



This activity is supported by an independent medical education grant from BridgeBio Pharma, Inc.



Learning Objectives

- 1. Recognize the clinical indicators for early screening and diagnosis of Transthyretin Cardiac Amyloidosis (ATTR-CM), particularly among a diverse population.
- 2. Identify the burden of health disparities in ATTR-CM disease management on health outcomes and access to care in the United States.
- 3. Distinguish the clinical efficacy, safety, monitoring, and patient selection criteria for new and emerging disease-modifying treatment options for ATTR-CM.
- Discuss managed care approaches to optimizing diagnosis and the referral process, health outcomes, and equitable access to care for managing ATTR-CM.





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 - ✓ Submit by October 13, 2025

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Faculty



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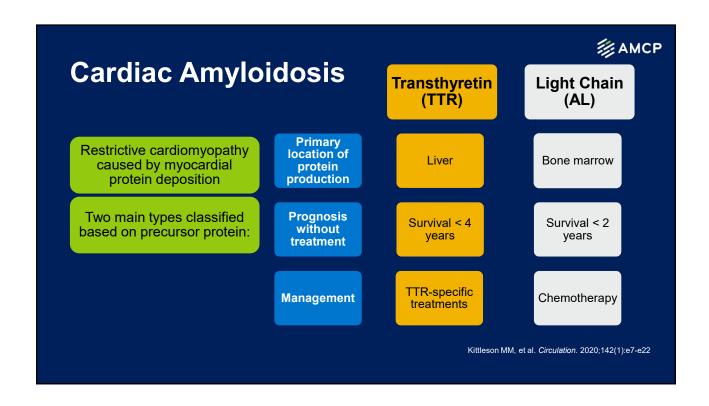


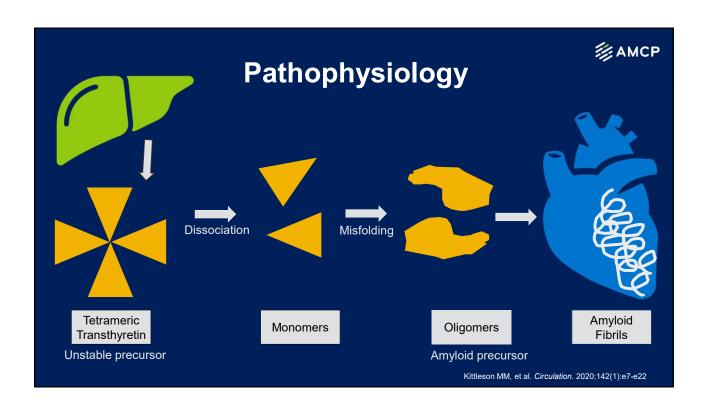
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ATTR-CM Overview







ATTR-CM: A Growing Concern

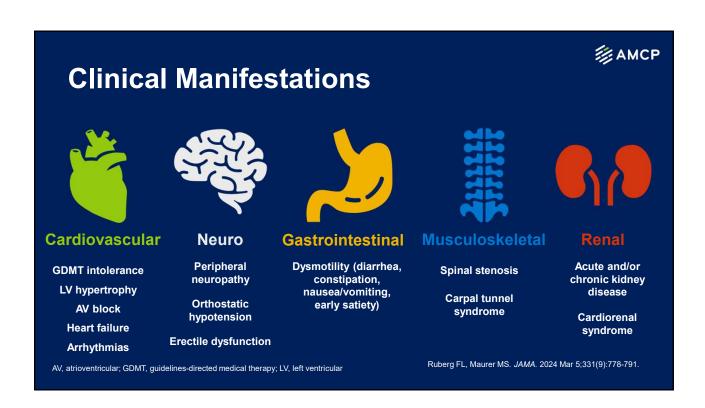
Туре	Estimated Frequency	Estimated Penetrance	Typical Onset Age
Wild-type (no genetic variants)	 12% HFpEF (↑ with age) 10% HFrEF 7% carpal tunnel surgery 7% HCM >8% severe AS 21% older patient autopsies 	Not genetically inherited	> 60 years
Variant (Hereditary) Val122Ile (AKA V122I or pV142I) most common in US	3.4% African Americans	Age > 60 years: ~7-100%Increases with ageMales > females	> 65 years

