Disease Modifying Therapies for the Treatment of Transthyretin Amyloid Cardiomyopathy (ATTR-CM): Effectiveness and Value

Public Meeting — September 20th, 2024

Meeting materials available at: https://icer.org/assessment/transthyretin-amyloid-cardiomyopathy-2024/

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Patient Experts

Milton Mitchell, Patient Advocate, Donate Life Ambassador and Active Amyloidosis Support Group Member

- *No conflicts to disclose.*

Sean Riley, Patient Advocate/Speaker, Mackenzie's Mission - Amyloidosis Speakers Bureau

- *Sean has had equity interests in excess of $10,000 for Alnylam and BridgeBio.*

Clinical Experts

Michelle Kittleson, MD, PhD, Professor of Medicine, Smidt Heart Institute at Cedars-Sinai

- *No conflicts to disclose.*

Mathew S. Maurer, MD, Professor of Cardiology, Columbia University Irving Medical Center

- *Dr. Maurer has received funds in excess of $5,000 from Novo-Nordisk and has received research support and consulting from Alnylam, Pfizer, Ionis, Intellia, and Attralus.*

ICER Speakers

Sarah K. Emond, MPP
President & CEO

Jason H. Wasfy, MD, MPhil
Evidence Author

David Rind, MD, MSc
Chief Medical Officer

Steven D. Pearson, MD, MSc
Special Advisor

Aaron Winn, MPP, PhD
Lead Modeler

Why are we here today?

“When complaining for years and years, everyone sent me to a different specialist until my cardiologist saw my AFib going into effect. I got tested by tons of doctors until they finally got me diagnosed. I have neuropathy in my feet, it is very hard for me to walk a couple hundred feet. I still go out with all my friends, they just know I walk slow. I’m living with this. Everybody I know, knows I have it and they are really accepting. They do everything they can to help me out and take me everywhere I need to go.”

Person with ATTR-CM

Why Are We Here Today?

- What happens the day these treatments receive FDA approval?
- Questions about:
  - What are the risks and benefits?
  - How do new treatments fit into the evolving landscape?
  - What are reasonable prices and costs to patients, the health system, and the government?
  - What lessons are being learned to guide our actions in the future?

The Impact on Rising Health Care Costs for Everyone

DIAGNOSIS: DEBT

100 Million People in America Are Saddled With Health Care Debt

By Noam N. Levey

JUNE 16, 2022

Why Delaware is eying a 27% premium hike on state employees' health insurance

Amanda Fries

Delaware News Journal

Published 4:35 a.m. ET Feb. 1, 2024 | **Updated 9:29 p.m. ET Feb. 6, 2024**

100 Million People in America Are Saddled With Health Care Debt (KFF Health News)

Why Delaware is eying a 27% premium hike on state employees' health insurance (Delaware Online)

Organizational Overview

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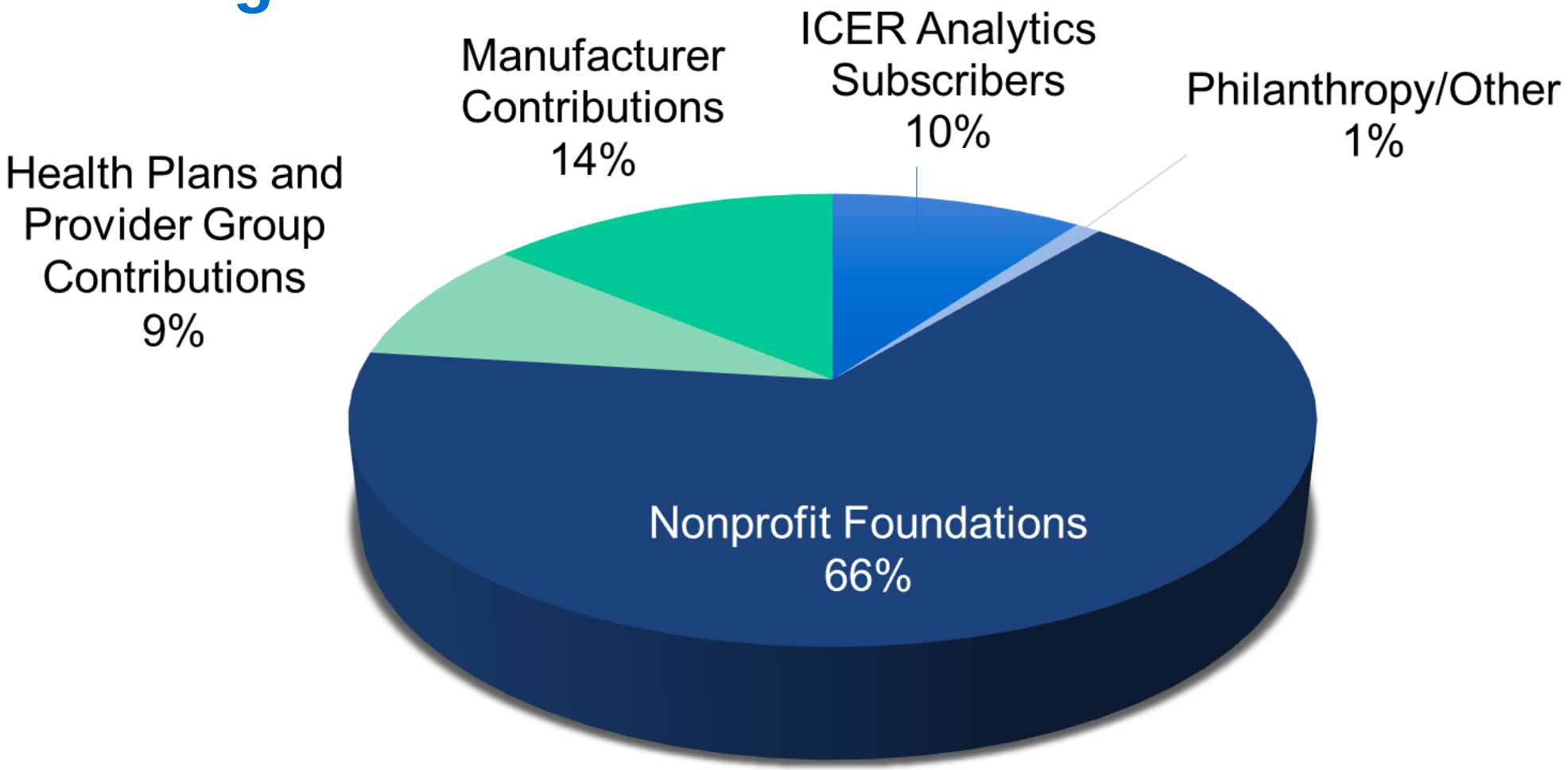
Funding 2024



ICER Policy Summit and non-report activities only

* ICER received significant funding from Arnold Ventures, The California Health Care Foundation, and The Commonwealth Fund, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, and Peterson Center on Healthcare, LLC. Source: https://icer.org/who-we-are/independentfunding/sources-of-funding/

How Was the ICER Report Developed?

