ACORAMIDIS LOWERS NT-proBNP IN A LARGER PROPORTION OF ATTRibute-CM STUDY PARTICIPANTS WITH TRANSTHYRETIN AMYLOID CARDIOMYOPATHY COMPARED WITH PLACEBO, INDEPENDENT OF ATRIAL FIBRILLATION STATUS

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DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIPS WITH INDUSTRY AND ACKNOWLEDGMENTS

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INTRODUCTION

- ATTR-CM is characterized by destabilization of TTR and aggregation of amyloid fibrils in the heart, leading to progressive heart failure, impaired quality of life, hospitalizations, and death[1,2]
- AF is a frequent complication of heart failure in ATTR-CM, and its presence is a marker of disease progression[3]
- A progressive rise in NT-proBNP levels is also an independent prognostic marker of ATTR-CM progression, and higher NT-proBNP levels are observed in patients with ATTR-CM with superimposed AF than in those without AF[3,4]
- 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 wild-type and variant ATTR-CM in adults[5–9]
- In the ATTRibute-CM study,[a] acoramidis blunted the progressive rise in NT-proBNP levels compared with placebo in participants with ATTR-CM[10]

OBJECTIVE:

To assess the effect of acoramidis on ATTR-CM disease progression (based on NT-proBNP levels) according to AF status at baseline

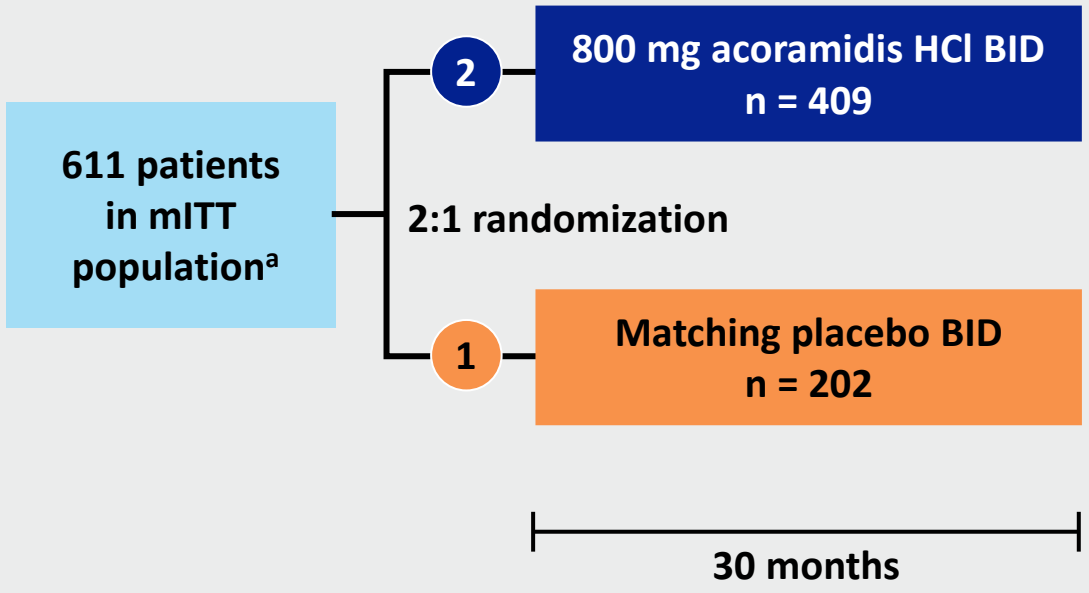
[a]ClinicalTrials.gov identifier: NCT03860935.

AF, atrial fibrillation; ATTR-CM, transthyretin amyloid cardiomyopathy; NT-proBNP, N-terminal pro-B-type natriuretic peptide; TTR, transthyretin.

1. Ruberg FL, Maurer MS. *JAMA*. 2024;331(9):778-791. **2.** Lane T, et al. *Circulation*. 2019;140:16-26. **3.** Witteles R, et al. *JACC CardioOncol*. 2024;6(4):592-598. **4.** Ioannou A, et al. *J Am Coll Cardiol*. 2024;83(14):1276-1291. **5.** Judge DP, et al. *J Am Coll Cardiol*. 2019;74(3):285-295. **6.** BridgeBio Pharma, Inc. Prescribing Information, Attruby (acoramidis). 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 3, 2025. https://mhraproducts4853.blob.core.windows.net/docs/a59718d1af5328302357b1f6a18908322e4eb7f8. **10.** Gillmore JD, et al. *N Engl J Med*. 2024;390(2):132-142.