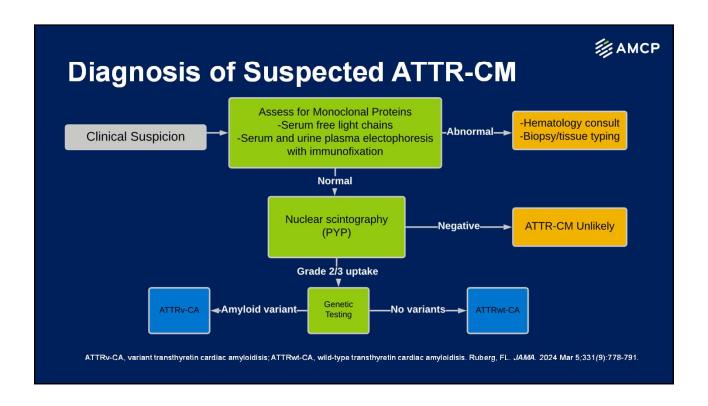
Prevalence increasing over time

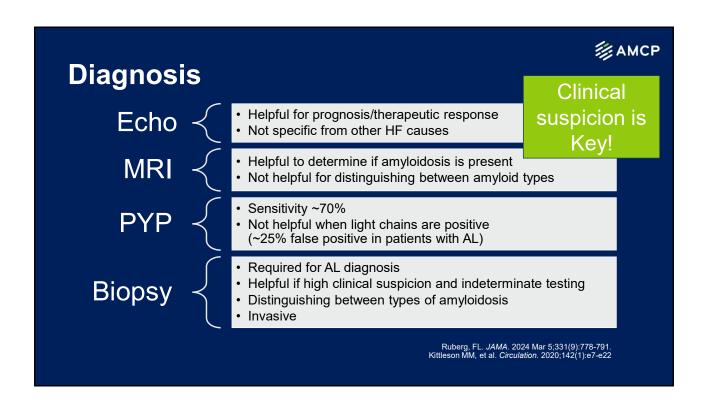
(improved awareness/diagnostics)
United States 2021: 6.1 per 1,000,000
(54.9 per 1,000,000 age 65+)
2018: 3.9 per 1,000,000
(36.6 per 1,000,000 age 65+)

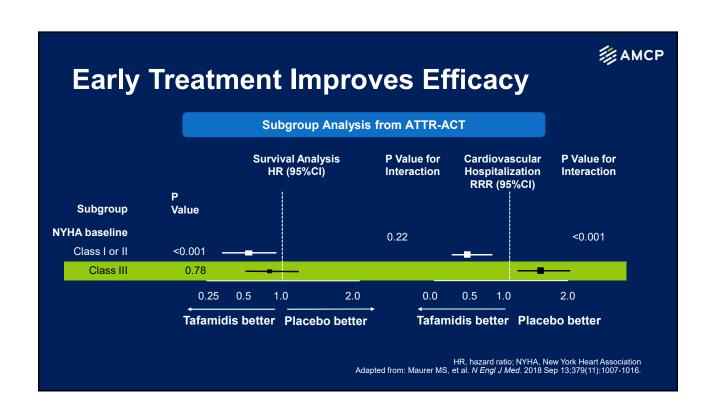
AS, aortic stenosis, HCM, hypertrophic cardiomyopathy; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; TTR, transthyretin; US, United States Ruberg FL, Maurer MS. JAMA. 2024 Mar 5;331(9):778-791.

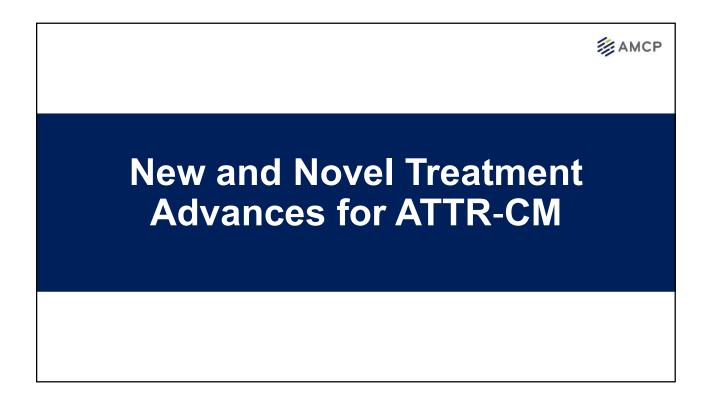
Brown D et al. J Am Coll Cardiol. 2021;77(18 suppl 1).