Guidance from patients, clinical experts, manufacturers, and other stakeholders

Evidence analysis in collaboration with **Harvard Medical School** and cost-effectiveness modeling in collaboration with the **University of Illinois at Chicago**

- **Muriel Finkel**, President, Amyloidosis Support Groups Inc.
- **Jerry H. Gurwitz**, MD, Professor of Medicine, UMass Chan Medical School
- **Mathew Maurer**, MD, Professor of Cardiology, Columbia University Irving Medical Center

Structured to support **Midwest CEPAC** voting and policy discussion

Value Assessment Framework: Long-Term Value for Money

Agenda (CT)

10:00 AM	Meeting Convened and Opening Remarks
10:20 AM	Presentation of the Clinical Evidence
11:00 AM	Presentation of the Economic Model
11:40 AM	Public Comments and Discussion
12:00 PM	Lunch Break
12:50 PM	Midwest CEPAC Deliberation and Vote
1:50 PM	Break
2:00 PM	Policy Roundtable Discussion
3:30 PM	Reflections from Midwest CEPAC
4:00 PM	Meeting Adjourned

Presentation of the Clinical Evidence

Jason H. Wasfy, MD, MPhil

Associate Professor, Harvard Medical School

Director of Outcomes Research, Massachusetts General Hospital Cardiology Division, Mass General Brigham

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Key Collaborators

Team Role	Assigned Team Member
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Research Assistants	Finn Raymond, BS and Emily Nhan, BA

Disclosures

Financial support provided to Dr. Wasfy from the Institute for Clinical and Economic Review (ICER).

Dr. Wasfy has no conflicts to disclose defined as more than $10,000 in healthcare company stock or more than $5,000 in honoraria or consultancies relevant to this report during the previous year from health care manufacturers or insurers.

Transthyretin Amyloid Cardiomyopathy (*ATTR-CM*)

- ATTR-CM is a heart muscle disease caused by amyloid fibril deposits in the heart tissue.
  - Hereditary ATTR-CM (ATTRv-CM): Caused by an inherited mutated transthyretin gene, often in younger individuals.
  - Wild-type ATTR-CM (ATTRwt-CM): No inherited mutation, but transthyretin still misfolds and deposits in the heart, generally at older ages.
- 50,000 to 150,000 US adults have ATTR-CM, likely more due to underdiagnosis.
- ATTR-CM is a progressive disease with high morbidity and poor life expectancy.
- ATTR-CM can co-exist with other amyloid disorders like neuropathy.

Impact on Patients

- Patients with ATTR-CM face significant challenges in obtaining an accurate and timely diagnosis due to:
  - Clinicians' unfamiliarity with this condition
  - Underdiagnosis or delayed diagnosis (often years)
- Employment and daily activities of living are hindered by symptoms (shortness of breath, arrhythmias, heart failure).
- High medication costs are burdensome and require patients to navigate complex health system.

New York Heart Association (NYHA) Functional Classification

The NYHA classification is a clinician-assessed measure of functional status broadly applicable to patients with cardiac disease.

Class	Definition
Class I	Patients with cardiac disease but without limitations of physical activity
Class II	Patients with cardiac disease resulting in slight limitation of physical activity
Class III	Patients with cardiac disease resulting in marked limitation of physical activity
Class IV	Patients with cardiac disease resulting in inability to exert physically at all and/or the presence of symptoms at rest

Standard of Care and Management

- Goals: Relieve symptoms and slow disease progression
- Previously, use of heart or heart-liver transplant
- Current guidelines recommend use of tafamidis for patients with wild-type or hereditary ATTR-CM and NYHA class I-III symptoms.
  - Consider use of alternatives when polyneuropathy also present

NYHA: New York Heart Association

Interventions

TTR Stabilizers

Tafamidis (Vyndamax™/Vyndagel™)

- 61 mg taken orally once a day (one 61 mg capsule)
- 80 mg taken orally once a day (four 20 mg capsules)
- Granted FDA approval in 2019

Acoramidis

- 800 mg taken orally twice daily
- Under evaluation by the FDA with a PDUFA date of November 29th, 2024

RNA Silencers

Vutrisiran (Amvuttra™)

- 25 mg subcutaneous injection once every three months
- Approved for hereditary ATTR amyloidosis with polyneuropathy
- Alnylam plans to file a U.S. supplemental NDA using a priority review voucher

FDA: Food and Drug Administration, NDA: New Drug Application, PDUFA: Prescription Drug User Fee Act

Image Source: Freepik

Scope of Review

- **Population**
  - Contemporary adult patients with ATTR-CM (wild-type or hereditary)
- **Intervention**
  - Tafamidis
  - Acoramidis
  - Vutrisiran
- **Comparator**
  - Each intervention compared to one another as well as vs. no disease-specific treatment. Given new evidence for vutrisiran in individuals receiving tafamidis, also comparing vutrisiran plus tafamidis vs. tafamidis alone.

Key Outcomes

All-Cause Mortality

- Heart transplantation or ventricular assist device treated as deaths

Cardiovascular-Related Hospitalizations

Primary Endpoint

- Composite of multiple outcomes including all-cause mortality and cardiovascular-related hospitalizations

Clinical Evidence

Key Clinical Trials: Design

Study	Treatment	Design	Population	Follow-up
ATTR-ACT	**Tafamidis** (20 mg or 80 mg) vs. placebo	Phase 3, randomized, double-blind	• Age 18-90 • NYHA I-III	30 months
ATTRibute-CM	**Acoramidis** vs. placebo	Phase 3, randomized, double-blind	• Age 18-90 • NYHA I-III	30 months
HELIOS-B	**Vutrisiran** (monotherapy or overall) vs. placebo	Phase 3, randomized, double-blind	• Age 18-85 • NYHA I-III*	30+ months

*Unless NYHA class of III with a National Amyloidosis Centre ATTR stage of 3 (defined as an NT-proBNP level of >3000 pg per milliliter and an eGFR of <45 ml per minute per 1.73 m2 of body-surface area).

