Acoramidis Reduces Cardiovascular Mortality: Results Through Month 42 from the ATTRibute-CM Open-label Extension Study

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Introduction

- ATTR-CM is a progressive cardiomyopathy resulting in substantial cardiovascular morbidity and mortality caused by destabilization of the TTR tetramer[1]
- Acoramidis is a highly selective, oral TTR stabilizer that achieves near-complete (≥ 90%) TTR stabilization, and is approved in the USA, Europe, Japan, and UK for treating wild-type or variant ATTR-CM in adults[2-5]
- In the phase 3 ATTRibute-CM study, acoramidis achieved a 36% reduction in ACM or first CVH, and 42% reduction in ACM or recurrent CVH compared to placebo at Month 30[6,7]
- In the OLE phase of ATTRibute-CM study (NCT04988386), continuous acoramidis treatment led to a 36% risk reduction in ACM through Month 42 versus switching from placebo to acoramidis ($p = 0.006$)[8]
  - No new clinically important safety issues were identified up to 42 months[8]

ACM, all-cause mortality; ATTR-CM, TTR amyloid cardiomyopathy; CVH, cardiovascular-related hospitalization; OLE, open-label extension; TTR, transthyretin.

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Objective

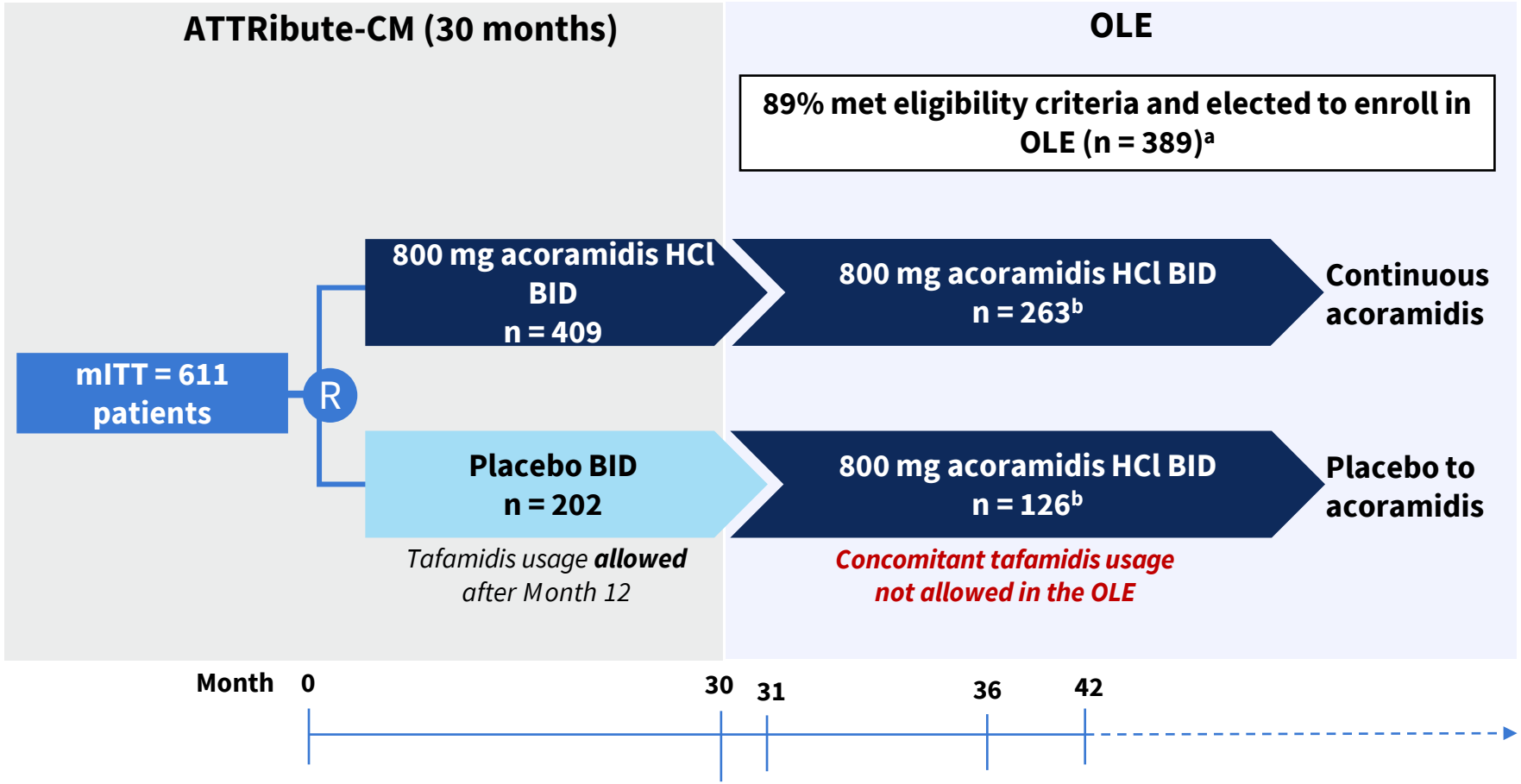
We report data from the OLE of ATTRibute-CM on prespecified secondary outcomes for:

1. **Time to CVM up to Month 42**

2. **Time to CVM or First CVH up to Month 42**

CVM, cardiovascular mortality.

ATTRibute-CM OLE Study Design



OLE endpoints[c]

Time to first event for CVM, CVM or first CVH, and first CVH[d,e]

Key OLE eligibility criteria

- Completed 30 months of study treatment in ATTRibute-CM study
- Discontinued concomitant tafamidis use before entering OLE
- No planned concomitant tafamidis or other investigational treatment during OLE

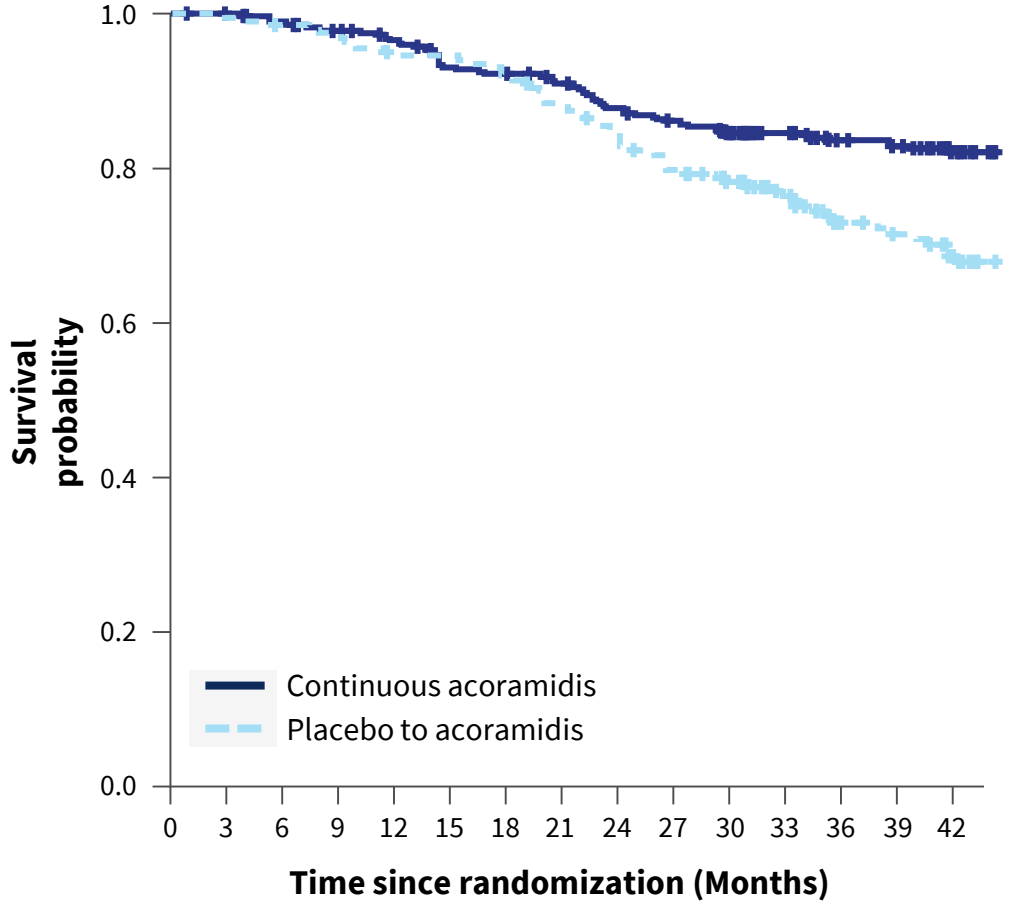
Figure adapted from: Judge DP, et al. *Circulation* 2025;151(9):601–611. (https://creativecommons.org/licenses/by/4.0/).
[a]11% elected not to enroll into OLE (n = 49). Most commonly due to desire to receive tafamidis after ATTRibute-CM. [b]Modified intent-to-treat (mITT) analysis was continuous from the start of ATTRibute-CM into the OLE. [c]For this study. [d]Cox proportional hazards model. [e]CVH was defined as a non-elective admission to an acute care setting for cardiovascular-related morbidity that resulted in at least a 24-hour stay, or an unplanned visit to an emergency department/ward, urgent care clinic, or day clinic of fewer than 24 hours for the management of decompensated heart failure requiring treatment with an intravenous diuretic.
BID, twice daily.

