ACORAMIDIS REDUCES THE RISK OF ALL-CAUSE MORTALITY AND CARDIOVASCULAR-RELATED HOSPITALIZATION COMPARED WITH PLACEBO IN PARTICIPANTS WITH TRANSTHYRETIN AMYLOID CARDIOMYOPATHY AND EARLY HEART FAILURE SEVERITY REGARDLESS OF ATRIAL FIBRILLATION HISTORY: INSIGHTS FROM ATTRibute-CM

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INTRODUCTION

- AF is a common manifestation of ATTR-CM that can impact quality of life and is associated with increased risk of CVH[1,2]
- NYHA class is an independent predictor of mortality in ATTR-CM[3]
  - Patients with late HF severity (NYHA class III/IV) have a worse prognosis than those with early HF severity (NYHA class I/II)[4]
- Acoramidis, an oral TTR stabilizer that achieves near-complete (≥ 90%) TTR stabilization, is approved in the USA, Europe, Japan, and the UK for the treatment of ATTR-CM in adults[5–9]
- In the phase 3 ATTRibute-CM study,[a] acoramidis significantly reduced the risk of ACM or first CVH at Month 30 vs placebo, including in those with early HF severity[10]
  - In the OLE,[b] continuous acoramidis treatment through Month 42 reduced the risk of ACM or first CVH vs placebo-to-acoramidis[11]

OBJECTIVE:
To assess the effect of acoramidis on ACM and CVH in participants with ATTR-CM and early HF severity according to AF diagnosis at baseline

[a]ClinicalTrials.gov identifier: NCT03860935. [b]ClinicalTrials.gov identifier: NCT04988386.
ACM, all-cause mortality; AF, atrial fibrillation; AFL, atrial flutter; ATTR-CM, transthyretin amyloid cardiomyopathy; CVH, cardiovascular-related hospitalization; HF, heart failure; NYHA, New York Heart Association; OLE, open-label extension; TTR, transthyretin.

1. Thrall G, et al. *Am J Med*. 2006;119(5):448.e1-19. **2.** Sinigiani G, et al. *Heart Rhythm*. 2024;21(6):725-732. **3.** Cheng RK, et al. *JACC CardioOncol.* 2020;2(3):414-424. **4.** Rozenbaum MH, et al. *Eur Heart J Qual Care Clin Outcomes.* 2022;8(5):529-538. **5.** Judge DP, et al. *J Am Coll Cardiol*. 2019;74(3):285-295. **6.** BridgeBio Pharma, Inc. Prescribing Information, Attruby (acoramidis). FDA, 2024. Accessed October 6, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/216540s000lbl.pdf. **7.** BridgeBio Europe B.V. SmPC, Beyonttra (acoramidis). EMA, 2024. Accessed October 6, 2025. https://www.ema.europa.eu/en/documents/product-information/beyonttra-epar-product-information_en.pdf. **8.** Alexion. SmPC, Beyonttra (acoramidis). MHLW Japan, 2025. Accessed October 6, 2025. https://www.pmda.go.jp/PmdaSearch/iyakuDetail/ResultDataSetPDF/870056_2190048F1029_1_01. **9.** Bayer plc. SmPC, Beyonttra (acoramidis). MHRA UK, 2025. Accessed October 6, 2025. https://mhraproducts4853.blob.core.windows.net/docs/a59718d1af5328302357b1f6a18908322e4eb7f8. **10.** Judge DP, et al. *J Am Coll Cardiol.* 2025;85(10):1003-1014. **11.** Judge DP, et al. *Circulation*. 2025;151(9):601-611.