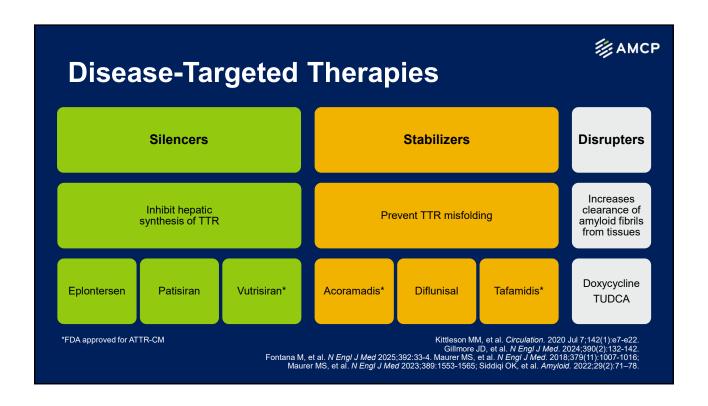


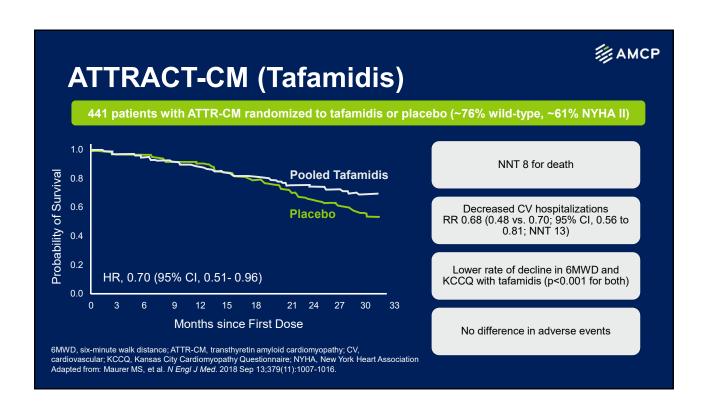


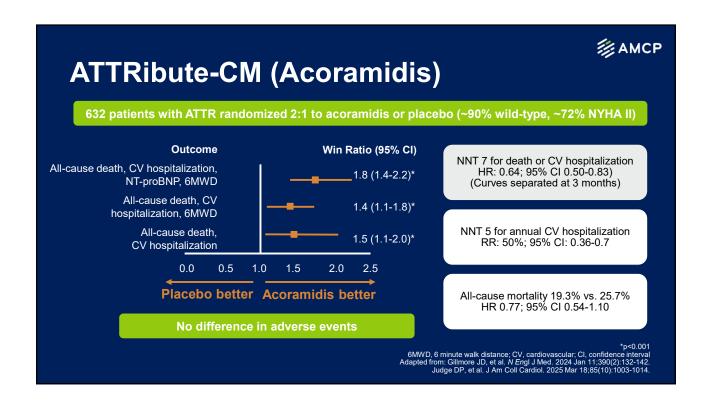


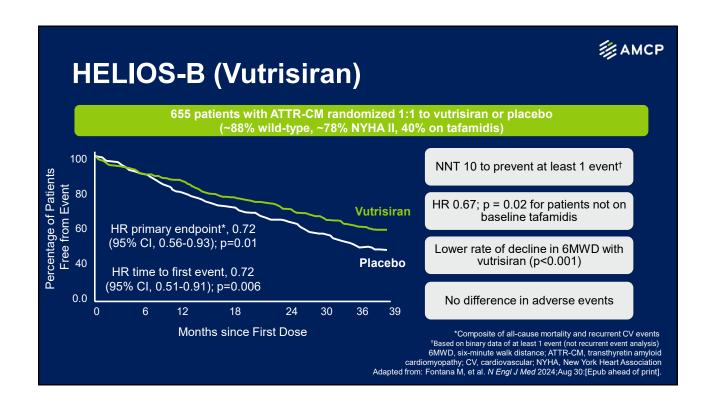














Comparing Phase 3 ATTR-CM Trials

ATTR-CM (wild-type or variant)			
Trial Criteria	ATTRACT-CM (Tafamidis)	ATTRibute-CM (Acoramidis)	HELIOS-B (Vutrisiran)
Tafamidis use	N/A	Only allowed after 12 months	40% at baseline
NYHA Class	I-III symptoms	I-III symptoms	I-III symptoms Excluded NYHA III at high risk
6MWD	≥100 m	≥150 m	≥150 m
NT-proBNP	≥600 pg/mL	≥300 pg/mL, ≤8500 pg/mL	>300 pg/mL, <8500 pg/mL (>600 pg/mL, <8500 pg/mL in AF)
Primary End Point	Hierarchical composite all- cause death and CV hospitalizations at 30 months	Hierarchical composite all-cause death, CV hospitalizations, ΔNT-proBNP, Δ6MWD at 30 months	Composite all-cause death and recurrent CV events over 36 months

