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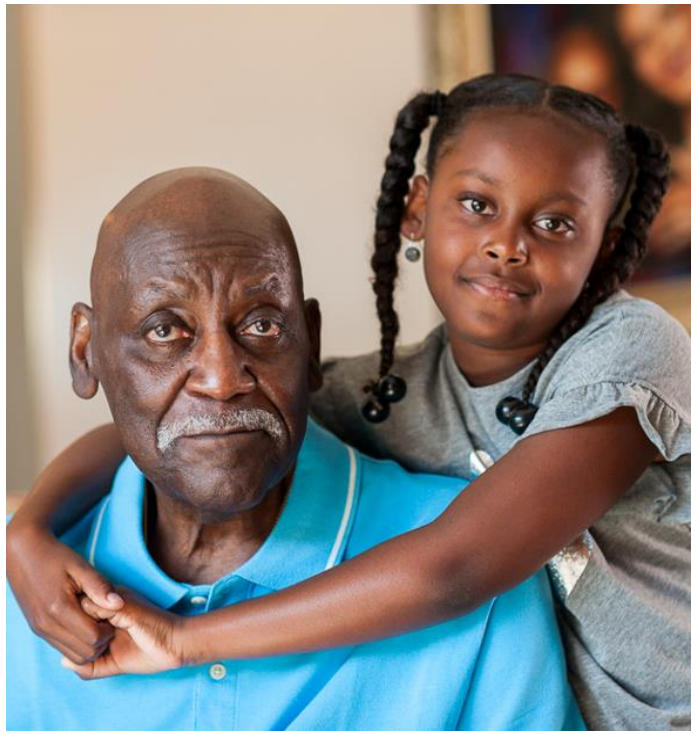
ATTRibute-CM
Part A topline results

December 2021



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ATTRibute-CM did not meet its Month 12 primary endpoint

Primary endpoint	p-value
Change from baseline in 6MWD	0.76

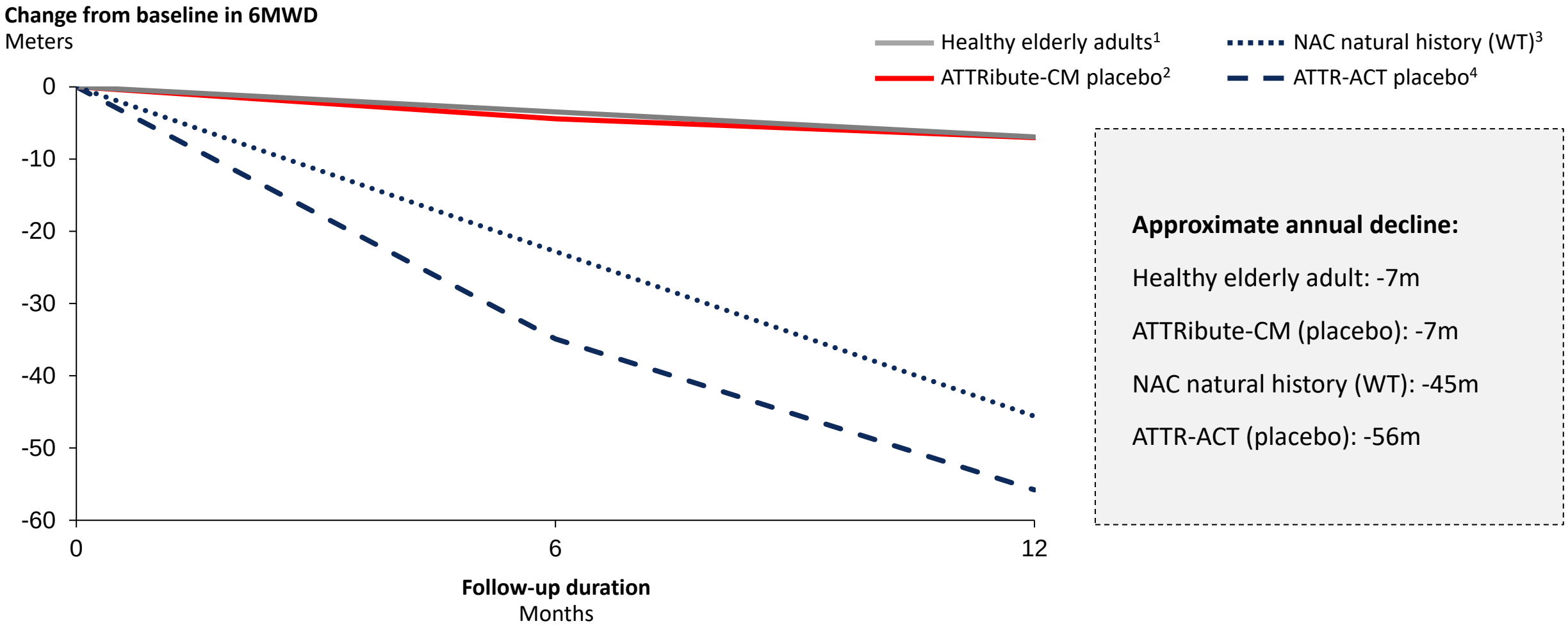
Observed change from baseline in 6MWD at Month 12