DEFINITIONS

AF diagnosis at baseline

1. AF medical history OR
2. The presence of AF or AFL on an electrocardiogram at enrollment

ACM

1. Death due to any cause OR
2. Receipt of a cardiac mechanical assist device OR
3. Receipt of a heart transplant

CVH

≥ 24 h: overnight stay

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

OR

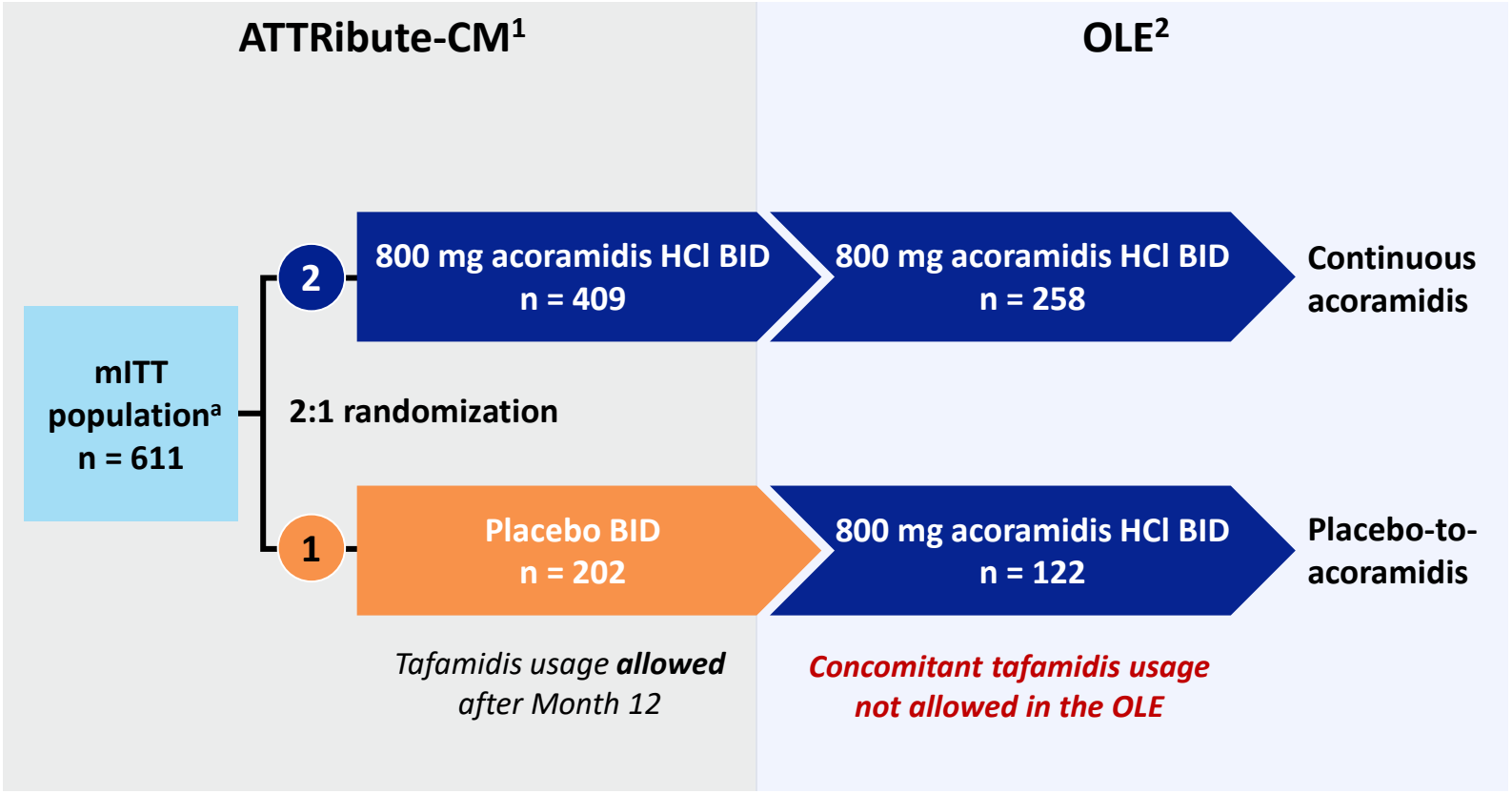
< 24 h: urgent HF visits

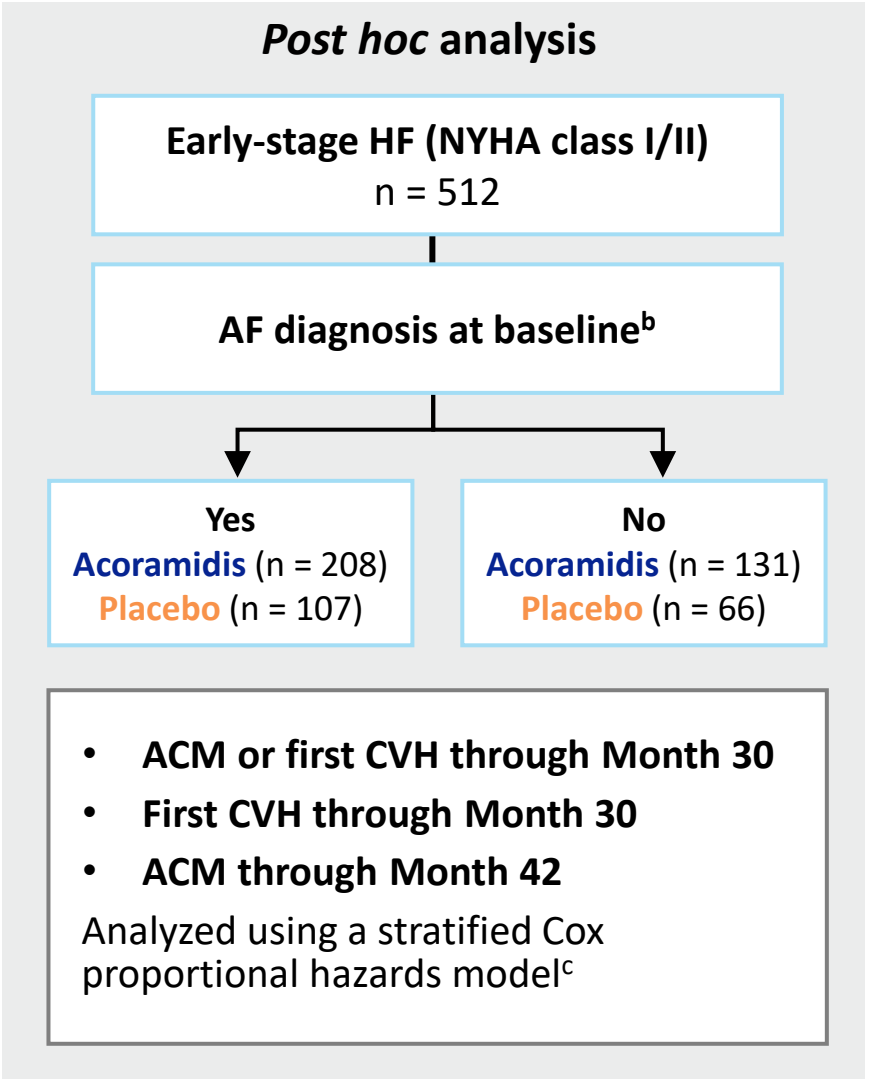
Visits to emergency department, urgent care, or day clinic for management of decompensated HF requiring treatment with an intravenous diuretic

- All events were adjudicated independently by the clinical events committee

ACM, all-cause mortality; AF, atrial fibrillation; AFL, atrial flutter; CVH, cardiovascular-related hospitalization; HF, heart failure.

POST HOC ANALYSIS OF ATTRibute-CM AND ITS OLE





[a]mITT population consisted of all randomized participants who received at least one dose of acoramidis or placebo, had at least one post-baseline efficacy evaluation, and had a baseline eGFR ≥ 30 mL/min/1.73 m^2. [b]Defined as AF medical history or the presence of AF or AFL on an electrocardiogram at enrollment. [c]With treatment, baseline 6MWD, and AF diagnosis at baseline and its interaction with treatment as model terms, and stratified by randomization stratification factors of genotype, NT-proBNP level, and eGFR from the interactive voice/web response system.

6MWD, 6-minute walk distance; ACM, all-cause mortality; AF, atrial fibrillation; AFL, atrial flutter; BID, twice daily; CVH, cardiovascular-related hospitalization; eGFR, estimated glomerular filtration rate; mITT, modified intention-to-treat; OLE, open-label extension; RCT, randomized controlled trial.

