# How treatment impacted outcomes in variant and wild-type ATTR-CM

Attruby® (acoramidis) 356 mg tablet

## The variant form of ATTR-CM is associated with earlier onset and faster disease progression[1]

**1 in 10** patients enrolled in ATTRibute-CM had ATTRv-CM[2]

**62%** of patients in the ATTRv-CM subgroup had **V122I**, the most prevalent TTR variant in the US[3]

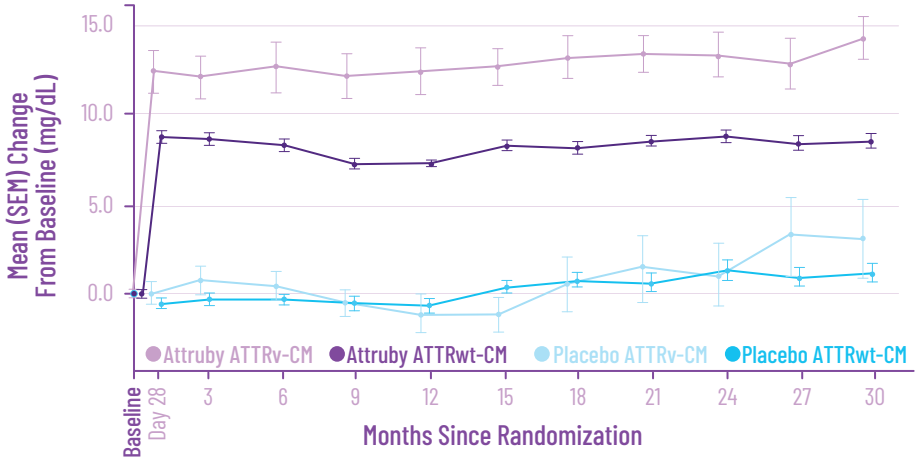
## Consistent early increase in serum TTR in patients with ATTRwt-CM and ATTRv-CM[4]

**Patients with ATTRv-CM had lower levels of serum TTR at baseline compared with ATTRwt-CM patients[4]**

### ATTRibute-CM Study Design

Attruby was assessed in adults with ATTRv-CM or ATTRwt-CM for efficacy (N=611) and safety (N=632) over 30 months in a phase 3, randomized (2:1), double-blind, placebo-controlled study.† Concomitant tafamidis permitted after Month 12. The primary endpoint was a 4-part hierarchical composite (ACM, CVH, CFB in NT-proBNP, CFB in 6MWD). Secondary endpoints included CFB in KCCQ-OS, CFB in serum TTR, and CVH‡.[3,6]

**Prespecified Subgroup Analysis: Change From Baseline in Serum TTR Level Through Month 30, mITT Population[4*†]**




**No. at Risk**

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Attruby ATTRwt-CM | 368 | 327 | 312 | 296 | 290 | 297 | 278 | 271 | 265 | 269 | 256 | 259 |
| Attruby ATTRv-CM | 38 | 36 | 36 | 28 | 29 | 31 | 29 | 29 | 29 | 28 | 24 | 24 |
| Placebo ATTRwt-CM | 179 | 158 | 156 | 149 | 148 | 156 | 146 | 149 | 142 | 132 | 122 | 128 |
| Placebo ATTRv-CM | 20 | 20 | 19 | 16 | 14 | 12 | 14 | 11 | 12 | 10 | 6 | 7 |

**These analyses were descriptive and exploratory in nature. Results were limited by small sample size.**

*From mITT population: 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. Serum TTR concentrations were determined using a standardized clinical assay for serum prealbumin performed in a central laboratory. Data are shown for participants who had non-missing CFB values. Serum TTR levels were measured at baseline, Day 28, Month 3, and every 3 months thereafter. Observed percentage changes from baseline at various timepoints were summarized by descriptive statistics in the mITT population.

†Efficacy assessment included 611 participants in the prespecified mITT population (eGFR ≥30 mL/min/1.73 m$^2$). A total of 632 patients underwent randomization. Of these patients, 21 who had stage 4 CKD were excluded from the primary analysis in the mITT population.[5]

‡Prespecified, non-alpha protected.[3,6]

6MWD=6-minute walk distance; ATTR-CM=transthyretin amyloid cardiomyopathy; ATTRv=variant transthyretin-mediated amyloidosis; ATTRwt=wild-type transthyretin-mediated amyloidosis; CFB=change from baseline; CKD=chronic kidney disease; CVH=cardiovascular-related hospitalization; eGFR=estimated glomerular filtration rate; KCCQ-OS=Kansas City Cardiomyopathy Questionnaire Overall Summary; mITT=modified intent-to-treat; NT-proBNP=N-terminal pro-B-type natriuretic peptide; SEM=standard error of the mean; TTR=transthyretin.

## INDICATION

Attruby® (acoramidis) is indicated for the treatment of the cardiomyopathy of wild-type or variant transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular death and cardiovascular-related hospitalization.

## IMPORTANT SAFETY INFORMATION

### Adverse Reactions

Diarrhea (11.6% vs 7.6%) and upper abdominal pain (5.5% vs 1.4%) were reported in patients treated with Attruby versus placebo, respectively. The majority of these adverse reactions were mild and resolved without drug discontinuation.

Discontinuation rates due to adverse events were similar between patients treated with Attruby versus placebo (9.3% and 8.5%, respectively).

