Tafamidis Efficacy Among Octogenarian Patients in the Phase 3 ATTR-ACT and Ongoing Long-Term Extension Study

Pablo Garcia-Pavia, MD, PhD,a,b,c Marla B. Sultan, MD, MBA,d Balarama Gundapaneni, MS,e Yoshiki Sekijima, MD,f Federico Perfetto, MD,g Mazen Hanna, MD,h Ronald Witteles, MDi

ABSTRACT

BACKGROUND Tafamidis was approved to treat patients with transthyretin amyloid cardiomyopathy (ATTR-CM) on the basis of findings from the phase 3 Tafamidis in Transthyretin Cardiomyopathy Clinical Trial (ATTR-ACT).

OBJECTIVES Post hoc analysis exploring tafamidis efficacy in octogenarian patients.

METHODS Analysis of patients aged <80 and ≥80 years in ATTR-ACT and its ongoing open-label long-term extension (LTE) study, where all patients receive tafamidis.

RESULTS After 30 months in ATTR-ACT, least squares (LS) mean change from baseline in 6-minute walk test (6MWT) distance, N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentration, and Kansas City Cardiomyopathy Questionnaire Overall Summary (KCCQ-OS) score were smaller (all \( P < 0.05 \)) in patients aged ≥80 years treated with tafamidis (n = 51) vs placebo (n = 37). At the LTE study interim analysis, patients aged ≥80 years treated continuously with tafamidis had a smaller decline in KCCQ-OS score (\( P < 0.05 \)) and trended toward longer median survival (45 vs 27 months; all-cause mortality HR: 0.6828 [95% CI: 0.4048-1.1517]; \( P = 0.1526 \)) than those initially treated with placebo in ATTR-ACT. Similar efficacy was observed in patients aged <80 years in ATTR-ACT, including smaller LS mean change from baseline in 6MWT distance, NT-proBNP concentration, and KCCQ-OS score, and lower rate of cardiovascular-related hospitalizations with tafamidis (n = 125) vs placebo (n = 140). In the LTE study, patients aged <80 years treated continuously with tafamidis had a longer median survival (80 vs 41 months; HR = 0.4513 [95% CI: 0.3176-0.6413]; \( P < 0.0001 \)) and a smaller decline in KCCQ-OS score than those initially treated with placebo.

CONCLUSIONS The findings demonstrate tafamidis efficacy for patients with ATTR-CM both in those aged <80 and those aged ≥80 years. (Tafamidis in Transthyretin Cardiomyopathy Clinical Trial [ATTR-ACT]; NCT01994889/Long-term Safety of Tafamidis in Subjects With Transthyretin Cardiomyopathy; NCT02791230) (J Am Coll Cardiol HF 2023;–:––:–). © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Translthyretin amyloid cardiomyopathy (ATTR-CM) is caused by the deposition of wild-type or variant transthyretin amyloid fibrils in the myocardium. It typically affects older adults and usually progresses to heart failure. The wild-type form of ATTR-CM is associated with aging, has a median age at onset of around 75 years, and is not typically seen in patients aged <60 years. The typical age at onset of variant ATTR-CM differs depending on the gene variation inherited. Although a substantial proportion of patients with ATTR-CM are elderly, variant ATTR-CM is often diagnosed at a younger age than is wild-type ATTR-CM.

The growing knowledge around transthyretin amyloidosis formation has allowed the development of therapies for ATTR-CM. Tafamidis was the first disease-modifying treatment proved to be efficacious, as assessed in the phase 3 Tafamidis in Transthyretin Cardiomyopathy Clinical Trial (Tafamidis in Transthyretin Cardiomyopathy Clinical Trial [ATTR-ACT]; NCT01994889). Despite being approved by the U.S. Food and Drug Administration and the European Medicines Agency without age restrictions, there are very few published evaluations of any heart failure therapies in octogenarian patients, leading to a general lack of age-specific disease management recommendations.

This post hoc analysis aimed to examine the long-term benefit of tafamidis treatment in octogenarian patients with ATTR-CM using data from ATTR-ACT and an interim analysis of the ongoing long-term extension (LTE) study.

