MDP857

EVOLVING BASELINE RISK IN PATIENTS WITH TRANSTHYRETIN AMYLOID CARDIOMYOPATHY: A SYSTEMATIC LITERATURE REVIEW OF CLINICAL TRIALS

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DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIPS WITH INDUSTRY AND ACKNOWLEDGMENTS

Ahmad Masri has acted as a researcher for Attralus, Cytokinetics, Ionis Pharmaceuticals, and Pfizer; and as a consultant, advisor, or speaker for Akros Pharma, Alexion Pharmaceuticals, Alnylam Pharmaceuticals, AstraZeneca, Attralus, BioMarin Pharmaceutical, BridgeBio Pharma (formerly Eidos Therapeutics), Bristol Myers Squibb, Cytokinetics, HAYA Therapeutics, Ionis Pharmaceuticals, Lexicon Pharmaceuticals, Pfizer, Prothena Biosciences, and Tenaya Therapeutics

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INTRODUCTION

- ATTR-CM is an underdiagnosed disease, characterized by the destabilization of TTR tetramers and accumulation of amyloid fibrils in the heart, leading to cardiac dysfunction and progressive heart failure[1–5]
- Increased awareness, early diagnosis, and the availability of a disease-modifying therapy have improved the prognosis for patients with ATTR-CM[6]
- We therefore hypothesize that patients with ATTR-CM enrolled in contemporary clinical trials may have less advanced disease than those in earlier clinical trials, indicated by lower NYHA class, lower NT-proBNP levels, and higher eGFR[2,3,7]

OBJECTIVE:

To report temporal trends in baseline disease characteristics and ACM of patients with ATTR-CM enrolled in clinical trials

ACM, all-cause mortality; ATTR-CM, transthyretin amyloid cardiomyopathy; eGFR, estimated glomerular filtration rate; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; TTR, transthyretin. 1. Brito D *et al. Glob Heart* 2023;18:59; 2. Garcia-Pavia P *et al. Eur J Heart Fail* 2021;23:512–26; 3. Kittleson MM *et al. Circulation* 2020;142:e7–22; 4. Ruberg FL *et al. J Am Coll Cardiol* 2019;73:2872–91; 5. Nativi-Nicolau J *et al. JACC Cardio Oncol* 2021;3:537–46; 6. Ioannou A *et al. Circulation* 2022;146:1657–70; 7. Garcia-Pavia P *et al. Eur J Heart Fail* 2021;23:895–905

SYSTEMATIC LITERATURE REVIEW[a]

- **Systematic literature search** conducted on November 23, 2023 in MEDLINE, Embase, Cochrane Central, key congress websites (ACC, AHA, ESC, ESCHF, HFSA, ISA), and clinical trial registries[b]
- Limited to English-language peer-reviewed journal articles (no date limit) and congress abstracts (past 2 years)

- Screening against eligibility criteria was performed by **two independent reviewers**
- A third reviewer resolved any disagreements

