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Survival in a Real-World Cohort of Patients With Transthyretin Amyloid Cardiomyopathy Treated With Tafamidis: An Analysis From the Transthyretin Amyloidosis Outcomes Survey (THAOS)

PABLO GARCIA-PAVIA, MD, PhD[1,2,3] ARNT V. KRISTEN, MD[4] BRIAN DRACHMAN, MD[5] MARTIN CARLSSON, MS[6] LESLIE AMASS, PhD[6] FRANCA STEDILE ANGELI, MD, PhD[6] and MATHEW S. MAURER, MD[7], on behalf of the THAOS investigators[a]

Madrid, and Pozuelo de Alarcon, Spain; Heidelberg, Germany; and Philadelphia, and New York, USA

From the [1]Hospital Universitario Puerta de Hierro Majadahonda, IDIPHISA, CIBERCV, Madrid, Spain; [2]Universidad Francisco de Vitoria, Pozuelo de Alarcon, Spain; [3]Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain; [4]Department of Cardiology, Angiology, and Respiratory Medicine, Medical University of Heidelberg, Heidelberg, Germany; [5]University of Pennsylvania Health System, Philadelphia, PA, USA; [6]Pfizer Inc, New York, NY and [7]Columbia University College of Physicians and Surgeons, New York, NY, USA.

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Reprint requests: Pablo Garcia-Pavia, Heart Failure and Inherited Cardiac Diseases Unit, Department of Cardiology, Hospital Universitario Puerta de Hierro Majadahonda, Manuel de Falla, 1, 28222 Majadahonda. Madrid, Spain. Tel: 34 91 191 7297; Fax: 34 91 191 7718. E-mail: pablogpavia@yahoo.es

[a]Additional THAOS investigators contributing to this analysis: Angela Dispenzieri, Mayo Clinic, Rochester, MN, USA; Martha Grogan, Mayo Clinic, Rochester, MN, USA; Eve Cariou, CHU de Toulouse - Hopital Rangueil, Toulouse, France; Igor Diemberger, University of Bologna, Bologna, Italy; Edward Miller, Smilow Cancer Hospital at Yale New Haven, New Haven, CT, USA; Mazen Hanna, Cleveland Clinic Foundation, Cleveland, OH, USA; Henning Moelgaard, Aarhus University Hospital, Skejby, Aarhus, Denmark; Calogero Lino Cirami, Azienda Ospedaliero-Universitaria di Careggi, Firenze, Italy; Michele Emdin, Fondazione Toscana Gabriele Monasterio Per La Ricerca Medica E Di Sanita Pubblica (Ftgm), Pisa, Italy; David Slosky, Vanderbilt University School of Medicine, Nashville, TN, USA; Olga Azevedo, Centro Hospitalar Do Alto Ave, Epe, Guimaraes, Portugal; Jose Tallaj, University of Alabama at Birmingham, Birmingham, AL, USA; Diego Delgado, Toronto General Hospital, Toronto, Canada; Jose Gonzalez Costello, Hospital Universitari de Bellvitge, Barcelona, Spain; Scott Hummel, University of Michigan, Ann Arbor, MI, USA; Carsten Tschoepe, Charite Campus Rudolf-Virchow-Klinikum, Berlin, Germany; Sanjiv Shah, Northwestern University, Chicago, IL, USA; Srinivas Murali, Wexford Health and Wellness Pavillion, Pittsburgh, PA, USA; Nowell Fine, University of Alberta Foothills Medical Centre, Calgary, Canada; Edileide de Barros Correia, Instituto Dante Pazzanese De Cardiologia, Sao Paulo, Brazil; Marcia Waddington-Cruz, Hospital Universitario Clementino Fraga Filho - HU, Rio de Janeiro, Brazil; Hector Ventura, John Ochsner Heart & Vascular Institute, New Orleans, LA, USA; Daniel Lenihan, Washington University School of Medicine, St. Louis, MO, USA; Christopher Mueller, Medical College of Wisconsin, Milwaukee, WI, USA; Yoshiki Sekijima, Shinshu University School of Medicine, Matsumoto, Japan; Jocelyn Inamo, Chu De Fort De France, Fort de France, France; Darae Kim, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; Ronald Witteles, Stanford University School of Medicine, Stanford, CA, USA; Miriam Freimer, The Ohio University College of Medicine, Columbus, OH, USA; William Cotts, Advocate Christ Medical Centre, Oak Lawn, IL, USA; Jose Nativi Nicolau, The University of Utah Health Sciences Center, Salt Lake City, UT, USA; James Tauras, Montefiore Medical Center-Jack D. Weiler Hospital, Bronx, NY, USA; Johan Van Cleemput, Afdeling Klinische Cardiologie, O&N I, Leuven, Belgium; Hans Nienhuis, University Medical Center Groningen, Groningen, Netherlands; Isabel Conceicao, Hospital Santa Maria, Lisboa, Portugal; Jonas Wixner, Umeå University Hospital, Umeå, Sweden; Dianna Quan, UC Denver, Aurora, CO, USA; Firas Al Badarin, Cleveland Clinic Abu Dhabi LLC, Abu Dhabi, United Arab Emirates; Mitsuharu Ueda, Kumamoto University, Kumamoto, Japan; Teresa Coelho, Unidade Clinica de Paramiloidose-Centro Hospitalar Porto, EPE-Hospital Geral Santo Antonio, Porto, Portugal; Dania Mohty, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia; Jeffrey Ralph, University of California – San Francisco, Department of Neurology, San Francisco, CA, USA; David Steidley, Mayo Clinic Arizona, Phoenix, AZ, USA; Robert Brunkhorst, University Hospital of RWTH Aachen, Aachen, Germany; Juan Gonzalez Moreno, Hospital Son Llàtzer, Palma de Mallorca, Spain; Violaine Plante-Bordeneuve, CHU Henri Mondor, Créteil, France; Marco Luigetti, Fondazione Policlinico Gemelli - Universita Cattolica del Sacro Cuore, Roma, Italy; Stephen Gottlieb, University of Maryland, Baltimore, MD, USA; Nitasha Sarswat, University of Chicago Medical Center, Chicago, IL, USA; Ivailo Tournev, Alexandrovska University Hospital Clinic of Neurology, Sofia, Bulgaria; Michael Praktiknjo, Universitatsklinikum Muenster - Transplant Hepatology, Münster, Germany; Roberto Fernandéz Torrón, Hospital Universitario Donostia, San Sebastian, Spain; Jeeyoung Oh, Konkuk University Medical Center, Seoul, Republic of Korea; Sorina Badelita, Institutul De Cardiologie Prof. Dr. C. C. Iliescu Spitalului Fundeni, Bucuresti, Romania; Michael Polydefkis, Johns Hopkins Hospital, Baltimore, MD, USA; James Hoffman, University of Miami Hospital & Clinics, Miami, FL, USA; Sasa Zivkovic, University of Pittsburgh Medical Center (UPMC), Pittsburgh, PA, USA; Alberta Warner, VA Greater Los Angeles Healthcare System, Los Angeles, CA, USA.

