Acoramidis Reduces All-Cause Mortality and Cardiovascular-Related Hospitalizations Through Month 42 in Transthyretin Amyloid Cardiomyopathy Across All Pre-specified Participant Subgroups

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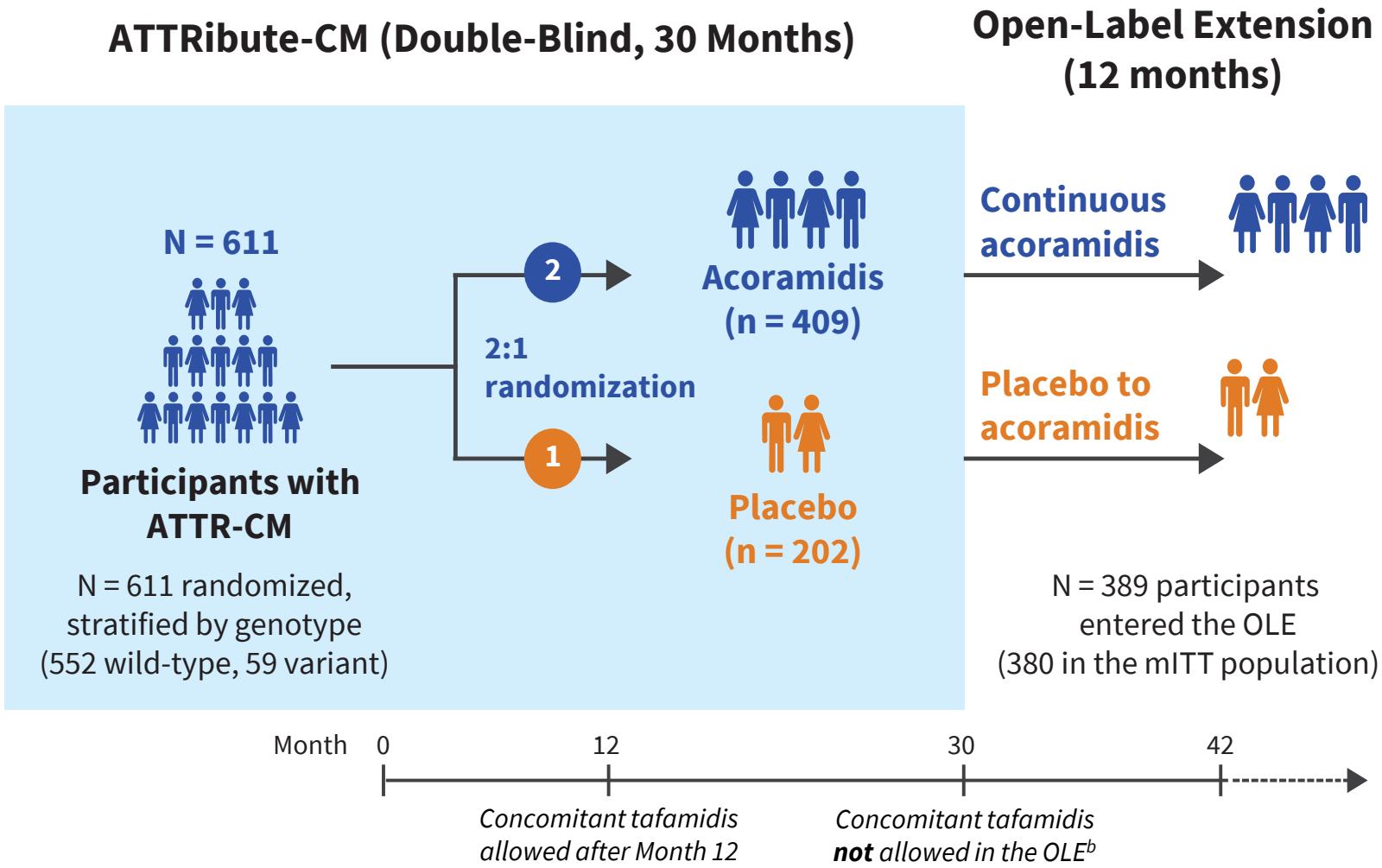
Introduction