Clinical Characteristics at Entry to the OLE

Participant characteristics[a,b]	Continuous acoramidis n = 263	Placebo to acoramidis n = 126
Age, years, mean (SD)[c]	78.8 (6.50)	79.7 (6.33)
Male sex, n (%)	244 (92.8)	115 (91.3)
ATTRwt-CM, n (%)[d]	242 (92.0)	120 (95.2)
ATTR-CM duration at randomization,[d,e] years, **n** **Mean (SD)**	 262 1.2 (1.10)	 126 1.2 (1.29)
NYHA class, n (%)[f] **I or II** **III** **IV**	 216 (82.1) 44 (16.7) 3 (1.1)	 79 (62.7) 45 (35.7) 1 (0.8)
NT-proBNP, pg/mL, **n** **Median (IQR)**	 257 2094.0 (1247.0–3566.0)	 125 2905.0 (1624.0–5166.0)
Serum TTR, mg/dL, **n** **Mean (SD)**	 258 32.8 (6.22)	 124 25.6 (6.53)
Participants who received tafamidis in the ATTRibute-CM study, n (%)	29 (11.0)	23 (18.3)

Table adapted from: Judge DP, et al. *Circulation* 2025;151(9):601–11. (https://creativecommons.org/licenses/by/4.0/).
[a]Data are for all participants who enrolled in the OLE and received at least one dose of open-label acoramidis. [b]Baseline values are the last non-missing assessment values completed before the first OLE acoramidis treatment. [c]Age calculated from the first OLE treatment date and date of birth/age. [d]Data at the time of randomization in ATTRibute-CM (not at OLE entry). [e]Calculated as (randomization date – date of ATTR-CM diagnosis)/365.25. [f]Data missing for one patient in the placebo to acoramidis group.
ATTRwt-CM, transthyretin amyloidosis wild-type cardiomyopathy; IQR, interquartile range; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; SD, standard deviation.

Continuous Acoramidis Reduced the Risk of CVM Through Month 42 Versus Placebo to Acoramidis (mITT Population[a])



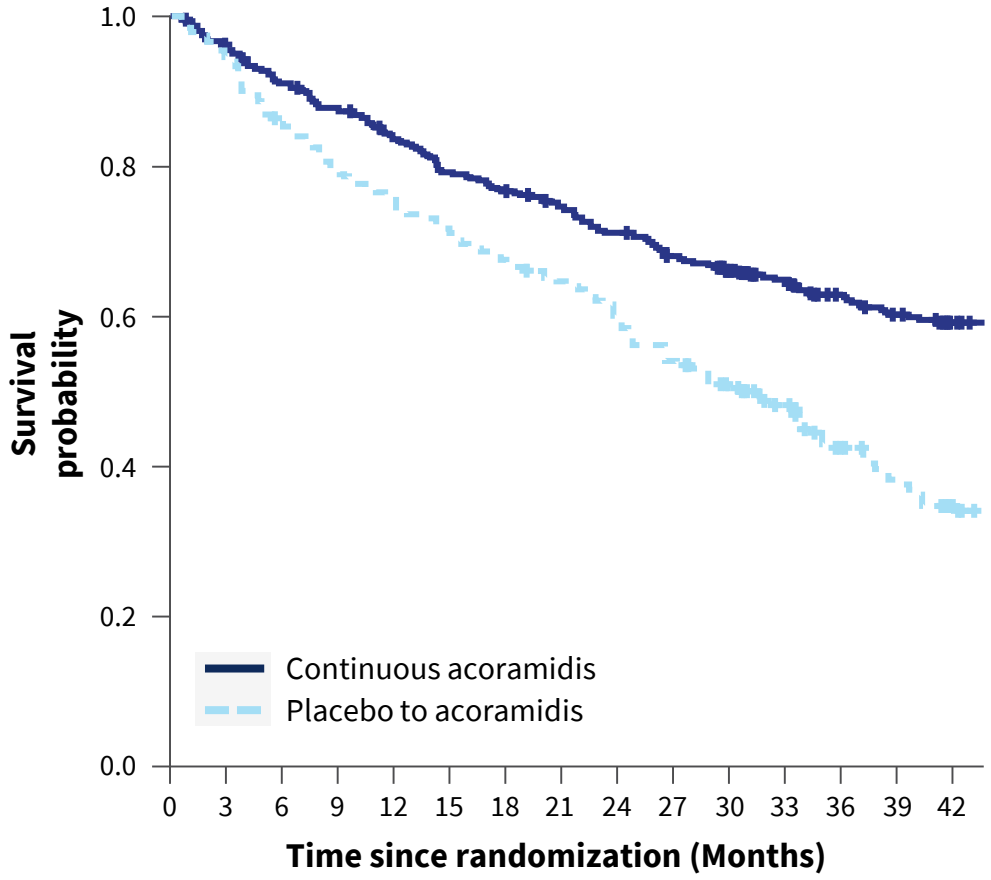
Subjects remaining at risk (Cumulative events)