See page 532 for disclosure information.

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ABSTRACT

Background: In the pivotal Tafamidis in Transthyretin Cardiomyopathy Clinical Trial (ATTR-ACT), tafamidis significantly reduced mortality rates, leading to its approval in many countries for the treatment of transthyretin amyloid cardiomyopathy (ATTR-CM). Real-world evidence on survival in patients with ATTR-CM following tafamidis treatment has not been extensively reported.

Methods and Results: The Transthyretin Amyloidosis Outcomes Survey (THAOS) was a longitudinal, observational, phase 4 study of patients with transthyretin amyloidosis and asymptomatic participants carrying pathogenic transthyretin variants. Patients from THAOS with a predominantly cardiac phenotype at enrollment were included, and survival was analyzed according to tafamidis treatment status (treated or untreated). Results are based on the completed THAOS dataset. In tafamidis-treated (n = 587) and tafamidis-untreated (n = 854) patients, respectively, median age at enrollment was 77.7 and 76.4 years, 91.8% and 90.0% were male, and 91.8% and 83.8% had wild-type disease. Survival rates (95% CI) at 30 and 42 months, respectively, were 84.4% (80.5−87.7) and 76.8% (70.9−81.7) in tafamidis-treated patients, and 70.0% (66.4-73.2) and 59.3% (55.2-63.0) in tafamidis-untreated patients. Survival rates in genotype subgroups (wild-type and variant) were similar to those of the overall cohort. Survival rates were better in a contemporary cohort, as reflected by a sensitivity analysis performed in patients enrolled after vs before 2019. No new safety signals were identified.

Conclusions: In this real-world cohort of patients with ATTR-CM, survival rates were higher than in ATTR-ACT and consistent with more recent reports, suggesting early diagnosis and treatment with tafamidis has improved life expectancy in ATTR-CM. These results provide further evidence supporting tafamidis' safety and effectiveness.

Trial registration: ClinicalTrials.gov identifier: NCT00628745 (*J Cardiac Fail 2025;31:525−533*)

Key Words: Transthyretin amyloid cardiomyopathy, tafamidis, real-world, survival.

Introduction

Transthyretin amyloid cardiomyopathy (ATTR-CM) is a progressive disease caused by the accumulation of misfolded transthyretin (TTR) amyloid fibrils in the extracellular matrix of the heart, leading to progressive heart failure, arrhythmias and conduction-system disease.[1−3] ATTR-CM can be caused by pathogenic variants in the *TTR* gene (hereditary or variant; ATTRv-CM) or the accumulation of wild-type TTR protein (wild-type; ATTRwt-CM).[1] Untreated ATTR-CM has a poor prognosis, with median survival estimates between 2 and 6 years.[4]