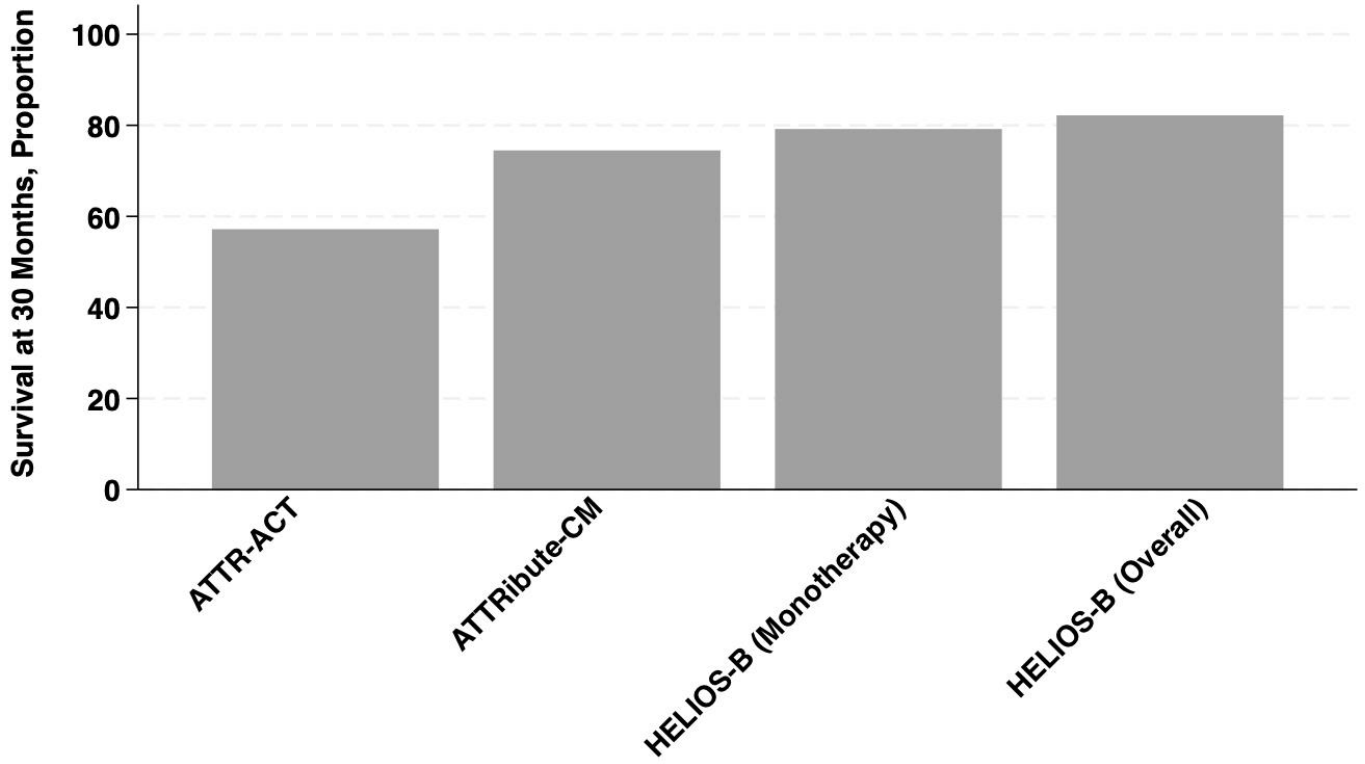
eGFR: estimated glomerular filtration rate, NYHA: New York Heart Association

Key Clinical Trials: Baseline Characteristics

Trial		ATTR-ACT	ATTRibute-CM	HELIOS-B
Year		2013-2015	2019-2020	2019-2021
N		353	632	654
Age, years (mean)		74	77	77
Sex, %	**Male**	90	90	93
TTR genotype, %	**ATTRwt**	76	90	88
NYHA class, %	**Class I**	8	11	13
	Class II	60	72	78
	Class III	32	17	9

ATTRwt: wild type, NYHA: New York Heart Association

Survival of Patients in Placebo Arms of Trials



Note: In the ATTRibute-CM trial, 22.8% of the placebo arm received tafamidis.
Note: The HELIOS-B monotherapy arm only includes patients randomized to placebo who were not receiving tafamidis at baseline (21% of this arm initiated tafamidis after randomization). The overall placebo arm had 40% on tafamidis at start of study.

Source: 2024 ESC Congress London

Impact on Mortality

Tafamidis

Survival at 30 months higher in tafamidis (20+80mg) vs placebo (70.5% vs. 57.1%, HR 0.70, 95% CI: 0.51-0.96).

Acoramidis

Survival at 30 months trended higher in acoramidis vs placebo (80.7% vs. 74.3%), but not statistically significant. (HR not calculated; sensitivity analyses were inconclusive).

Vutrisiran

After 33-36 months, survival was higher in vutrisiran vs placebo (84% vs. 79%; HR: 0.69, 95% CI: 0.49-0.98). In group without tafamidis at baseline, mortality reduction not statistically significant vs placebo (HR: 0.71, 95% CI: 0.47 to 1.06, p=0.12) but significant in both groups at month 42.

CI: confidence interval, HR: hazard ratio

Cardiovascular-related Hospitalizations

Tafamidis

Participants taking tafamidis (20+80mg) experienced fewer cardiovascular-related hospitalizations compared to those on placebo (0.48 vs. 0.70 hospitalizations per year; relative risk 0.68, 95% CI 0.56 to 0.81).

Acoramidis

The risk of cardiovascular-related hospitalization was lower in patients taking acoramidis than placebo (RR 0.50, 95% CI 0.36 to 0.70).

Vutrisiran

Vutrisiran was superior to placebo in reducing CV-related hospitalizations and urgent heart failure visits for both the monotherapy (HR: 0.68, 95% CI: 0.53 to 0.86) and overall (HR: 0.73, 95% CI: 0.61 to 0.88) study populations.