ATTRibute-CM: *POST HOC* ANALYSIS

ATTRibute-CM[1]

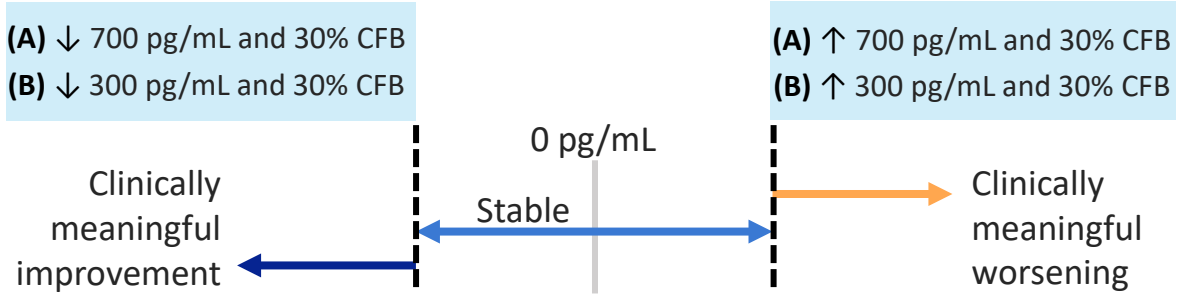


Post Hoc Descriptive Analysis[b]

Effect of acoramidis on NT-proBNP levels in subgroups with or without:

1. AF diagnosis at baseline (recorded AF medical history or presence of AF/AFL on an ECG at enrollment)
2. ≥ 1 AF/AFL TEAE during the study[c]
3. AF/AFL at any time (defined as 1 and/or 2)

NT-proBNP Cut-Off Levels and Percentage CFB for Disease Progression Categories for Analysis



Threshold definitions based on two reports:

(A) An increase > 700 pg/mL and > 30% (associated with increased risk of death[2])

(B) An increase > 300 pg/mL and > 30% (defined by expert consensus[3])

[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]Conducted in mITT population participants who had baseline and Month 30 NT-proBNP assessments available. [c]AF/AFL TEAEs were identified using 'atrial fibrillation', 'atrial flutter', and 'cardiac flutter' MedDRA preferred terms.

AF, atrial fibrillation; AFL, atrial flutter; BID, twice a day; CFB, change from baseline; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; mITT, modified intention-to-treat; NT-proBNP, N-terminal pro-B-type natriuretic peptide; TEAE, treatment-emergent adverse event.

1. Gillmore JD, et al. *N Engl J Med*. 2024;390(2):132-142. **2.** Ioannou A, et al. *J Am Coll Cardiol*. 2024;83(14):1276-1291. **3.** Garcia-Pavia P, et al. *Eur J Heart Fail*. 2021;23(6):895-905.