Tafamidis, a selective TTR stabilizer, is the first disease-modifying therapy for patients with ATTR-CM and has regulatory approval in over 50 countries worldwide. The approval was based on positive findings from the Tafamidis in Transthyretin Cardiomyopathy Clinical Trial (ATTR-ACT) (NCT01994889), a phase-3 study, conducted from 2013−2018, that investigated the efficacy and safety of tafamidis in patients with ATTRv-CM or ATTRwt-CM.[5] Patients in ATTR-ACT were randomized 2:1:2 to tafamidis meglumine 80 mg, tafamidis meglumine 20 mg or placebo for 30 months. Primary results showed a reduction in all-cause mortality (hazard ratio 0.70; 95% confidence interval [CI] 0.51−0.96) and a lower rate of cardiovascular-related hospitalizations (relative risk ratio 0.68; 95% CI 0.56−0.81) with tafamidis vs placebo.[5] Follow-up analyses of ATTR-ACT, combined with data from its long-term extension study (NCT02791230), found that patients initially treated with tafamidis in ATTR-ACT had substantially better survival rates than those initially treated with placebo after a median follow-up of ∼ 58 months,[6] which highlights the importance of early diagnosis and treatment in patients with ATTR-CM.

The Transthyretin Amyloidosis Outcomes Survey (THAOS) (NCT00628745) was a global, longitudinal, observational, phase 4 study open to patients with ATTR amyloidosis (inclusive of ATTR-CM and transthyretin amyloid polyneuropathy [ATTR-PN]) who were treatment-naïve or receiving tafamidis, as well as asymptomatic participants with pathogenic *TTR* variants. THAOS was completed on June 16, 2023, and remains the largest and longest transthyretin amyloidosis disease registry to date, enrolling 6718 participants across 33 countries over a 16-year period. The objective of this analysis from THAOS was to examine real-world survival in a tafamidis-treated and tafamidis-untreated ATTR-CM population.

Methods

Study Design and Patients

Full details of study design and eligibility criteria of THAOS have been published.[7] All THAOS sites received ethical or institutional review board approval before patient enrollment, and each patient provided written informed consent. The study followed the Good

Pharmacoepidemiology Practice guidelines and the principles of the Declaration of Helsinki. Individual study sites entered patients' data into the THAOS database, which is managed by Pfizer.

This analysis included all patients from THAOS with predominantly cardiac phenotypes at enrollment, which was defined as patients with ATTR-CM without signs and symptoms suggestive of associated ATTR amyloidosis-related neuropathy. Full details of the predominantly cardiac phenotype definition are provided in Supplementary Methods. Patients were categorized as tafamidis-treated if they received tafamidis while enrolled in THAOS, or as tafamidis-untreated if they never received tafamidis while enrolled in THAOS. Patients were not receiving any other investigational treatments for ATTR-CM, and data were censored during any period of time when a patient participated in another clinical trial.

Outcomes and Analysis

The tafamidis-untreated set included all available data from patients enrolled in THAOS who never received tafamidis during THAOS. The tafamidis-treated set included: (1) all available data from enrollment to final discontinuation of tafamidis or end of follow-up in THAOS (whichever was earlier) from patients receiving tafamidis at or prior to enrollment; and (2) all available data from first tafamidis dose to final discontinuation of tafamidis or end of follow-up in THAOS (whichever was earlier) from patients who initiated tafamidis after enrollment. Patients who received any dose of tafamidis were included to provide an accurate representation of the real-world experience of this patient population.

Baseline demographic and clinical characteristics are reported as number (percentage) for categorical data and median (10th and 90th percentiles) for continuous data. Clinical characteristics included *TTR* genotype, New York Heart Association (NYHA) functional class, left ventricular (LV) septum thickness, LV ejection fraction, modified body mass index; calculated by multiplying body mass index by the serum albumin level to compensate for fluid accumulation), past or current clinical trial participation, diagnostic method, N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentration, estimated glomerular filtration rate, troponin I and T concentration, and National Amyloidosis Centre stage.

Survival was analyzed using the Kaplan-Meier method. Kaplan-Meier curves for the tafamidis-treated and tafamidis-untreated sets are presented up to month 42, and overall survival estimates and 2-sided 95% CIs are provided at months 30 and 42. Patients were censored at last follow-up, the last treatment date (for treated patients), the study discontinuation date, or at enrollment in another clinical trial. Sensitivity analyses were conducted to examine survival in patients with a wild-type or variant *TTR* genotype, in patients enrolled in THAOS before and after 2019, and in patients treated with tafamidis meglumine 80 mg/free acid 61 mg only. After the study was closed, additional information was received from a single study site in the United States that called into question the tafamidis exposure status of 99 untreated patients with predominantly cardiac phenotypes from that site. We were no longer able to verify whether these patients were treated with tafamidis or not, so an additional sensitivity analysis was conducted to exclude these 99 patients from the untreated cohort.

Safety data were collected prospectively from the time patients began tafamidis while enrolled in THAOS or at the time of the patients' informed consent if the patients were being treated at enrollment. The safety-data collection period continued through the end of the observation period of the study, which must have included $\geq$ 28 days after the last administration of tafamidis.

The first patient included in this analysis was enrolled on December 20, 2007, and the final data cutoff date was July 24, 2023.

