Improved Health-Related Quality of Life in Patients With ATTR-CM Treated With Acoramidis Demonstrated by Improvements in KCCQ Scores

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PURPOSE

- **To evaluate the effects of acoramidis on Kansas City Cardiomyopathy Questionnaire overall summary (KCCQ-OS) and KCCQ domain scores in participants of ATTRibute-CM**

BACKGROUND

- Transthyretin amyloid cardiomyopathy (ATTR-CM) is a rare, progressive, and fatal cardiomyopathy associated with poor quality of life (QoL)[1-3]
- The self-administered KCCQ is used to assess the perception of health status and health-related QoL in patients with heart failure (HF)[4,5]
  - It comprises 23 questions corresponding to 7 domains, including frequency and burden of HF symptoms, limitations of physical and social functions, and HF impact on QoL (**Figure 1**)[4,5]
  - It is a commonly used assessment tool in studies of HF interventions and represents an independent predictor of survival[6]
- Acoramidis is a novel, investigational transthyretin (TTR) stabilizer that increases serum TTR (also known as prealbumin) for the treatment of patients with ATTR-CM[7-9]
- Acoramidis met its four-step primary hierarchical endpoint of mortality, cardiovascular-related hospitalization, change in N-terminal pro-B-type natiuretic peptide, and six-minute walk test (p<0.0001) in a pivotal phase 3 trial (ATTRibute-CM, NCT03860935) and was generally well tolerated[9]
- Change from baseline to Month 30 in the KCCQ-OS score was a key secondary endpoint in ATTRibute-CM[9]

FIGURE 1. KCCQ Domains[5]

Symptom Burden	Symptom Frequency	Physical Limitation	QoL	Social Limitation	Symptom Stability	Self-Efficacy
Total Symptom Score						
Clinical Summary Score						
KCCQ-OS Score						

METHODS

- ATTRibute-CM was a placebo-controlled, randomized, phase 3 clinical trial for ATTR-CM—participants were randomized 2:1 to receive 800 mg acoramidis or matching placebo twice daily for 30 months[9]
- The efficacy analysis was conducted in the modified intent-to-treat (mITT) population, which consisted of randomized participants who had a baseline estimated glomerular filtration rate of ≥30 mL/min/1.73 m^2 [9]
- Participants completed the KCCQ at baseline, every 3 months for the first year, and every 6 months thereafter until Month 30
- The change from baseline in KCCQ-OS was analyzed using a mixed effect model with repeated measures via the Jump to Reference method and has been previously described in Gillmore et al[9]
- Summary statistics for change from baseline in KCCQ domain scores at Month 30 were also evaluated
- For post hoc analysis, the percentage of patients with a net improvement in KCCQ-OS at Month 30 compared with baseline was calculated; participants with missing KCCQ-OS scores were counted as "not improved" and contributed to the denominator when calculating the percentage

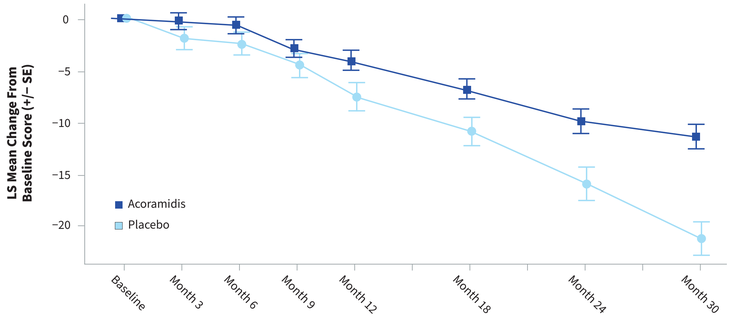
CONCLUSIONS

- **In ATTRibute-CM, acoramidis reduced the decline in health status and QoL shown by statistically significant and clinically meaningful benefits in KCCQ-OS, supported by numerical and consistent benefits in individual KCCQ domains**