	Mean (SD)	Median
Acoramidis	-9.28m (62.7)	-4.83m
Placebo	-7.04m (59.7)	-6.25m

ATTRibute-CM placebo group outperformed tafamidis-treated participants in ATTR-ACT by more than 70%[1]

[1]Maurer, M.S. et al. NEJM 2018

Observed ATTRibute-CM placebo substantially outperformed historical controls



Approximate annual decline:

Healthy elderly adult: -7m

ATTRibute-CM (placebo): -7m

NAC natural history (WT): -45m

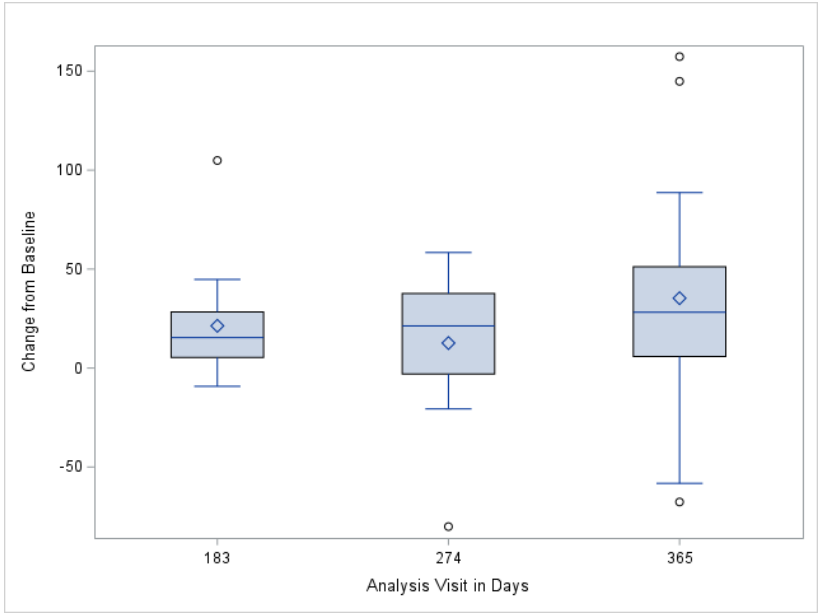
ATTR-ACT (placebo): -56m

[1]Enright, P.L. et al. Am J Respir Crit Care Med 1998. N = 117 healthy elderly adults
[2] Observed ATTRibute-CM draft results, N = 160 at Month 12
[3]Lane, T. et al., Circulation 2019. N = 289 ATTRwt-CM at Month 12
[4]Maurer, M.S. et al. NEJM 2018. N = 136 at Month 12