Results

Baseline Characteristics and Treatment

Of 6718 patients enrolled in THAOS, 1441 had a predominantly cardiac phenotype (tafamidis-treated, n = 587; tafamidis-untreated, n = 854) and were included in this analysis (Supplementary Fig. S1). Patients in this analysis were enrolled in 18 countries (Fig. 1). In tafamidis-treated and tafamidis-untreated patients, respectively, median age at enrollment was 77.7 and 76.4 years, and 91.8% and 90.0% were male (Table 1). The largest proportion of tafamidis-treated patients (73.4%) enrolled in THAOS between 2019 and 2023, whereas the largest proportion of tafamidis-untreated patients (54.8%) enrolled between 2013 and 2018. The proportion of patients with a variant *TTR* genotype (8.2% vs 16.2%) and in NYHA class III (21.1% vs 26.9%) was numerically lower in tafamidis-treated vs tafamidis-untreated patients. The most common *TTR* variant in both groups was V122I (p. V142I); the proportion of patients with the V122I variant was numerically lower in tafamidis-treated vs tafamidis-untreated patients (3.6% vs 8.1%). In patients with available data, the median LV septal thickness was 17.0 mm in both groups, and the median LV ejection fraction was 50.0% in tafamidis-treated patients and 49.0% in tafamidis-untreated patients. Median NT-proBNP levels were lower in the 157 tafamidis-treated patients vs the 487 tafamidis-untreated patients with available data (1883.0 vs 2498.0 pg/mL). The proportions of patients in National Amyloidosis Centre stage I–III were generally similar between groups, although data were missing for a majority of patients (Supplementary Table S1). Median follow-up time was 2.2 years in the treated group and 2.3 years in

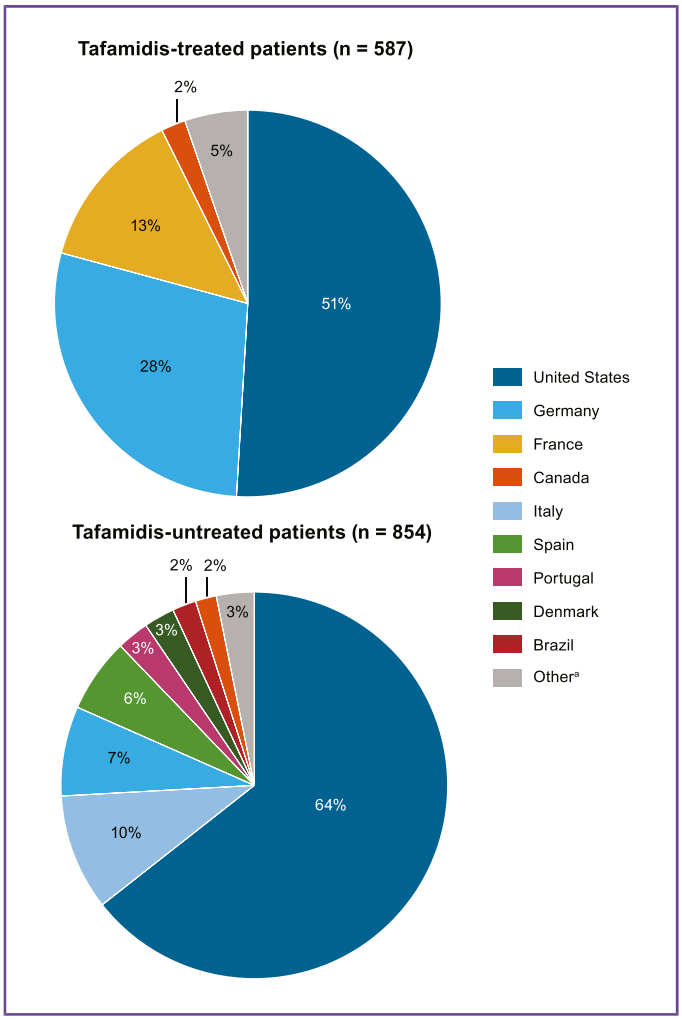


Fig. 1. Country of enrollment for tafamidis-treated and tafamidis-untreated patients. [a]Includes countries with fewer than 10 enrolled patients.

the untreated group; 11 and 67 patients, respectively, were lost to follow-up.

In the tafamidis-treated group, a majority of patients (n = 455 [77.5%]) received tafamidis meglumine 80 mg or bioequivalent free acid 61 mg throughout the study. The remaining patients received tafamidis meglumine 20 mg throughout the study (n = 52 [8.9%]), initially received tafamidis meglumine 20 mg, then switched to tafamidis meglumine 80 mg/free acid 61 mg (n = 73 [12.4%]) or received another dose (n = 7 [1.2%]). Median (10th, 90th percentile) treatment duration was 2.0 (0.6, 3.5) years. Among tafamidis-treated patients, 43.4% received concomitant medication for cardiovascular disease prior to tafamidis (Supplementary Table S2), and 22.3% received concomitant medication for cardiovascular disease on or after the first dose of tafamidis (Supplementary Table S3). Among tafamidis-untreated patients, 45.9% received concomitant medication for cardiovascular disease (Supplementary Table S2).

