Acoramidis Improves Serum Transthyretin Levels in Patients With Wild-Type or Variant Transthyretin Amyloid Cardiomyopathy – Results From ATTRibute-CM

Prem Soman,[1] Mathew S. Maurer,[2] Nitasha Sarswat,[3] Martha Grogan,[4] Amrut Ambardekar,[5] Anique Ducharme,[6] Steen Hvitfeldt Poulsen,[7] Justin L. Grodin,[8,9] John Berk,[10] Alan X. Ji,[11] Satish Rao,[11] Jean-François Tamby,[11] Adam Castaño,[11] Jonathan C. Fox,[11] and Uma Sinha[11]

[1]Division of Cardiology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA; [2]Columbia College of Physicians and Surgeons, New York, NY, USA; [3]University of Chicago Medicine, Chicago, IL, USA; [4]Mayo Clinic, Rochester, MN, USA; [5]University of Colorado, Aurora, CO, USA; [6]Department of Medicine, Montreal Heart Institute, Université de Montréal, Montreal, Quebec, Canada; [7]Aarhus University Hospital, Aarhus, Denmark; [8]Parkland Health and Hospital System, Dallas, TX, USA; [9]University of Texas Southwestern Medical Center, Dallas, TX, USA; [10]Boston University School of Medicine, Boston, MA, USA; [11]BridgeBio Pharma, Inc., San Francisco, CA, USA

Poster: 118-11

Scan QR code to access a PDF copy of the poster

PURPOSE

- **To determine the effect of acoramidis on serum transthyretin (sTTR) levels in participants with variant (ATTRv-CM) or wild-type (ATTRwt-CM) transthyretin amyloid cardiomyopathy from the ATTRibute-CM study (NCT03860935)**

CONCLUSIONS

- In ATTRibute-CM, acoramidis treatment resulted in rapid (by Day 28) and sustained increases in sTTR levels through Month 30 in participants with ATTRv-CM or ATTRwt-CM
  - At baseline, sTTR levels were lower in participants with ATTRv-CM than in those with ATTRwt-CM
  - Acoramidis treatment led to greater mean changes from baseline in sTTR levels in participants with ATTRv-CM than in those with ATTRwt-CM, resulting in similar absolute sTTR levels in the two genotype groups from Day 28 to Month 30
- These results demonstrate the ability of acoramidis to increase sTTR levels (a measure of TTR stabilization), irrespective of *TTR* genotype, and to overcome the lower baseline sTTR levels observed in the variant patient population
- Given the higher risk posed by ATTRv-CM than ATTRwt-CM, these results are of particular clinical relevance in meeting the distinct medical needs of the variant patient population

BACKGROUND

- Transthyretin amyloid cardiomyopathy (ATTR-CM) is a progressive disease characterized by the destabilization of transthyretin (TTR), which can occur owing to age-related factors (ATTRwt-CM) or inherited mutations in the *TTR* gene that produce pathogenic variants (ATTRv-CM)[1–3]
  - Greater TTR destabilization generally results in lower sTTR levels and an elevated risk of worse clinical disease[3–5]
  - Patients with ATTRv-CM typically have lower sTTR levels and earlier disease onset followed by more rapid clinical progression than patients with ATTRwt-CM[3,6]
- 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 adults with ATTR-CM[7–11]
- In the pivotal phase 3 ATTRibute-CM study, acoramidis treatment resulted in early (by Day 28) increases in sTTR levels that were sustained to Month 30, led to improved clinical outcomes compared with placebo ($p < 0.0001$), and was well tolerated[12]