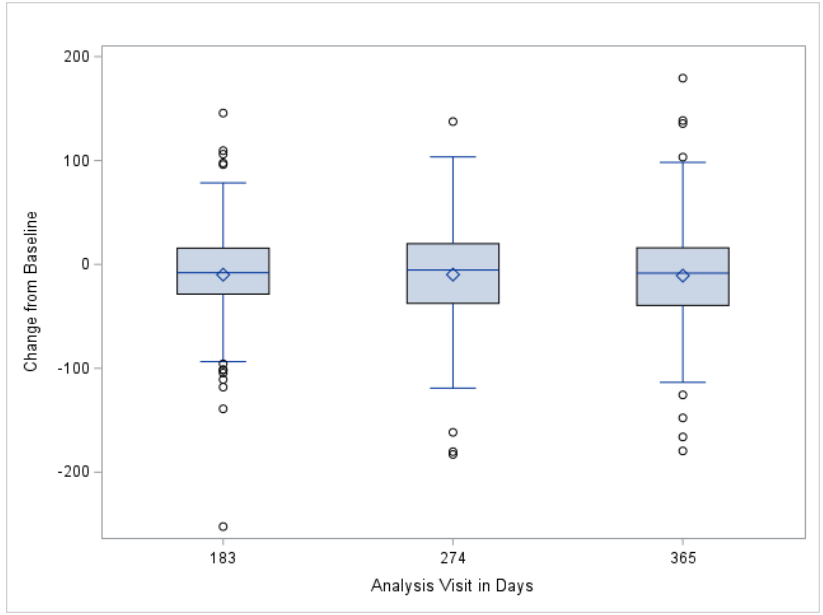
Lack of placebo deterioration across NYHA classes is baffling

Change from baseline in 6MWT total distance at months 6, 9, 12

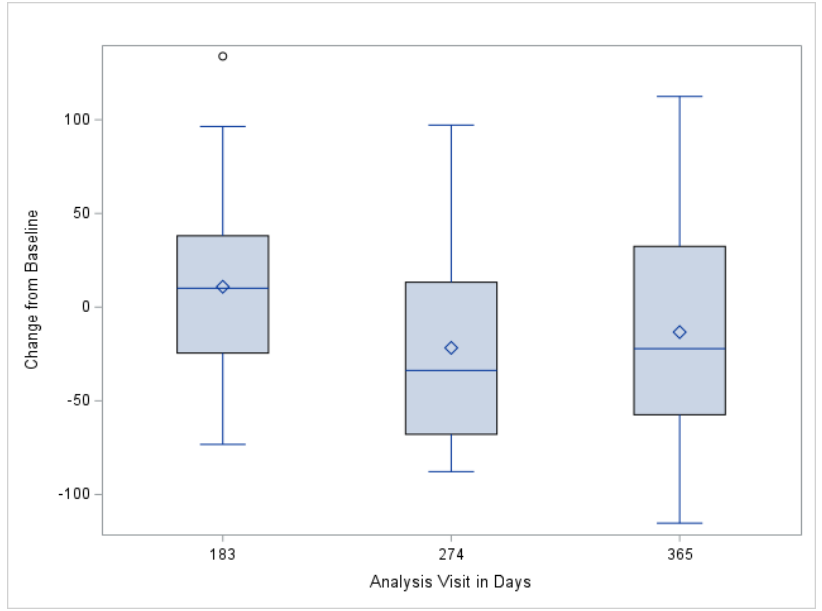
Baseline NYHA Class I



Baseline NYHA Class II



Baseline NYHA Class III



ATTRibute-CM enrolled a similar population as ATTR-ACT

Baseline Trait	ATTRibute-CM (mITT)	ATTR-ACT
Age		
Mean	77.0	74.3
Median	78.0	74.6
NYHA Class		
Class I	11.2%	8.4%
Class II	72.7%	59.6%
Class III	16.1%	32.0%
6MWT (m)		
Mean	360	352
Genetic TTR status		
Variant	9.7%	24.0%
Wildtype	90.3%	76.0%
Geography		
US	19.3%	63.3%
Ex-US	80.7%	36.7%