Survival

Survival rates at 30 and 42 months, respectively, were 84.4% (95% CI 80.5–87.7) and 76.8% (95% CI 70.9–81.7) in tafamidis-treated patients, and 70.0% (95% CI 66.4–73.2) and 59.3% (95% CI 55.2–63.0) in tafamidis-untreated patients (Visual take home graphic). When the 99 patients from a single site in the United States with uncertain tafamidis-treatment status were removed from the untreated cohort, the survival rates at 30 (69.0% [95% CI 65.3–72.5]) and 42 months (58.0% [53.9–62.0]) were similar and within 1% of the rates in the original untreated cohort (Supplementary Fig. S2).

Survival rates did not differ numerically between patients with wild-type and variant *TTR* genotype among tafamidis-treated patients (Supplementary Fig. S3, A) and tafamidis-untreated (Supplementary Fig. S3, B) patients, although the number of patients with a variant *TTR* genotype was small, especially after month 12.

In patients enrolled in THAOS prior to 2019, survival rates at 30 and 42 months, respectively, were 77.7% (95% CI 69.5–84.0) and 66.0% (95% CI 55.6–74.6) in tafamidis-treated patients, and 68.7% (95% CI 64.6–72.4) and 58.0% (95% CI 53.6–62.1) in tafamidis-untreated patients (Supplementary Fig. S4, A). In patients enrolled in THAOS in 2019 or later, survival rates at 30 and 42 months, respectively, were 87.3% (95% CI 82.6–90.8) and 82.8% (95% CI 75.7–87.9) in tafamidis-treated patients and 77.2% (95% CI 69.8–83.1) and 67.3% (95% CI 56.9–75.8) in tafamidis-untreated patients (Supplementary Fig. S4, B). In patients who received tafamidis meglumine 80 mg/free acid 61 mg only, survival rates were 83.1% (95% CI 78.4–87.0) at month 30 and 81.1% (95% CI 75.7–85.4) at month 42 (Supplementary Fig. S5, A). In patients who received tafamidis meglumine 80 mg/free acid 61 mg only and who enrolled in 2019 or later, the survival rate was 86.3% (95% CI 80.4–90.5) at months 30 and 42 (Supplementary Fig. S5, B).

Safety

All-causality, treatment-emergent adverse events (AEs) occurred in 161 (27.4%) tafamidis-treated patients (Table 2). No tafamidis-treated patient had a dosage reduction due to AEs, and 16 (2.7%) had the study drug withdrawn (temporarily, permanently or delayed) due to AEs.

During the study period, 44 (7.5%) tafamidis-treated patients and 354 (41.5%) tafamidis-untreated patients died, and 138 (23.5%) and 263 (27.6%) were hospitalized. Hospitalizations in 52 (8.9%) tafamidis-treated patients and 138 (16.2%) tafamidis-untreated patients were related to ATTR amyloidosis, as assessed by the investigator.

Discussion

In this real-world analysis of the final database of THAOS, the survival rate at 42 months was 76.8% in tafamidis-

Table 1 Baseline demographic and clinical characteristics

	Tafamidis-treated (n = 587)	Tafamidis-untreated (n = 854)	*P* Value
Sex, n (%)			0.25
Male	539 (91.8)	769 (90.0)	
Female	48 (8.2)	85 (10.0)	
Race/ethnicity,*n (%)	502	767	<0.001
Afro-Caribbean	1 (0.2)	8 (1.0)	
American Hispanic	1 (0.2)	0	
Asian	9 (1.8)	8 (1.0)	
Black or African American	28 (5.6)	72 (9.4)	
Latino American	0	12 (1.6)	
White	463 (92.2)	659 (85.9)	
Other	0	8 (1.0)	
Age at symptom onset (y), n	500	783	0.86
Median (10th, 90th percentile)	72.5 (59.5, 82.5)	72.5 (57.5, 82.5)	
Time from symptom onset to diagnosis (y), n	495	726	0.45
Median (10th, 90th percentile)	1.6 (0.0, 13.0)	1.4 (0.0, 10.7)	
Year of enrollment, n (%)			<0.001
2007–2012	13 (2.2)	147 (17.2)	
2013–2018	143 (24.4)	468 (54.8)	
2019–2023	431 (73.4)	239 (28.0)	
Age at enrollment (y), median (10th, 90th percentile)	77.7 (68.0, 85.9)	76.4 (65.2, 85.7)	0.02
Symptom duration at enrollment (y), n	500	783	0.30
Median (10th, 90th percentile)	3.0 (0.4, 13.7)	2.7 (0.3, 11.9)	
Follow-up time,† (y), median (10th, 90th percentile)	2.2 (0.5, 5.3)	2.3 (0.6, 5.7)	0.07
TTR genotype, n (%)			<0.001
Variant	48 (8.2)	138 (16.2)	
Wild-type	539 (91.8)	716 (83.8)	
Most Common *TTR* Variants,‡ n (%)			0.01
V122I (p. V142I)	21 (3.6)	69 (8.1)	
V30M (p.V50M)§	3 (0.5)	18 (2.1)	
I68L (p.I88L)	5 (0.9)	10 (1.2)	
Heart failure, n (%)	509 (86.7)	787 (92.2)	<0.001
NYHA functional class, n (%)	484	769	<0.001
I	76 (15.7)	80 (10.4)	
II	305 (63.0)	456 (59.3)	
III	102 (21.1)	207 (26.9)	
IV	1 (0.2)	26 (3.4)	
NT-proBNP (pg/mL), n	157	487	0.04
Median (10th, 90th percentile)	1883.0 (459.0, 6837.0)	2498.0 (466.0, 8256.0)	
LV septum thickness (mm), n	464	611	0.13
Median (10th, 90th percentile)	17.0 (13.0, 22.0)	17.0 (13.0, 22.0)	
LV ejection fraction (%), n	472	609	0.02
Median (10th, 90th percentile)	50.0 (33.0, 63.0)	49.0 (29.0, 62.0)	
mBMI, n	403	473	0.23
Median (10th, 90th percentile)	1077.6 (851.8, 1346.5)	1060.2 (806.4, 1344.1)	
Past or current clinical trial participation, ‖ n (%)	581	752	0.70
Yes	120 (20.7)	149 (19.8)	
Tafamidis trial	7 (1.2)	0	
Non-tafamidis trial	113 (19.4)	149 (19.8)	
No	461 (79.3)	603 (80.2)	
Diagnostic method,¶ n (%)			-
Clinical symptoms	546 (93.0)	734 (85.9)	
Amyloid confirmed on tissue biopsy	244 (41.6)	460 (53.9)	
TTR confirmed as precursor protein on tissue biopsy	218 (37.1)	401 (47.0)	
Scintigraphy	352 (60.0)	228 (26.7)	
Other	66 (11.2)	34 (4.0)	