**Please see additional Important Safety Information throughout and accompanying Full Prescribing Information for Attruby.**

# Attruby showed consistent treatment benefit in both ATTRwt-CM and ATTRv-CM

**IN ATTRibute-CM**

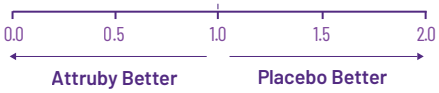
**Attruby demonstrated a significant reduction in the combination of ACM and CVH at Month 30 (*P*=0.018, F-S test)[2,5]**

- CVH was reported in 27% and 43% of participants in the Attruby and placebo groups, respectively[5]
- 10-point difference (95% CI: 5.97-13.91; *P*<0.0001) in KCCQ-OS in favor of Attruby[2,5]
- Discontinuations due to adverse events were similar for Attruby (9.3%) and placebo (8.5%)[5]

## PRESPECIFIED SUBGROUP ANALYSIS

Composite of ACM or First CVH[7]

| Subgroup | No (%) of Patients | Hazard Ratio (95% CI) | *P* Value |
|---|---|---|---|
| **Overall** | 611 (100.0) | 0.65 (0.50-0.83) | 0.0008 |
| **ATTR-CM Genotype** | | | |
| **ATTRv-CM** | **59 (9.7)** | 0.41 (0.21-0.81) | **0.0109*** |
| ATTRwt-CM | 552 (90.3) | 0.69 (0.52-0.90) | 0.0073* |




In patients with ATTRv-CM

**59%**

**RRR IN COMPOSITE OF ACM OR FIRST CVH OBSERVED** WITH ATTRUBY VS PLACEBO


### Select secondary outcomes in ATTRv-CM patients

**62%** **RRR** IN FREQUENCY OF **CVH** WITH ATTRUBY VS PLACEBO[2]
95% CI: 0.139-1.027

**20** **POINT DIFFERENCE** LS MEAN CFB IN **KCCQ-OS** SCORE OBSERVED WITH ATTRUBY VS PLACEBO[8]

**These analyses were descriptive and exploratory in nature. Results were limited by small sample size.**

*Nominal *P* value.

ACM=all-cause mortality; ATTR-CM=transthyretin amyloid cardiomyopathy; ATTRv=variant transthyretin-mediated amyloidosis; ATTRwt=wild-type transthyretin-mediated amyloidosis; CFB=change from baseline; CVH=cardiovascular-related hospitalization; F-S test=Finkelstein-Schoenfeld test; KCCQ-OS=Kansas City Cardiomyopathy Questionnaire Overall Summary; LS mean=least-squares mean; RRR=relative risk reduction.

**References: 1.** Hornstrup LS, Frikke-Schmidt R, Nordestgaard BG, Tybjaerg-Hansen A. Genetic stabilization of transthyretin, cerebrovascular disease, and life expectancy. *Arterioscler Thromb Vasc Biol.* 2013;33(6):1441-1447. doi:10.1161/ATVBAHA.113.301273 **2.** Gillmore JD, Judge DP, Cappelli F, et al. Efficacy and safety of acoramidis in transthyretin amyloid cardiomyopathy. *N Engl J Med.* 2024;390(2):132-142. doi:10.1056/NEJMoa2305434 **3.** Data on file. BridgeBio Pharma, Inc.; 2024-2025. **4.** Maurer M, Sarswat N, Grogan M, et al. Acoramidis improves serum TTR levels in patients with wild-type or variant transthyretin amyloid cardiomyopathy-results from ATTRibute-CM. Poster presented at: Annual Congress of the Heart Failure Association of the European Society of Cardiology; May 17-20, 2025; Belgrade, Serbia. **5.** Attruby. Prescribing information. BridgeBio Pharma, Inc.; 2024. **6.** Gillmore JD, Judge DP, Cappelli F, et al. Efficacy and safety of acoramidis in transthyretin amyloid cardiomyopathy [protocol]. *N Engl J Med.* 2024;390(2):132-142. doi:10.1056/NEJMoa2305434 **7.** Davis MK, Alexander KM, Ambardekar A, et al. Acoramidis increases serum TTR levels in patients with wild-type or variant transthyretin amyloid cardiomyopathy. Poster presented at: American College of Cardiology 74th Annual Scientific Session and Expo; March 29-31, 2025; Chicago, IL. **8.** Fontana M, Kumar V, Sheridan P, et al. Descriptive analysis of unmet need in a contemporary cohort of tafamidis-treated patients with ATTR-CM. Poster presented at: Heart Failure Society of America Annual Scientific Meeting; September 27-30, 2024; Atlanta, GA.

## IMPORTANT SAFETY INFORMATION (cont'd)

### Laboratory Tests

Mean increase in serum creatinine of 0.2 and 0.0 mg/dL and a mean decrease in eGFR of 8.2 and 0.7 mL/min/1.73 $m^2$ was observed in the adults with ATTR-CM treated with Attruby versus placebo, respectively, at Day 28 and then stabilized. These changes were reversible after treatment discontinuation.

### Use in Specific Populations

**Pregnancy & Lactation:** There are no data on the use of Attruby in pregnant women. Animal data have not shown developmental risk associated with the use of Attruby in pregnancy. There are no available data on the presence of Attruby in either human or animal milk or the effects of the drug on the breastfed infant or maternal milk production.

**Please see additional Important Safety Information throughout and accompanying Full Prescribing Information for Attruby.**

bridgebio