ATTRibute-CM was relatively well-balanced

Baseline Trait	Acoramidis (mITT)	Placebo (mITT)
Age		
Mean	77.2	76.9
Median	78.0	77.8
NYHA Class		
Class I	12.6%	8.5%
Class II	70.2%	77.6%
Class III	17.2%	13.9%
6MWT (m)		
Mean (SD)	364 (103)	351 (102)
Genetic TTR status		
Variant	9.1%	9.5%
Wildtype	90.6%	90.0%
Geography		
US	18.5%	20.9%
Ex-US	81.5%	79.1%

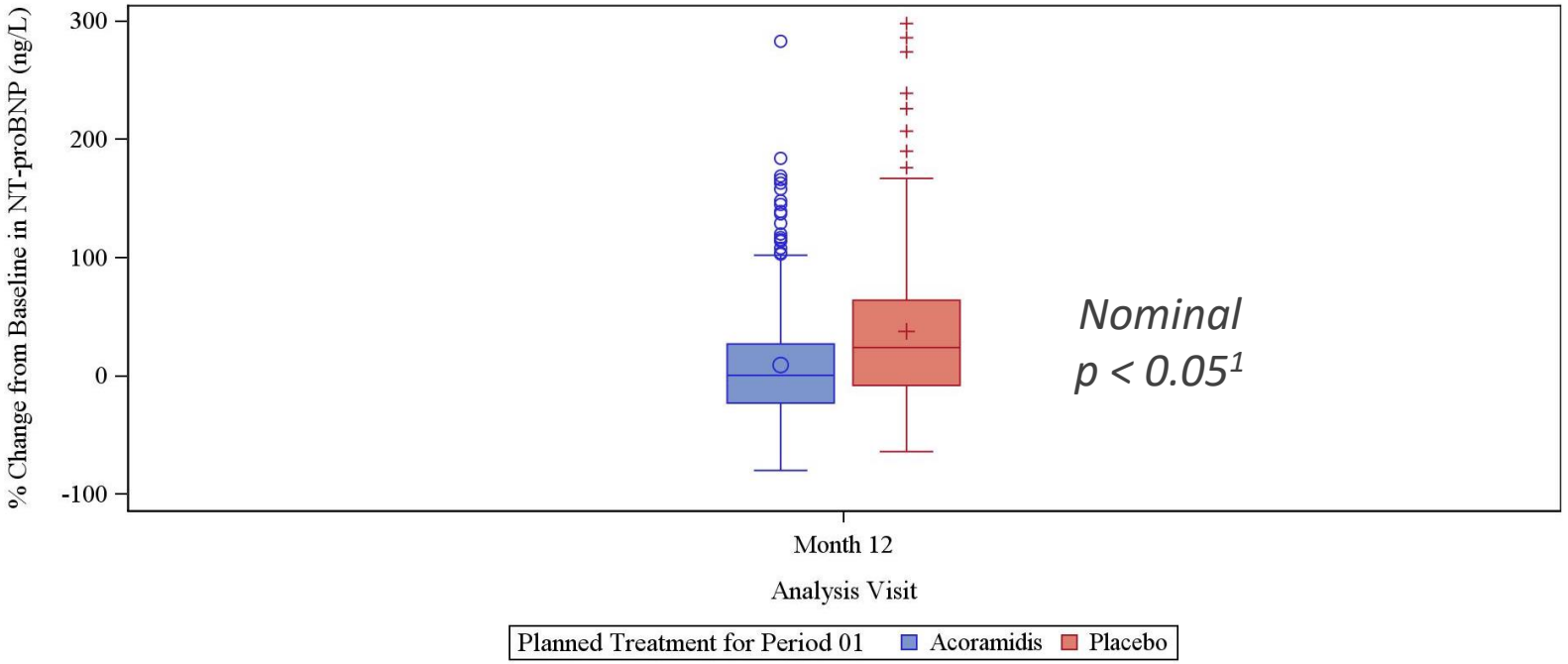
Trial population differences unlikely to contribute to lack of 6MWT benefit