- ATTR-CM is a progressive cardiomyopathy resulting in substantial cardiovascular morbidity and mortality caused by destabilization of the TTR tetramer[1]
- Acoramidis is an oral TTR stabilizer that achieves ≥90% TTR stabilization and is approved in the USA, Europe, Japan, and UK for treating variant or wild-type ATTR-CM in adults[2-6]
- In the ATTRibute-CM study, acoramidis reduced the risk of time to ACM or first CVH by 36% ($p = 0.0008$) compared with placebo[7]
- In the ongoing OLE (NCT04988386), continuous acoramidis treatment led to risk reductions of 43% in ACM or first CVH and 36% in ACM alone through Month 42 (30 months ATTRibute-CM + 12 months OLE) versus participants randomized to placebo who switched to acoramidis after Month 30[8]
  - No new clinically important safety issues were identified up to 42 months[8]

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

1. Rapezzi C, et al. *Nat Rev Cardiol* 2010;7(7):398–408. **2.** Ji A, et al. Poster presented at the European Society of Cardiology Congress 2023; August 25–28, 2023; Amsterdam, Netherlands. **3.** ATTRUBY™ (acoramidis) tablets, for oral administration. BridgeBio Pharma, Inc. November 2024. http://www.accessdata.fda.gov/drugsatfda_docs/label/2024/216540s000lbl.pdf. Accessed October 2025. **4.** BEYONTTRA 356 mg film-coated tablets summary of product characteristics. BridgeBio Pharma, Inc. 2025. https://www.ema.europa.eu/en/documents/product-information/beyonttra-epar-product-information_en.pdf. Accessed October 2025. **5.** BridgeBio Pharma, Inc. https://investor.bridgebio.com/news/news-details/2025/beyonttra-acoramidis-the-first-near-complete-ttr-stabilizer-90-approved-in-japan-to-treat-attr-cm-03-27-2025/default.aspx. Accessed October 2025. **6.** Medicines and Healthcare Products Regulatory Agency. https://www.gov.uk/government/news/acoramidis-approved-to-treat-wild-type-or-variant-transthyretin-amyloidosis-in-adults-with-cardiomyopathy. Accessed October 2025. **7.** Judge DP, et al. *J Am Coll Cardiol* 2025;85(10):1003–1014. **8.** Judge DP, et al. *Circulation*. 2025;151(9):601–611.

Study Design & Objective



OBJECTIVE[a]

To assess the long-term clinical benefits of continuous acoramidis treatment through Month 42 across participant subgroups for:

1. **Composite of ACM or first CVH**
2. **ACM alone**

[a]For this study. [b]Participants who received tafamidis during the double-blind period were required to discontinue it before entering the OLE.
mITT, modified intent-to-treat.

Definitions of ACM and CVH in ATTRibute-CM

ACM

- Death due to any cause
- Receipt of a cardiac mechanical assist device placement
- Receipt of a heart transplant

CVH

≥24 hour CVH:

- Non-elective admission to an acute care setting for cardiovascular-related morbidity

<24 hour CVH for HF (urgent HF visit):

- Unplanned visit to an ER/urgent care/day clinic for management of decompensated HF requiring treatment with an intravenous diuretic

All events were independently adjudicated by a Clinical Events Committee

ER, emergency room; HF, heart failure.

At Entry Into the OLE, Placebo to Acoramidis Participants Had More Severe Disease Than Continuous Acoramidis Participants[a]

- **Placebo to acoramidis participants had higher median NT-proBNP (2905 vs 2094 pg/mL) and a higher proportion of NYHA Class III (35.7% vs 16.7%) versus continuous acoramidis participants**

Participant Characteristic[b,c]	Continuous Acoramidis n = 263	Placebo to Acoramidis n = 126
Age, years, mean (SD)[d]	78.8 (6.50)	79.7 (6.33)
Sex, male, n (%)	244 (92.8)	115 (91.3)
Race, n (%)[e]		
Caucasian	232 (88.2)	118 (93.7)
Black or African American	12 (4.6)	1 (0.8)
Asian	6 (2.3)	3 (2.4)
Other	1 (0.4)	0
Multiple races	1 (0.4)	0
Genotype, n (%)[f]		
ATTRv-CM	21 (8.0)	6 (4.8)
ATTRwt-CM	242 (92.0)	120 (95.2)
ATTR-CM duration at randomization,[f,g] years	n = 262	n = 126
Mean (SD)	1.2 (1.10)	1.2 (1.29)
Participants who received tafamidis in the ATTRibute-CM study, n (%)	29 (11.0)	23 (18.3)