NT-proBNP, N-terminal pro-B-type natriuretic peptide; AF, atrial fibrillation; NYHA, New York Heart Association; 6MWD, 6-minute walk distance.

Hellenbart EL et al. Pharmacotherapy. 2024;45(2):124-144; Maurer MS et al. N Engl J Med. 2018;379(11):1007-1016;

Gillmore JD et al. N Engl J Med. 2024;390(2):132-142; Fontana M et al. N Engl J Med. 2025;392(1):33-44.

Comparing Phase 3 ATTR-CM Trials

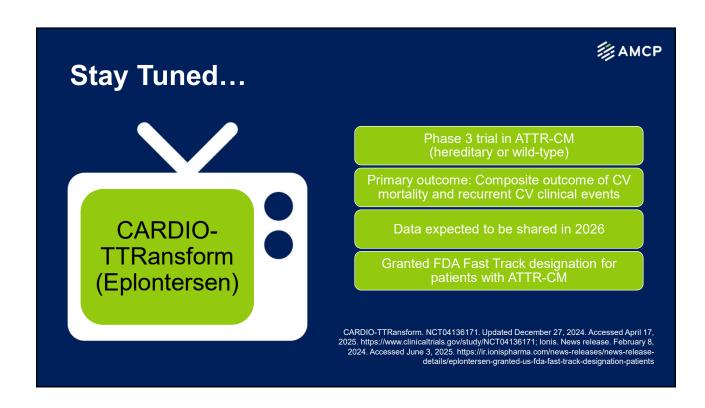


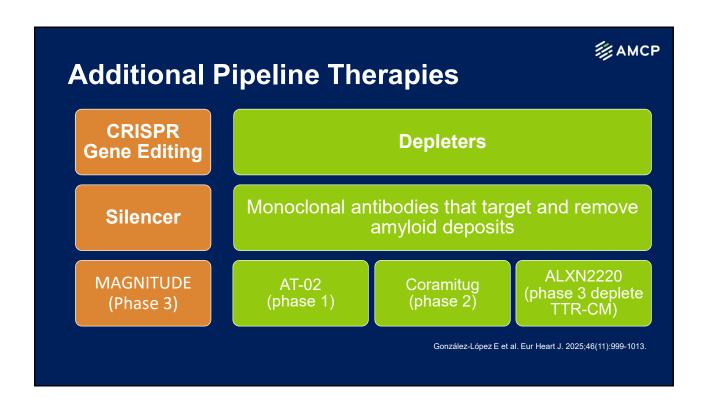
Baseline Characteristic	ATTR-ACT (Tafamidis)	ATTRibute-CM (Acoramidis)	HELIOS-B (Vutrisiran)
Age, years (median)	74	77	77
NYHA class, % I II III	8 60 32	11 72 17	13 78 9
6MWD, m (mean)	353	348	375
NT-proBNP, pg/mL (median)	3161	2306	1813
ATTRv (%)	24	10	12

NT-proBNP, N-terminal pro-B-type natriuretic peptide; AF, atrial fibrillation; NYHA, New York Heart Association; 6MWD, 6-minute walk distance.

