MDP858

RELATIONSHIP BETWEEN CVH AND SURVIVAL IN THE ACORAMIDIS-TREATED PARTICIPANTS WITHIN ATTRibute-CM

Kevin Alexander,[1] Margot K Davis,[2] Amrut Ambardekar,[3] Jose Nativi-Nicolau,[4] Keyur Shah,[5] Mazen Hanna,[6] Simon DJ Gibbs,[7,8] Jing Du,[8] Jean-François Tamby,[8] Suresh Siddhanti,[8] John Whang,[8] Jonathan C Fox,[8] and Richard K Cheng[9]

[1]Stanford University School of Medicine, Palo Alto, CA, USA; [2]University of British Columbia, Vancouver, Canada; [3]University of Colorado, Aurora, CO, USA; [4]Mayo Clinic, Jacksonville, FL, USA; [5]Virginia Commonwealth University Health, Richmond, VA, USA; [6]Cleveland Clinic, Cleveland, OH, USA; [7]Eastern Health, Melbourne, Australia; [8]BridgeBio Pharma, Inc., San Francisco, CA, USA; [9]University of Washington Medicine, Seattle, WA, USA

Presenter: Kevin Alexander

Scan the QR code to access a PDF version and plain language summary of this poster

Presented on November 17, at the AHA Scientific Sessions 2024, McCormick Place Convention Center, Chicago, IL, USA

DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIPS WITH INDUSTRY AND ACKNOWLEDGMENTS

Kevin Alexander has acted as a consultant, advisor, or speaker for Arbor Biotechnologies, Attralus, Intellia Therapeutics, and Prothena

MKD has received honoraria for participation in advisory boards from Akcea, Alnylam, AstraZeneca, Bayer, Boehringer Ingelheim, Ferring, Ionis, Janssen, and Pfizer; has received consulting fees from Janssen and Novo Nordisk; has received speaking fees from Bayer, Ferring, Janssen, and Pfizer, and has received research funding from Pfizer. **AA** has no relevant financial relationships to disclose. **JNN** has received research funding from Alnylam, AstraZeneca, Eidos, and Pfizer. **KS** is a consultant, advisor, and speaker for Pfizer. **MH** has acted as a consultant, advisor, or speaker for Alexion Pharmaceuticals, Alnylam Pharmaceuticals, BridgeBio Pharma (formerly Eidos Therapeutics), Ionis Pharmaceuticals, and Pfizer. **SDJG** is an employee of BridgeBio Pharma; and has acted as a speaker, advisory board member, or steering committee member for AbbVie, Alnylam Pharmaceuticals, Bristol Myers Squibb, Intellia Therapeutics, Ionis Pharmaceuticals, Janssen Pharmaceuticals, Pfizer, and Takeda**. JD**, **JFT**, **SS**, **JW**, and **JCF** are employees and stakeholders of BridgeBio Pharma. **RKC** has nothing to disclose

Funding

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

Acknowledgments

- The authors would like to thank the patients who participated in the ATTRibute-CM trial and their families
- The authors would also like to thank the ATTRibute-CM investigators
- Under the direction of the authors, medical writing assistance was provided by Heather Booth, DPhil, of Oxford PharmaGenesis Inc., and supported by BridgeBio Pharma, Inc. Editorial support and critical review were provided by Dana Walters, PhD, and Shweta Rane, PhD, CMPP, of BridgeBio Pharma, Inc.

INTRODUCTION

- ATTR-CM is characterized by the destabilization of TTR tetramers, and accumulation of amyloid fibrils in the heart, leading to cardiac dysfunction and progressive heart failure[1–3]
- Occurrence of cardiovascular-related hospitalization (CVH) is associated with a higher risk of subsequent mortality in patients with ATTR-CM[4,5]
- Acoramidis is an investigational, selective TTR stabilizer for the treatment of patients with ATTR-CM that achieves near-complete (≥ 90%) TTR stabilization[6–8]
- In the phase 3 ATTRibute-CM study (NCT03860935), acoramidis reduced the risk of frequency of CVH by 50% vs placebo (RRR: 0.496; 95% CI: 0.355–0.695) with beneficial effects of acoramidis observed by Month 3[8]

OBJECTIVE:

To report the relationship between CVH events and survival rate in participants with ATTR-CM treated with acoramidis in ATTRibute-CM

ATTR-CM, transthyretin amyloid cardiomyopathy; CI, confidence interval; RRR, relative risk ratio; TTR, transthyretin.

