

BridgeBio Response to 12-month Follow-up for Evidence Regarding ICER’s October 2024 Final Evidence Report on Treatments for Transthyretin Amyloid Cardiomyopathy (ATTR-CM)

BridgeBio welcomes the opportunity to describe new evidence underscoring connections between acoramidis and meaningful outcomes. Regarding relationships between transthyretin (TTR) stabilization and clinical outcomes, ICER’s 2024 report states: “A study...found that acoramidis raised [serum TTR (sTTR)] more than tafamidis, and found an association between [sTTR] and clinical outcomes...experts had sharply divergent opinions as to whether [sTTR] is an adequate surrogate to allow such comparisons...”¹ A 2025 systematic review concluded that sTTR is a predictor of cardiovascular events, all-cause mortality (ACM), and cardiovascular mortality (CVM).² Emerging evidence, described here, continues to advance understanding of ATTR-CM and underscores therapeutic potential of acoramidis, whose TTR-stabilizing mechanism may address persistent unmet needs and meaningfully modify disease trajectory.

1. Early Increase in [sTTR] by Acoramidis Independently Predicts Improved Survival in [ATTR-CM]³

This post-hoc analysis of sTTR in the ATTRibute-CM study (n=557) supports the importance of early, sustained TTR stabilization:

- Acoramidis patients experienced sharp, early Δ TTR: mean sTTR increase of 9.1 mg/dL within 28 days, sustained over 30 months of treatment
- sTTR correlated with survival:
 - Early (Day 28) Δ TTR was associated with reduced ACM (HR: 0.96 per 1 mg/dL increase in early Δ TTR; 95% CI: 0.93-0.98; P=0.002)
 - Adjusting for TTR variant status and baseline NYHA functional class, National Amyloidosis Centre stage, and sTTR, early Δ TTR was independently associated with reduced ACM (P<0.001)

2. Effect of Acoramidis on Recurrent and Cumulative Cardiovascular Outcomes in ATTR-CM: Exploratory Analysis From ATTRibute-CM⁴

Another ATTRibute-CM exploratory analysis demonstrated progressive benefits of acoramidis vs placebo over 30 months (phase 3, N=611) plus 12-month open-label extension:

- Acoramidis patients showed numeric reduction in CVM or recurrent cardiovascular hospitalization (CVH) at all timepoints (Months 1-30)
 - The authors note that, while this treatment effect may partially relate to enrollment of participants with less advanced disease, this pattern of fewer

cumulative CV events has not occurred until later timepoints in other recent phase 3 ATTR-CM trials^{5,6}

- This effect increased progressively, with 53 events avoided/100 treated patients by Month 30
- Separation of treatment and placebo curves occurred early and progressively increased
- 19% of CVM/recurrent CVH and 22% of CVH occurred within the first 6 months, highlighting the importance of timely diagnosis and treatment

The authors suggest a possible underlying mechanism: acoramidis-mediated near-complete TTR stabilization, resulting in early, sustained increases in sTTR, a marker of TTR stabilization.

3. Efficacy of Acoramidis in Wild-Type and Variant [ATTR-CM]: Results From ATTRibute-CM and Its Open-Label Extension⁷

Patients with variant ATTR-CM, including V124I, historically face high disease burden, limited treatment options, and care inequities. This prespecified, post-hoc analysis confirmed high unmet need: variant (n=20) and V142I (n=12) placebo recipients experienced high ACM and CVH (70% to 80%) through Months 30-42.

Consistent treatment benefits further differentiated acoramidis vs placebo:

- Month 30: acoramidis reduced ACM/1st CVH by 59% (variant) and 69% (V142I), the first evidence of this level of benefit in these subgroups
- Month 42: acoramidis reduced ACM by 59% (variant) and 69% (V142I)

Authors concluded that acoramidis confers consistent efficacy across the genotype spectrum for multiple endpoints (e.g., ACM, CVH, sTTR), reinforcing benefits of near-complete TTR stabilization.

Thank you for considering this evidence.

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