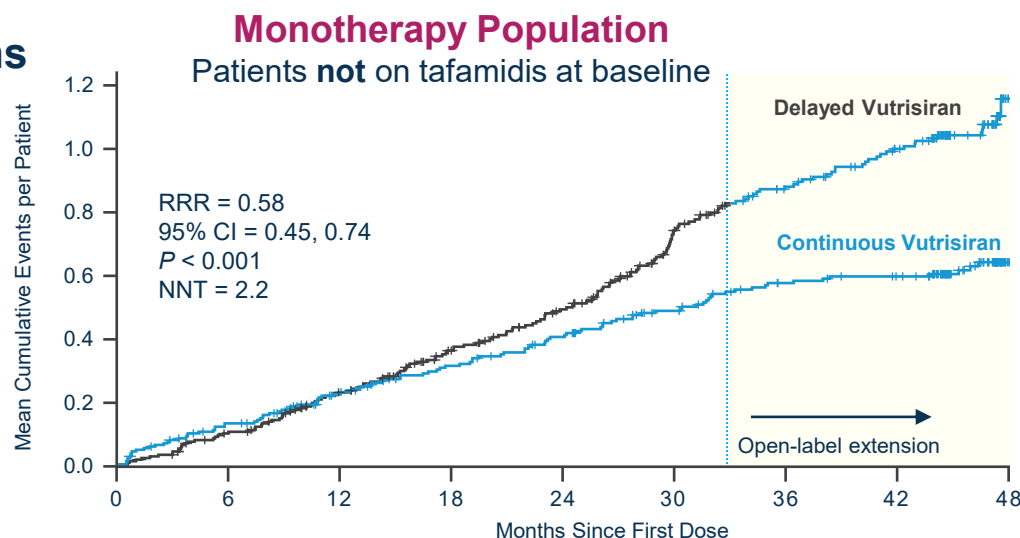
Significant Benefit on Hospitalizations with Long-Term, Continuous Vutrisiran in the Overall and Monotherapy Populations



42% and 37% risk reduction in CV and non-CV hospitalizations in the monotherapy population, respectively

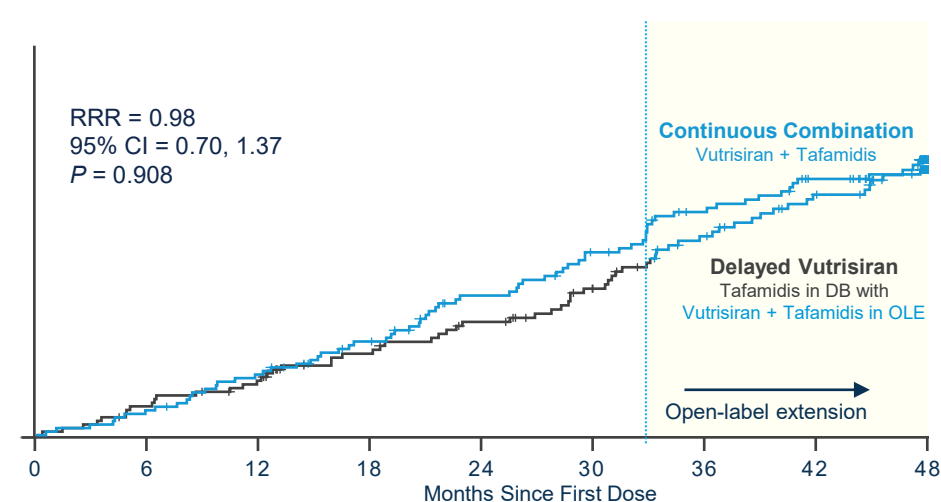
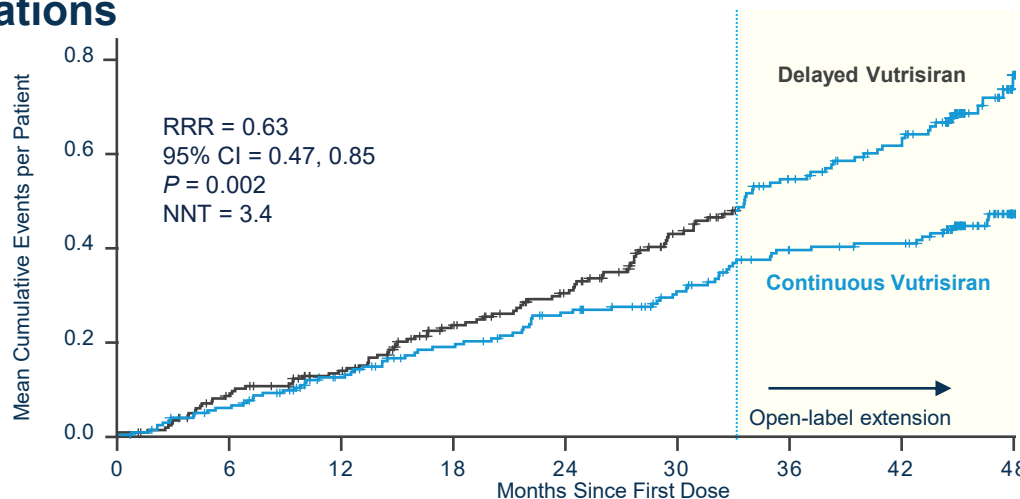
CV Hospitalizations