METHODS

- The study design of ATTRibute-CM has been described previously[12]
- Briefly, adults aged 18–90 years with ATTR-CM were randomized 2:1 to receive acoramidis HCl 800 mg or matching placebo twice daily for 30 months[12]
  - Participants could initiate concomitant open-label tafamidis from Month 12 onwards, at the discretion of the investigator[12]
- Participants were diagnosed with ATTR-CM by either an endomyocardial biopsy or a positive technetium-99m-pyrophosphate or -bisphosphonate scan
- Efficacy analyses were conducted in the modified intention-to-treat (mITT) population, consisting of all randomized participants who had received at least one dose of acoramidis or placebo, had at least one efficacy evaluation after baseline, and had a baseline estimated glomerular filtration rate ≥ 30 mL/min/1.73 m^2
- sTTR concentrations were determined at baseline, on Day 28, and then every 3 months until Month 30 using a standardized clinical assay for sTTR performed in a central laboratory
- Percentage changes from baseline in sTTR levels were summarized descriptively

RESULTS

- In the mITT population at randomization, 59 participants were identified as having ATTRv-CM (acoramidis, n = 39; placebo, n = 20) and 552 participants were identified as having ATTRwt-CM (acoramidis, n = 370; placebo, n = 182; **Table 1**)
- Baseline demographics and characteristics were generally similar between treatment groups and genotypes in the mITT population (N = 611; **Table 1**)
  - The three most common *TTR* variants were p.V142I (n = 35), p.I88L (n = 7), and p.T80A (n = 5; **Table 2**)
- Median (first quartile [Q1], third quartile [Q3]) baseline sTTR levels were lower in participants with ATTRv-CM (acoramidis, 19.0 [13.0, 21.0] mg/dL; placebo, 18.0 [12.5, 20.0] mg/dL) than in those with ATTRwt-CM (acoramidis, 23.0 [20.0, 27.0] mg/dL; placebo, 24.0 [21.0, 28.0] mg/dL; **Table 1**)

TABLE 1: Baseline Demographics and Characteristics by ATTR-CM Genotype; mITT Population (N = 611)[a]

Baseline Demographic/Characteristic	Acoramidis (n = 409)		Placebo (n = 202)	
	ATTRv-CM (n = 39)	ATTRwt-CM (n = 370)	ATTRv-CM (n = 20)	ATTRwt-CM (n = 182)
Age, years, mean (SD)	73.9 (7.60)	77.7 (6.25)	71.2 (7.84)	77.6 (6.32)
Sex, n (%)				
Male	33 (84.6)	341 (92.2)	14 (70.0)	167 (91.8)
Female	6 (15.4)	29 (7.8)	6 (30.0)	15 (8.2)
NT-proBNP, pg/mL, median (Q1, Q3)	2326.0 (1312.0, 4567.0)	2264.5 (1315.0, 3729.0)	2340.5 (1521.5, 3534.0)	2273.5 (1105.0, 3590.0)
NYHA functional class, n (%)				
I	2 (5.1)	49 (13.2)	1 (5.0)	16 (8.8)
II	35 (89.7)	253 (68.4)	16 (80.0)	140 (76.9)
III	2 (5.1)	68 (18.4)	3 (15.0)	26 (14.3)
sTTR, mg/dL, median (Q1, Q3)	19.0 (13.0, 21.0)	23.0 (20.0, 27.0)	18.0 (12.5, 20.0)	24.0 (21.0, 28.0)

[a]In total, 59/611 participants were categorized as having ATTRv-CM at randomization; subsequently, mutations were identified in the clinical database in 56/611 participants.