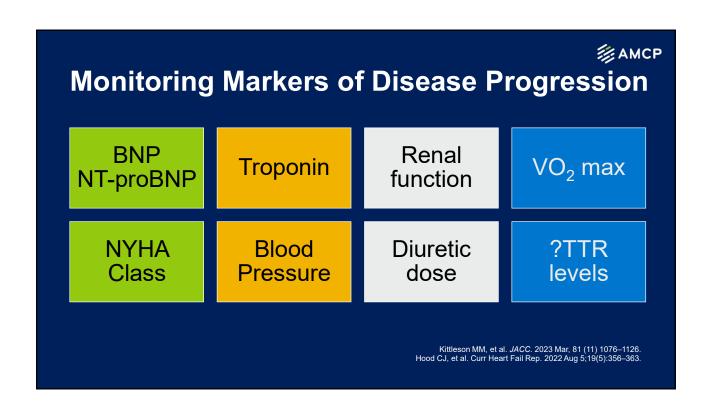
Hellenbart EL et al. Pharmacotherapy. 2024;45(2):124-144; Maurer MS et al. N Engl J Med. 2018;379(11):1007-1016;

Gillmore JD et al. N Engl J Med. 2024;390(2):132-142; Fontana M et al. N Engl J Med. 2025;392(1):33-44.





MAMCP Pharmacotherapy for ATTR Medication Diflunisal Tafamidis **Eplontersan Patisiran** Mechanism TTR stabilizers TTR Silencers+ ATTR-CM Only approved for ATTR **FDA** 2024 Off-Label 2019 March 2025 polyneuropathy **Approval** Landmark Cardio-ATTRibute-CM ATTR-ACT APOLLO-B **HELIOS-B** Trial in **TTRansform** 2023 2018 2022 2024 2026 ATTR-CM 0.3 mg/kg 45 mg SC once 712 mg orally 250 mg orally 61 mg orally 25 mg SC (max 30 mg) IV Dose twice daily twice daily once daily every 3 months monthly every 3 weeks Renal Infusion-related/site reactions*, Adverse Well tolerated dysfunction, Well tolerated **Effects** vitamin A deficiency bleeding Kittleson MM, et al. *Circulation*. 2020 Jul 7;142(1):e7-e22. Gillmore JD, et al. *N Engl J Med*. 2024;390(2):132-142. Fontana M, et al. *N Engl J Med* 2025;392:33-4. Maurer MS, et al. *N Engl J Med*. 2018;379(11):1007-1016. Maurer MS, et al. *N Engl J Med*. 2023;389:1553-1565 Siddiqi OK, et al. *Amyloid*. 2022;29(2):71–78. ATTR, Transthyretin amyloidosis; ATTR-CM, Transthyretin amyloidosis cardiomyopathy; FDA, Food and Drug Administration; GI, gastrointestinal; IV, intravenous; PDUFA, Prescription Drug User Fee Act; SC, subcutaneous; TTR, transthyretin



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Breaking data from the European Society of Cardiology Annual **Congress**

Acoramidis

- Acoramidis reduces cardiovascular mortality: results through month 42 from the
- ACTRibute-CM open-label extension study

 Acoramidis-mediated improvement in NT-proBNP at month 30 compared with placebo in patients with ATTR-CM: results from the ATTRibute-CM study

 Acoramidis has a beneficial effect compared with placebo on change from baseline in NAC ATTR stage at month 30 in patients with ATTR-CM: results from the ATTRibute CM study ATTRibute-CM study



Vutrisiran

- Vutrisiran Reduces Days Lost to Death and/or Hospitalization Versus Placebo in Patients with Transthyretin Amyloidosis with Cardiomyopathy in the HELIOS-B Trial HELIOS-B: 12-Month Results from the Open-Label Extension Period of Vutrisiran
- in Patients with Transthyretin Amyloidosis with Cardiomyopathy