Overall Population
RRR = 0.68
95% CI = 0.56, 0.82
 $P < 0.001$
NNT = 3.2



Non-CV Hospitalizations

Overall Population
RRR = 0.75
95% CI = 0.60, 0.94
 $P = 0.013$
NNT = 5.7



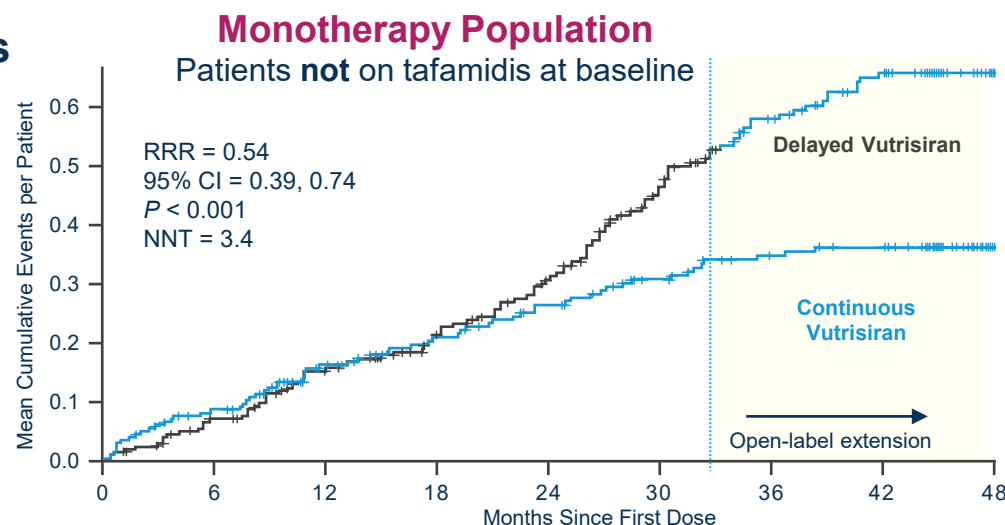
Significant Benefit on HF Hospitalizations and Urgent HF Visits

70% risk reduction in urgent HF visits with long-term, continuous combination therapy vs. tafamidis monotherapy with vutrisiran add-on in the OLE