CI: confidence interval, CV: cardiovascular, HR: hazard ratio

Comparisons Among Disease Modifying Therapies

Acoramidis Versus Tafamidis

- In ATTRibute-CM, 1 mg/dL increase in TTR levels at day 28 a/w 5.5% lower risk of CV-related mortality at 30 months.[1]
- In a cross-trial comparison, acoramidis-treated patients had greater increase in serum TTR levels compared to tafamidis 80 mg-treated (39% versus 30%). Within-trial comparison of serum TTR levels between the acoramidis and placebo to tafamidis crossover arm in ATTRibute-CM showed a ~3 mg/dL difference in favor of acoramidis.[2]
- In a retrospective cohort study that compared the outcomes of 10 patients receiving acoramidis to 137 patients taking tafamidis, there was numerically better survival with acoramidis that was not statistically significant (p=0.19) in the matched cohort. This compares trial patients getting acoramidis versus real-world patients getting tafamidis.[3]

CV: cardiovascular, mg/dL: milligrams per deciliter, TTR: Transthyretin
1. Ambardekar et al. 2024, 2. BridgeBio Pharma. 2024,
3. Bampatsias et al. 2024

Comparisons Among Disease Modifying Therapies

Vutrisiran Versus Acoramidis or Tafamidis

- There were insufficient data to directly compare the net health benefit of vutrisiran monotherapy for ATTR-CM versus tafamidis or acoramidis.

Tafamidis 80 mg Versus Tafamidis 20 mg

- The LTE analysis comparing the two doses of tafamidis was not a direct randomized comparison. Bias could result if there were differential enrollment of patients with different severities of disease in the LTE; we lack the data to assess this.[1]

LTE: long-term extension
1. Damy et al. 2021

Harms

Key Points

- Across all trials the incidence of adverse events during treatment was similar in the intervention and placebo groups and favored the intervention with respect to serious adverse events.
- Vutrisiran has been associated with certain AEs, including joint pain, difficulty breathing, and reduced vitamin A levels. The FDA-approved label for vutrisiran recommends supplementation with vitamin A to mitigate the risk of these events.

AE: adverse event, FDA: Food and Drug Administration

Subgroup Analyses and Heterogeneity

- **Tafamidis (ATTR-ACT):** Subgroup analyses showed no significant effects on mortality but a slight increase in CV-related hospitalization for NYHA class III patients, possibly due to longer survival with tafamidis.
- **Acoramidis (ATTRibute-CM):** No notable subgroup effects on mortality or CV-related outcomes, including hospitalization and NT-proBNP levels.
- **Vutrisiran (HELIOS-B):** Subgroup effects were inconsistent, though greater improvements were observed in younger patients (<75) and those with lower baseline levels of NT-proBNP. Similar effects in those on tafamidis and not.

CV: cardiovascular, NT-proBNP: N-terminal pro–B-type natriuretic peptide, NYHA: New York Heart Association

Controversies and Uncertainties

- Tafamidis shows potential benefits for earlier-stage ATTR-CM patients.
- Comparing tafamidis and acoramidis is difficult given uncertain relevance of TTR levels as a surrogate marker.
- Further data is needed to compare trial populations (placebo arms of all 3 trials had different mortality).
- More data needed to determine whether combination therapy (TTR stabilizer + RNA silencer) is superior to monotherapy.
- Any mortality benefit of acoramidis was difficult to show, while vutrisiran demonstrated a statistically significant reduction in mortality in a longer trial.
- There is uncertainty around tafamidis dosing, with the FDA approved 80 mg while some formularies prefer the less expensive 20 mg dose based on suggestive evidence of TTR levels.

FDA: Food and Drug Administration, TTR: Transthyretin

Benefits Beyond Health and Special Ethical Priorities

- ATTR-CM is widely underdiagnosed, and access to the one approved therapy (tafamidis) is limited due to high costs.
- Black patients in the U.S. are underrepresented in clinical trials compared to White patients despite more affects by hereditary version.
- Women are underrepresented in trials and more underdiagnosed in practice (although disease affects many more men).
- New therapies for ATTR-CM could reduce the burden on caregivers.
- Acoramidis and tafamidis are oral medications, while vutrisiran is subcutaneous, with no indication that delivery method impacts treatment access.

Public Comments Received

- Comparison of tafamidis and acoramidis on TTR stabilization difficult, both manufacturers submitted comments/arguments for each of their options.
- Many data gaps remain: impact of treatments on patients with multi-organ involvement.

Summary

- Three disease-modifying therapies have shown significant potential in reducing mortality and cardiovascular events in patients with early-stage ATTR-CM.
- Current comparative evidence is limited, offering no clear advantage between the three therapies.
- All three agents seem to possess a favorable safety profile.

ICER Evidence Ratings

Treatment	Comparator	Evidence Rating
Acoramidis	No disease-specific treatment	B+
Tafamidis	No disease-specific treatment	B+
Acoramidis	Tafamidis	I
Vutrisiran	No disease-specific treatment	A
Vutrisiran as add-on to current therapy	Current therapy alone	A
Vutrisiran	Tafamidis	I
Vutrisiran	Acoramidis	I

A: Superior – High certainty of a substantial (moderate-large) net health benefit
B+: Incremental or Better - Moderate certainty of a small or substantial net health benefit, with high certainty of at least a small net health benefit
I: Insufficient - Any situation in which the level of certainty in the evidence is low

Questions?

Disease Modifying Therapies for the Treatment of Transthyretin Amyloid Cardiomyopathy (ATTR-CM): Effectiveness and Value

Aaron Winn, MPP, PhD

Associate Professor

University of Illinois at Chicago

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Key Review Team Members

Team Role	Assigned Team Member
Modelers	Aaron Winn MPP, PhD, Kanya Shah PharmD, MS, MBA, Sodam Kim PharmD, MA, Daniel R. Touchette PharmD, MA
Economics Leads	Marina Richardson PhD, MSc, Woojung Lee PharmD, PhD

Disclosures

Financial support provided to the UIC Economic Modeling Team from the Institute for Clinical and Economic Review (ICER).

UIC Economic Modeling Team, with the exception of Dr. Winn, has no conflicts to disclose defined as more than $10,000 in healthcare company stock or more than $5,000 in honoraria or consultancies relevant to this report during the previous year from health care manufacturers or insurers. Dr. Winn has consulted for Takeda, Novo Nordisk and CorMedix.

Objective

ATTR-CM

To evaluate the lifetime cost-effectiveness of transthyretin stabilizing agents added to best supportive care compared to best supportive care alone for the treatment of transthyretin amyloidosis cardiomyopathy (ATTR-CM) in US adults.