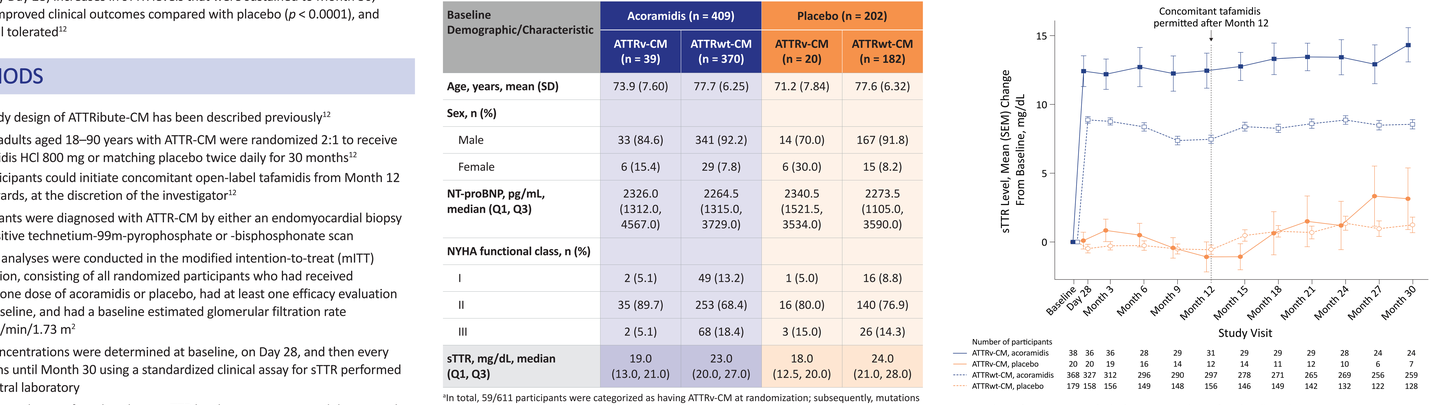
TABLE 2: Most Common *TTR* Variants; ATTRv-CM mITT Population (n = 56)[a]

TTR Variant Genotype, n (%)	Acoramidis (n = 37)	Placebo (n = 19)
p.V142I	23 (62.2)	12 (63.2)
p.I88L	4 (10.8)	3 (15.8)
p.T80A	3 (8.1)	2 (10.5)

[a]In total, 59/611 participants were categorized as having ATTRv-CM at randomization; subsequently, mutations were identified in the clinical database in 56/611 participants.

- Acoramidis treatment led to rapid increases from baseline in sTTR levels at Day 28, which were sustained through Month 30 in participants with ATTRv-CM and those with ATTRwt-CM (**Figure 1**)

FIGURE 1: Mean Change From Baseline in sTTR Levels to Month 30; mITT Population (N = 611)



Data are shown for participants who had non-missing change from baseline values.

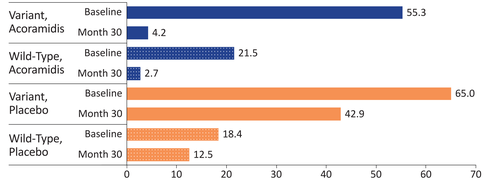
- Although participants with ATTRv-CM had lower baseline sTTR levels than those with ATTRwt-CM (**Table 1**), acoramidis treatment led to a greater mean change from baseline in sTTR levels in participants with ATTRv-CM than in those with ATTRwt-CM, resulting in similar absolute sTTR levels in the two genotype groups from Day 28 to Month 30 (**Table 3**)
  - Mean (SD) sTTR levels were 30.0 (6.5) mg/dL and 32.5 (6.5) mg/dL at Day 28, and 33.3 (6.3) mg/dL and 32.7 (6.2) mg/dL at Month 30, for participants with ATTRv-CM and ATTRwt-CM, respectively

TABLE 3: Absolute sTTR Levels at Day 28 and Month 30 Following Acoramidis Treatment; mITT Population (N = 611)

		ATTRv-CM (n = 39)	ATTRwt-CM (n = 370)
Day 28	n	37	328
	sTTR, mg/dL, mean (SD)	**30.0 (6.5)**	**32.5 (6.5)**
Month 30	n	24	260
	sTTR, mg/dL, mean (SD)	**33.3 (6.3)**	**32.7 (6.2)**

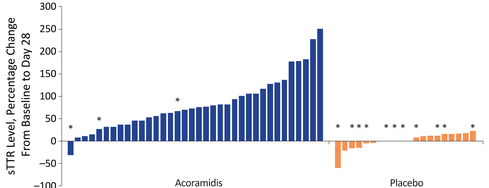
- At baseline in the acoramidis group, sTTR levels were below the reference range (< 20 mg/dL) in 55.3% of participants with ATTRv-CM and in 21.5% of participants with ATTRwt-CM (**Figure 2**)
- At Month 30, fewer than 5% of participants with ATTRv-CM and ATTRwt-CM had sTTR levels below the reference range following acoramidis treatment (**Figure 2**)
  - sTTR levels were below the reference range in a greater proportion of participants in the placebo group than in the acoramidis group at Month 30