HF Hospitalizations

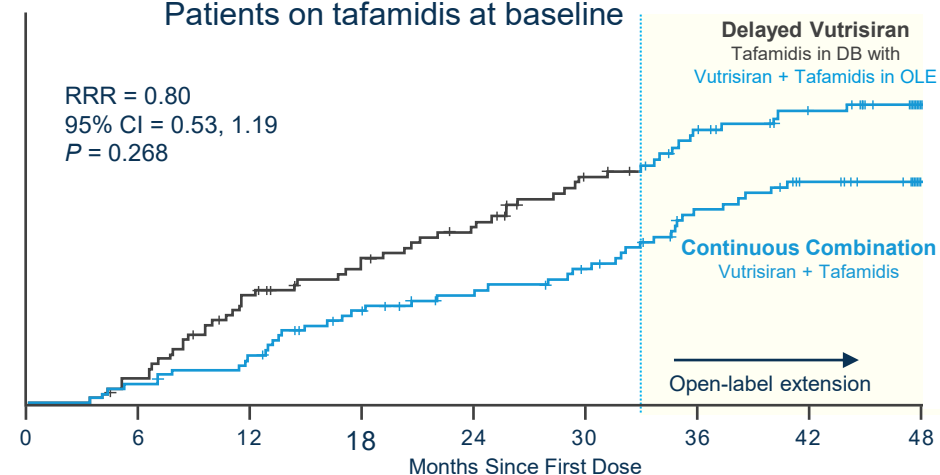
Overall Population
RRR = 0.63
95% CI = 0.49, 0.80
 $P < 0.001$
NNT = 4.5



Baseline Tafamidis Subgroup

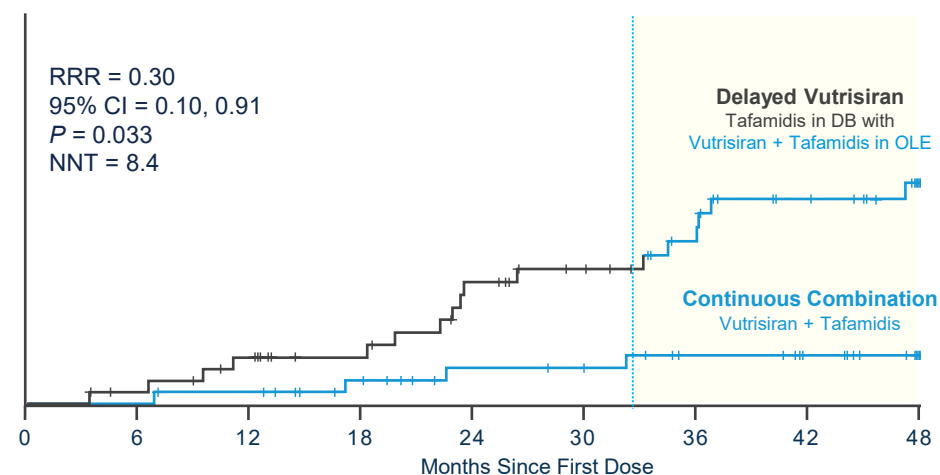
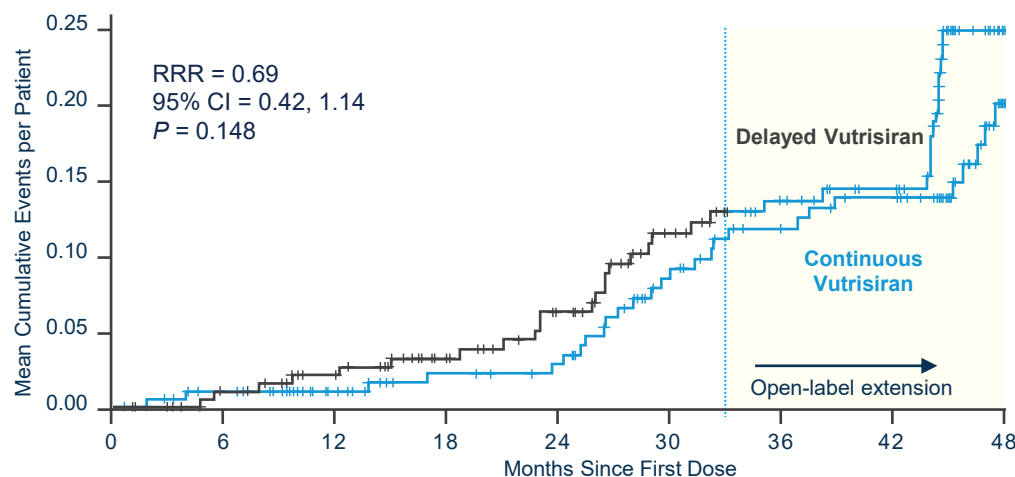
Patients on tafamidis at baseline