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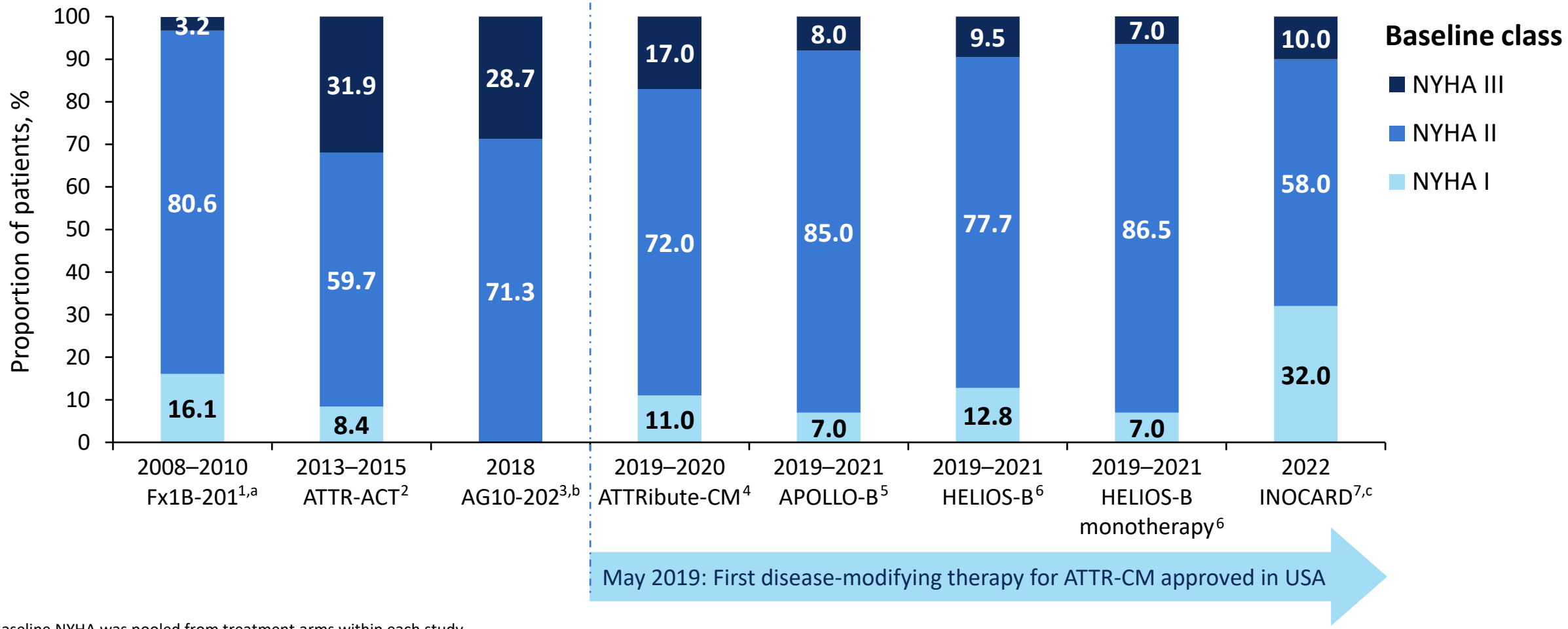
- A total of **9 unique trials in ATTR-CM** were included
  - **7** trials identified during screening (**3** RCTs, **4** single-arm trials)
  - **2** additional RCTs published after the search cut-off date

- Baseline data for **age, sex, and race were comparable** across studies.
- Baseline characteristics of interest were available for **7/9** trials
  - **ACM** data were available for **4/9** trials
  - **2/9** trials did not include data eligible for this analysis

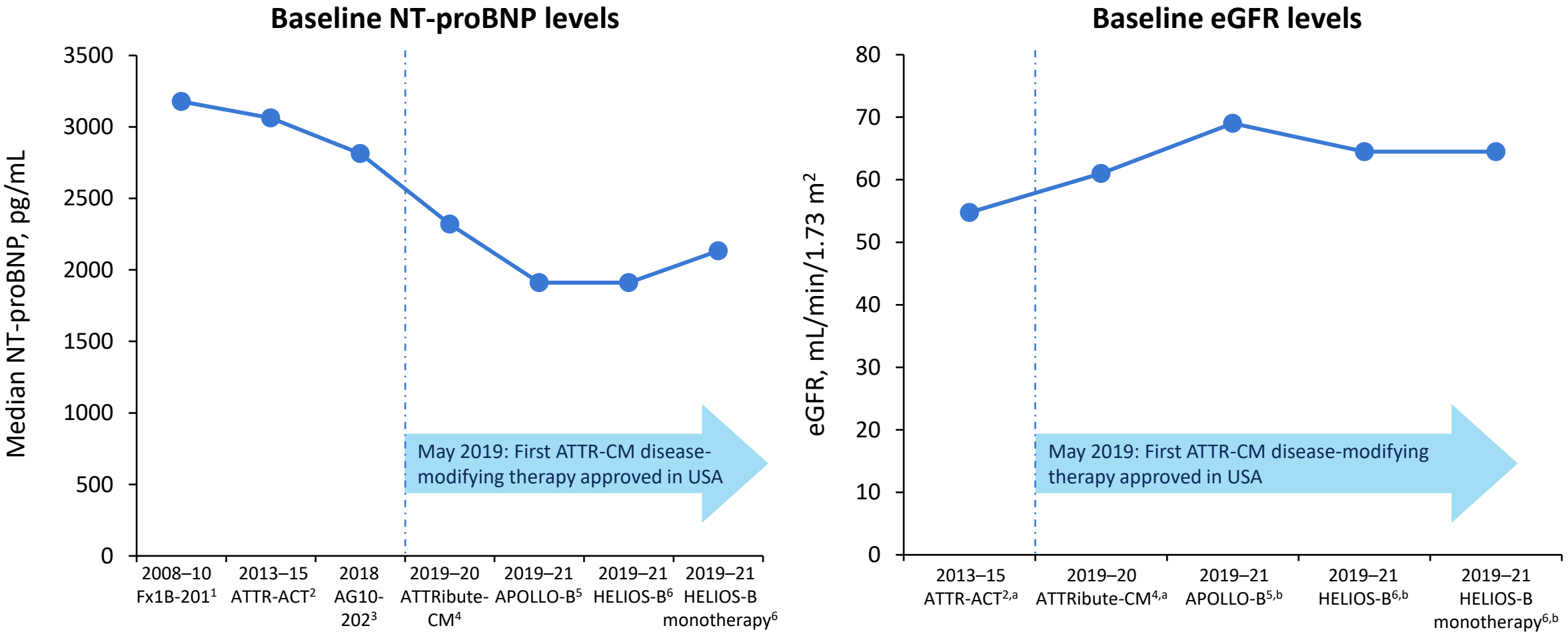
[a]The systematic literature review was conducted broadly following the standards set out in the Preferred Reporting Items for Systematic Reviews and Meta-analyses and the Cochrane Handbook for Systematic Reviews of Interventions, as well as the rigorous standards required by the National Institute for Health and Care Excellence and most health technology assessment bodies.
[b]ClinicalTrials.gov and World Health Organization.
ACC, American College of Cardiology; ACM, all-cause mortality; AHA, American Heart Association; ATTR-CM, transthyretin amyloid cardiomyopathy; ESC, European Society of Cardiology; ESCHF, European Society of Cardiology Heart Failure; HFSA, Heart Failure Society of America; ISA, International Symposium on Amyloidosis; RCT randomized controlled trial

