ACORAMIDIS IMPROVED CLINICAL OUTCOMES, FUNCTION, QUALITY OF LIFE, AND NT-proBNP IN PATIENTS WITH TRANSTHYRETIN AMYLOID CARDIOMYOPATHY REGARDLESS OF ATRIAL FIBRILLATION STATUS AT BASELINE

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INTRODUCTION

- AF is a common manifestation of ATTR-CM that can impact quality of life and is associated with poor outcomes, including an increased risk of CVH[1–3]
- 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 wild-type and variant ATTR-CM in adults[4–8]
- In the phase 3 ATTRibute-CM study,[a] acoramidis treatment significantly reduced the risk of ACM or first CVH through Month 30, and improved 6MWD, KCCQ-OS scores, and NT-proBNP levels relative to placebo[9]
- The clinical efficacy of acoramidis in patients with ATTR-CM, stratified by their baseline AF diagnosis, has not yet been reported

OBJECTIVE:

To assess the effect of acoramidis on ACM or first CVH, 6MWD, KCCQ-OS score, and NT-proBNP level to Month 30 in participants with ATTR-CM according to AF status at baseline

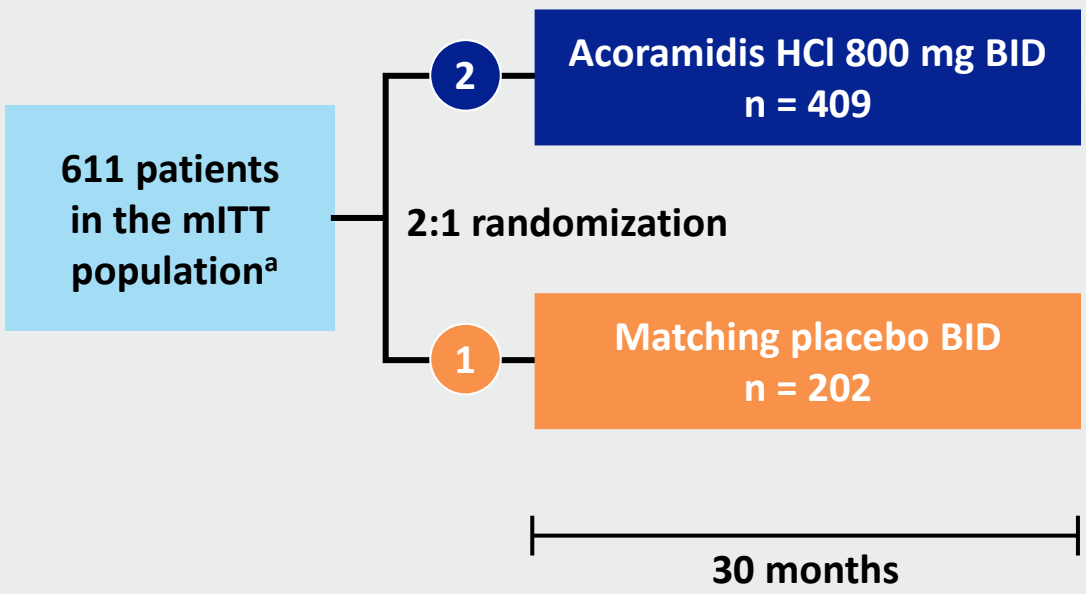
[a]ClinicalTrials.gov identifier: NCT03860935.

6MWD, 6-minute walk distance; ACM, all-cause mortality; AF, atrial fibrillation; ATTR-CM, transthyretin amyloid cardiomyopathy; CVH, cardiovascular-related hospitalization; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire-Overall Summary; NT-proBNP, N-terminal pro-B-type natriuretic peptide; TTR, transthyretin.