Patient Perspective



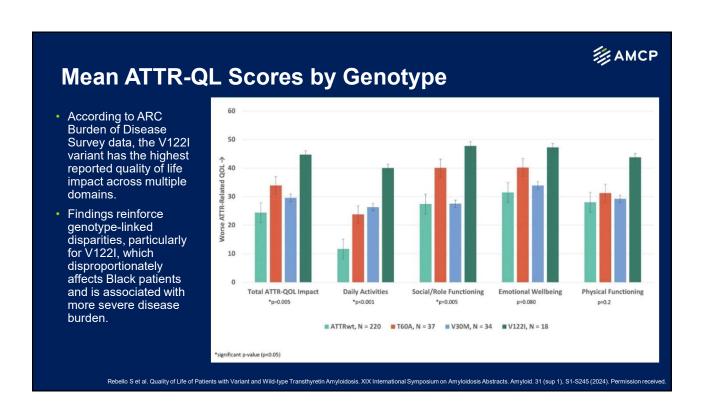
Patient Testimonial Video





Health Disparities Impacting ATTR-CM Disease Management

MAMCP Patient-Level & Social Disparities • Mean age = 74.5 years (SD 9.7) • Estimated payer mix ~ 80% Medicare, 15% Commercial, 5% Other **Genetic Disparity: V122I Variant** Specific mutation in TTR gene · Majority of ATTR-CM patients are White (55.4%) males (61%) • Under recognition in women; different clinical presentation Predominantly found in individuals of African descent **Regional Disease Burden** Estimated 3.4% of Black individuals in the U.S. carry the mutation • ATTR-CM prevalence highest in Northeast (38.6%) and South (24%) (~1.5 million people) Predisposes individuals to ATTR-CM Associated with more aggressive • Black patients with low socioeconomic status (SES) face greater risk of underdiagnosis and worse outcomes vs. White patients. disease • 66% of Black vs. 28% of White patients were in the "most deprived" category, based on national area deprivation index (P = 0.004). Higher rates of heart failure hospitalization/death over 5 years vs. White patients (P < 0.001).





Regional Impact - California Spotlight

Race

- California has the fifth-largest Black population in the U.S. with ~ 2.8 million individuals.
 - The V122I variant may affect an estimated ~100,00 individuals in California alone, based on population prevalence.
- Individuals are at increased risk of disease and disease may be more severe/progressive.

Age

- California has the largest number of Medicare beneficiaries nationally, ~7 million individuals.
- Significant variation in ATTR-CM therapy utilization across Medicare plans.

Plan Size	Utilizers	Utilization Rate per 1,000
45,000 members	30	0.67
14,500 members	4	0.28
7,000 members	16	2.29
4,600 members	3	0.65
3,500 members	6	1.71

Kaiser Family Foundation (KFF). Total Medicare Beneficiaries. KFF State Health Facts. 2024. Available from: https://www.kff.org/medicare/state-indicator/total-medicare-beneficiaries
World Population Review. Black Population by State [Internet]. 2024. Available from: https://worldpopulationreview.com/state-rankings/black-population-by-state

MAMCP System-Level & Access Disparities California Amyloidosis Median 2-to-3-year delay from Diagnostic Delays **Treatment Centers:** symptom onset to ATTR-CM diagnosis California Pacific Medical Center -San Francisco, CA Cedars-Sinai Hospital Underutilized in high-risk populations **Genetic Screening** City of Hope despite known genetic predisposition Kaiser Permanente San Francisco **Medical Center** Scripps Clinic John R. Anderson V **Medical Pavilion** EHR and claims often lack **Data Equity** Stanford Health Care race/genotype granularity Hematology Program Stanford Hospital & Clinics -**Amyloid Center** Few treatment centers statewide, **Specialty Care** UC San Diego Health access limited outside major metro Accessibility **UCSF** Spencer-Bonilla G. Curr Cardiovasc Risk Rep. 2021 June; 15(6 enbaum MH et al. Impact of Delayed Diagnosis and Misdiagnosis for Patients with Transthyretin Amyloid Cardiomyopathy (ATTR-CM): A Targeted Literature Review. Cardiol Ther. 2021 Apr; 10(1):141–159. doi: 10.1007/s40119-021-00219-5



Considerations for Managed Care Management of ATTR-CM in the U.S.

