Health-Related Quality of Life in Patients With Symptomatic Transthyretin Amyloid Cardiomyopathy Treated With Acoramidis: an Analysis From the ATTRibute-CM Study

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PURPOSE

- **We report the effects of acoramidis on health-related quality of life (HRQoL), as measured by the EuroQoL 5-dimensions 5-levels Health Outcomes Assessment (EQ-5D-5L) in patients with symptomatic transthyretin amyloid cardiomyopathy (ATTR-CM)**

BACKGROUND

- ATTR-CM is a rare, progressive, and fatal cardiomyopathy associated with poor quality of life (QoL)[1-5]
- Acoramidis is a novel, potent, investigational transthyretin oral stabilizer for the treatment of patients with ATTR-CM[6-8]
- 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[8]
- A planned analysis of ATTRibute-CM was the assessment of HRQoL via EQ-5D-5L, a widely used evaluation of general QoL[9]

METHODS

- ATTRibute-CM, a phase 3, multicenter, double-blind, placebo-controlled trial, randomized participants with ATTR-CM to receive either acoramidis or placebo in a 2:1 ratio, previously described in Gillmore et al[8]
- The EQ-5D-5L is a brief, self-administered, generic health status instrument that includes 2 parts: the EQ-5D-5L descriptive system and the EQ visual analog scale (EQ VAS)[9,10]
  - The EQ-5D-5L descriptive system measures mobility, self-care, usual activities, pain/discomfort, and anxiety/depression
  - The EQ VAS records respondent's health from 0 to 100 (the worst and best imaginable health, respectively) on a VAS
- Analyses of EQ-5D-5L results were performed on the modified intent-to-treat (mITT) population of ATTRibute-CM
- Change from baseline via least squares (LS) mean difference in EQ-5D-5L index score and VAS was analyzed using a mixed model for repeated measures (MMRM) using the jump to reference (J2R) method

CONCLUSIONS

- **In addition to improving clinical outcomes at month 30, treatment with acoramidis resulted in a statistically significant and clinically important reduction in the progressive decline in HRQoL associated with ATTR-CM**

RESULTS

Baseline demographics and disease characteristics

- Baseline demographics and clinical characteristics were well balanced between the treatment groups and have been previously published[8] **(Table 1)**

TABLE 1. Baseline Demographics and Clinical Characteristics[8] (ITT population)

	Acoramidis N=421	Placebo N=211
Age, years, mean (SD)	77.4 (6.5)	77.1 (6.8)
Male sex, n (%)	384 (91.2)	186 (88.2)
Race/ethnicity, White, n (%)	368 (87.4)	187 (88.6)
Transthyretin genotype[a], ATTRv-CM, n (%)	39 (9.3)	19 (9.0)
V122I, n (% of ATTRv-CM)	24 (61.5)	12 (63.2)
NT-proBNP, pg/mL, median (IQR)	2326 (1332-4019)	2306 (1128-3754)
eGFR, mL/min/1.73 m², mean (SD)	61 (18)	61 (19)
NYHA class, n (%)		
I	51 (12.1)	17 (8.1)
II	293 (69.6)	162 (76.8)
III	77 (18.3)	32 (15.2)
NAC stage[b], n (%)		
I	241 (57.2)	120 (56.9)
II	134 (31.8)	69 (32.7)
III	46 (10.9)	22 (10.4)
Serum transthyretin, mg/dL, mean (SD)	23 (6)	24 (6)

The ITT population (N=632) was defined as all randomized participants who received at least 1 dose of study drug and had at least 1 postbaseline efficacy evaluation.
[a]Genetic status may differ from interactive voice/web response system stratification factor, as classification of a variant for the latter was at the discretion of the investigator. For this electronic case report form, all variants were documented as a mutation.
[b]NAC ATTR staging criteria: stage I (NT-proBNP ≤3000 pg/mL and eGFR ≥45 mL/min/1.73 m²); stage II (all remainder results when both NT-proBNP and eGFR are not missing); stage III (NT-proBNP >3000 pg/mL and eGFR <45 mL/min/1.73 m²).