**METHODS**

**STUDIES.** ATTR-ACT was an international, multicenter, double-blind, placebo-controlled, randomized phase 3 trial of patients with ATTR-CM. Patients were required to be between 18 and 90 years of age, to have biopsy-confirmed ATTR-CM, and a history of heart failure. Patients must also have had an N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentration of ≥600 pg/mL and a 6-minute walk test (6MWT) distance of >100 m at baseline. Exclusion criteria included NYHA functional class IV symptoms, a history of liver or heart transplantation, an implanted cardiac mechanical assist device, an estimated glomerular filtration rate <25 mL/min/1.73 m² of body surface area, liver transaminase levels more than twice the upper limit of the normal range, a modified body mass index <600 (calculated as [weight in kg/height in m²] × serum albumin concentration in g/L), or current treatment with certain nonsteroidal anti-inflammatory drugs, tauroursodeoxycholate, doxycycline, calcium channel blockers, or digitalis.

Treatment randomization was stratified by transthyretin genotype (wild-type or variant) and NYHA functional class (I or II/III). Patients received daily tafamidis meglumine 80 mg, tafamidis meglumine 20 mg, or placebo (2:1:2) for 30 months before being invited to join an open-label LTE study, where all patients received tafamidis for up to an additional 60 months (Long-term Safety of Tafamidis in Subjects With Transthyretin Cardiomyopathy; NCT02791230). Patients receiving tafamidis in ATTR-ACT initially continued this dose in the LTE study. Those who had received placebo in ATTR-ACT were randomized 2:1 to tafamidis meglumine 80 mg or 20 mg, stratified by genotype. After a protocol amendment in July 2018, all patients were transitioned to the approved tafamidis dose age of once-daily tafamidis free acid 61 mg, which is bioequivalent to tafamidis meglumine 80 mg. The LTE study is currently ongoing.

Both studies were approved by the independent review board or ethics committee at each participating center and were conducted in accordance with the Declaration of Helsinki and the International Council for Harmonisation for Good Clinical Practice Guideline. All patients provided written informed consent.

**ANALYSIS GROUPS.** This post hoc analysis includes data for all patients who were randomized to tafamidis meglumine 80 mg (the approved dose for ATTR-CM) or placebo in ATTR-ACT. Patients who were randomized to tafamidis 20 mg in ATTR-ACT are not included in this analysis, which used data spanning from the ATTR-ACT baseline to the interim data cut of the ongoing LTE study on August 1, 2021. Data were summarized by patient age at baseline (<80 years or ≥80 years) and treatment (continuous tafamidis in ATTR-ACT and the LTE study [80 mg and 61 mg], or placebo in ATTR-ACT and tafamidis in the LTE study), resulting in 4 groups.

**VARIABLES.** Demographic and clinical characteristics at the ATTR-ACT baseline are summarized descriptively.
Key efficacy measures collected up until the end of ATTR-ACT were compared between treatments (tafamidis 80 mg vs placebo) for patients aged <80 and ≥80 years. These included: 1) least squares (LS) mean change from baseline in 6MWT distance; 2) LS mean geometric fold change from baseline in NT-proBNP concentration, both compared using a mixed model for repeated measures with an unstructured covariance matrix, with center and subject within center as random effects, and treatment, visit, transthyretin genotype, and visit-by-treatment interaction as fixed effects, and baseline score as covariate; 3) LS mean change from baseline in Kansas City Cardiomyopathy Questionnaire Overall Summary (KCCQ-OS) score, compared using a mixed model for repeated measures with unstructured covariance matrix, with fixed effects of treatment, visit, transthyretin genotype, and visit-by-treatment interaction; and 4) mean rate of cardiovascular-related hospitalizations per patient, per year, compared using a Poisson regression analysis with treatment, transthyretin genotype, baseline NYHA functional class (I/II [combined] or III), treatment by transthyretin genotype interaction, and treatment by NYHA functional class interaction as factors adjusted for treatment duration.

Cardiovascular-related hospitalizations, 6MWT, and NT-proBNP were not adjudicated/monitored in the LTE study. Efficacy measures collected in the interim analysis of the LTE study (August 1, 2021) were compared between treatment groups (continuous tafamidis [tafamidis in ATTR-ACT and the LTE)
vs placebo to tafamidis (placebo in ATTR-ACT then tafamidis in the LTE study) for patients aged <80 and ≥80 years. Evaluated efficacy measures included: 1) KCCQ-OS score as described earlier; and 2) all-cause mortality, calculated by the Kaplan-Meier method and compared by a Cox proportional hazard model with treatment, baseline NYHA functional class (I/II [combined] and III), and transthyretin genotype as covariates. Patients who were discontinued because of a heart transplantation or implantation of a cardiac mechanical assist device were treated as death. The Cox proportional hazard model was also used to explore the interaction between treatment and age group. The number of patients needed to be treated to avoid 1 all-cause mortality event was calculated for each age group.