1. Gillmore JD, et al. *N Engl J Med*. 2024;390(2):132-142; **2.** Judge DP, et al. *Circulation.* 2025;151(9):601-611.

BASELINE DEMOGRAPHICS AND CHARACTERISTICS BY BASELINE AF STATUS IN PARTICIPANTS WITH EARLY HF SEVERITY

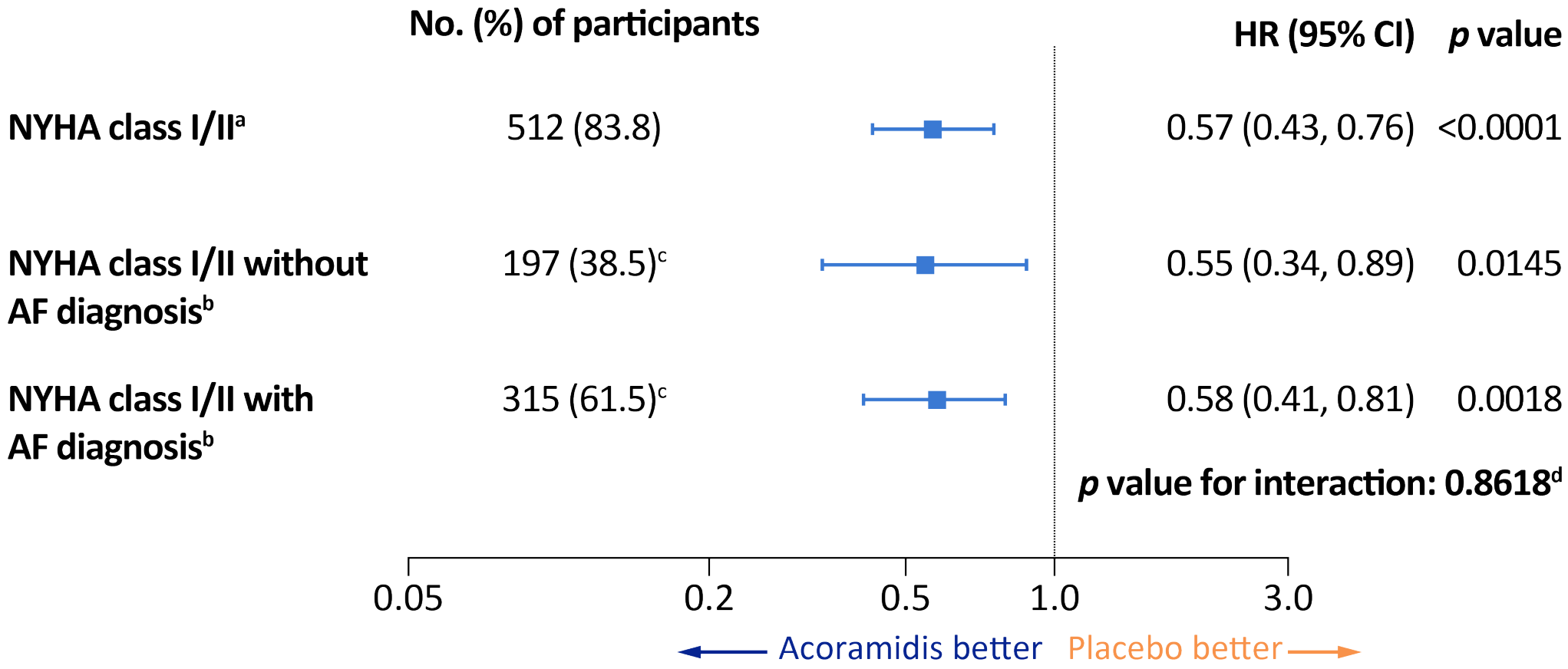
Baseline Demographic/Characteristic (mITT Population)		AF at Baseline			No AF at Baseline		
		Acoramidis (n = 208)	Placebo (n = 107)	Overall (N = 315)	Acoramidis (n = 131)	Placebo (n = 66)	Overall (N = 197)
Age, years	Mean (SD)	77.2 (6.6)	77.0 (6.7)	77.1 (6.6)	76.5 (6.8)	76.2 (6.7)	76.4 (6.7)
Sex, male	n (%)	196 (94.2)	101 (94.4)	297 (94.3)	115 (87.8)	57 (86.4)	172 (87.3)
Wild-type ATTR-CM[a]	n (%)	183 (88.0)	99 (92.5)	282 (89.5)	119 (90.8)	57 (86.4)	176 (89.3)
NYHA class							
NYHA class I	n (%)	30 (14.4)	8 (7.5)	38 (12.1)	21 (16.0)	9 (13.6)	30 (15.2)
NYHA class II	n (%)	178 (85.6)	99 (92.5)	277 (87.9)	110 (84.0)	57 (86.4)	167 (84.8)
6MWD, m	n Mean (SD)	208 364.9 (98.9)	107 363.2 (88.1)	315 364.3 (95.2)	130 403.9 (98.0)	66 374.2 (86.6)	196 393.9 (95.1)
KCCQ-OS score	n mean (SD)	207 72.4 (19.1)	107 73.4 (18.8)	314 72.7 (19.0)	131 77.8 (15.8)	66 75.8 (16.9)	197 77.1 (16.2)
NT-proBNP, pg/mL	n Median (Q1, Q3)	208 2485 (1524, 4181)	107 2363 (1240, 3851)	315 2449 (1435, 4086)	131 1542 (897, 2523)	66 1610 (752, 2852)	197 1543 (851, 2614)