n represents the total number of patients at baseline; n represents the number of patients with recorded data.

ATTR amyloidosis, transthyretin amyloidosis; LV, left ventricular; mBMI, modified body mass index; NYHA, New York Heart Association; THAOS, Transthyretin Amyloidosis Outcomes Survey; TTR, transthyretin.

*Race was not collected in France or Portugal.

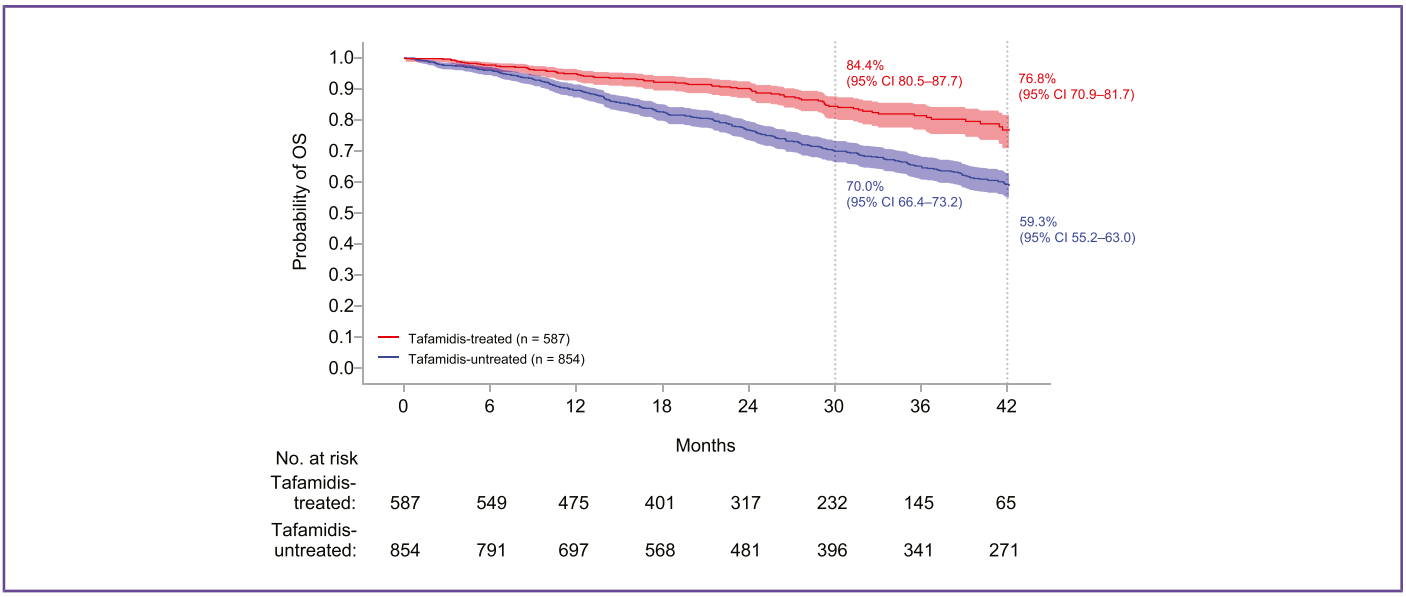
†Follow-up time is based on consent date to last available follow-up date.

‡Genotypes recorded in ≥ 10 patients at enrollment in either group are shown.

§Includes patients with G6S (p.G26S) in addition to V30M (p.V50M).

‖Data were censored during the time period of clinical trial participation.

¶Patients could be diagnosed based on > 1 diagnostic method. *P* value not included because observations are not independent.