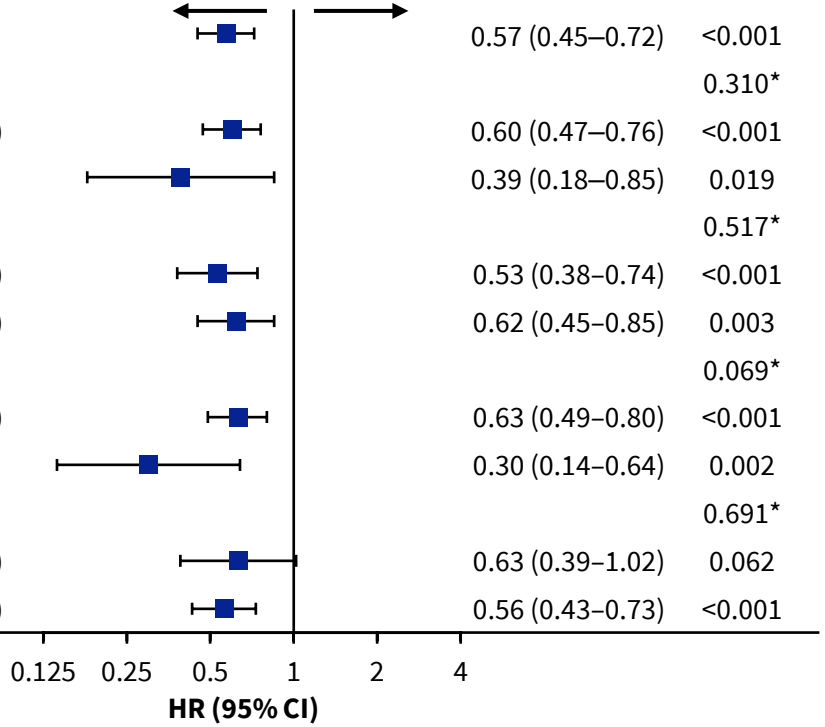
Participant Characteristic[b,c]	Continuous Acoramidis n = 263	Placebo to Acoramidis n = 126
NYHA Class, n (%)[h]		
I or II	216 (82.1)	79 (62.7)
III	44 (16.7)	45 (35.7)
IV	3 (1.1)	1 (0.8)
NAC ATTR stage, n (%)[i]		
I	136 (51.7)	52 (41.3)
II	66 (25.1)	46 (36.5)
III	53 (20.2)	26 (20.6)
eGFR, n (%)		
≥45 mL/min/1.73 m^2	228 (86.7)	104 (82.5)
<45 mL/min/1.73 m^2	35 (13.3)	22 (17.5)
NT-proBNP, pg/mL	n = 257	n = 125
Median (IQR)	2094.0 (1247.0–3566.0)	2905.0 (1624.0–5166.0)
Serum TTR, mg/dL	n = 258	n = 124
Mean (SD)	32.8 (6.22)	25.6 (6.53)

Table adapted from: Judge DP, et al. *Circulation.* 2025;151(9):601–611. (https://creativecommons.org/licenses/by/4.0/).
[a]Baseline characteristics at randomization in the ATTRibute-CM double-blind were mostly similar. [b]Data are for all participants who enrolled in the OLE and received at least one dose of open-label acoramidis. [c]Baseline values are the last non-missing assessment values completed before the first OLE acoramidis treatment. [d]Age calculated from the first OLE treatment date and date of birth/age from 'Date of Birth' in the electronic case report form. [e]Data not reported for 11 participants in the continuous acoramidis group and 4 in the placebo to acoramidis group. [f]Data at the time of randomization in ATTRibute-CM (not at OLE entry). [g]Calculated as (randomization date – date of ATTR-CM diagnosis)/365.25. [h]Data missing for 1 participant in the placebo to acoramidis group. [i]Data missing for 8 participants in the continuous acoramidis group and 2 in the placebo to acoramidis group.
eGFR, estimated glomerular filtration rate; IQR, interquartile range; NAC, National Amyloidosis Center; NT-proBNP, B-type natriuretic peptide; NYHA, New York Heart Association; SD, standard deviation; v, variant; wt, wild type.