- Participants with early HF severity and with an AF diagnosis at baseline had lower mean 6MWD and KCCQ-OS scores, and higher median NT-proBNP levels at study entry compared with those without an AF diagnosis at baseline

[a]TTR genotype was reported in the interactive voice/web response system at randomization.

6MWD, 6-minute walk distance; AF, atrial fibrillation; ATTR-CM, transthyretin amyloid cardiomyopathy; HF, heart failure; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire Overall Summary; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; Q1, first quartile; Q3, third quartile; SD, standard deviation.

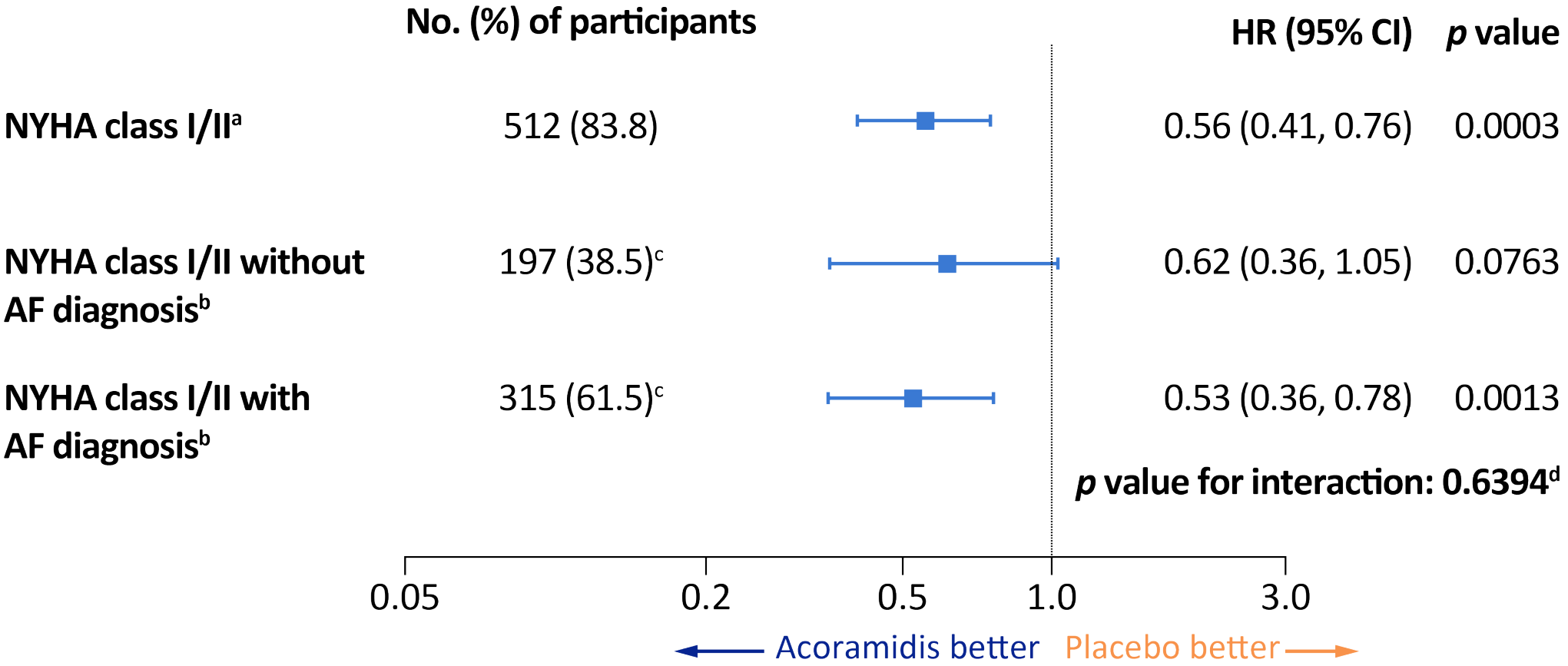
ACORAMIDIS REDUCED THE RISK OF ACM OR FIRST CVH THROUGH MONTH 30 IN PARTICIPANTS WITH EARLY HF SEVERITY, REGARDLESS OF AF DIAGNOSIS AT BASELINE