RRR = 0.80
95% CI = 0.53, 1.19
 $P = 0.268$



Urgent HF Visits

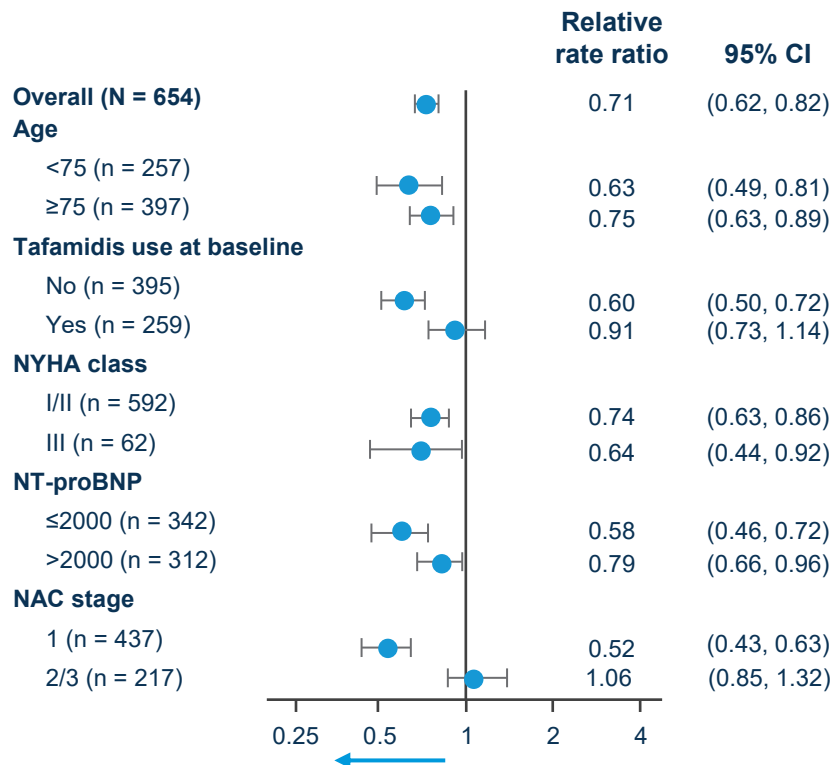
Overall Population
RRR = 0.46
95% CI = 0.27, 0.77
 $P = 0.003$
NNT = 11.6