MAMCP Managed Care Challenges in ATTR-CM · High-Cost Therapies - lack of head-to-head data comparing the approved therapies makes coverage decisions challenging. Growing **High-Cost** Growing Patient Population – steady increase in Patient **Therapies** utilization of ATTR-CM therapies since tafamidis **Population** approval in 2019. Diagnostic Challenges – ensure timely access and coverage of appropriate tests and procedures; genetic sequencing to distinguish hATTR and Specialized Diagnostic Care Specialized Care Coordination – care coordination Challenges Coordination between multiple discipline including PCP, cardiologist, neurologist, pharmacist, social worker, genetic counselor and/or access to an amyloidosis treatment center to help effectively manage ATTR-CM patients.



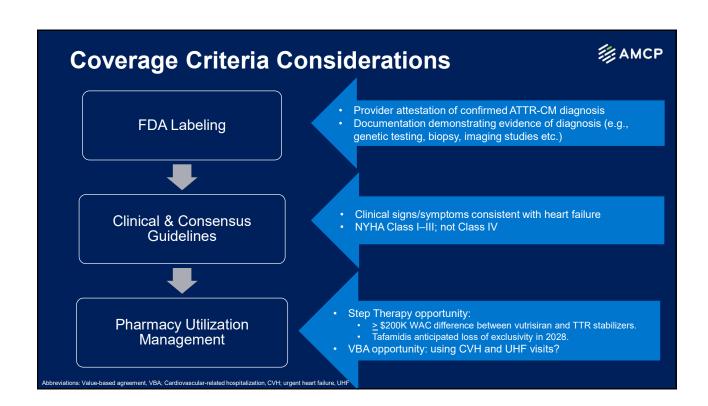
ATTR-CM Treatment Landscape

Prescribers are quickly adopting newly approved therapies for ATTR-CM.

- May 2019 tafamidis became the first and only FDA-approved therapy for ATTR-CM.
- November 2024 approval of acoramidis provided another 1st-line option, especially considering its improved TTR stabilization profile and lower WAC.
- March 2025 availability of vutrisiran since end of March 2025 further expands the patient population being treated; TTR silencer provided differentiated MOA.
- Cardiologists expect the availability of additional therapies will increase treatment uptake, particularly among patients with Stage I HF.

Drug	Vyndaqel/ Vyndamax (tafamidis)	Attruby (acoramidis)	Amvuttra (vutrisiran)
MOA	TTR Stabilizer	TTR Stabilizer	TTR Silencer
ATTR-CM Approval	2019	2024	2025
Dosing	Oral, daily	Oral, twice daily	HCP- administered SC, every 3 months
Annual WAC	\$271,710	\$244,539	\$477,404

Abbreviations: Mechanism of action, MOA; Healthcare professional, HCP; Subcutaneous, SC; Wholesale acquisition cost, WAC.
Source: IPD Analytics, July 2025.



Coverage Criteria Considerations - Combination Therapy?



- ICER research team rated vutrisiran + tafamidis "A" for added benefit over monotherapy, based on HELIOS-B trial results (ICER, 2024).
- HELIOS-B did not show heterogeneity between monotherapy and overall populations, supporting the combination rating.
- However, ICER's public appraisal panel unanimously disagreed, stating the evidence is not adequate to confirm combination superiority.
- Cardiologist experts noted the trial was not specifically powered or designed to evaluate combination therapy, and current data suggest but do not prove additional benefit.
- Despite ICER's "A" rating, clinical and payer consensus does not currently support routine coverage of vutrisiran in combination with tafamidis.
- Therefore, payers may reasonably restrict coverage for combination use until more definitive evidence is available.

Combination therapy is a top concern for payers due to the high costs across the category.

With monotherapy alone approaching \$3 PMPM for a 1 MM Medicare plan, the potential of combination therapy raises significant budgetary concerns.

Wasfy JH, et al. ICER. 2024, October 21.