Could the lack of 6MWD benefit be caused by…	Preliminary answer
…higher proportion of NYHA II vs III participants?	**Unlikely** – our 6MWD result was modestly better in NYHA I/II than NYHA III participants
…higher proportion of ex-US vs. US participants?	**Unlikely** – our 6MWD result was modestly better in ex-US participants than US participants
…higher proportion of wild-type vs. variant participants?	**Unlikely** – although a 6MWD benefit was observed in variant participants, a similar proportion of variant participants as ATTR-ACT would not have corrected the outcome

Current hypotheses for the differential placebo result include context bias, training bias, and an evolution in ATTR-CM diagnostic approach and standard of care

Acoramidis improved NT-proBNP relative to placebo

Percent change from baseline in NT-proBNP at Month 12 – mITT population



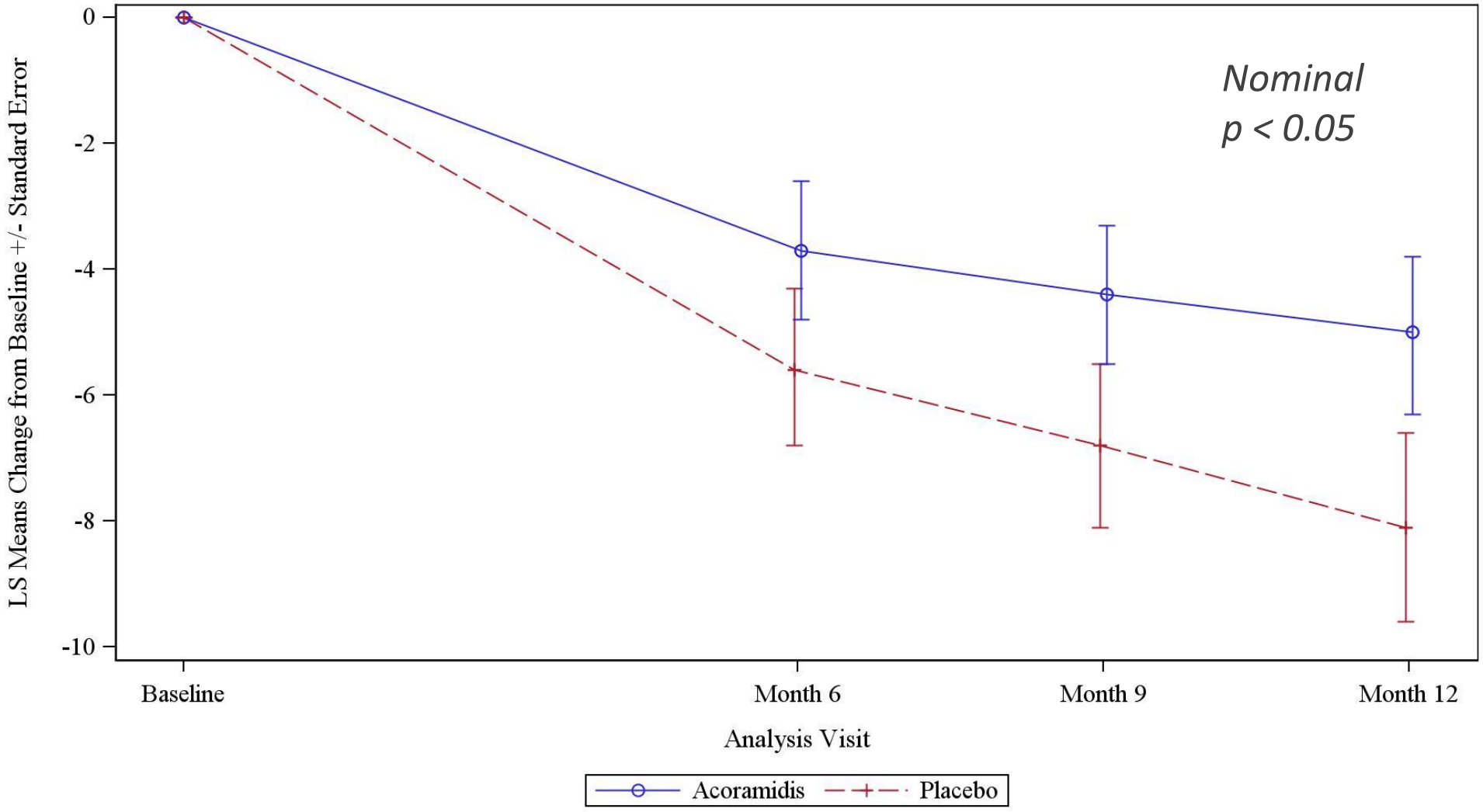
Note: to facilitate a focused review of the vast majority of the data, outliers greater than 300% change from baseline are not included in this plot.