[a]Analysis conducted in all mITT population participants, using a stratified Cox proportional hazards model with treatment, baseline 6MWD, NYHA class HF at baseline (I/II vs III) and its interaction with treatment as model terms, and stratified by randomization stratification factors of genotype, NT-proBNP level, and eGFR from the interactive voice/web response system. [b]Subgroup analyses conducted in mITT population participants with NYHA class I/II HF, using a stratified Cox proportional hazards model with treatment, baseline 6MWD, and AF diagnosis at baseline and its interaction with treatment as model terms, and stratified by randomization stratification factors of genotype, NT-proBNP level, and eGFR from the interactive voice/web response system. [c]Total number of participants with NYHA class I/II HF was used as the denominator. [d]*p* value from testing the interaction of subgroup x treatment.

6MWD, 6-minute walk distance; ACM, all-cause mortality; AF, atrial fibrillation; CI, confidence interval; CVH, cardiovascular-related hospitalization; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; mITT, modified intention-to-treat; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association.

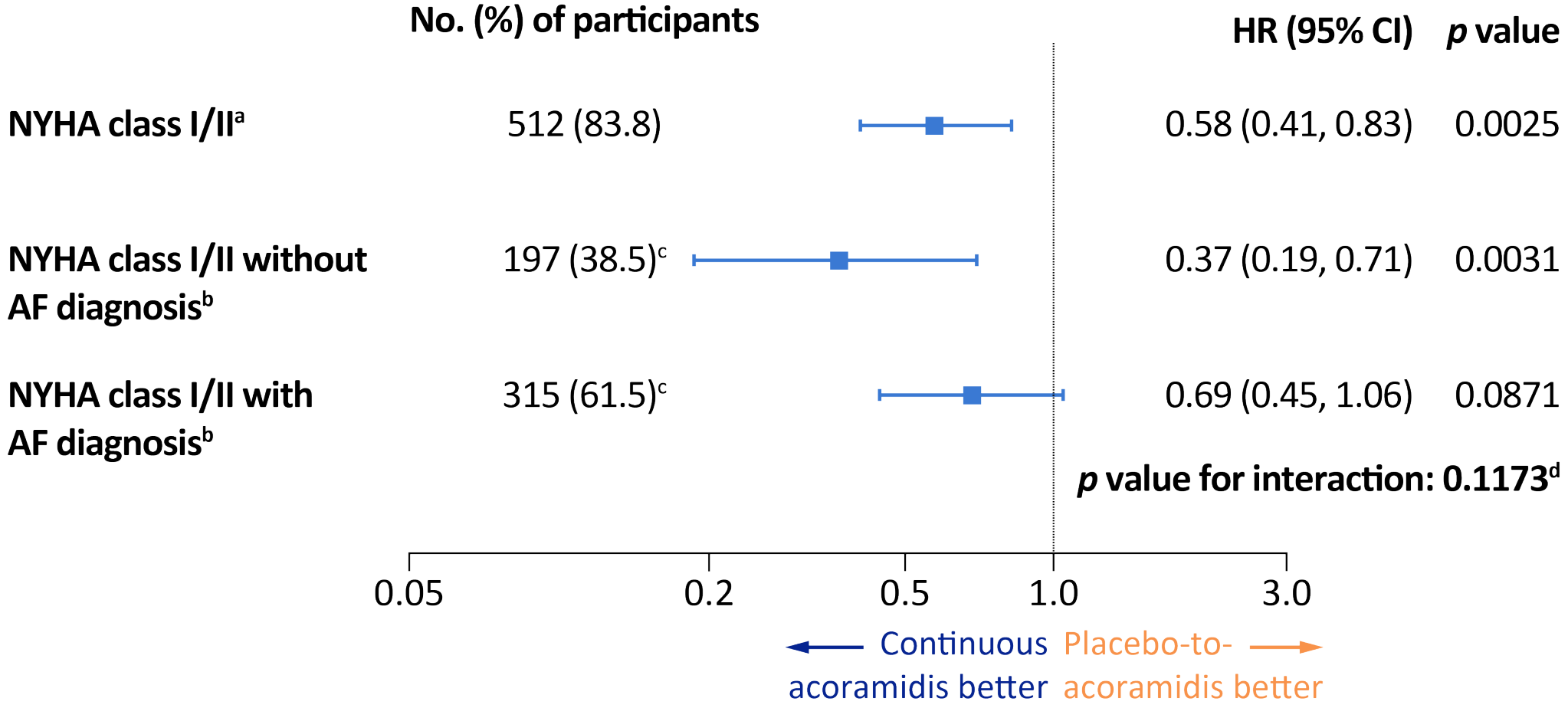
POINT ESTIMATES FAVORED ACORAMIDIS OVER PLACEBO FOR FIRST CVH THROUGH MONTH 30 IN PARTICIPANTS WITH EARLY HF SEVERITY, REGARDLESS OF AF DIAGNOSIS AT BASELINE