Unmet Need

Condition	Absolute evLY Shortfall	Proportional evLY Shortfall
ATTR-CM	5.5	63.9%
Other Example Conditions		
Multiple Sclerosis	18.9	52%
Osteoporosis	2.6	19%

evLY: equal value of life years gained

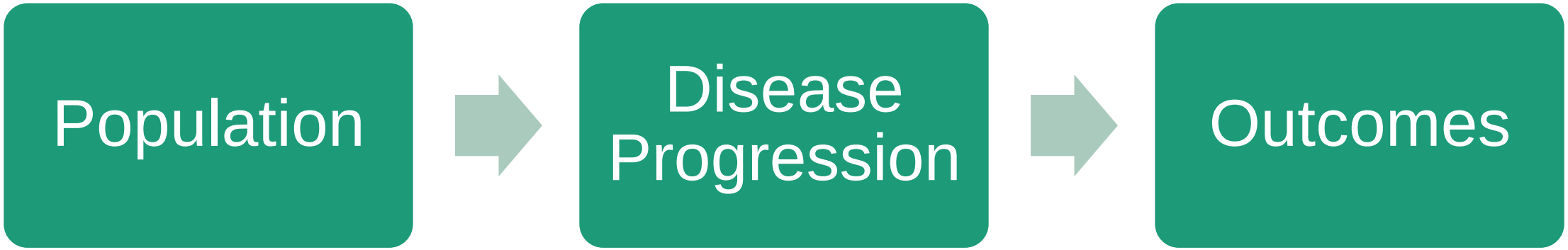
Methods in Brief

Methods Overview

Domain	Approach
Model	Markov Model
Setting	United States
Perspective	Health Care Sector Perspective and Modified Societal Perspective
Time Horizon	Lifetime
Discount Rate	3% per year (costs and outcomes)
Cycle Length	6 months
Primary Outcome	Cost per quality-adjusted life years (QALYs) gained; equal value life years (evLYs) gained, time spent in NYHA Class I and II

evLY: equal value of life years gained, QALY: quality-adjusted life years
NYHA: New York Heart Association

Simplified Model Components

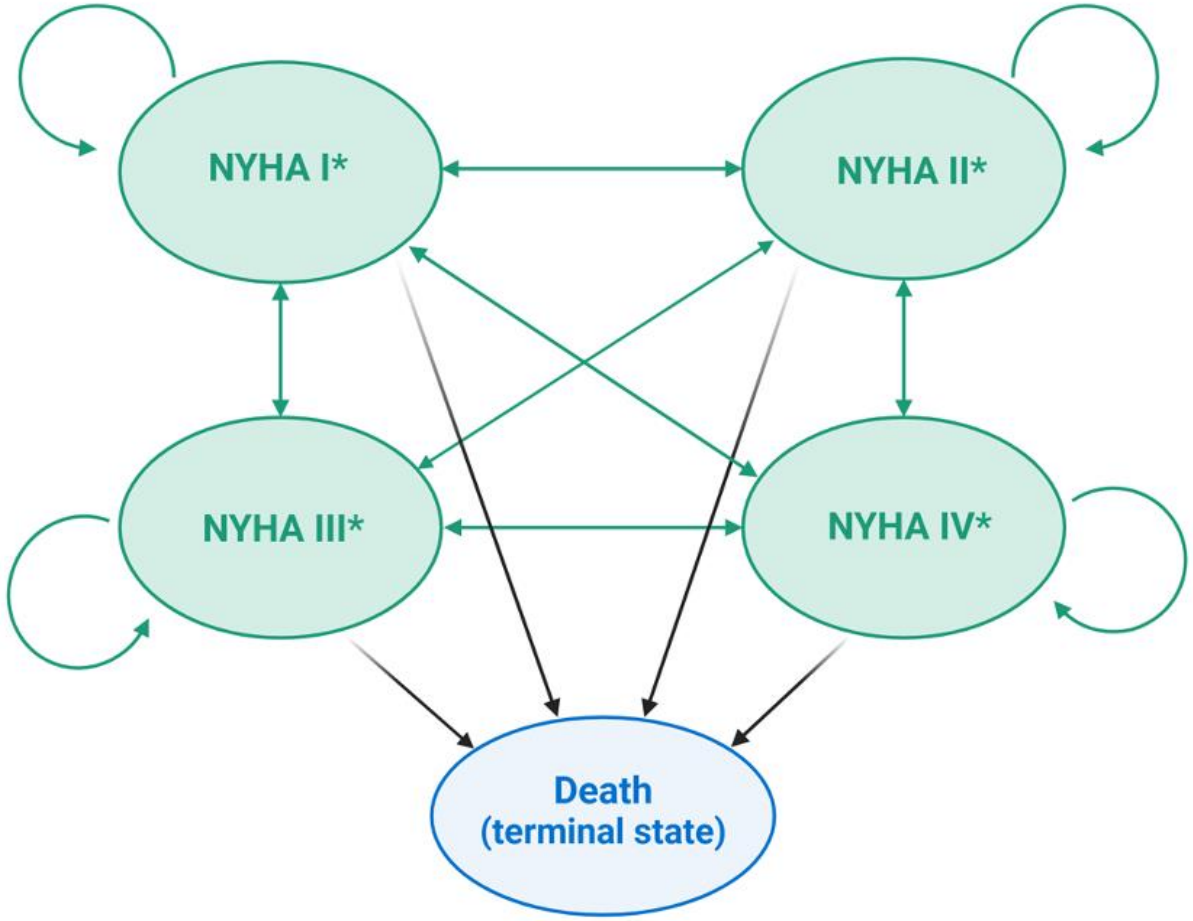


Population Characteristics

Baseline Characteristic	ATTRibute-CM (Acoramidis) N=632	ATTR-ACT (Tafamidis) N=441
Mean Age (±SD)	77.3±6.6	74.3±6.7
Gender		
Male	570 (90.2%)	398 (90.2%)
Female	62 (9.8%)	43 (9.8%)
NYHA Functional Class		
I	68 (10.8%)	37 (8.4%)
II	455 (72.0%)	263 (59.6%)
III	109 (17.2%)	141 (31.9%)
IV	0 (0%)	0 (0%)

NYHA: New York Heart Association

Disease Progression in the Model



*Each NYHA functional class health state includes a potential for a hospitalization event, with different probabilities of hospitalization for each NYHA functional class.