1. Prasad P, et al. *Circulation*. 2022;146(22):1730-1732. **2.** Thrall G, et al. *Am J Med*. 2006;119(5):448.e1-19. **3.** Chew DS, et al. *Circ Arrhythm Electrophysiol*. 2022;15(2):e010304. **4.** Judge DP, et al. *J Am Coll Cardiol*. 2019;74(3):285-295. **5.** BridgeBio Pharma, Inc. Prescribing Information, Attruby (acoramidis). FDA, 2024. Accessed October 6, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/216540s000lbl.pdf. **6.** 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. **7.** Alexion. SmPC, Beyonttra (acoramidis). MHLW Japan, 2025. Accessed October 6, 2025. https://www.pmda.go.jp/PmdaSearch/iyakuDetail/ResultDataSetPDF/870056_2190048F1029_1_01. **8.** Bayer plc. SmPC, Beyonttra (acoramidis). MHRA UK, 2025. Accessed October 6, 2025. https://mhraproducts4853.blob.core.windows.net/docs/a59718d1af5328302357b1f6a18908322e4eb7f8. **9.** Gillmore JD, et al. *N Engl J Med*. 2024;390(2):132-142.

ATTRibute-CM: *POST HOC* ANALYSIS

ATTRibute-CM[1]



Post Hoc Analysis

AF diagnosis at baseline
(recorded medical history of AF
or presence of AF or atrial flutter on ECG at baseline)

Yes
Acoramidis: n = 255 (62.3%)
Placebo: n = 129 (63.9%)

No
Acoramidis: n = 154 (37.7%)
Placebo: n = 73 (36.1%)

ACM or first CVH through Month 30

- Stratified Cox proportional hazards model,[b] stratified by randomization factors[c]

6MWD, KCCQ-OS scores, NT-proBNP levels

- Changes from baseline to Month 30 were analyzed using an MMRM

[a]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 of ≥ 30 mL/min/1.73 m^2. [b]With treatment as an explanatory factor and baseline 6MWD, AF diagnosis at baseline, and the interaction between AF diagnosis at baseline and treatment as covariates. [c]Genotype, NT-proBNP level, and eGFR.
6MWD, 6-minute walk distance; ACM, all-cause mortality; AF, atrial fibrillation; BID, twice a day; CVH, cardiovascular-related hospitalization; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire-Overall Summary; mITT, modified intention-to-treat; MMRM, mixed effects model for repeated measures; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