[a]Analysis conducted in all mITT population participants, using a stratified Cox proportional hazards model with treatment, baseline 6MWD, NYHA class HF at baseline (I/II vs III) and its interaction with treatment as model terms, and stratified by randomization stratification factors of genotype, NT-proBNP level, and eGFR from the interactive voice/web response system. [b]Subgroup analyses conducted in mITT population participants with NYHA class I/II HF, using a stratified Cox proportional hazards model with treatment, baseline 6MWD, and AF diagnosis at baseline and its interaction with treatment as model terms, and stratified by randomization stratification factors of genotype, NT-proBNP level, and eGFR from the interactive voice/web response system. [c]Total number of participants with NYHA class I/II HF was used as the denominator. [d]*p* value from testing the interaction of subgroup x treatment.

6MWD, 6-minute walk distance; AF, atrial fibrillation; CI, confidence interval; CVH, cardiovascular-related hospitalization; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; mITT, modified intention-to-treat; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association.

POINT ESTIMATES FAVORED ACORAMIDIS OVER PLACEBO FOR ACM THROUGH MONTH 42 IN PARTICIPANTS WITH EARLY HF SEVERITY, REGARDLESS OF AF DIAGNOSIS AT BASELINE



[a]Analysis conducted in all mITT population participants, using a stratified Cox proportional hazards model with treatment, baseline 6MWD, NYHA class HF at baseline (I/II vs III) and its interaction with treatment as model terms, and stratified by randomization stratification factors of genotype, NT-proBNP level, and eGFR from the interactive voice/web response system. [b]Subgroup analyses conducted in mITT population participants with NYHA class I/II HF, using a stratified Cox proportional hazards model with treatment, baseline 6MWD, and AF diagnosis at baseline and its interaction with treatment as model terms, and stratified by randomization stratification factors of genotype, NT-proBNP level, and eGFR from the interactive voice/web response system. [c]Total number of participants with NYHA class I/II HF was used as the denominator. [d]*p* value from testing the interaction of subgroup x treatment.

6MWD, 6-minute walk distance; ACM, all-cause mortality; AF, atrial fibrillation; CI, confidence interval; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; mITT, modified intention-to-treat; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association.

CONCLUSIONS

- A lower risk for ACM and CVH outcomes was observed with acoramidis vs placebo in participants with early HF severity, regardless of AF diagnosis at baseline
- The findings are consistent with previously reported results from ATTRibute-CM and its OLE that demonstrate reduced disease progression with acoramidis[1,2]

ACM, all-cause mortality; AF, atrial fibrillation; CVH, cardiovascular-related hospitalization; HF, heart failure; OLE, open-label extension.

1. Judge DP, et al. *Circulation.* 2025;151(9):601-611. **2.** Gillmore JD, et al. *N Engl J Med*. 2024;390(2):132-142.