Reductions in ACM/First CVH Through Month 42 With Continuous Acoramidis Were Consistently Observed in all Subgroups

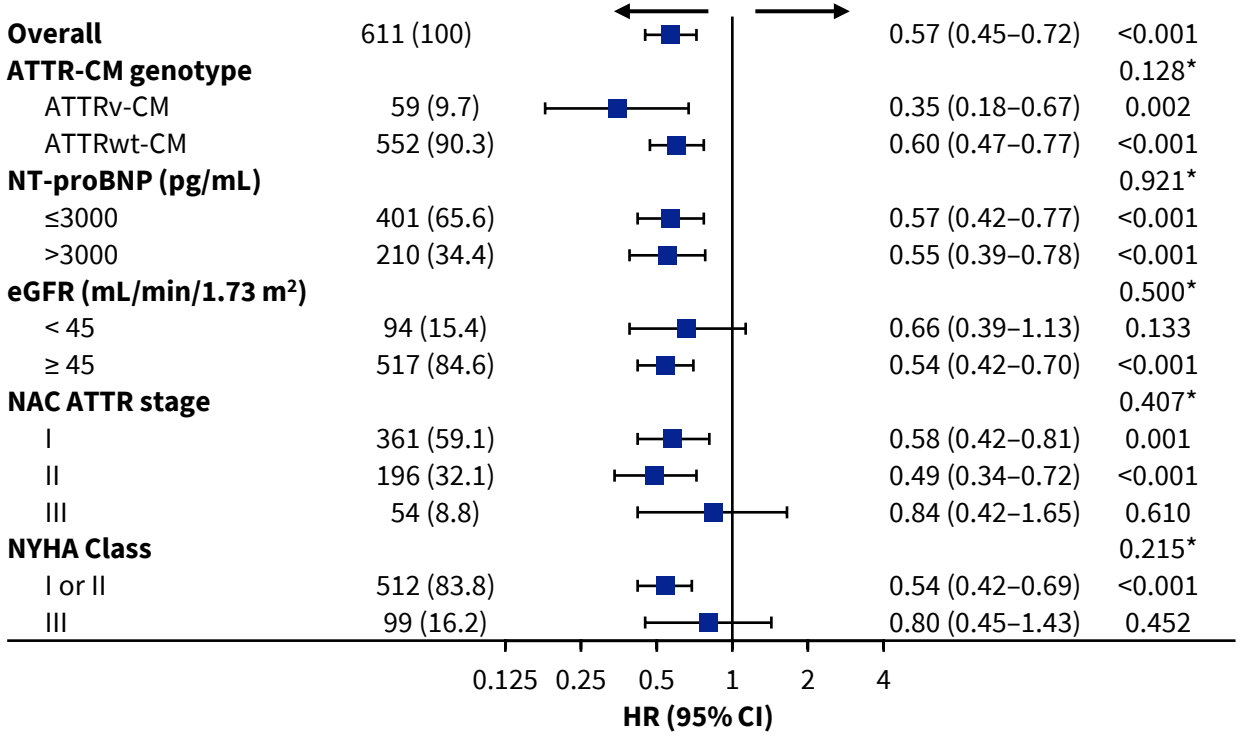
ACM/First CVH by Participant Demographics

Subgroup	No. of participants (%)	HR (95% CI)	*p* value
Overall	611 (100)	0.57 (0.45–0.72)	<0.001
Sex			0.310*
Male	555 (90.8)	0.60 (0.47–0.76)	<0.001
Female	56 (9.2)	0.39 (0.18–0.85)	0.019
Age (years)			0.517*
<78	299 (48.9)	0.53 (0.38–0.74)	<0.001
≥78	312 (51.1)	0.62 (0.45–0.85)	0.003
Race			0.069*
Caucasian	537 (87.9)	0.63 (0.49–0.80)	<0.001
Non-Caucasian	74 (12.1)	0.30 (0.14–0.64)	0.002
Country			0.691*
United States	119 (19.5)	0.63 (0.39–1.02)	0.062
Rest of world	492 (80.5)	0.56 (0.43–0.73)	<0.001