PRELIMINARY ANALYSIS – NOT VALIDATED

[1]Inference analysis (p-value) based on absolute change from baseline between groups

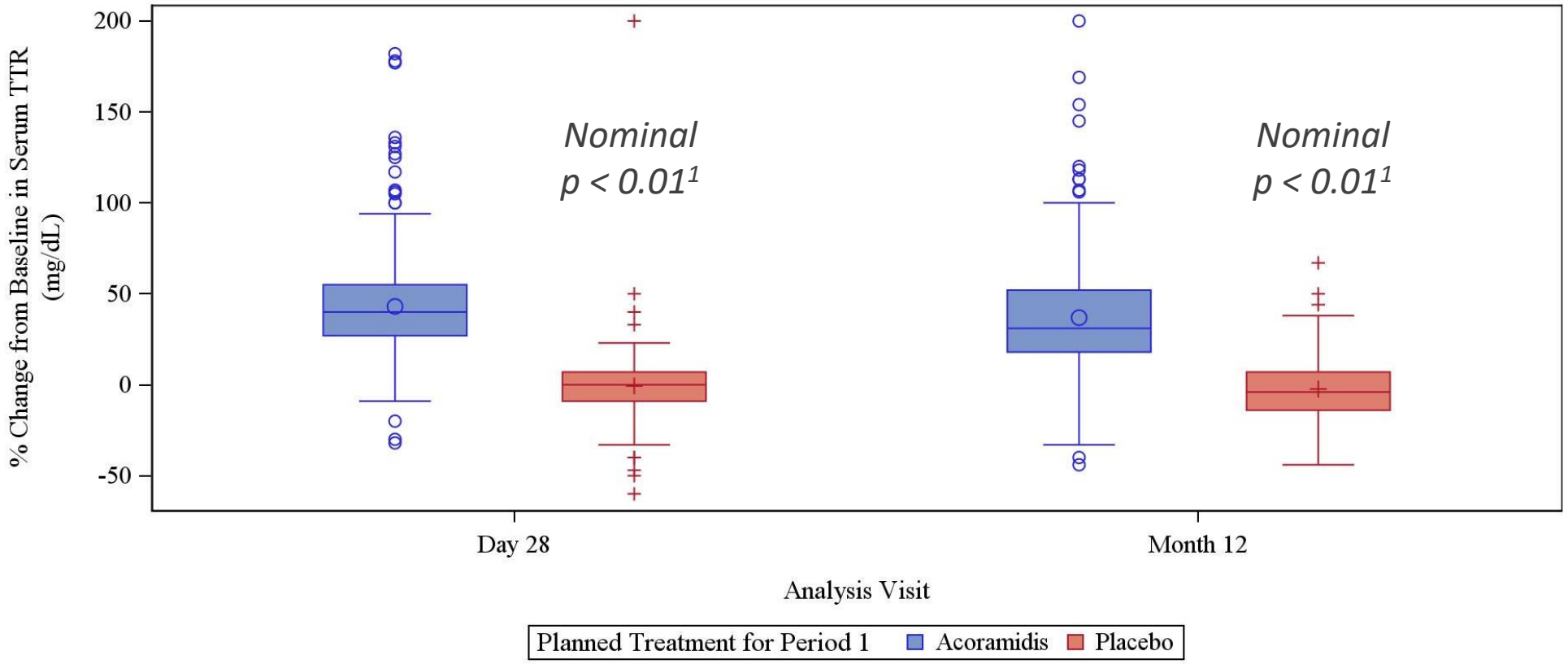
Acoramidis improved KCCQ-OS relative to placebo

KCCQ-OS by treatment and visit – MMRM without imputation



Acoramidis increased serum TTR concentrations

Percent change from baseline in serum TTR by treatment and visit – mITT population



Note: to facilitate a focused review of the vast majority of the data, outliers greater than 200% change from baseline are not included in this plot.