**RESULTS**

The results are summarized in the Central Illustration and in the plain language summary available in the Supplemental Appendix.

**BASELINE CHARACTERISTICS.** Of the 441 patients randomized in ATTR-ACT, 51 of 176 receiving tafamidis 80 mg and 37 of 177 receiving placebo were aged ≥80 years. Their demographics and clinical characteristics are summarized by age and treatment in Table 1. Aside from having a higher age, patients aged ≥80 years had broadly similar demographics to those aged <80 years. Higher proportions of patients aged ≥80 years had a wild-type transthyretin genotype and NYHA functional class III symptoms than in patients aged <80 years. Consistent with symptoms indicating more advanced disease, patients aged ≥80 years had higher median NT-proBNP concentrations, shorter 6MWT distances, and slightly lower mean KCCQ-OS scores at baseline than those aged <80 years.

**EFFICACY MEASURES AFTER 30 MONTHS IN ATTR-ACT.** Reflecting findings in the overall ATTR-ACT population over 30 months, patients aged <80 years and ≥80 years showed signs of disease progression that was attenuated by tafamidis treatment. Whereas all 4 groups (patients aged <80 or ≥80 years taking either tafamidis or placebo) had reductions in 6MWT distances (–50 to –156 m) (Figure 1) and increases in NT-proBNP concentration (1.18- to 2.24-fold) at
**FIGURE 1** Reduction in 6MWT Distance During ATTR-ACT by Patient Age

**A** <80 years

![Graph A](image1)

**B** ≥80 years

![Graph B](image2)

*P < 0.05 between treatment groups. 6MWT = 6-minute walk test; ATTR-ACT = Tafamidis in Transthyretin Cardiomyopathy Clinical Trial; LS = least squares.
KCCQ-OS scores were collected up to the interim analysis of the LTE study (August 1, 2021), but analysis of LS mean change stopped at month 66 because of low numbers. At the furthest timepoint (month 84) there was 1 patient remaining in the continuous tafamidis <80- and ≥80-year groups, and none in the placebo to tafamidis <80- and ≥80-year groups. Patients in the continuous tafamidis group took 80 mg tafamidis in ATTR-ACT and tafamidis in the LTE study. Patients in the placebo to tafamidis group took placebo in ATTR-ACT and tafamidis in the LTE study. *P < 0.05 between treatment groups. KCCQ-OS = Kansas City Cardiomyopathy Questionnaire Overall Summary; LTE = long-term extension.
At the interim data cut of the LTE study. The median follow-up times at the end of the LTE study were 60 months in patients aged <80 years treated with continuous tafamidis, and 56 months in patients aged ≥80 years treated with placebo in ATTR-ACT then tafamidis in the LTE study. The median follow-up times in equivalent groups of patients aged <80 years were 61 and 60 months.

The change from baseline in KCCQ-OS score from the start of ATTR-ACT to month 54 is shown in Figure 2. KCCQ-OS score continued to decline over the course of the LTE study in all 4 groups, but this decline was attenuated by tafamidis treatment in patients aged both <80 and ≥80 years. The magnitude of decline in KCCQ-OS score was generally larger in patients aged ≥80 years than in those aged <80 years; however, this decline appeared to stabilize in the LTE study for both age groups. Treatment-related statistical separation was stunted in patients aged ≥80 years because of low patient numbers.

In patients aged ≥80 years, median survival was 45 months in those treated with continuous tafamidis and 27 months in those initially treated with placebo (Figure 3). The HR for all-cause mortality trended in favor of continuous tafamidis but was not statistically significant (HR: 0.6828 [95% CI: 0.4048–1.1517]; P = 0.5721). The number of patients needed to be treated to avoid 1 event was 4.74. In patients aged <80 years, median survival was 80 months in those treated with continuous tafamidis and 41 months in those initially treated with placebo. The HR for all-cause mortality was statistically significant in favor