FIGURE 2: Percentage of Participants With sTTR Levels Below the Reference Range (< 20 mg/dL) at Baseline and Month 30; mITT Population (N = 611)



- In participants with ATTRv-CM, acoramidis treatment led to increases in sTTR levels from baseline to Day 28 in 35 of 36 (97.2%) participants, whereas there was very little change in sTTR levels in the placebo group (**Figure 3**)

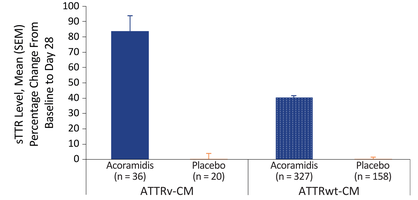
FIGURE 3: Percentage Change From Baseline to Day 28 in sTTR Levels for Each Participant With ATTRv-CM; mITT Population (N = 611)



Data are shown for participants who had sTTR levels recorded at baseline and Day 28. Asterisks indicate participants with sTTR levels below the lower limit of the reference range (< 20 mg/dL) at Day 28.

- Acoramidis treatment led to a greater mean percentage increase in sTTR levels at Day 28 in participants with ATTRv-CM than in those with ATTRwt-CM (83.7% vs 40.5%), whereas sTTR levels remained unchanged at Day 28 in the placebo group (**Figure 4**)

FIGURE 4: Mean Percentage Change From Baseline to Day 28 in sTTR Levels for Participants With ATTRv-CM and ATTRwt-CM; mITT Population (N = 611)



Data are shown for participants who had sTTR levels recorded at baseline and Day 28.

CORRESPONDING AND PRESENTING AUTHOR: Prem Soman, somanp@upmc.edu

REFERENCES: 1. Rapezzi C, et al. *Nat Rev Cardiol*. 2010;7(7):398-408. **2.** Sanguinetti C, et al. *Biomedicines*. 2022;10(8):1906. **3.** Lane T, et al. *Circulation*. 2019;140(1):16-26. **4.** Porcari A, et al. *Cardiovasc Res*. 2022;118(18):3517-3535. **5.** Hammarström P, et al. *Proc Natl Acad Sci U S A*. 2002;99(suppl 4):16427-16432. **6.** Greve AM, et al. *JAMA Cardiol*. 2021;6(3):258-268. **7.** Judge DP, et al. *J Am Coll Cardiol*. 2019;74(3):285-295. **8.** BridgeBio Pharma, Inc. Prescribing Information, Attruby (acoramidis). FDA, 2024. Accessed July 10, 2025. www.accessdata.fda.gov/drugsatfda_docs/label/2024/216540s000lbl.pdf. **9.** BridgeBio Europe B.V. SmPC, Beyonttra (acoramidis). EMA, 2024. Accessed July 10, 2025. www.ema.europa.eu/en/documents/product-information/beyontra-epar-product-information_en.pdf. **10.** Alexion. SmPC, Beyonttra (acoramidis). MHLW Japan, 2025. **11.** Bayer plc. SmPC, Beyonttra (acoramidis). MHRA UK, 2025. Accessed July 10, 2025. https://mhraproducts4853.blob.core.windows.net/docs/2b28fbdb53c2078600da92ae212cabe0ba041449. **12.** Gillmore JD, et al. *N Eng J Med*. 2024;390(2):132-142.

FUNDING: This study was sponsored by BridgeBio Pharma, Inc., San Francisco, CA, USA.

ABBREVIATIONS: ATTR-CM, transthyretin amyloid cardiomyopathy; ATTRv-CM, variant transthyretin amyloid cardiomyopathy; ATTRwt-CM, wild-type transthyretin amyloid cardiomyopathy; mITT, modified intention-to treat; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; Q1, first quartile; Q3, third quartile; SD, standard deviation; SEM, standard error of the mean; sTTR, serum transthyretin; TTR, transthyretin.