Impact of Medicare Part D Redesign Under IRA



2024 change:

- 1. 5% coinsurance in catastrophic phase eliminated (i.e., \$0 patient responsibility in catastrophic phase).
- Effectively capped patient out-of-pocket (OOP) spend to ~\$3,300 per year.

2025 changes:

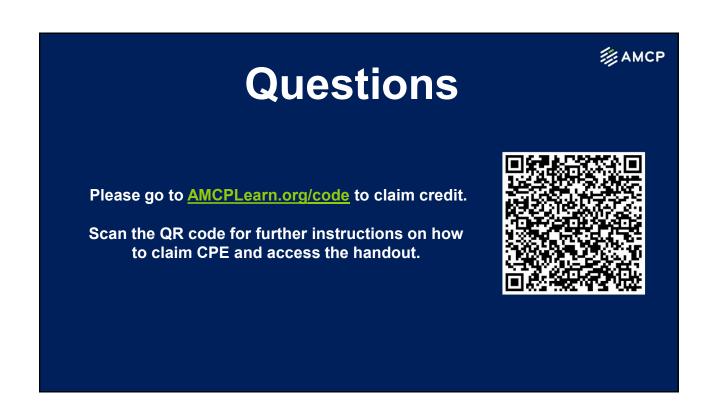
- 1. "Donut hole" coverage gap eliminated no separate, higher-cost phase when initial coverage is exhausted. 3 phases only deductible, initial and catastrophic.
- 2. \$2,000 annual OOP cap on all prescription drug costs for Part D enrollees.
- Copay smoothing mechanism enables patients to spread OOP costs throughout the year; may improve adherence and reduce cost-related abandonment, especially among fixed-income Medicare patients.
- 3. Part D plans' share of cost will increase from 15% to 60% above the cap.
- Higher cost share = Increase access barriers (especially for high-cost specialty drugs).

A 2021 Medicare Part D data analysis found that the mean OOP cost per 30-day fill for tafamidis was \$505.59 (\$6,067.08 per year). IQVIA stated that in the years before 2024, Standard Medicare patients had OOP cost between \$700-\$900 per month.

According to an IPD Primary Market Insights survey, the majority of providers report that higher patient OOP costs influence their treatment decisions — reinforcing the access impact of recent Part D changes.

Blatt PJ et al. JAMA Netw Open. 2024;7;(9):e2426086. doi:10.1001/jamanetworkopen.2024.26086





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Cardiology Pharmacy Specialist Atrium Health Carolinas Medical Center Dr. Gale is a cardiology clinical pharmacy specialist and cardiology clinical coordinator at Atrium Health Carolinas Medical Center in Charlotte, NC. She earned her Doctor of Pharmacy from Wingate University. She completed her PGY1 at Novant Health Presbyterian Medical Center and her PGY2 cardiology specialty residency at the University of Maryland School of Pharmacy. Dr. Gale is a Fellow of the Heart Failure Society of America and actively involved in the American College of Cardiology and American College of Clinical Pharmacy.

FACULTY BIOGRAPHY

Fiona Tillman, PharmD

Director, Market & Financial Insights IPD Analytics

Fiona Tillman is a Director of Market & Financial Insights at IPD Analytics, where she specializes in pharmaceutical financial forecasting and strategic analysis, providing actionable insights that inform key decisions in a complex and rapidly evolving pharmaceutical landscape. One of her key areas of expertise is the rare disease space, with a particular focus on conditions such as spinal muscular atrophy, Friedreich ataxia, Prader-Willi syndrome, and ATTR amyloidosis.

Prior to joining IPD Analytics, Fiona served as Pharmacy Manager for Utilization Management (UM) at Health Care Service Corporation (HCSC)—the parent company of five Blue Cross and Blue Shield plans (Illinois, Montana, New Mexico, Oklahoma, and Texas). There, she led pharmacy UM programs across the commercial line of business. Earlier in her career, she was a clinical pharmacist at CVS Caremark, supporting the Pharmacy & Therapeutics (P&T) Committee and contributing formulary recommendations for the National Formulary.

Fiona holds a Bachelor of Science in Pharmacology and Toxicology from the University of Toronto and earned her Doctor of Pharmacy (PharmD) from the University of Illinois at Chicago.

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