NYHA: New York Heart Association

Key Assumptions

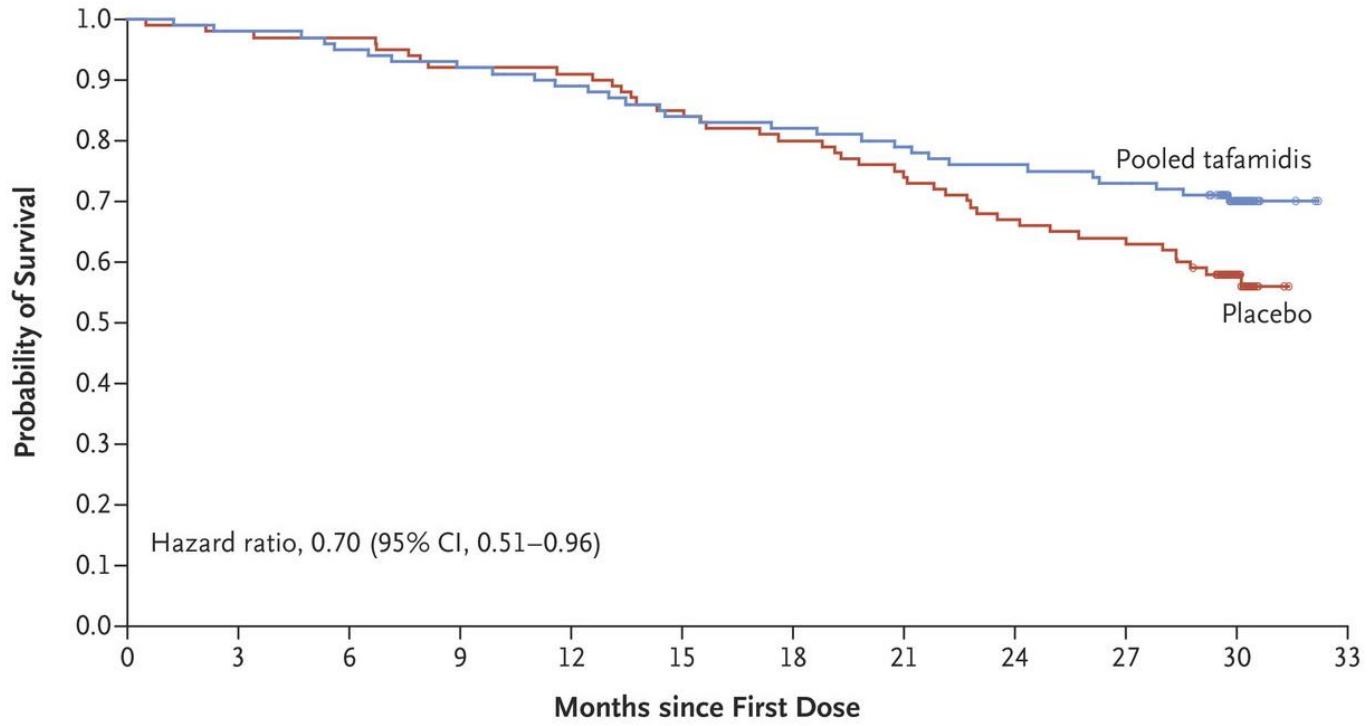
Treatment efficacy was defined by observed progression through the NYHA functional class

The modeled intervention is transthyretin stabilizing agents as a class

NYHA: New York Heart Association

Key Model Inputs: Mortality Inputs

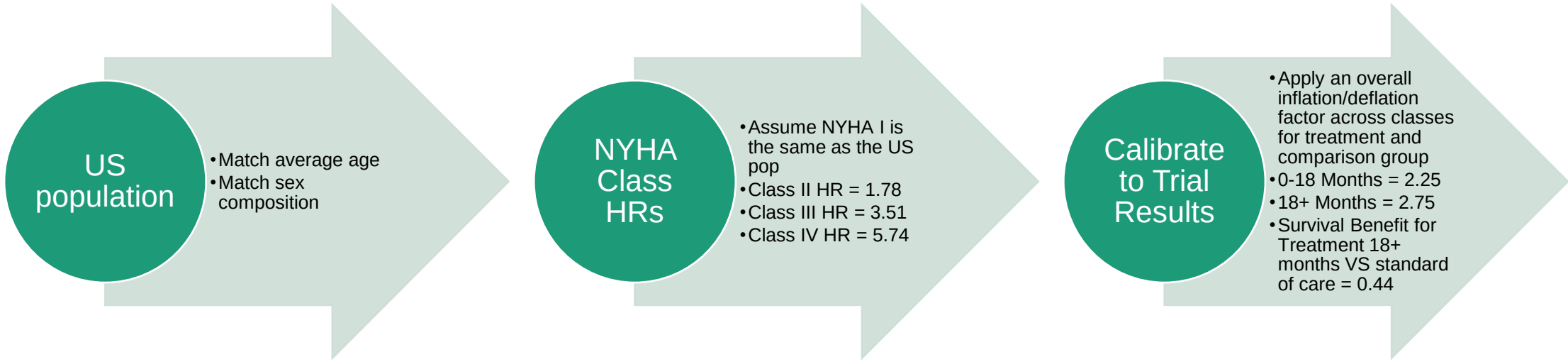
B Analysis of All-Cause Mortality



No. at Risk (cumulative no. of events)

Pooled tafamidis	264 (0)	259 (5)	252 (12)	244 (20)	235 (29)	222 (42)	216 (48)	209 (55)	200 (64)	193 (71)	99 (78)	0 (78)
Placebo	177 (0)	173 (4)	171 (6)	163 (14)	161 (16)	150 (27)	141 (36)	131 (46)	118 (59)	113 (64)	51 (75)	0 (76)

Key Model Inputs: Mortality Inputs



NYHA: New York Heart Association

Key Assumptions

- Utility, cost, and hospitalization inputs were NYHA functional class dependent, but not treatment dependent
- Price of treatment based on current tafamadis prices
- Discontinuation: Individuals discontinued transthyretin stabilizing treatment when they progress to NYHA Class IV
- Adverse Reactions: The effect of adverse events was incorporated only as treatment discontinuation, with no effect on costs or utilities

NYHA: New York Heart Association

Key Model Inputs: Utilities

Utility Input*	Trial Based Estimate, Normalized to National Average
NYHA Class I	0.82
NYHA Class II	0.729
NYHA Class III	0.633
NYHA Class IV	0.333

*Adjusted from ATTR-ACT [tafamidis]

NYHA: New York Heart Association

Scenario Analysis

Scenario Analysis	Description
Modified Societal Perspective	Included patient and caregiver productivity costs
Tafamidis Trial Population	Population characteristics (age, gender, and baseline NYHA functional class proportions) emulated the ATTR-ACT [tafamidis] clinical trial
Mortality Calibrated to Attribute-CM [acoramidis] Clinical Trial	Calibrated survival in our mode to match the Attribute-CM [acoramidis] clinical trial
Unadjusted Utility Values	Used the health state utility values as reported in the ATTR-ACT [tafamidis] clinical trial, without adjusting to the population averages
Exclude Disutility Due to Hospitalization	Did not incorporate a disutility for those experiencing a hospitalization
Cost of Reduced Dose (20 mg)	Drug cost input was lowered 25% of the base case cost, to reflect that some payers provide coverage for the 20 mg dosage of tafamidis