1. Gillmore JD, et al. *N Engl J Med*. 2024;390(2):132-142.

BASELINE DEMOGRAPHICS AND CHARACTERISTICS BY BASELINE AF STATUS

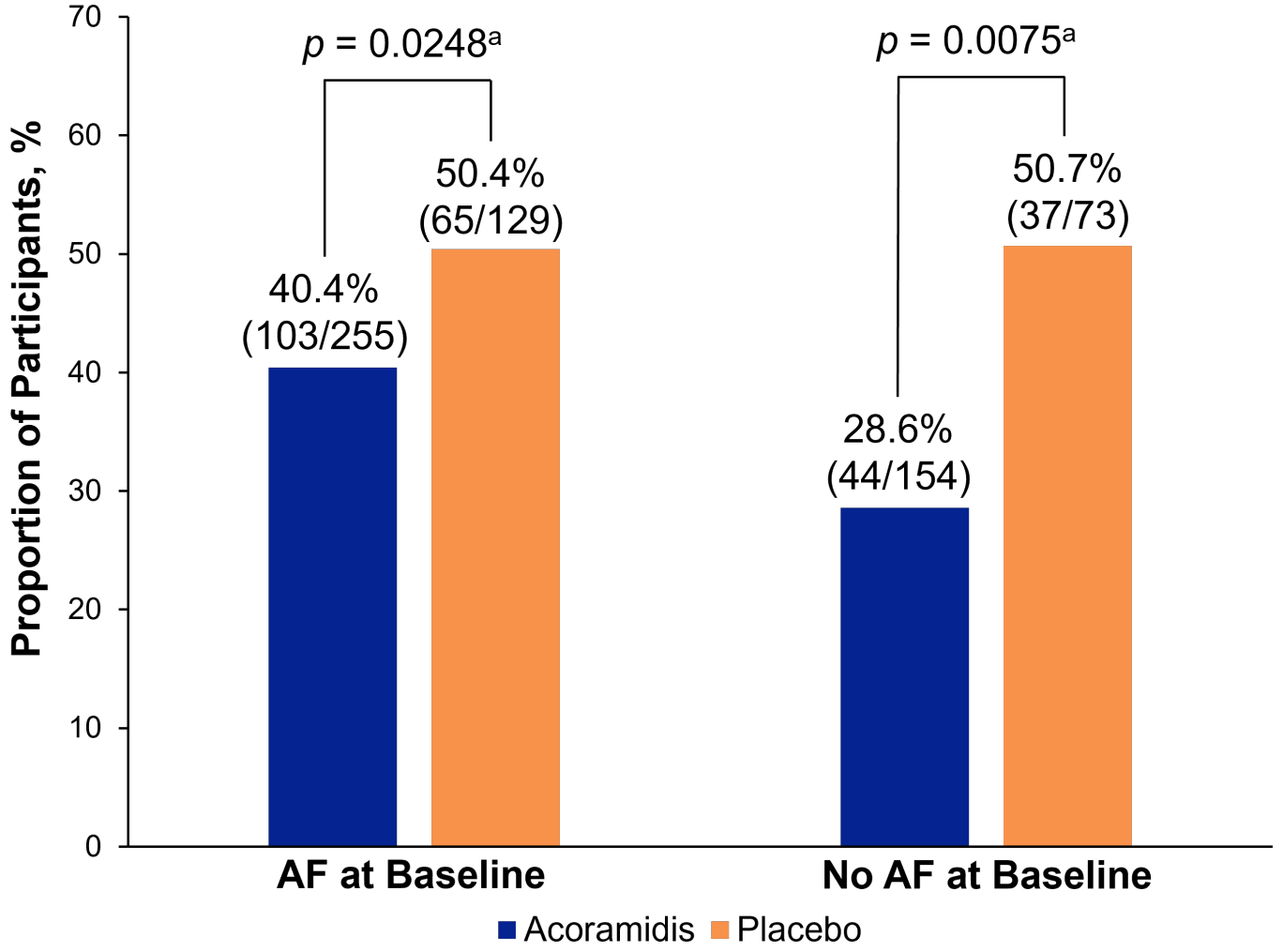
Baseline Demographic/Characteristic (mITT Population)		AF at Baseline			No AF at Baseline		
		Acoramidis (n = 255)	Placebo (n = 129)	Overall (N = 384)	Acoramidis (n = 154)	Placebo (n = 73)	Overall (N = 227)
Age, years	**Mean (SD)**	77.7 (6.4)	77.4 (6.7)	77.6 (6.5)	76.8 (6.7)	76.2 (6.7)	76.6 (6.7)
Sex, male	**n (%)**	238 (93.3)	118 (91.5)	356 (92.7)	136 (88.3)	63 (86.3)	199 (87.7)
Wild-type ATTR-CM[a]	**n (%)**	229 (89.8)	121 (93.8)	350 (91.1)	141 (91.6)	61 (83.6)	202 (89.0)
NYHA functional class I II III	**n (%)**	 30 (11.8) 178 (69.8) 47 (18.4)	 8 (6.2) 99 (76.7) 22 (17.1)	 38 (9.9) 277 (72.1) 69 (18.0)	 21 (13.6) 110 (71.4) 23 (14.9)	 9 (12.3) 57 (78.1) 7 (9.6)	 30 (13.2) 167 (73.6) 30 (13.2)
6MWD, m	**n** **Mean (SD)**	255 348.1 (100.8)	129 344.6 (95.0)	384 347.0 (99.0)	152 387.3 (103.6)	73 363.7 (91.0)	225 380.0 (100.1)
KCCQ-OS score	**n** **Mean (SD)**	254 69.3 (20.4)	129 68.5 (21.6)	383 69.0 (20.8)	154 75.8 (16.7)	73 74.1 (18.5)	227 75.2 (17.3)
NT-proBNP, pg/mL	**n** **Median (Q1, Q3)**	255 2613 (1733, 4519)	129 2433 (1307, 4115)	384 2566 (1555, 4383)	154 1562 (915, 2573)	73 1882 (817, 2895)	227 1717 (880, 2852)

› Participants with an AF diagnosis at baseline generally had lower mean 6MWD and KCCQ-OS scores and higher median NT-proBNP levels than those without an AF diagnosis at baseline; other baseline characteristics were comparable between groups

[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; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire-Overall Summary; mITT, modified intention-to-treat; n, number of participants who had data available at baseline; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; Q1, first quartile; Q3, third quartile; SD, standard deviation; TTR, transthyretin.