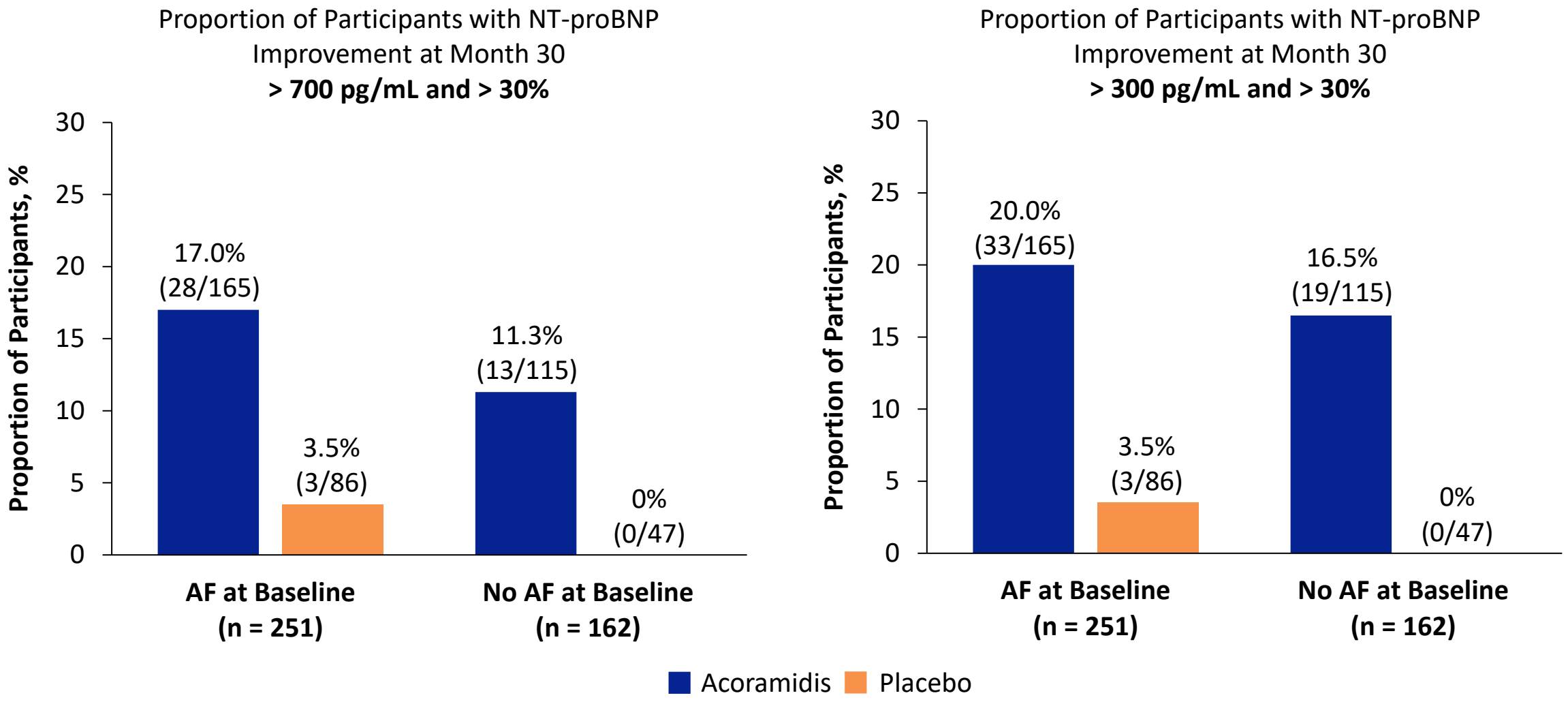
BASELINE DEMOGRAPHICS AND CHARACTERISTICS BY BASELINE AF STATUS

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)
NAC ATTR stage[b]	n (%)						
I		138 (54.1)	70 (54.3)	208 (54.2)	103 (66.9)	50 (68.5)	153 (67.4)
II		88 (34.5)	49 (38.0)	137 (35.7)	42 (27.3)	17 (23.3)	59 (26.0)
III		29 (11.4)	10 (7.8)	39 (10.2)	9 (5.8)	6 (8.2)	15 (6.6)
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 6MWD and KCCQ-OS scores and higher NT-proBNP levels, and were more frequently categorized as having higher NAC ATTR stages, than those without an AF diagnosis at baseline