ACKNOWLEDGMENTS: The authors thank Jing Du, MD, MS, of BridgeBio Pharma, Inc., for statistical analysis support. Under the direction of the authors, medical writing assistance was provided by Oxford PharmaGenesis, Inc., and was funded by BridgeBio Pharma, Inc. Editorial support and critical review were provided by Shweta Rane, PhD, CMPP, BCMAS, of BridgeBio Pharma, Inc.

DISCLOSURES: P.S. has received grants from Pfizer; and acted as a consultant, advisor, or speaker for Alnylam Pharmaceuticals, BridgeBio Pharma, Inc., Pfizer, and Spectrum Dynamics. **M.S.M.** has acted as a researcher for Alnylam Pharmaceuticals, Attralus, BridgeBio Pharma, Inc., Intellia Therapeutics, Ionis Pharmaceuticals, the National Institutes of Health (R01HL139671 and R01AG081582-01), and Pfizer; and as a consultant or advisor for Akcea Therapeutics, Alnylam Pharmaceuticals, AstraZeneca, Attralus, BridgeBio Pharma, Inc., Intellia Therapeutics, Ionis Pharmaceuticals, Novo Nordisk, and Pfizer. **N.S.** has acted as a researcher for Pfizer; and as a consultant, advisor, or speaker for Alnylam Pharmaceuticals, AstraZeneca, BridgeBio Pharma, Inc., Novo Nordisk, and Pfizer. **M.G.** has received research funding/grants or acted as a contractor for Alnylam Pharmaceuticals, Anumana, AstraZeneca, BridgeBio Pharma, Inc., Intellia Therapeutics, Janssen Pharmaceuticals, Novo Nordisk, and Pfizer; and as an advisor for Alnylam Pharmaceuticals. **A.A.** has no relevant financial relationships to disclose. **A.D.** has acted as a consultant, advisor, or speaker for Abbott, AstraZeneca, Bayer, Boehringer Ingelheim, Novartis, and Novo Nordisk; and as a researcher for Abbott, AstraZeneca, Bayer, BridgeBio Pharma, Inc., Merck, and Novo Nordisk. **S.H.P.** has acted as a consultant for Bayer, BridgeBio Pharma, Inc., and Pfizer; and received research support from Novo Nordisk. **J.L.G.** has received grant support from BridgeBio Pharma, Inc., the National Heart, Lung, and Blood Institute, Pfizer, and the Texas Health Resources Clinical Scholars Fund; and has acted as a consultant, advisor, or speaker for Alexion Pharmaceuticals, AstraZeneca, BridgeBio Pharma, Inc., Intellia Therapeutics, Pfizer, and Tenax Therapeutics. **J.B.** has received research funding/grants or acted as a contractor for Alnylam Pharmaceuticals, AstraZeneca, BridgeBio Pharma, Inc., Intellia Therapeutics, and Ionis Pharmaceuticals; royalties from Purpose Pharma International; and honoraria from Alnylam Pharmaceuticals, AstraZeneca, BridgeBio Pharma, Inc., and Intellia Therapeutics; and has acted as an advisor for Alnylam Pharmaceuticals, AstraZeneca, BridgeBio Pharma, Inc., and Intellia Therapeutics. **A.X.J., S.R., J-F.T., A.C., J.C.F.,** and **U.S.** are employees and stakeholders of BridgeBio Pharma, Inc.

PRESENTED AT THE 30TH ANNUAL SCIENTIFIC SESSION AND EXHIBITION OF THE AMERICAN SOCIETY OF NUCLEAR CARDIOLOGY (ASNC), SEPTEMBER 4–7, 2025, ORLANDO, FL, USA

DATA WERE PREVIOUSLY PRESENTED AT THE ANNUAL CONGRESS OF THE HEART FAILURE ASSOCIATION OF THE EUROPEAN SOCIETY OF CARDIOLOGY (ESC), MAY 17–20, 2025, BELGRADE, SERBIA