ACM/First CVH by Disease Characteristics

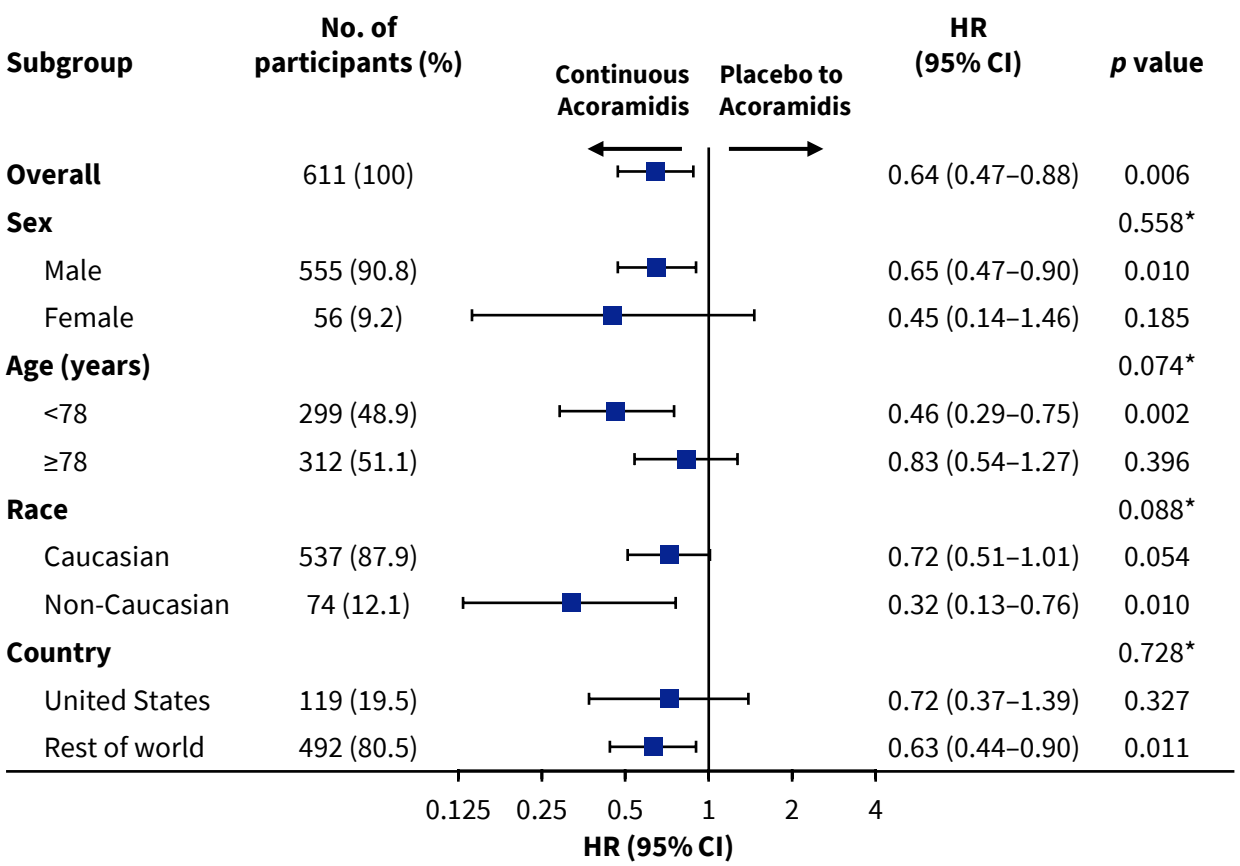
Subgroup	No. of participants (%)	HR (95% CI)	*p* value
Overall	611 (100)	0.57 (0.45–0.72)	<0.001
ATTR-CM genotype			0.128*
ATTRv-CM	59 (9.7)	0.35 (0.18–0.67)	0.002
ATTRwt-CM	552 (90.3)	0.60 (0.47–0.77)	<0.001
NT-proBNP (pg/mL)			0.921*
≤3000	401 (65.6)	0.57 (0.42–0.77)	<0.001
>3000	210 (34.4)	0.55 (0.39–0.78)	<0.001
eGFR (mL/min/1.73 m²)			0.500*
< 45	94 (15.4)	0.66 (0.39–1.13)	0.133
≥ 45	517 (84.6)	0.54 (0.42–0.70)	<0.001
NAC ATTR stage			0.407*
I	361 (59.1)	0.58 (0.42–0.81)	0.001
II	196 (32.1)	0.49 (0.34–0.72)	<0.001
III	54 (8.8)	0.84 (0.42–1.65)	0.610
NYHA Class			0.215*
I or II	512 (83.8)	0.54 (0.42–0.69)	<0.001
III	99 (16.2)	0.80 (0.45–1.43)	0.452