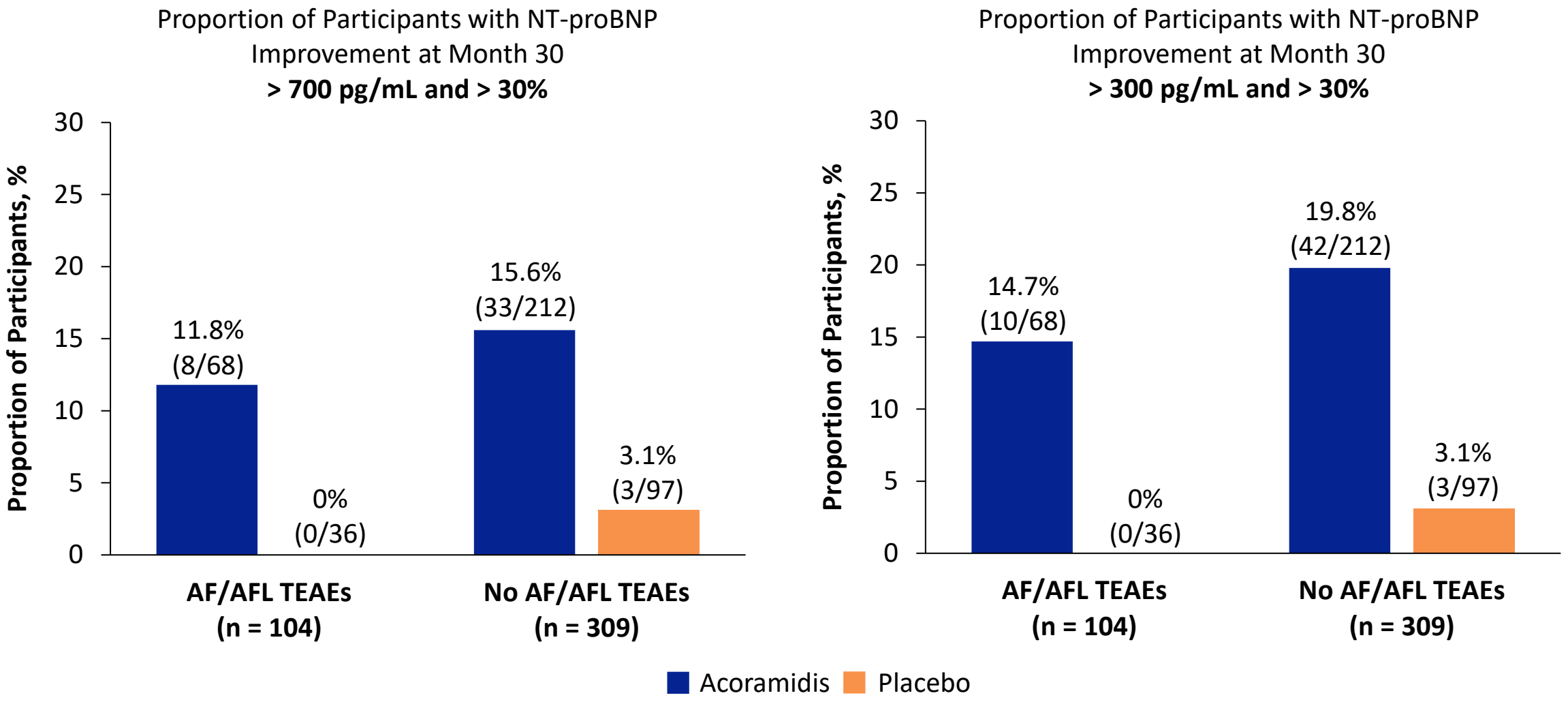
[a]TTR genotype was reported in the interactive voice/web response system at randomization. [b]NAC ATTR stage: NAC ATTR stage I, defined as NT-proBNP ≤ 3000 pg/mL and eGFR ≥ 45 mL/min/1.73 m^2; stage III, defined as NT-proBNP > 3000 pg/mL and eGFR < 45 mL/min/1.73 m^2; the remainder were categorized as stage II when both NT-proBNP and eGFR were not missing.
6MWD, 6-minute walk distance; AF, atrial fibrillation; ATTR, transthyretin amyloidosis; eGFR, estimated glomerular filtration rate; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire Overall Summary; mITT, modified intention-to-treat; n, number of participants who had data available at baseline; NAC, National Amyloidosis Centre; NT-proBNP, N-terminal pro-B-type natriuretic peptide; Q1, first quartile; Q3, third quartile; SD, standard deviation; TTR, transthyretin.