Results

Base-Case Results

Drug	Cost*	QALYs	evLYs	Years In NYHA Class I and II
Transthyretin Stabilizing Agent + Best Supportive Care	$858,000	2.9	3.2	2.7
Best Supportive Care Alone	$76,000	2.0	2.0	1.8
Incremental Change	$782,000	0.9	1.2	0.9

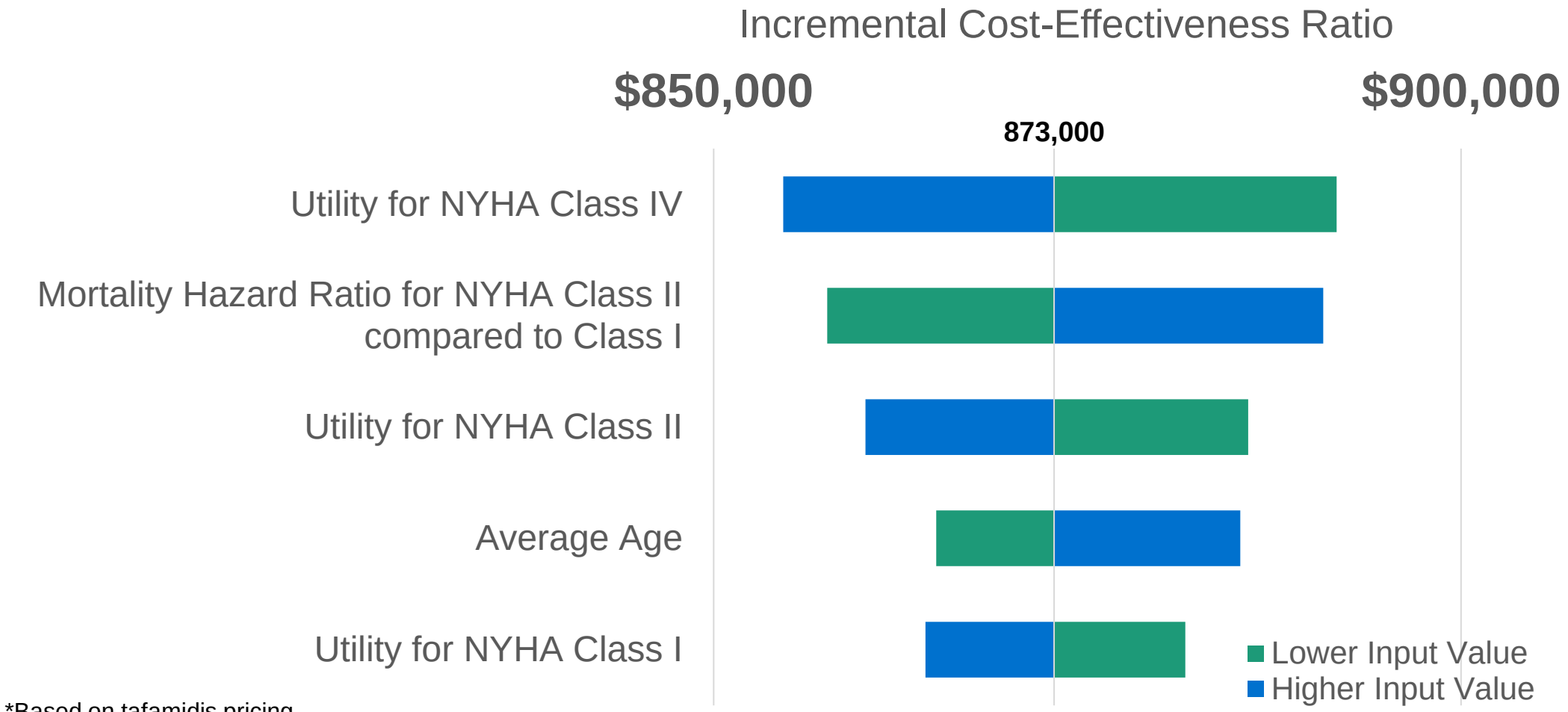
*Based on tafamidis pricing

Base-Case Incremental Ratio Results

Treatment	Comparator	Cost per QALY Gained*	Cost per evLY Gained*
Transthyretin Stabilizing Agent + Best Supportive Care	**Best Supportive Care Alone**	$873,000	$627,000

*Based on tafamidis pricing

One Way Sensitivity Analyses



*Based on tafamidis pricing

NYHA: New York Heart Association

Probabilistic Sensitivity Analysis

Drug	Cost-Effective at $50,000 per QALY*	Cost-Effective at $100,000 per QALY*	Cost-Effective at $150,000 per QALY*
Transthyretin Stabilizing Agent + Best Supportive Care	0%	0%	0%

*Based on tafamidis pricing

QALY: quality-adjusted life years

Scenario Analyses

	Scenario	Cost per QALY Gained*	Cost per evLY Gained*
	Base-Case Results	$873,000	$627,000
1	**Modified Societal Perspective**	$1,016,000	$731,000
2	**Mortality Calibrated to ATTRibute-CM [acoramidis] Clinical Trial**	$1,155,000	$859,000
3	**Tafamidis Trial Population**	$826,000	$579,000
4	**Unadjusted Utility Values**	$784,000	$627,000
5	**Exclude Disutility due to Hospitalization**	$838,000	$634,000

*Based on tafamidis pricing

evLY: equal value of life years gained, QALY: quality-adjusted life years

Scenario Analyses

	Scenario	Cost per QALY Gained*	Cost per evLY Gained*
	Base-Case Results	$873,000	$627,000
6	**Cost of Reduced Dose (20 mg)**	$250,000	$179,000
7	**Exclude Non-Drug Costs (Both Hospital and Supportive Care Costs)**	$831,000	$597,000
8	**Exclude Hospital Costs Only**	$847,000	$609,000
9	**Exclude Supportive Care Costs Only**	$857,000	$616,000

*Based on tafamidis pricing

evLY: equal value of life years gained, QALY: quality-adjusted life years

Health Benefit Price Benchmark (HBPB)

Intervention	Annual WAC*	Annual Price at $100,000 Threshold (per QALY)	Annual Price at $150,000 Threshold (per evLY)	Discount from WAC to Reach Threshold Prices
Transthyretin Stabilizing Agent + Best Supportive Care	$267,987	$13,600	$39,000	85.4% - 94.9%

*Based on tafamidis pricing

WAC: wholesale acquisition cost

Limitations

Top Limitations

- Lack of available data to inform a differentiated effect between acoramidis and tafamidis
- Limited ATTR-CM specific cost and mortality data
- Uncertainty on disease progression in ATTR-CM

Comments Received

- Mortality Estimation: To respond to concerns of the accuracy of the mortality calculation, we recalibrated mortality using the two-phase method.
- Hospitalization Rates: After concerns of bias in the initial hospitalization rates, which were different between treatment and comparator arms, we updated the inputs to pooled estimates from the ATTR-ACT [tafamidis] clinical trial.