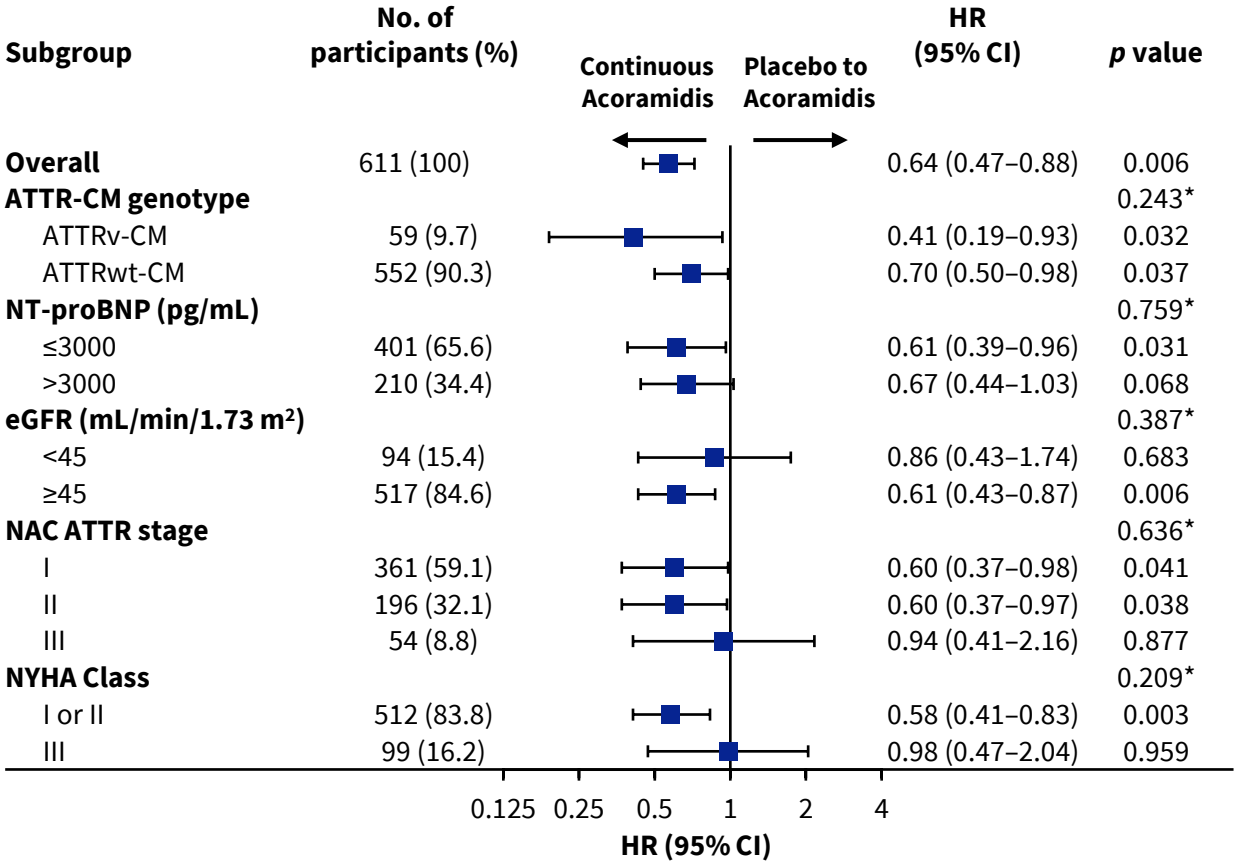
p values with * are from testing the interaction of subgroup × treatment; other *p* values are for testing the treatment difference at a given value of subgroup variable.
CI, confidence interval; HR, hazard ratio.

Reductions in ACM Through Month 42 With Continuous Acoramidis Were Consistently Observed in all Subgroups

ACM by Participant Demographics



ACM by Disease Characteristics



*p values with * are from testing the interaction of subgroup × treatment; other p values are for testing the treatment difference at a given value of subgroup variable.

Conclusions

Continuous acoramidis through Month 42 of the ATTRibute-CM OLE was associated with consistent clinical benefits across multiple clinically relevant subgroups

These 1-year findings from the ongoing ATTRibute-CM OLE show that long-term acoramidis treatment delivers durable risk reduction across ATTR-CM subgroups

The findings also highlight that early initiation of acoramidis is critical in reducing the long-term risks of ACM/first CVH and ACM alone

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