ACORAMIDIS IMPROVED NT-proBNP LEVELS AT MONTH 30 VS PLACEBO, REGARDLESS OF AF DIAGNOSIS AT BASELINE



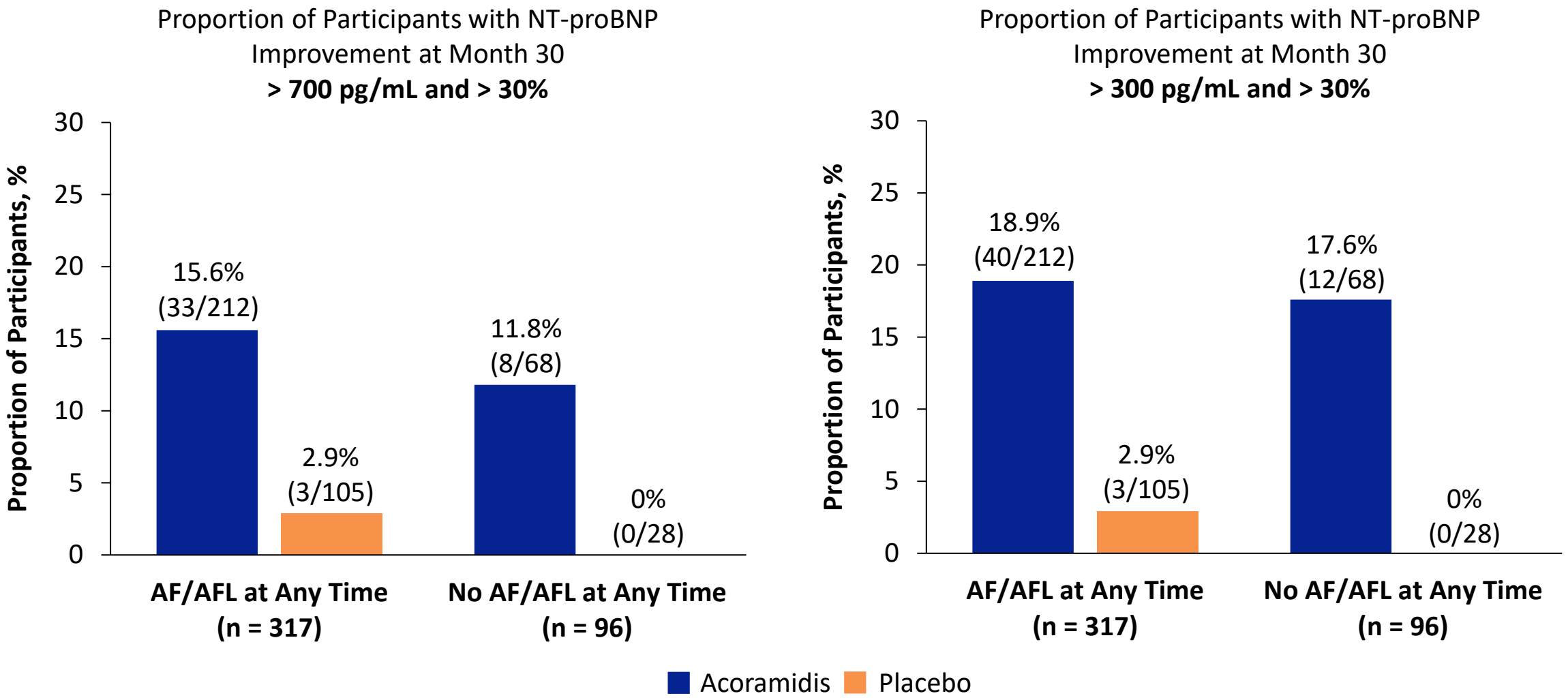
Data are for participants with non-missing NT-proBNP levels at baseline and Month 30 in the mITT population.
AF, atrial fibrillation; mITT, modified intention-to-treat; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

ACORAMIDIS IMPROVED NT-proBNP LEVELS AT MONTH 30 VS PLACEBO, REGARDLESS OF OCCURRENCE OF AF/AFL TEAEs DURING THE STUDY



Data are for participants with non-missing NT-proBNP levels at baseline and Month 30 in the mITT population.
AF, atrial fibrillation; AFL, atrial flutter; mITT, modified intention-to-treat; NT-proBNP, N-terminal pro-B-type natriuretic peptide; TEAE, treatment-emergent adverse event.

ACORAMIDIS IMPROVED NT-proBNP LEVELS AT MONTH 30 VS PLACEBO, REGARDLESS OF AF/AFL AT ANY TIME (AT BASELINE OR DURING THE STUDY[a])



Data are for participants with non-missing NT-proBNP levels at baseline and Month 30 in the mITT population.
[a]AF diagnosis at baseline or incidence of an AF/AFL TEAE during the study.
AF, atrial fibrillation; AFL, atrial flutter; mITT, modified intention-to-treat; NT-proBNP, N-terminal pro-B-type natriuretic peptide; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- Absolute proportions of participants with clinically meaningful NT-proBNP improvements at Month 30 were about 15% higher with acoramidis than with placebo, regardless of baseline AF status or AF/AFL during the study
- Findings were consistent across NT-proBNP reduction thresholds (> 700 pg/mL and > 30%, OR > 300 pg/mL and > 30%)
- Limitations of these analyses are that participants were not randomized by their AF status at baseline and that AF occurrence was not evaluated as a time-dependent variable
- Durability and long-term clinical effects of acoramidis are being assessed in the ongoing open-label extension study[a]

[a]ClinicalTrials.gov identifier: NCT04988386.
AF, atrial fibrillation; AFL, atrial flutter; NT-proBNP, N-terminal pro-B-type natriuretic peptide.