STARTING WITH ATTR-ACT, EARLIER TRIALS HAD HIGHER PROPORTIONS OF PATIENTS WITH NYHA CLASS III THAN MORE RECENT TRIALS



Baseline NYHA was pooled from treatment arms within each study.
[a]Study enrolled patients with NYHA class I or II, or from TRACS. [b]Study enrolled patients with NYHA class II or III. [c]Study period extrapolated from year of publication.
ATTR-CM, transthyretin amyloid cardiomyopathy; NYHA, New York Heart Association; TRACS, FoldRx Study Fx-001 natural history study.
1. Maurer MS *et al. Circ Heart Fail* 2015;8:519–26; 2. Maurer MS *et al. N Engl J Med* 2018;379:1007–16; 3. Judge DP *et al. J Am Coll Cardiol* 2019;74:285–95; 4. Gillmore JD *et al. N Engl J Med* 2024;390:132–42;
5. Maurer MS *et al. N Engl J Med* 2023;389:1553–65; 6. Fontana M *et al. N Engl J Med* 2024; doi:10.1056/NEJMoa2409134; 7. Giblin GT *et al.* 2022. Presented at the XVIII. Meeting of the International Society of Amyloidosis, Heidelberg, Germany, 2022

RECENT TRIALS SHOWED A TREND TOWARDS LOWER NT-proBNP LEVELS AND HIGHER eGFR COMPARED WITH EARLIER TRIALS



Baseline NT-proBNP and baseline eGFR were pooled from treatment arms within each study. Higher NT-proBNP levels and lower eGFR indicate worse prognosis. Data calculations used weighted averages of the medians
[a]Mean. [b]Median.
ATTR-CM, transthyretin amyloid cardiomyopathy; eGFR, estimated glomerular filtration rate; NT-proBNP, N-terminal pro-B-type natriuretic peptide.
1. Maurer MS *et al. Circ Heart Fail* 2015;8:519–26; 2. Maurer MS *et al. N Engl J Med* 2018;379:1007–16; 3. Judge DP *et al. J Am Coll Cardiol* 2019;74:285–95; 4. Gillmore JD *et al. N Engl J Med* 2024;390:132–42;
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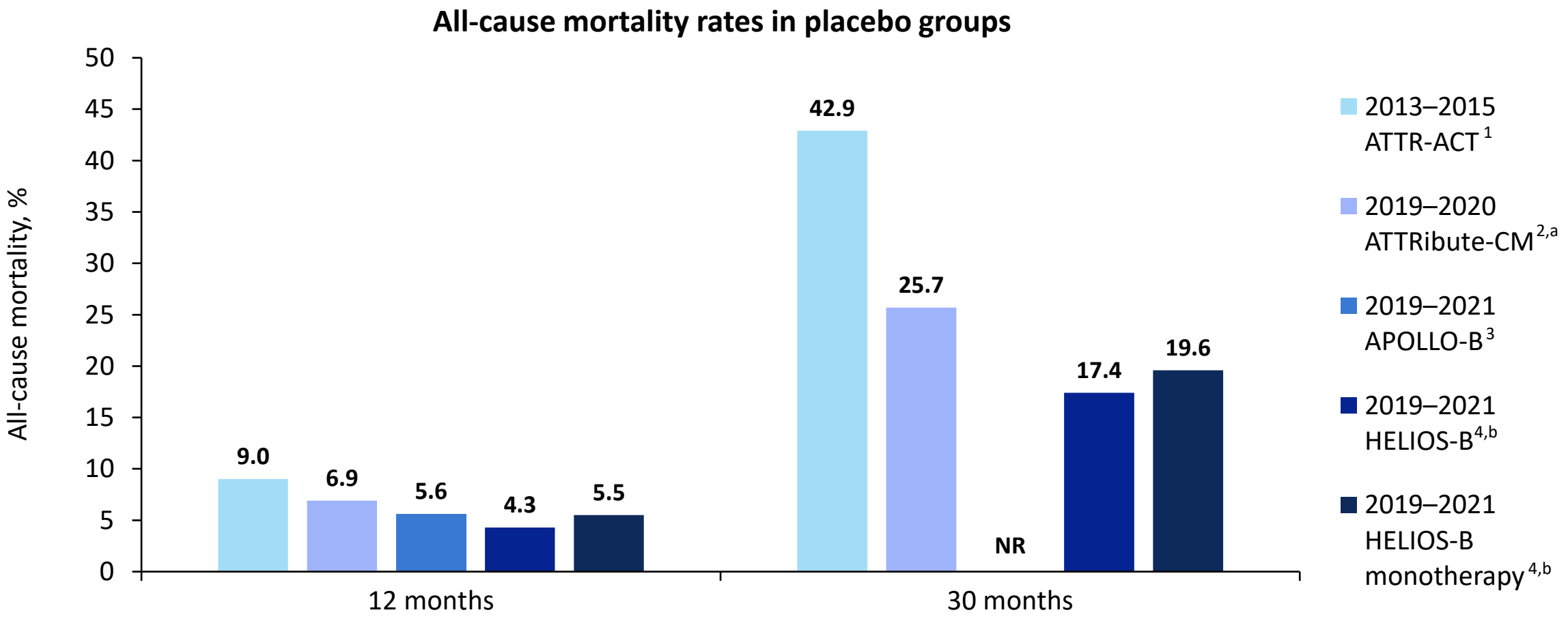
RECENT TRIALS HAD LOWER ALL-CAUSE MORTALITY AT 12 MONTHS AND 30 MONTHS IN THE PLACEBO GROUPS COMPARED WITH EARLIER TRIALS



[a]Treatment with tafamidis was permitted after Month 12 in the ATTRibute-CM trial; 23% of participants in the placebo group started tafamidis after Month 12.
[b]Treatment with tafamidis was allowed in the HELIOS-B trial; 40% of participants in the placebo group were taking tafamidis at baseline; among participants in the monotherapy population, 21% in the placebo group started tafamidis during the trial.
NR, not reported.
1. Maurer MS *et al. N Engl J Med* 2018;379:1007–16; 2. Gillmore JD *et al. N Engl J Med* 2024;390:132–42; 3. Maurer MS *et al. N Engl J Med* 2023;389:1553–65; 4. Fontana M *et al. N Engl J Med* 2024; doi:10.1056/NEJMoa2409134

CONCLUSIONS

- Recent clinical trials in ATTR-CM appear to have enrolled patients with better prognosis compared with earlier clinical trials in ATTR-CM

- As ATTR-CM is increasingly recognized and patients are diagnosed earlier after symptom onset, potentially with a lower amyloid burden, it is important to assess the benefits of disease-modifying therapies in contemporary populations

ATTR-CM, transthyretin amyloid cardiomyopathy