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Change in 6MWT Distance, NT-proBNP Concentration, and KCCQ-OS Score at 30 Months, and Cardiovascular-Related Hospitalizations During ATTR-ACT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>80 mg Tafamidis (n = 125)</td>
</tr>
<tr>
<td>Change from baseline in 6MWT distance at the end of ATTR-ACT</td>
<td></td>
</tr>
<tr>
<td>N with data at 30 mo</td>
<td>76</td>
</tr>
<tr>
<td>LS mean change</td>
<td>−50.22</td>
</tr>
<tr>
<td>Difference from placebo (95% CI)</td>
<td>74.46 (53.07–95.85)</td>
</tr>
<tr>
<td>Geometric fold change from baseline in NT-proBNP concentration at the end of ATTR-ACT</td>
<td></td>
</tr>
<tr>
<td>N with data at 30 mo</td>
<td>82</td>
</tr>
<tr>
<td>LS mean change</td>
<td>1.26</td>
</tr>
<tr>
<td>Difference from placebo (95% CI)</td>
<td>0.56 (0.47–0.68)</td>
</tr>
<tr>
<td>Change from baseline in KCCQ-OS score at the end of ATTR-ACT</td>
<td></td>
</tr>
<tr>
<td>N with data at 30 mo</td>
<td>82</td>
</tr>
<tr>
<td>LS mean change</td>
<td>−4.2</td>
</tr>
<tr>
<td>Difference from placebo (95% CI)</td>
<td>14.31 (9.39–19.24)</td>
</tr>
<tr>
<td>Cardiovascular-related hospitalizations during the 30 mo of ATTR-ACT</td>
<td></td>
</tr>
<tr>
<td>Patients with hospitalizations, n (%)</td>
<td>65 (52.0)</td>
</tr>
<tr>
<td>Mean rate of hospitalizations per y</td>
<td>0.44</td>
</tr>
<tr>
<td>Rate ratio for tafamidis vs placebo (95% CI)</td>
<td>0.63 (0.50–0.80)</td>
</tr>
</tbody>
</table>

6MWT = 6-minute walk test; KCCQ-OS = Kansas City Cardiomyopathy Questionnaire Overall Summary; NT-proBNP = N-terminal pro B-type natriuretic peptide.
FIGURE 3  All-Cause Mortality in ATTR-ACT and the LTE Study by Patient Age

**A** <80 years

<table>
<thead>
<tr>
<th>Months</th>
<th>0</th>
<th>14</th>
<th>28</th>
<th>42</th>
<th>56</th>
<th>70</th>
<th>84</th>
<th>98</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONT</td>
<td>125</td>
<td>112</td>
<td>94</td>
<td>71</td>
<td>51</td>
<td>25</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PLACEBO</td>
<td>140</td>
<td>121</td>
<td>92</td>
<td>52</td>
<td>30</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**B** ≥80 years

<table>
<thead>
<tr>
<th>Months</th>
<th>0</th>
<th>14</th>
<th>28</th>
<th>42</th>
<th>56</th>
<th>70</th>
<th>84</th>
<th>98</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONT</td>
<td>51</td>
<td>38</td>
<td>32</td>
<td>24</td>
<td>10</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>PLACEBO</td>
<td>37</td>
<td>32</td>
<td>18</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Patients who underwent heart transplantation or implantation of a cardiac mechanical assist device were treated as deceased. There were 52 events in the continuous tafamidis group who were aged <80 years, comprising 43 deaths, 7 heart transplantations, and 2 cardiac mechanical assist device implantations. Comparable values in the placebo to tafamidis group who were aged <80 years, the continuous tafamidis group who were aged ≥80 years, and the placebo to tafamidis group who were aged ≥80 years are 90, 84, 6, 0; 32, 32, 0; 31, 31, 0. Analysis from ATTR-ACT baseline to LTE study interim analysis dated August 1, 2021. Patients in the continuous tafamidis group took 80 mg tafamidis in ATTR-ACT and tafamidis in the LTE study. Patients in the placebo to tafamidis group took placebo in ATTR-ACT and tafamidis in the LTE study. Abbreviations as in Figures 1 and 2.
of continuous tafamidis treatment (HR: 0.4513 [95% CI: 0.3176-0.6413]; \( P < 0.0001 \)). The number of patients needed to be treated to avoid 1 event was 4.41. The interaction between treatment and age subgroups (\( \geq 80 \) and \(< 80 \) years) was not significant (\( P = 0.8696 \)).

**DISCUSSION**

The efficacy of tafamidis was proven among patients with ATTR-CM aged 46 to 90 during ATTR-ACT and continues to be demonstrated in the ongoing LTE study.\(^8,16,17\) This post hoc analysis further supports the efficacy of tafamidis treatment in octogenarian patients.