Visual take home graphic. Kaplan-Meier plot of overall survival in tafamidis-treated and tafamidis-untreated patients. CI, confidence interval; OS, overall survival.

treated patients and 59.3% in tafamidis-untreated patients. The survival rate at 30 months in tafamidis-treated patients (84.4%) was higher than that reported in the treatment arm of ATTR-ACT (70.5%),[5] and a similar trend was noted between tafamidis-untreated patients (70.0%) and the placebo arm of ATTR-ACT (57.1%).[5] A recent report from the United Kingdom National Amyloidosis Centre reported that the median survival rate in patients with ATTR-CM has been steadily increasing with time, from 34.9 months in patients referred between 2002 and 2006 to > 60 months in patients referred between 2017 and 2021.[8] These improvements in survival rates are likely the result of advances in cardiac imaging and increased awareness among physicians that facilitate earlier detection of ATTR-CM,[8,9] as well as the availability of new treatments, especially those for heart failure.[10] Indeed, patients in this THAOS analysis appeared to be in earlier stages of the disease compared with patients in ATTR-ACT, as evidenced by a numerically higher proportion of patients in NYHA class I (12.5% vs 8.4%) and a lower proportion in NYHA class III (24.7% vs 32.0%), as well as lower median NT-proBNP concentrations (treated: 1883.0 vs 2995.9 pg/mL; untreated/placebo: 2498.0 vs 3161.0 pg/mL), which reinforces that early diagnosis and treatment translate to improved outcomes. To further examine whether survival rates are increasing with time, we conducted a sensitivity analysis to examine survival rates in those patients enrolled in THAOS in 2019 or later, and we found that 30-month survival rates in this subgroup were higher for tafamidis-treated (87.3%) and tafamidis-untreated (77.2%) patients compared with the entire treated and untreated cohorts.

The importance of early diagnosis and treatment in ATTR-CM has also been demonstrated in a follow-up analysis of ATTR-ACT combined with the long-term extension study, wherein patients who initiated treatment after ATTR-ACT had poorer outcomes than patients on continuous tafamidis treatment, despite showing a reduction in mortality rates when compared with an extrapolation of survival with placebo.[6] Further analysis of these studies confirmed improved survival rates in patients in NYHA class III who received continuous tafamidis compared with those who received placebo, then tafamidis.[11] The benefit of early treatment with tafamidis has also been

Table 2 Summary of all-causality, treatment-emergent adverse events in tafamidis-treated patients

	Tafamidis dose				
	20 mg (n = 52)	80/61 mg (n = 455)	20 to 80/61 mg (n = 73)	Other doses (n = 7)	All doses (n = 587)
Number of AEs, n	22	258	61	11	352
Patients with AEs, n (%)	11 (21.2)	120 (26.4)	28 (38.4)	2 (28.6)	161 (27.4)
Patients with serious AEs, n (%)	10 (19.2)	91 (20.0)	20 (27.4)	2 (28.6)	123 (21.0)
Patients with severe AEs, n (%)	8 (15.4)	77 (16.9)	16 (21.9)	2 (28.6)	103 (17.5)
Patients for whom treatment was withdrawn due to AEs,* n (%)	1 (1.9)	12 (2.6)	2 (2.7)	1 (14.3)	16 (2.7)
Patients with dose reduction due to AEs, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

*Treatment temporarily or permanently withdrawn or delayed, but patient continued in the study.AE, adverse event.

demonstrated in ATTR-PN. Results from a randomized clinical trial and long-term extension study showed that patients with ATTR-PN who received continuous tafamidis for up to 6 years had less disease progression than those who received placebo for 18 months, then tafamidis.[12] However, disease progression slowed in the latter group following initiation of tafamidis to the same rate seen in the continuously treated group.[12]

Although tafamidis is currently the only approved treatment for ATTR-CM, results of the phase 3 ATTRibute-CM (Transthyretin amyloid cardiomyopathy-CM) trial of the TTR stabilizer acoramidis were recently published. Patients in ATTRibute-CM trial had a median age of 78 years, 90% were male, 90% had ATTRwt-CM, and 72.0% had NYHA class II symptoms.[13] In addition, 18% of patients received concomitant tafamidis, which was allowed after month 12.[13] Although not statistically different, results revealed a 30-month survival rate of 81% vs 74% with acoramidis vs placebo,[13] reinforcing how the survival rate in patients with ATTR-CM has been steadily increasing with time with the availability of approved and investigational treatments that delay disease progression.

Safety and tolerability are key components for achieving full therapeutic benefit in chronic diseases. In this report, the proportion of patients for whom tafamidis treatment was withdrawn or delayed due to AEs was small, and no patient required a dosage reduction due to AEs. Overall, no new safety signals were detected, and the data collected confirm the long-term safety and tolerability profile of tafamidis in a real-world setting.

Strengths of this analysis include the large sample size of > 1400 patients with ATTR-CM and the representation of patients from 18 countries. Furthermore, patients who received any dosage of tafamidis were included in this analysis (rather than only those who received the approved dosage of tafamidis meglumine 80 mg/free acid 61 mg) to provide an accurate representation of the real-world management of this patient population outside the parameters of randomized controlled clinical trials. The administration of tafamidis dosages other than the approved dosage of tafamidis meglumine 80 mg/free acid 61 mg may have been due to differences in drug availability and local practices, as well as the time period when the patient was treated. A sensitivity analysis that included only patients who received the approved dosage revealed a 30-month survival rate of 83.1%, which is similar to that of the entire cohort.