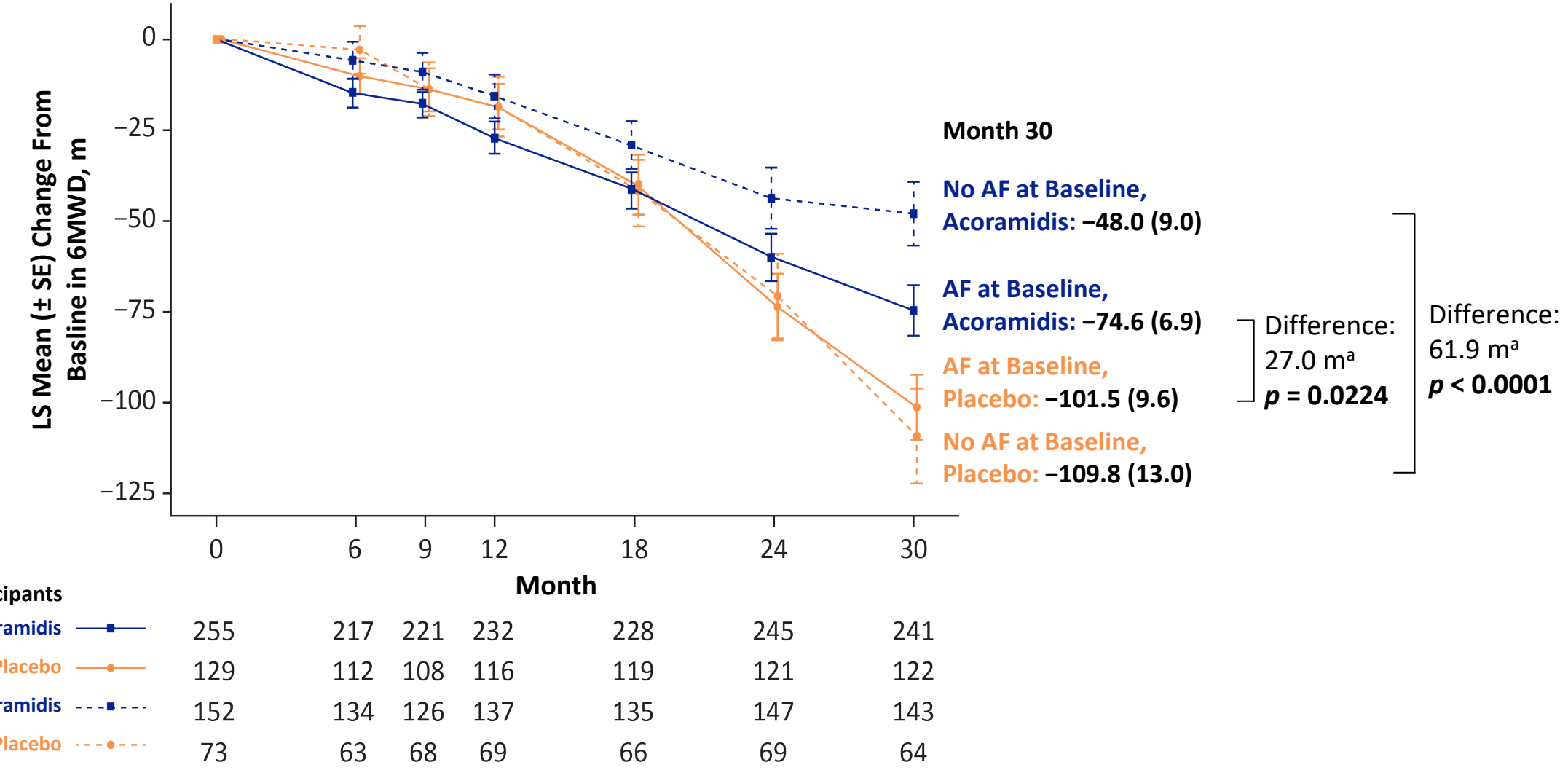
OCCURRENCE OF ACM OR FIRST CVH THROUGH MONTH 30 WAS SIGNIFICANTLY LOWER WITH ACORAMIDIS VS PLACEBO



[a]The occurrence of ACM or first CVH through Month 30 was compared between groups using a stratified Cox proportional hazards model that included treatment as an explanatory factor, and baseline 6MWD, AF diagnosis at baseline, and the interaction between AF diagnosis at baseline and treatment as covariates.