Greatest Benefit Seen with Earlier Treatment

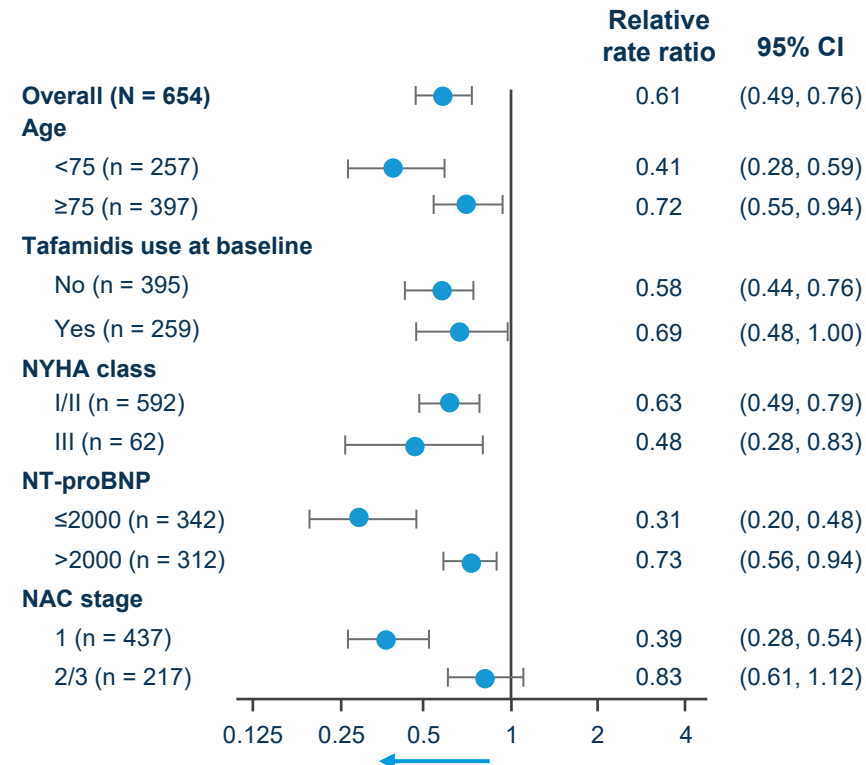
Lower event rates were observed with continuous vutrisiran in patients who were younger, lower risk, NAC stage 1, and receiving vutrisiran as first-line therapy

All-Cause Hospitalizations



Favors Continuous Vutrisiran

Composite HF Hospitalizations and Urgent HF Visits



Favors Continuous Vutrisiran

Overall Population	RRR = 0.71, 95% CI = 0.62, 0.82; $P < 0.001$, NNT = 2.0
Monotherapy Population	RRR = 0.60, 95% CI = 0.50, 0.72; $P < 0.001$, NNT = 1.3
Baseline Tafamidis Subgroup	RRR = 0.91, 95% CI = 0.73, 1.14; $P = 0.423$

Overall Population	RRR = 0.61, 95% CI = 0.49, 0.76; $P < 0.001$, NNT = 3.3
Monotherapy Population	RRR = 0.58, 95% CI = 0.44, 0.76; $P < 0.001$, NNT = 2.9
Baseline Tafamidis Subgroup	RRR = 0.69, 95% CI = 0.48, 1.00; $P = 0.05$, NNT = 4.1

Subgroups are defined at study baseline.

CI, confidence interval; HF, heart failure; NAC, National Amyloidosis Centre; NNT, number needed to treat; NT-proBNP, N-terminal prohormone of brain-type natriuretic peptide; NYHA, New York Heart Association; RRR, relative rate ratio.

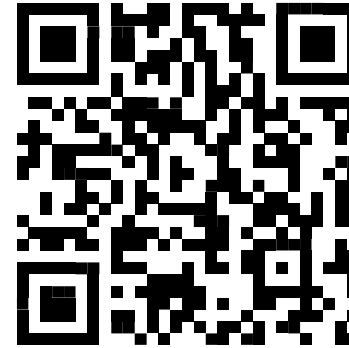
Conclusions



- Long-term, **continuous vutrisiran reduced the risk of hospitalizations and urgent HF visits** relative to patients receiving vutrisiran after a 3-year delay.
- At 48 months, the **NNT for all-cause hospitalization was 2** in both the overall and monotherapy populations.
- The **significant reduction in non-CV hospitalizations** in the overall and monotherapy populations may suggest a **systemic effect of therapy**.
- There was a **significant benefit in urgent HF visits** in patients receiving long-term, continuous **combination vutrisiran and tafamidis** relative to patients on stabilizer monotherapy with vutrisiran added in the OLE.
- Continuous vutrisiran **reduced the proportion of patients with recurrent events by half** on many outcomes.
- Benefits were greatest in patients who were **younger, lower risk, earlier in their disease course**, or **receiving vutrisiran as first line therapy**.

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