Limitations

One limitation of this analysis was that the current cohort was restricted to patients with a predominantly cardiac phenotype. The rationale was that these patients represent a homogeneous cardiac population, but additional analyses that focus on the broader population of patients in THAOS with ATTR-CM, including those who had a mixed phenotype at enrollment, will be included in a future report. Another limitation is that a majority of the data came from U.S. study sites. Additionally, although we do not have detailed information on unblinded treatment allocation and, in many cases, the exact date that treatment started and ended, ~ 20% of patients in both the tafamidis-treated and tafamidis-untreated groups were enrolled in other clinical trials before or during THAOS, which may have contributed, at least in part, to our findings. Also, registry data, by nature, are not always complete, and baseline data for certain variables, treatment histories and details, and measures of disease severity were not available for all patients. The observational nature of this study also had the potential to introduce selection or ascertainment bias and, thus, may impact the external validity of the conclusions of the study. Notably, treated patients had less severe disease than untreated patients, as indicated by lower median NT-proBNP values, and were more likely to have been enrolled in THAOS in 2019 or later. These differences complicate comparisons among the groups. However, the intent of this analysis was to provide a real-world picture of the experiences of patients with ATTR-CM, not to conduct formal comparisons by treatment status. Propensity-matched analyses were not possible, given the amount of incomplete data. Additionally, the median follow-up time was 2 years in both groups, thus limiting the reliability of the survival analyses in later months. Data on the use of SPECT (single-photon emission computed tomography) imaging used in patients diagnosed by scintigraphy are not available, so it is possible that patients may have been misdiagnosed, because scintigraphy in the absence of SPECT can lead to false-positives. Last, the small number of patients with variant *TTR* genotypes precludes making robust conclusions about survival in genotype subgroups; future analyses should confirm results in patients with ATTRv-CM.

Conclusions

This THAOS analysis of a real-world population of patients with ATTR-CM showed that survival rates were higher than those observed in ATTR-ACT and were consistent with other recent reports. These results reinforce the importance of early diagnosis and treatment in this patient population and continue to support the safety and effectiveness of tafamidis.

Pablo Garcia-Pavia.

How does this work apply to patients?

These data show that patients with ATTR-CM are living longer than before.

This is likely due to earlier diagnosis and treatment with tafamidis.

Tafamidis may help patients with ATTR-CM live even longer than those who do not receive tafamidis.

Lay Summary

Tafamidis is approved to treat ATTR-CM and was shown to improve survival in a clinical trial compared with placebo. This analysis looked at survival in real-world patients with ATTR-CM enrolled in a registry called THAOS; 587 patients received tafamidis, and 854 did not. Survival rates at 30 and 42 months, respectively, were 84.4% and 76.8% in patients who received tafamidis, and 70.0% and 59.3% in those who did not. These survival rates are higher than those reported in the clinical trial. This suggests that patients with ATTR-CM are living longer, which is likely due to earlier diagnosis and treatment with tafamidis.

Disclosures

PG-P served as a speaker in scientific meetings for Alnylam, BridgeBio, Ionis, Intellia, AstraZeneca, Novo Nordisk, and Pfizer, received funding from Alnylam and Pfizer for scientific meeting expenses, received consultancy fees from Alnylam, Attralus, BridgeBio, Neuroimmune, AstraZeneca, Novo Nordisk, Alexion, Intellia, and Pfizer, and his institution received research grants/educational support from Alnylam, BridgeBio, AstraZeneca, Novo Nordisk, Intellia, and Pfizer. AVK received research support from and attended advisory boards for Pfizer, Neurimmune, Alnylam, Intellia, Ionis, Akcea, Novo Nordisk, Astra Zeneca, and Alexion. BD received consultancy fees from Alnylam and Eidos. MC, LA and FSA are full-time employees of Pfizer and hold stock and/or stock options in Pfizer. MSM received grant support from NIH R01HL139671 and grants from Pfizer during the conduct of the study and grants and personal fees from Alnylam, Pfizer, BridgeBio, Prothena, and Ionis and personal fees from Astra Zeneca, Ionis, Intellia, and Novo Nordisk.

CRediT Authorship Contribution Statement

PABLO GARCIA-PAVIA: Writing – review & editing, Supervision, Data curation, Conceptualization. **ARNT V. KRISTEN:** Writing – review & editing, Data curation. **BRIAN DRACHMAN:** Writing – review & editing, Data curation. **MARTIN CARLSSON:** Writing – review & editing, Data curation. **LESLIE AMASS:** Writing – review & editing, Formal analysis, Data curation, Conceptualization. **FRANCA STEDILE ANGELI:** Writing – review & editing, Formal analysis, Conceptualization. **MATHEW S. MAURER:** Writing – review & editing, Formal analysis, Data curation, Conceptualization.

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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/data-and-results for more information.

Supplementary Materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cardfail.2024.06.003.

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