RESULTS

- Baseline characteristics were well balanced between groups[9]
- As previously reported, at Month 30, acoramidis showed a statistically significant and clinically meaningful benefit in KCCQ-OS score favoring acoramidis vs placebo (KCCQ-OS score least squares mean difference 9.94 [95% CI 5.97-13.91]; p<0.0001), with the curve separation beginning at Month 3 and increasing in magnitude through Month 30 (**Figure 2**)[9]

FIGURE 2. LS Mean (±SE) Change From Baseline in KCCQ-OS Score Over Time[9]



	Baseline	Month 3	Month 6	Month 9	Month 12	Month 18	Month 24	Month 30
Acoramidis	408	263	389	390	397	404	407	405
Placebo	202	134	192	194	196	199	201	201

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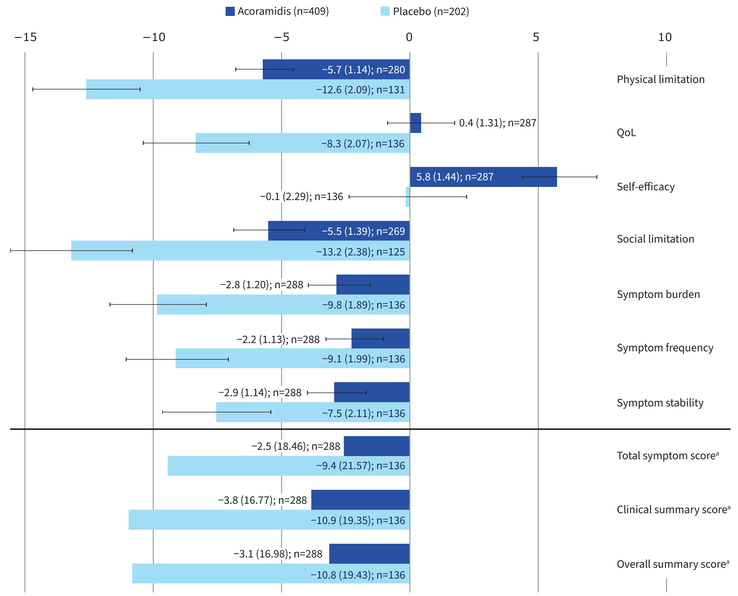
TABLE 1. Mean (SD) Baseline KCCQ Domain Scores (mITT Population, Observed Values)

Domain	Acoramidis N=409	Placebo N=202
Physical limitation	n=406 73.0 (21.70)	n=202 72.2 (20.88)
QoL	n=407 67.1 (21.64)	n=202 66.4 (24.08)
Self-efficacy	n=407 78.4 (22.51)	n=202 80.1 (23.77)
Social limitation	n=400 68.8 (26.03)	n=196 67.7 (27.65)
Symptom burden	n=408 78.3 (19.03)	n=202 75.9 (21.24)
Symptom frequency	n=408 77.4 (20.41)	n=201 75.1 (22.31)
Symptom stability	n=408 52.5 (14.24)	n=202 53.1 (17.09)
Total symptom score	*n=408* *77.8 (18.76)*	*n=202* *75.3 (21.18)*
Clinical summary score	*n=408* *75.4 (18.79)*	*n=202* *73.8 (19.34)*
Overall summary score	*n=408* *71.7 (19.37)*	*n=202* *70.5 (20.65)*

FIGURE 3. Change From Baseline (Mean± SE) at Month 30 in KCCQ Domain Scores (mITT, Observed Values)



[a]SD is provided for summary scores.

- Individual KCCQ domain scores at baseline are shown in **Table 1**. A numerical improvement from baseline at Month 30 in KCCQ domain scores was observed across all KCCQ domain scores for the acoramidis group vs the placebo group **(Figure 3)**
- In a post hoc analysis, 30.8% of participants in the acoramidis group exhibited a net increase in KCCQ-OS score relative to baseline at Month 30, revealing a clinical improvement in health status, compared to 17.8% of participants in the placebo group (stratified CMH; nominal p value=0.0005)

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ABBREVIATIONS: ATTR-CM, transthyretin amyloid cardiomyopathy; HF, heart failure; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire overall summary; LS, least squares; mITT, modified intent-to-treat; QoL, quality of life.

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