Continuous acoramidis	409	407	401	393	385	369	365	358	344	336	297	260	247	243	216
	(0)	(0)	(4)	(9)	(14)	(28)	(31)	(36)	(49)	(55)	(61)	(61)	(64)	(66)	(68)
Placebo to acoramidis	202	201	198	196	188	188	183	175	166	156	143	118	102	98	87
	(0)	(1)	(3)	(5)	(11)	(11)	(16)	(23)	(31)	(40)	(43)	(46)	(51)	(53)	(58)

	Continuous acoramidis (n = 409)	Placebo to acoramidis (n = 202)
CVM, n (%)	68 (16.6%)	58 (28.7%)
Relative risk reduction	**42.1%**	
Hazard ratio (95% CI)[b]	0.56 (0.389–0.791)	
***p* value**	0.0011	

[a]mITT analysis was continuous from the start of ATTRibute-CM into the OLE. [b]Stratified Cox proportional hazards model that included treatment group as an explanatory factor and baseline 6-minute walk distance as a covariate and was stratified by the ATTRibute-CM randomization stratification factors of genotype, NT-proBNP level and estimated glomerular filtration rate as recorded in the interactive voice/web response system.

Continuous Acoramidis Reduced the Risk of CVM/First CVH Through Month 42 Versus Placebo to Acoramidis (mITT Population[a])



Subjects remaining at risk (Cumulative events)

Continuous acoramidis	409 (0)	389 (18)	370 (36)	355 (50)	337 (66)	319 (84)	308 (94)	298 (102)	284 (116)	270 (128)	233 (136)	203 (140)	189 (146)	179 (154)	156 (157)
Placebo to acoramidis	202 (0)	191 (11)	172 (29)	159 (42)	152 (49)	143 (58)	135 (66)	129 (71)	121 (79)	108 (92)	97 (99)	80 (103)	63 (112)	54 (119)	45 (124)

	Continuous acoramidis (n = 409)	Placebo to acoramidis (n = 202)
CVM/first CVH, n (%)	157 (38.4%)	124 (61.4%)
Relative risk reduction	**37.5%**	
Hazard ratio (95% CI)[b]	0.54 (0.429–0.691)	
***p* value**	<0.0001	

[a]mITT analysis was continuous from the start of ATTRibute-CM into the OLE. [b]Stratified Cox proportional hazards model that included treatment group as an explanatory factor and baseline 6-minute walk distance as a covariate and was stratified by the ATTRibute-CM randomization stratification factors of genotype, NT-proBNP level and estimated glomerular filtration rate as recorded in the interactive voice/web response system.

Conclusions

Acoramidis treatment administered for 42 months led to a 42% relative risk reduction in CVM compared with the placebo to acoramidis treatment group

Acoramidis treatment administered for 42 months led to a 38% relative risk reduction in time to CVM or first CVH compared with the placebo to acoramidis treatment group, with a benefit observed as early as after 3 months of treatment initiation

Findings demonstrate the long-term clinical benefits of acoramidis, a near-complete TTR stabilizer, for reducing CVM in ATTR-CM, and the importance of early treatment

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