ACC.25

1659
JACC April 1, 2025
Volume 85, Issue 12, Suppl A

Heart Failure and Cardiomyopathies

ACORAMIDIS-MEDIATED EARLY INCREASE IN SERUM TRANSTHYRETIN LEVEL REDUCES CARDIOVASCULAR-RELATED HOSPITALIZATIONS AND MORTALITY: INSIGHTS FROM THE ATTRIBUTE-CM STUDY

Poster Contributions
South Hall
Monday, March 31, 2025, 9:00 a.m.-10:00 a.m.

Session Title: Heart Failure and Cardiomyopathies 11
Abstract Category: 24. Heart Failure and Cardiomyopathies: Pharmacology
Presentation Number: 1235-176

Authors: Nitasha Sarswat, Amrut Ambardekar, Jorg Taubel, Justin Lee Grodin, Julian D. Gillmore, Matthias Dupont, Richard F. Wright, Jing Du, Suresh Siddhanti, Jean Francois Tamby, Alan Ji, Uma Sinha, Jonathan C. Fox, Mathew S. Maurer, Richard Kar-Hang Cheng, BridgeBio Pharma, Inc., San Fransisco, CA, USA

Background: Patients with transthyretin amyloid cardiomyopathy (ATTR-CM) can have lower circulating serum TTR (sTTR) levels; this is associated with a greater risk of mortality. Acoramidis is an investigational TTR stabilizer with near complete (≥90%) TTR stabilization. In a phase 3 study, ATTRibute-CM, acoramidis treatment resulted in a rapid (by Day 28) and sustained increase in sTTR levels, and reduced the risk of cardiovascular hospitalizations (CVH) and mortality (CVM). In this post-hoc analysis of ATTRibute-CM, we evaluated the association between acoramidis-mediated early increase in sTTR levels with the risk of CVM and of first CVH.

Methods: Analyses were conducted in the ATTRibute-CM modified intent-to-treat (mITT) population (acoramidis: 409; placebo: 202). Relationships between change from baseline in TTR (ΔTTR) at Day 28 and subsequent risk of CVM and of first CVH over 30 months were analyzed as separate endpoints using stratified Cox proportional hazard model.

Results: Each 5 mg/dL increase in sTTR levels at Day 28 mediated by acoramidis was associated with a risk reduction of 24.5% in CVM and 21.2% for first CVH over 30 months. Risk reductions for CVM and of first CVH were greater for each 10 mg/dL increase in sTTR levels at Day 28, Table. Observations were independent of baseline sTTR and treatment groups.

Conclusion: Incremental increases in sTTR levels on Day 28, achieved with acoramidis, may independently predict greater reduction in risks of CVM and of first CVH in patients with ATTR-CM.

Table: Stratified Cox Proportional Model Analysis of CVM and first CVH and Hazard Ratio for 1, 5, 10 mg/dL Change From Baseline in Serum TTR at Day 28, mITT population (N=611)

	Acoramidis (n = 409)	Placebo (n = 202)
Cardiovascular-related Mortality (CVM)[a], n (%)	61 (14.9)	43 (21.3)
Cox Proportional Hazard Model[b] for CVM		
HR associated with 1 mg/dL ΔTTR (95% CI) p-value Risk Reduction, %	0.95 (0.90, 0.99) 0.021 5.5	
HR associated with 5 mg/dL ΔTTR (95% CI) p-value Risk Reduction, %	0.76 (0.59, 0.96) 0.021 24.5	
HR associated with 10 mg/dL ΔTTR (95% CI) p-value Risk Reduction, %	0.57 (0.35, 0.92) 0.021 43.1	
Cardiovascular-related Hospitalization (CVH)[c], n (%)	109 (26.7)	86 (42.6)
Cox Proportional Hazard Model[b] for CVH		
HR associated with 1 mg/dL ΔTTR (95% CI) p-value Risk Reduction, %	0.95 (0.92, 0.99) 0.012 4.7	
HR associated with 5 mg/dL ΔTTR (95% CI) p-value Risk Reduction, %	0.79 (0.66, 0.95) 0.012 21.2	
HR associated with 10 mg/dL ΔTTR (95% CI) p-value Risk Reduction, %	0.62 (0.43, 0.90) 0.012 37.9	

CI = confidence interval; CVM = cardiovascular-related mortality; CVH = cardiovascular-related hospitalization; mITT = modified intent-to-treat.

a. CVM includes all adjudicated CV-related and undetermined cause death; 1 participant received heart transplantation, and 1 participant received a cardiac mechanical assist device, both in the placebo group.

b. Stratified Cox proportional hazards model includes baseline 6MWT and change from baseline in TTR level at day 28 as covariates and is stratified by treatment group and randomization stratification factors of genotype (ATTRwt-CM vs ATTRv-CM), NT-proBNP level (≤3000 or >3000 pg/mL), eGFR level (< or ≥45 mL/min/1.73m^2) and Baseline TTR group (≥20 vs. <20).

c. CVH was defined as a nonelective admission to an acute care setting for cardiovascular-related morbidity that resulted in at least a 24-hour stay (or a date change if the time of admission/discharge was not available) or an unscheduled medical visit of <24 hours due to heart failure requiring treatment with IV diuretics.