2019 American Association of Heart Failure Nurses (AAHFN) Annual Meeting, Thursday, June 27 - Saturday, June 29, 2019 at the JW Marriott, Austin, TX.

Abstract Submission Deadline: December 3, 2018
The AAHFN Annual Meeting is designed to meet the educational needs of nurses interested in heart failure patient care.

Abstract Category: Research

Presentation Type: Oral or Poster

Word Limit: 500 words

Please note:

- Accepted abstracts will be published in Heart & Lung: The Journal of Acute and Critical Care
- AAHFN welcomes abstracts previously submitted to other national or international meetings
- Authors may submit an unlimited number of abstracts
- Submitted Abstracts will be peer reviewed
- Abstracts may be accepted for oral or poster presentation

Funding Acknowledgements: This study was sponsored by Pfizer.

Trial Registration number: NCT01994889.

Prior Presentation: These data were previously presented at the European Society of Cardiology Congress 2018, at the Heart Failure Society of America - 22nd Annual Scientific Meeting 2018, and have been published in the New England Journal of Medicine (Maurer et al., 2018;379[11]:1007-1016.)

Efficacy of Tafamidis in Transthyretin Amyloid Cardiomyopathy in the ATTR-ACT Trial

Terrell A. Patterson[1], Mathew S. Maurer[2], Jeffrey H. Schwartz[3], Balarama Gundapaneni[4], Perry Elliott[5], Giampaolo Merlini[6], Márcia Waddington Cruz[7], Martha Grogan[8], Ronald Witteles[9], Thibaud Damy[10], Brian M. Drachman[11], Sanjiv J. Shah[12], Mazen Hanna[13], Daniel P. Judge[14], Stephen S. Gottlieb[15], John L. Berk[16], Daniel J. Lenihan[17], James E. Hoffman[18], Scott L. Hummel[19], Eric J. Velazquez[20],, Marla B. Sultan[3], Claudio Rapezzi[21]

[1]Pfizer, Groton, Connecticut, USA. [2]Columbia University College of Physicians and Surgeons, New York, NY, USA. [3]Pfizer Inc, New York, NY, USA. [4]Syneos Health, Raleigh, North Carolina , USA. [5]University College London, London, UK. [6]Amyloidosis Center, IRCCS Policlinico San Matteo and University of Pavia, Pavia, Italy. [7]Federal University of Rio de Janeiro, National Amyloidosis Referral Center, CEPARM, Rio de Janeiro, Brazil. [8]Amyloidosis Center, Department of Cardiology, Heidelberg University, Heidelberg, Germany. [8]Department of Cardiovascular Diseases, Mayo Clinic, Rochester, MN, USA. [9]Stanford University School of Medicine, Stanford, California, USA. [10]French Referral Center for Cardiac Amyloidosis, Amyloidosis Mondor Network, GRC Amyloid Research Institute and Department of Cardiology, all at APHP, CHU Henri Mondor, and INSERM U955, Clinical Investigation Center 006, and DHU ATVB all at Creteil, France. [11]Penn Presbyterian Medical Center, University of Pennsylvania Health System, Philadelphia, Pennsylvania, USA. [12]Division of Cardiology, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA. [13]Cleveland Clinic, Cleveland, Ohio, USA. [14]Medical University of South Carolina, Charleston, South Carolina, USA. [15]University of Maryland School of Medicine, Baltimore, Maryland, USA. [16]Boston University School of Medicine, Boston Massachusetts, USA. [17]Washington University School of Medicine in St. Louis, St. Louis, Missouri, USA. [18]University of Miami, Miami, Florida, USA. [19]University of Michigan, Ann Arbor, Michigan, USA. [20]Heart and Vascular Center, Yale New Haven Health System, New Haven, Connecticut, USA. [21]Cardiology, Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Italy.

Background: Transthyretin cardiomyopathy (ATTR-CM) is an underdiagnosed, fatal disease caused by the deposition of transthyretin amyloid fibrils in the heart leading to heart failure (HF). It can be hereditary due to mutations in the *TTR* gene (ATTRm) or acquired (wild-type [ATTRwt]). Tafamidis is a selective transthyretin stabilizer which prevents tetramer dissociation and amyloidogenesis. The Tafamidis in Transthyretin

Cardiomyopathy Clinical Trial (ATTR-ACT) was an international, multicenter, double-blind, placebo-controlled, randomized trial of Tafamidis in patients with ATTR-CM.
Objectives: Given the limited number of patients with ATTR-CM, a novel study design was utilized to enable rigorous testing of the efficacy of tafamidis on hard cardiovascular (CV) endpoints in a study of relatively modest size compared with traditional CV trials. The primary results of this trial were further supported through the application of pre-specified sensitivity analyses.
Methods: Patients with ATTR-CM were randomized (2:1:2) to tafamidis (80 mg or 20 mg of tafamidis meglumine), or placebo (orally, once daily), for 30 months. Enrollment was stratified by NYHA class and genotype. The primary efficacy analysis was a hierarchical combination of all-cause mortality and frequency of CV-related hospitalizations comparing the pooled tafamidis groups (20 mg and 80 mg) vs. the placebo group using the Finkelstein–Schoenfeld (F-S) method. The primary efficacy analysis result was examined using a series of sensitivity analyses. Key secondary endpoints were change from baseline to Month 30 in the six-minute walk test distance and the Kansas City Cardiomyopathy Questionnaire (KCCQ) overall score. Safety assessments included adverse events, vital signs, and clinical laboratory tests.
Results: A total of 441 patients were randomized (tafamidis=264, placebo=177). Tafamidis was associated with a significant reduction in the hierarchical combination of all-cause mortality and CV-related hospitalizations (P<0.001). Tafamidis also significantly reduced the decline in both the six-minute walk distance (by 75.68 m [standard error, 9.24] P<0.001]),and KCCQ overall score (by 13.65 [2.13]; P<0.001) as compared with placebo. Sensitivity analyses consistently confirmed the efficacy of tafamidis in patients with ATTR-CM: there was a 30% reduction in risk of all-cause mortality (heart transplant and implantation of a cardiac mechanical assist device treated as death) with tafamidis compared with placebo (P=0.0259); and when heart transplant and implantation of a cardiac mechanical assist device were not treated as death, there was a 33% reduction in risk of all-cause mortality with tafamidis compared with placebo (P=0.018). Tafamidis was safe and well tolerated in this population.
Conclusions: ATTR-ACT, the largest randomized controlled trial in ATTR-CM, showed that tafamidis is the first treatment to improve survival and quality of life in ATTR-CM. Significant and clinically meaningful improvements were observed in functional capacity as measured by the six-minute walk distance and quality of life by KCCQ overall score. Sensitivity analyses confirmed the robustness of these results. Tafamidis was safe and well tolerated. The primary trial results, along with the sensitivity analyses described here, provide strong rationale for the use of tafamidis as first-line therapy in ATTR-CM.