HRQoL measured by EQ-5D-5L

- The baseline assessment of EQ-5D-5L endpoints in the mITT population are presented in **Table 2**

TABLE 2. Baseline Assessment of EQ-5D-5L Endpoints, mITT Population

	Acoramidis N=409	Placebo N=202	Overall N=611
EQ-5D-5L index score			
N	405	202	607
Mean (SD)	0.7862 (0.19923)	0.7762 (0.22016)	0.7829 (0.20631)
Median (Q1, Q3)	0.8340 (0.7110, 0.9400)	0.8350 (0.6810, 0.9320)	0.8340 (0.7050, 0.9400)
Min, Max	0.037, 1.000	−0.216, 1.000	−0.216, 1.000
EQ-5D-5L VAS			
N	405	202	607
Mean (SD)	72.3 (16.41)	72.0 (16.92)	72.2 (16.57)
Median (Q1, Q3)	75.0 (60.0, 85.0)	75.0 (65.0, 82.0)	75.0 (60.0, 85.0)
Min, max	20, 100	20, 100	20, 100

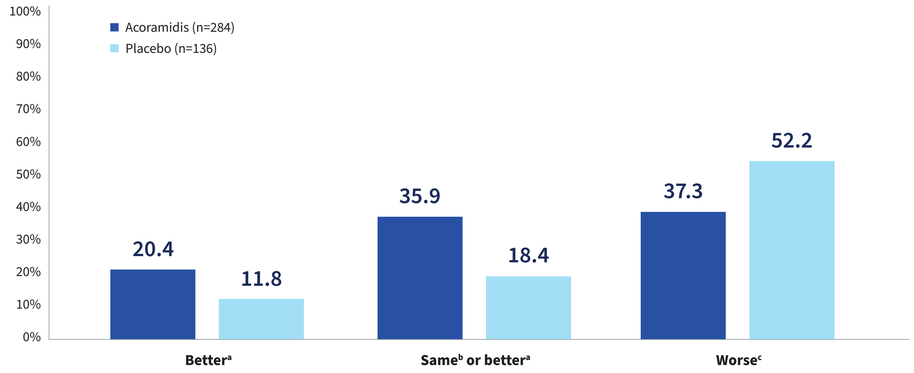
- Compared with baseline, treatment with acoramidis demonstrated clinically meaningful treatment benefit on EQ-5D-5L VAS (p<0.0001) at Month 30, with a 10-point change from baseline LS mean difference observed between treatment groups **(Table 3)**

TABLE 3. MMRM (J2R) Analysis of Change From Baseline in EQ-5D-5L VAS at Month 30

	Acoramidis N=409	Placebo N=202
Change from Baseline in EQ-5D-5L index score		
n	401	201
LS mean (95% CI)	−0.17 (−0.20, −0.14)	−0.30 (−0.34, −0.25)
LS mean difference (95% CI): acoramidis − placebo	0.13 (0.07, 0.18)	
p value	<0.0001	
Change from Baseline in EQ-5D-5L VAS		
n	402	200
LS mean (95% CI)	−10.12 (−12.49, −7.74)	−19.66 (−22.95, −16.37)
LS mean difference (95% CI): acoramidis − placebo	9.55 (5.50, 13.59)	
p value	<0.0001	

- More participants in the acoramidis groups indicated "better" or "same/better" in their health status change from baseline at Month 30 compared with placebo **(Figure)**

FIGURE. EQ-5D-5L Health Status Change From Baseline at Month 30



[a]Their health state is better (ie, better on at least 1 dimension and is no worse in any other dimension).
[b]Their health state is exactly the same (ie, same state on each dimension).
[c]Their health state is worse (ie, worse in at least 1 dimension and no better in any other dimension).

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ABBREVIATIONS: ATTR-CM, transthyretin amyloid cardiomyopathy; ATTRv-CM, variant ATTR-CM; eGFR, estimated glomerular filtration rate; EQ-5D-5L, EuroQol 5-dimensions 5-levels Health Outcomes Assessment; J2R, jump to reference; LS, least squares; max, maximum; min, minimum; mITT, modified intent-to-treat; MMRM, mixed model for repeated measures; NAC, National Amyloidosis Centre; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; NYHA, New York Heart Association; Q, quartile; VAS, visual analog scale.

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