6MWD, 6-minute walk distance; ACM, all-cause mortality; AF, atrial fibrillation; CVH, cardiovascular-related hospitalization.

ACORAMIDIS REDUCED THE DECLINE IN 6MWD VS PLACEBO REGARDLESS OF AF DIAGNOSIS AT BASELINE



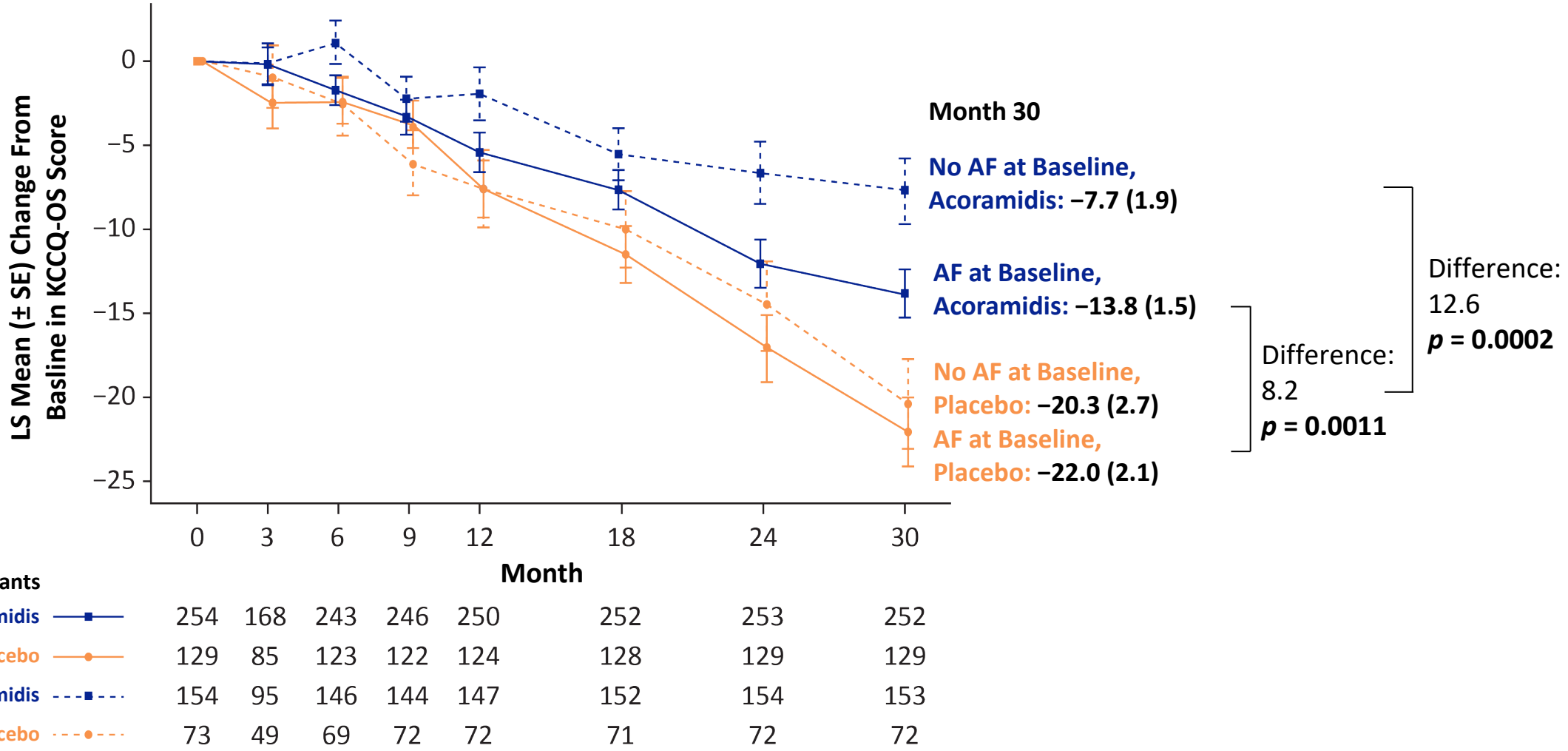
Number of Participants	0	6	9	12	18	24	30
AF at Baseline, Acoramidis	255	217	221	232	228	245	241
AF at Baseline, Placebo	129	112	108	116	119	121	122
No AF at Baseline, Acoramidis	152	134	126	137	135	147	143
No AF at Baseline, Placebo	73	63	68	69	66	69	64