[1]Inference analysis (p-value) based on absolute change from baseline between groups

No safety signals of potential clinical concern identified

To protect the integrity of Part B, Sponsor's access to adverse event data for Part A excludes AEs leading to a cardiovascular hospitalization excepting events with the outcome of death

Preliminary safety results	Treatment emergent adverse events (AEs)	
Subjects with one or more event(s)	Acoramidis n (%)	Placebo n (%)
Adverse events	387 (91.9%)	180 (85.3%)
Serious adverse events	85 (20.2%)	49 (23.2%)
Adverse events with outcome of death	19 (4.5%)	13 (6.2%)

27% fewer treatment emergent adverse events (AEs) leading to death occurred in participants receiving acoramidis than in participants receiving placebo

Note: n=number of subjects experiencing an adverse event (the subject is counted only once for each AE). Adverse event attributed by investigator as the reason for a cardiovascular-related hospitalization or EOCI are not included in the Part A adverse event tables, excepting events with the outcome of death. An adverse event occurring during the treatment period is considered a treatment emergent adverse event if it was not present before the first dose of study drug or if it was present before the first dose of study drug but increased in severity during the treatment period. An AE that occurs more than 30 days after the last dose of IMP will not be counted as an AE. Serious adverse event (SAE) meets seriousness criteria.

Preliminary summary and next steps

After 12 months of ATTRibute-CM, acoramidis demonstrated relative to placebo:

- No improvement in functional status as measured by 6MWD
- Other measures positive, including improvements in:
  - KCCQ-OS
  - NT-proBNP
  - Serum TTR
- No safety signals of clinical concern and lower rates of AEs leading to death and SAEs

The independent data monitoring committee recommends continuing the study based on unblinded data reviews

Major catalysts across the pipeline anticipated over the next 12 months

Core value drivers	Pipeline upside
☐ **Low-dose infigratinib (FGFRi) for achondroplasia:** Ph2 proof-of-concept data (1H22)	☐ **COL7 replacement for RDEB:** Data from Ph2 study (early ’22)
☐ **AAV5 gene therapy for CAH:** Initial data from Ph1/2 study (mid-22)	☐ **AAV9 gene therapy for GALT:** IND submission (2H22)
☐ **KRAS inhibitor program:** Clinical candidate selection (2022)	☐ **AAV9 gene therapy for ASPA:** Initial data from Ph1/2 study (2H22)
☐ **Acoramidis (ATTR stabilizer) for ATTR-CM:** Ph3 topline data (mid-23)	☐ **GO inhibitor for hyperoxaluria:** Data from Ph1 study (2022)
☐ **KRAS inhibitor program:** IND submission (2023)	☐ **SHP2 inhibitor for RAS and RTK driven cancer:** Monotherapy Phase 2 dose selection (2022)
☐ **Encaleret (CaSRi) for ADH1:** Ph3 topline data (2023)	☐ **Ribitol for LGMD2i:** Ph2 proof-of-concept data (2022)
	☐ **SHP2 inhibitor for RAS and RTK driven cancer:** Combination therapy initial data (2023)
	☐ **GO inhibitor for hyperoxaluria:** Data from Ph2 study (2023)

Approx. $800M current cash balance[1] plus access to up to an additional $300M upon achievement of portfolio proof-of-concepts through 2022 expected to provide runway into 2024

[1]Unaudited cash, cash equivalents and marketable securities

(acoramidis for ATTR-CM)

A sincere thank you to patients and families, investigators, referring physicians, clinical research staff, Eidos/BridgeBio employees, and collaborating research partners