ATTR-CM is a condition that predominantly affects older adults, with a substantial proportion of patients aged \( \geq 80 \) years.\(^5,18-20\) In particular, an age-associated increase in wild-type ATTR-CM prevalence has been found in autopsy studies, demonstrating a relationship with aging.\(^2,21\) Elderly patients with heart failure of various causes are known to have a shorter median survival and more cardiovascular-related hospitalizations than younger patients.\(^22,23\) Although very few clinical trials have included patients aged \( \geq 80 \) years, limited data suggest that the efficacy of heart failure treatments remains demonstrable in elderly patients; however, in the real world, patients aged \( \geq 80 \) years are commonly undertreated with the guideline-recommended therapies.\(^13,15,22,24\) The reasons for this undertreatment are poorly defined, but likely they relate to difficulties navigating factors common to older individuals, such as comorbidities, intolerances, frailty, polypharmacy, and patient expectations for their life.\(^10\) Although ATTR-CM (in particular wild-type ATTR-CM) is an age-related and progressive disease, no studies have specifically looked at the long-term effects of treatment in octogenarian patients.

This analysis of ATTR-ACT data found that patients aged \( \geq 80 \) years had more advanced disease than did those aged \(< 80 \) years at enrollment. The proportion of patients aged \( \geq 80 \) years with NYHA functional class III symptoms was higher than among patients aged \(< 80 \) years, as was median NT-proBNP concentration, whereas 6MWT distance and mean KCCQ-OS scores were lower. Given that damage to the heart in ATTR-CM is considered irreversible, this puts patients with advanced disease at a disadvantage in terms of potential outcomes with treatment. Among patients receiving the same treatment over the 30 months of ATTR-ACT (ie, tafamidis or placebo), those who were aged \( \geq 80 \) years showed a higher mean rate of cardiovascular-related hospitalizations per year and a larger decline in 6MWT distance and KCCQ-OS score than did those aged \(< 80 \) years. These findings presumably reflect the more advanced disease processes in these patients and the expected decrease in physicality associated with aging. Interestingly, fold changes in NT-proBNP over the duration of ATTR-ACT were slightly lower in patients aged \( \geq 80 \) years than in those aged \(< 80 \) years. This may be due to the already high concentrations of NT-proBNP at baseline in these patients (median: 3,828 to 4,007 pg/mL in patients aged \( \geq 80 \) years vs 2,681 to 3,015 pg/mL in those aged \(< 80 \) years).

Across both age groups, we found that treatment with tafamidis was associated with attenuated disease progression measures; namely, smaller reductions in 6MWT distance and KCCQ-OS score, and smaller increases in NT-proBNP as compared with placebo treatment over the 30 months of ATTR-ACT. Treatment with tafamidis was associated with a lower rate of cardiovascular-related hospitalizations (significant in patients aged \(< 80 \) years, but not in those aged \( \geq 80 \) years). In interim data from the LTE study, the decline in KCCQ-OS score was smaller in patients treated with continuous tafamidis in ATTR-ACT and the LTE study as compared with those who initially received placebo in ATTR-ACT and then tafamidis in the LTE study. Median survival was also longer in patients treated with continuous tafamidis vs placebo in ATTR-ACT then tafamidis in the LTE study among patients aged \(< 80 \) years (80 vs 41 months) and \( \geq 80 \) years (45 vs 27). The treatment effect on all-cause mortality among patients aged \( \geq 80 \) years was favorable but not statistically significant, likely because of the smaller numbers of patients. Tafamidis safety data from this interim analysis have been previously published, and they demonstrated a profile that was consistent with that reported in ATTR-ACT and at earlier timepoints in the LTE study.\(^8,16,17\) Overall, these findings reflect the efficacy established in the overall ATTR-ACT population and demonstrate both an initial and an enduring benefit of early tafamidis treatment in patients aged \( \geq 80 \) years.\(^8,16,17\)

**STUDY LIMITATIONS.** The limitations of this analysis include the low patient numbers toward the interim analysis of the LTE study, particularly in the placebo to tafamidis group aged \( \geq 80 \) years. The patients in this group were elderly at the start of ATTR-ACT (\(< 83 \) years), and the latest interim analysis was more than 5 years after enrollment, so this is presumably related to the additional mortality expected in this group as a result of old age. Patients enrolled in ATTR-ACT must have been able to walk \( \geq 100 \) m in the
6MWT, which would have excluded otherwise eligible elderly patients who were wheelchair bound or had poor mobility. This was not a prespecified analysis, and patient numbers were not planned to allow for statistical power. Further, despite the ability to detect a long-term value of early tafamidis treatment, as all patients received tafamidis in the LTE study, the ability to demonstrate the full value of long-term treatment is limited.