Changes from baseline were analyzed using an MMRM, with treatment group, visit, AF diagnosis at baseline, genotype, NT-proBNP level, eGFR, treatment-group-by-visit interaction, Baseline AF-diagnosis-by-treatment-group interaction, Baseline AF-diagnosis-by-visit interaction, and baseline AF-diagnosis-by-treatment-group-by-visit interaction as factors, and baseline value as a covariate.

[a]After rounding.

6MWD, 6-minute walk distance; AF, atrial fibrillation; eGFR, estimated glomerular filtration rate; MMRM, mixed effects model for repeated measures; NT-proBNP, N-terminal pro-B-type natriuretic peptide; SE, standard error.

ACORAMIDIS REDUCED THE DECLINE IN KCCQ-OS SCORE VS PLACEBO REGARDLESS OF AF DIAGNOSIS AT BASELINE

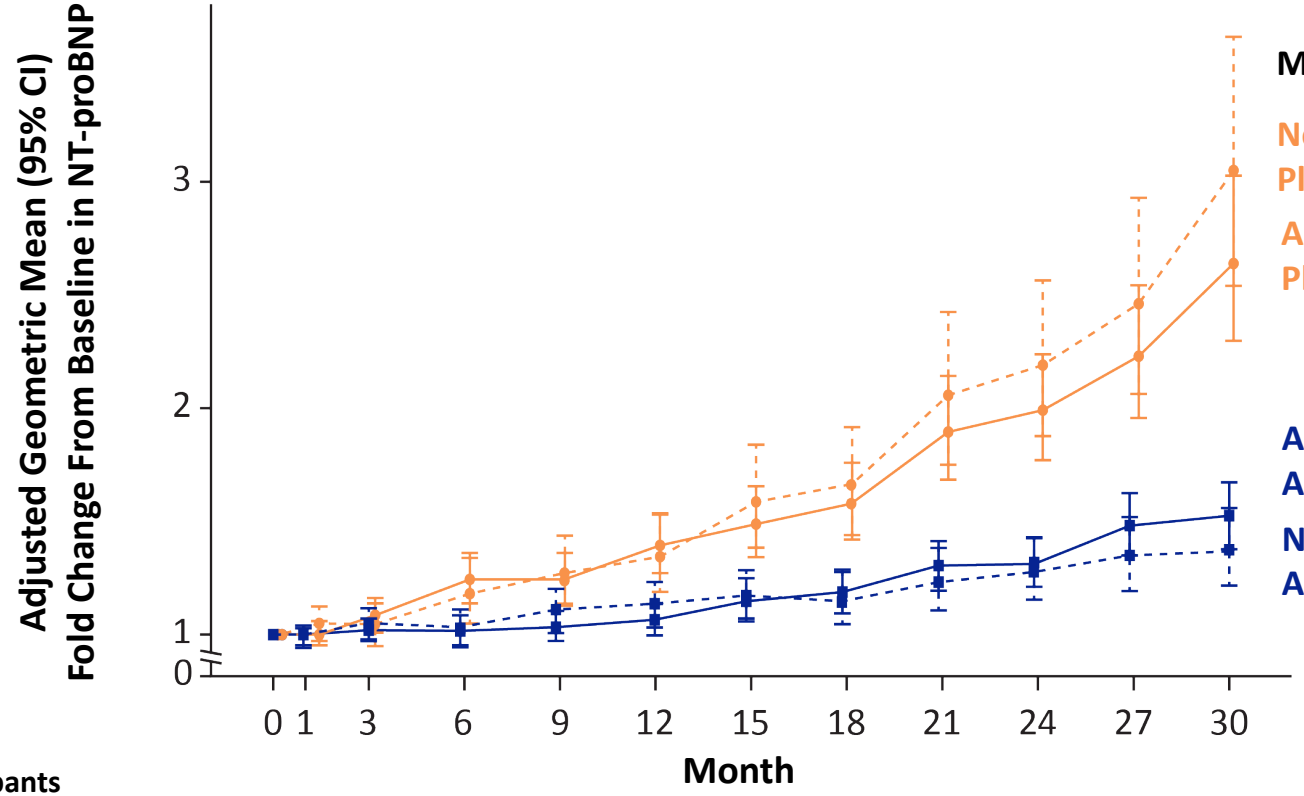


Number of Participants	0	3	6	9	12	18	24	30
AF at Baseline, Acoramidis	254	168	243	246	250	252	253	252
AF at Baseline, Placebo	129	85	123	122	124	128	129	129
No AF at Baseline, Acoramidis	154	95	146	144	147	152	154	153
No AF at Baseline, Placebo	73	49	69	72	72	71	72	72

Changes from baseline were analyzed using an MMRM, with treatment group, visit, AF diagnosis at baseline, genotype, NT-proBNP level, eGFR, treatment-group-by-visit interaction, Baseline AF-diagnosis-by-treatment-group interaction, Baseline AF-diagnosis-by-visit interaction, and baseline AF-diagnosis-by-treatment-group-by-visit interaction as factors, and baseline value as a covariate.

AF, atrial fibrillation; eGFR, estimated glomerular filtration rate; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire-Overall Summary; LS, least-squares; MMRM, mixed effects model for repeated measures; NT-proBNP, N-terminal pro-B-type natriuretic peptide; SE, standard error.

ACORAMIDIS ATTENUATED THE RISE IN NT-proBNP VS PLACEBO REGARDLESS OF AF DIAGNOSIS AT BASELINE