Conclusions

- Transthyretin stabilizing agent (plus best supportive care) generate greater length of life and quality of life with much greater costs compared to best supportive care alone.
- The cost-effectiveness of transthyretin stabilizing agents (plus best supportive care) exceeded commonly used cost-effectiveness thresholds in the US.

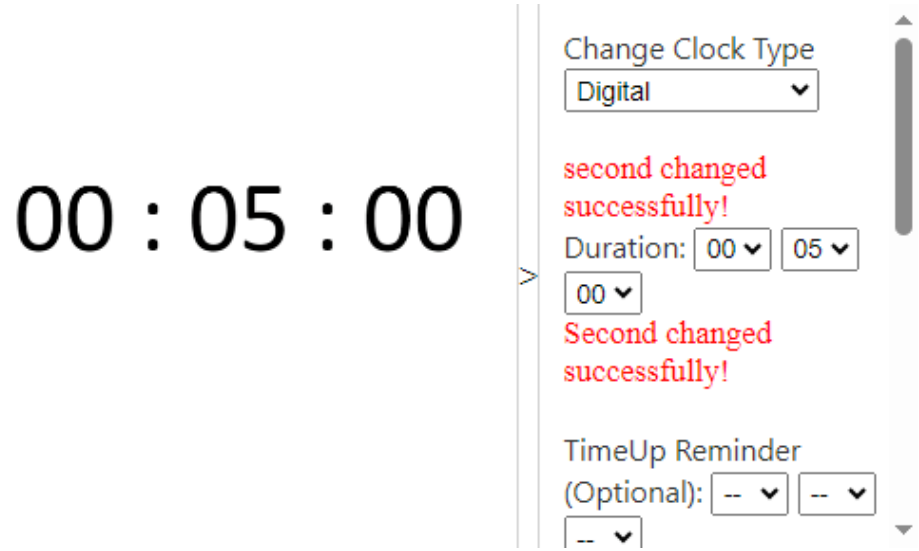
Questions?

Manufacturer Public Comment and Discussion

Marianna Bruno, PharmD, MPH, MBA
US Rare Cardiology Medical Team Lead, Pfizer

Conflicts of Interest:

- *Dr. Bruno is a full-time employee at Pfizer.*



Lunch

Meeting will resume at 12:50PM CT

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Voting Questions

Patient Population for all questions: *Adults with transthyretin amyloid cardiomyopathy (ATTR-CM).*

Clinical Evidence

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1. For adults with ATTR-CM is the current evidence adequate to demonstrate that the net health benefit of tafamidis is greater than that of no disease-specific treatment?

ⓘ Start presenting to display the poll results on this slide.

slido

2. For adults with ATTR-CM is the current evidence adequate to demonstrate that the net health benefit of acoramidis is greater than that of no disease-specific treatment?

ⓘ Start presenting to display the poll results on this slide.

slido

3. For adults with ATTR-CM is the current evidence adequate to demonstrate that the net health benefit of vutrisiran is greater than that of no disease-specific treatment?

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slido

4. For adults with ATTR-CM is the current evidence adequate to demonstrate that the net health benefit of vutrisiran added to tafamidis is greater than that of tafamidis alone?

ⓘ Start presenting to display the poll results on this slide.

slido

5. Is the currently available evidence adequate to distinguish the net health benefit among the interventions when used as monotherapy (tafamidis, acoramidis, vutrisiran)?

ⓘ Start presenting to display the poll results on this slide.

slido

5a. If “Yes”, which therapy has the greatest net health benefit?

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Benefits Beyond Health and Special Ethical Priorities

To help inform judgments of overall long-term value for money, please indicate your level of agreement with the following statements:

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6. There is substantial unmet need despite currently available treatments.

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slido

7. This condition is of substantial relevance for people from a racial/ethnic group that have not been equitably served by the healthcare system.

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The following questions are about the specific treatments:

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8. The TTR stabilizers are likely to produce substantial improvement in caregivers' quality of life and/or ability to pursue their own education, work, and family life.

ⓘ Start presenting to display the poll results on this slide.

slido

9. Acoramidis offers a substantial opportunity to improve access to effective treatment by means of its mechanism of action or method of delivery.

ⓘ Start presenting to display the poll results on this slide.

Long-Term Value for Money

10. Given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering benefits beyond health and special ethical priorities…

slido

10. What is the long-term value for money of tafamidis compared to no disease-specific treatment at current pricing?

ⓘ Start presenting to display the poll results on this slide.

11. Given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering benefits beyond health and special ethical priorities…

slido

11. What is the long-term value for money of acoramidis compared to no disease-specific treatment at assumed pricing?

ⓘ Start presenting to display the poll results on this slide.

Break

Meeting will resume at 2:00PM CT

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Policy Roundtable

Policy Roundtable

Participant	Conflict of Interest
Alyssa Guest, PharmD, Associate Director, Clinical Pharmacy, IPD Analytics	Alyssa is a full-time employee at IPD Analytics.
Michelle Kittleson, MD, PhD, Professor of Medicine, Smidt Heart Institute at Cedars-Sinai	No conflicts to disclose.
Mathew S. Maurer, MD, Professor of Cardiology, Columbia University Irving Medical Center	Dr. Maurer has received funds in excess of $5,000 from Novo-Nordisk and has received research support and consulting from Alnylam, Pfizer, Ionis, Intellia, and Attralus.
Milton Mitchell, Patient Advocate, Donate Life Ambassador and Active Amyloidosis Support Group Member	No conflicts to disclose.
Sean Riley, Patient Advocate/Speaker, Mackenzie's Mission - Amyloidosis Speakers Bureau	Sean has had equity interests in excess of $10,000 for Alnylam and BridgeBio.
John Watkins, PharmD, MPH, BCPS, Senior Clinical Pharmacist, Premera Blue Cross	John is a full-time employee at Premera Blue Cross.

Midwest CEPAC Council Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around October 21st, 2024
    - Includes description of Midwest CEPAC votes, deliberation, policy roundtable discussion
- Materials available at: https://icer.org/assessment/transthyretin-amyloid-cardiomyopathy-2024

Adjourn

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