**CONCLUSIONS**

Patients with ATTR-CM aged <80 and ≥80 years who received tafamidis treatment had better outcomes than did patients who initially received placebo across several measures. Octogenarians treated with tafamidis in ATTR-ACT had a smaller decline in quality of life and in functional capacity, and a smaller change in a biomarker of heart function at 30 months compared with those treated with placebo. In the LTE study, octogenarians treated with continuous tafamidis maintained a smaller decline in quality of life and had a nonsignificant trend toward longer survival than did octogenarians who received placebo in ATTR-ACT, then tafamidis in the LTE study. Patients aged <80 years had similar findings, additionally with a lower rate of cardiovascular-related hospitalizations in ATTR-ACT among those treated with tafamidis vs placebo, and a statistically longer survival in the LTE study among those who took tafamidis continuously vs those who initially received placebo in ATTR-ACT. These findings demonstrate the efficacy of tafamidis across age groups, including octogenarian patients.

**ACKNOWLEDGMENTS** Medical writing support was provided by Jennifer Bodkin of Engage Scientific Solutions and was funded by Pfizer.

**DATA AVAILABILITY STATEMENT** Upon request, and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions, and exceptions, Pfizer may also provide access to the related individual de-identified participant data. See https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information.

**FUNDING SUPPORT AND AUTHOR DISCLOSURES**

This study was sponsored by Pfizer. Pfizer contributed to the design and conduct of the study and management and collection of data. In their role as authors, employees of Pfizer were involved in the analysis and interpretation of data, preparation, review, and approval of the manuscript and the decision to submit for publication, along with their co-authors. The study sponsor approved the manuscript from an intellectual property perspective but had no right to veto the publication. Dr Garcia-Pavia has served as a speaker in scientific meetings for Alexion, Alnylam, BridgeBio, Ionis, AstraZeneca, Novo Nordisk, and Pfizer; has received funding from Alnylam and Pfizer for scientific meeting expenses; has received consultancy fees from Alnylam, Attralus, BridgeBio, NeuroImmune, AstraZeneca, Novo Nordisk, Alexion, Intellia, and Pfizer; and his institution has received research grants/educational support from Alnylam, AstraZeneca, BridgeBio, Intellia, and Pfizer. Dr Sultan and Mr Gundapaneni are full-time employees of Pfizer and hold stock/stock options. Dr Sekijima has a patent concerning tafamidis; has received honoraria for lectures and advisory board participation from Pfizer and Alnylam; and his institution has received research grants from Pfizer and Alnylam. Dr Perfetto has received honoraria for advisory board participation from Pfizer, Alnylam, and Akcea. Dr Hanna has received honoraria for advisory board participation from Pfizer, Alnylam, Akcea, Alexion, and Eisai; and has served as a speaker for a scientific meeting session funded by Alnylam. Dr Witteles has received honoraria for advisory board participation from Pfizer, Alnylam, Ionis, AstraZeneca, Janssen, Intellia, BridgeBio, Novo Nordisk, and Alexion.

**ADDRESS FOR CORRESPONDENCE:** Dr Pablo Garcia-Pavia, Heart Failure and Inherited Cardiac Diseases Unit, Department of Cardiology, Hospital Universitario Puerta de Hierro, Manuel de Falla, 2, Madrid 28222, Spain. E-mail: pablogpavia@yahoo.es.

**PERSPECTIVES**

**COMPETENCY IN MEDICAL KNOWLEDGE:** This analysis confirms the efficacy of tafamidis versus placebo in patients with ATTR-CM, including octogenarians, who had a significantly smaller decline in KCCQ-OS score, 6MWT distance, and increase in NT-proBNP concentration after 30 months of treatment in ATTR-ACT. In the LTE study, octogenarians treated with continuous tafamidis maintained a smaller decline in KCCQ-OS score and trended toward having longer survival than octogenarians who had been treated with placebo in ATTR-ACT and then received tafamidis in the LTE study.

**TRANSLATIONAL OUTLOOK:** Further studies and guidelines on the treatment of older patients with heart failure can help guide optimal management, including for those with ATTR-CM.
REFERENCES


KEY WORDS age, amyloidosis, elderly, heart failure with preserved ejection fraction, survival

APPENDIX For a supplemental appendix, please see the online version of this paper.