Number of Participants	0	1	3	6	9	12	15	18	21	24	27	30
AF at Baseline, Acoramidis	255	237	235	221	230	241	239	241	247	250	245	248
AF at Baseline, Placebo	129	116	118	117	113	119	122	125	127	128	120	128
No AF at Baseline, Acoramidis	154	135	130	135	131	142	143	142	146	151	150	149
No AF at Baseline, Placebo	73	69	66	64	67	71	68	70	72	69	69	70

Changes from baseline were analyzed using an MMRM, with treatment group, visit, baseline AF diagnosis, genotype, eGFR, treatment-group-by-visit interaction, baseline AF-diagnosis-by-treatment-group interaction, baseline AF-diagnosis-by-visit interaction, and baseline AF-diagnosis-by-treatment-group-by-visit interaction as factors, and baseline value as a covariate.

AF, atrial fibrillation; CI, confidence interval; eGFR, estimated glomerular filtration rate; MMRM, mixed effects model for repeated measures; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

CONCLUSIONS

- Regardless of baseline AF status, acoramidis was consistently associated with:
  - a reduction in ACM or first CVH
  - reduced declines in 6MWD and KCCQ-OS scores and
  - an attenuated rise in NT-proBNP levels, compared with placebo

- The limitations of this study include that participants were not randomized by their AF status at baseline and that AF occurrence was not evaluated as a time-dependent variable

- The durability and long-term clinical effects of acoramidis are being assessed in the open-label extension study[a]

[a]ClinicalTrials.gov identifier: NCT04988386.
6MWD, 6-minute walk distance; ACM, all-cause mortality; AF, atrial fibrillation; CVH, cardiovascular-related hospitalization; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire-Overall Summary; NT-proBNP, N-terminal pro-B-type natriuretic peptide.