1. Rapezzi C *et al. Nat Rev Cardiol* 2010;7:398–408; 2. Lane T *et al. Circulation* 2019;140:16–26; 3. Ruberg FL *et al. J Am Coll Cardiol* 2019;73:2872–91; 4. Bello NA *et al. Circ Heart Fail* 2014;7:590–5; 5. Masri A *et al.* 2024. Presented at the 2024 International Symposium on Amyloidosis, Rochester, NY, USA, and virtually; 6. Penchala SC *et al. Proc Natl Acad Sci USA* 2013;110:9992–7; 7. Miller M *et al. Med Chem* 2018;61:7862–76; 8. Gillmore JD *et al. N Engl J Med* 2024;390:132–42

ATTRibute-CM PHASE 3 STUDY DESIGN AND POST HOC ANALYSIS

Study design[1]

Screening and randomization

- **Placebo BID (n = 211)**
- **Acoramidis HCl 800 mg BID (n = 421)**

Key eligibility criteria

- Diagnosed ATTR-CM (wt or variant)
- NYHA class I–III
- ATTR-positive biopsy or ^{99m}Tc scan
- Light-chain amyloidosis excluded if diagnosis by ^{99m}Tc

Post hoc analysis:
relationship, within acoramidis group, between CVH and all-cause mortality at Month 30[a]

Acoramidis HCl 800 mg BID
Patients with CVH (n = 109)

vs

Acoramidis HCl 800 mg BID
Patients with no CVH (n = 300)

[a]This analysis was performed for the modified intention-to-treat population.
^{99m}Tc, technetium-labeled pyrophosphate or bisphosphonate; ATTR-CM, transthyretin amyloid cardiomyopathy; BID, twice daily; CVH, cardiovascular-related hospitalization; NYHA, New York Heart Association; wt, wild-type.
1. Gillmore JD *et al. N Engl J Med* 2024;390:132–42

MEAN AGE, SEX, AND GENOTYPE DISTRIBUTIONS WERE SIMILAR BETWEEN ACORAMIDIS-TREATED PARTICIPANTS WITH AND WITHOUT CVH EVENTS

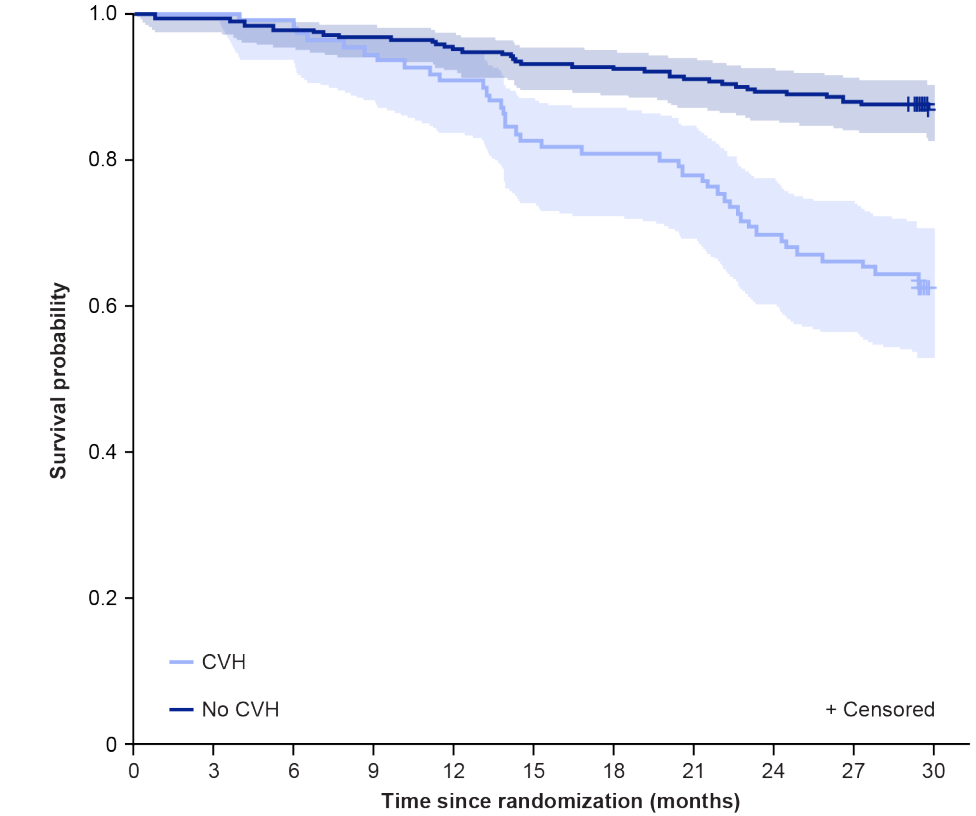
Baseline demographics and characteristics	Acoramidis (n = 409)	
	CVH (n = 109)	No CVH (n = 300)
Age, years, mean (SD)	77.8 (5.8)	77.1 (6.7)
Male, n (%)	99 (90.8)	275 (91.7)
ATTRv-CM genotype, n (%)	14 (12.8)	25 (8.3)
NYHA class, n (%)		
I	4 (3.7)	47 (15.7)
II	83 (76.1)	205 (68.3)
III	22 (20.2)	48 (16.0)
NAC stage,[a] n (%)		
I	53 (48.6)	188 (62.7)
II	41 (37.6)	89 (29.7)
III	15 (13.8)	23 (7.7)
Serum TTR, mg/dL, mean (SD)	22.7 (6.6)	23.1 (5.2)
KCCQ-OS score, mean (SD)	67.0 (20.5)	73.5 (18.7)
6MWD, m, mean (SD)	332.3 (102.9)	373.7 (101.7)
NT-proBNP, ng/L, mean (SD)	3410.8 (2160.5)	2667.1 (2114.6)
eGFR, mL/min/1.73 m^2, mean (SD)	57.7 (17.4)	63.5 (17.1)

Compared with participants without CVH events, participants with CVH events had:

- lower proportion with NAC stage I disease
- higher mean NT-proBNP level
- lower mean eGFR

Data shown are for the modified intention-to-treat population.
[a]Stage I, NT-proBNP level ≤ 3000 ng/L and eGFR ≥ 45 mL/min/1.73 m^2; Stage III, NT-proBNP level > 3000 ng/L and eGFR < 45 mL/min/1.73 m^2; the remainder were categorized as Stage II when data for NT-proBNP level and eGFR were available.
6MWD, 6-minute walk distance; ATTRv-CM, variant transthyretin amyloid cardiomyopathy; CVH, cardiovascular-related hospitalization; eGFR, estimated glomerular filtration rate; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire overall summary; NAC, National Amyloidosis Center; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; SD, standard deviation; TTR, transthyretin

SURVIVAL RATE WAS SIGNIFICANTLY HIGHER IN ACORAMIDIS-TREATED PARTICIPANTS WITH NO CVH EVENTS VERSUS THOSE WITH ≥ 1 CVH EVENT



Participants remaining at risk (cumulative events)

CVH	109 (0)	109 (0)	108 (1)	103 (6)	99 (10)	90 (19)	88 (21)	85 (24)	76 (33)	72 (37)	0 (41)
No CVH	300 (0)	298 (2)	293 (7)	290 (10)	286 (14)	279 (21)	277 (23)	273 (27)	268 (32)	264 (36)	0 (38)

30-month survival rate

CVH: 62.4%
(95% CI: 52.6, 70.7)

No CVH: 86.8%
(95% CI: 82.2, 90.3)

***p* < 0.0001[a]**

[a]*p* value calculated using the log-rank test.
CI, confidence interval; CVH, cardiovascular-related hospitalization

CONCLUSIONS

- In the ATTRibute-CM study, survival rate was significantly higher in participants with no CVH events compared with those with ≥ 1 CVH event
- CVH remains a powerful predictor of mortality in patients with ATTR-CM
- Results from this post hoc analysis reinforce the importance of an effective therapy that reduces CVH in patients with ATTR-CM and that, in turn, may improve survival

ATTR-CM, transthyretin amyloidosis cardiomyopathy; CVH, cardiovascular-related hospitalization