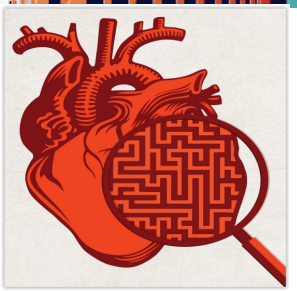
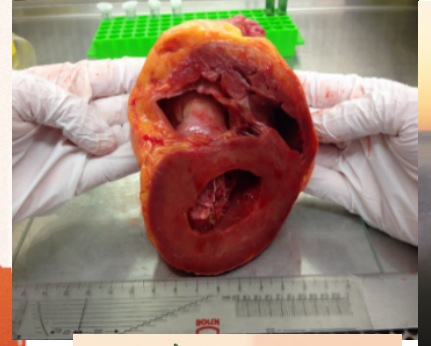
campi modulo

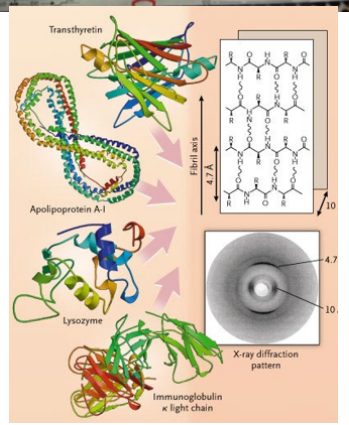
SEDE DEI LAVORI

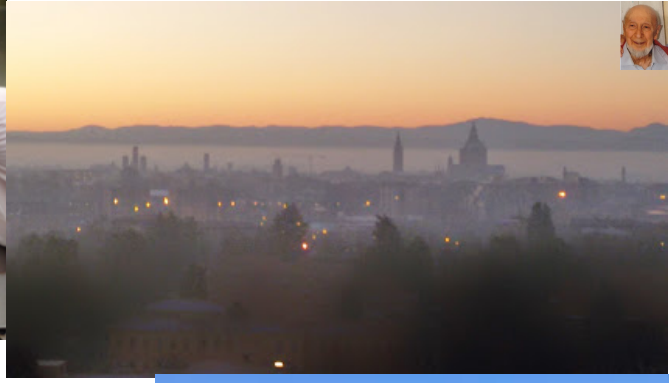
A. Roma Lifestyle Hotel
Via Giorgio Zoega 59, Roma



PLACE 2026
PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE







Approccio terapeutico e gestione del follow up

Stefano Perlini
Department of Internal Medicine, Center for Diagnosis and Treatment of Systemic Amyloidosis,
IRCCS Policlinico San Matteo Foundation, University of Pavia, Italy
Roma, 24 giugno 2026

Dislosures: Pfizer, Alnylam, Sanofi, Prothena, Accurate

Amyloidosis: protein misfolding disease

aggregation of normally soluble proteins into soluble β-sheet fibrils which are deposited in **target tissues** causing **progressive organ dysfunction**

Amyloid precursor

Increased conc.

Increased synthesis
- Monoclonal LC*
- SAA

Reduced clearance
- β2-microglobulin

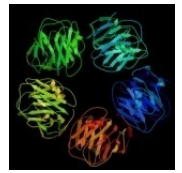
Mutations*
- Transthyretin
- Apolipoprotein AI
- Lysozyme, etc.

Aging
- Transthyretin wt

Interactions with microenvironment of target organs

Proteolysis

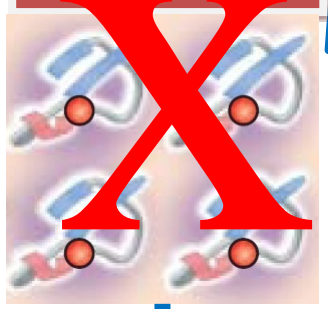
Lysosomal enzymes
Metalloproteases
metal ions,
matrix components



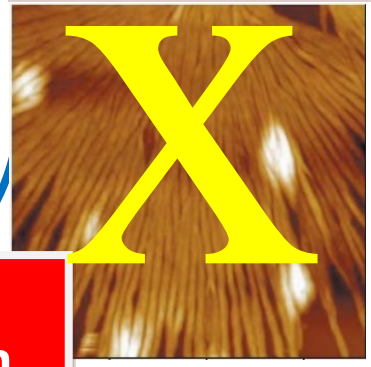
GAGs

SAP

Oligomers



Amyloid fibrils



misfolded

Structural instability

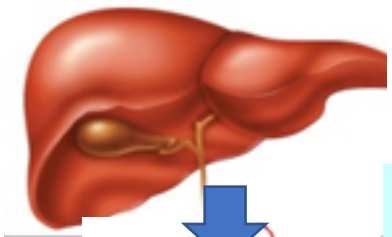
Organ dysfunction

Pavia Amyloidosis Center,, unpublished

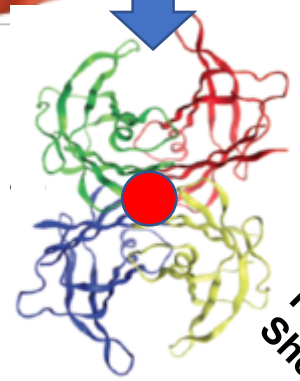
ATTR: Therapeutic opportunities

Obici & Merlini. *Expert Opin Investig Drugs.* 2014;23:1239-51

Suppression of the synthesis
- Liver transplantation



Tetramer stabilizers
- Tafamidis
- Diflunisal
- SOM0226
- Tolcapone



Amyloid fibril degradation/ reabsorption
- Anti-SAP therapy
- Anti-amyloid mAb

Amyloid fibrils

Aggregation inhibitors
- non-natural peptides

Proteolysis
Shear forces

rate-limiting tetramer dissociation

misfolding

Folded monomer

Aggregation

Small oligomers --> Oxidative stress Inflammation

- Anti-cytokines

Amorphous aggregates

Redirecting oligomers off-pathway
- EGCG

1. Ericzon et al, *Transplantation* 2015. 2. Coelho T, et al. *N Engl J Med*. 2013. 3. Coelho T, et al. *Neurology*. 2012 4. Berk JL, et al. *JAMA* 2013. 5. Ehrnhoefer, et al. *Nat SMB.* 2008. 6. Bodin et al, *Nature.* 2010. 6a. Richards et al, *NEJM* 2015 7. Cardoso I, et al. *J Transl Med.* 2010. 8. Merlini et al, *XIV Int Symposium on Amyloidosis, 2014.* 9. Pereira et al, *J Neuropathol Exp Neurol* 2015. Marcoux et al, *EMBO Mol Med 2015. 10* Sant'Anna et al, *Nat Comm 2016*

TABLE 3 ATTR Specific Disease Modifying Therapies

	Mechanism of Action	Stage of Approval	Route of Administration	Dose	Phase 3 Clinical Trial	Cardiovascular Trial Outcomes	Side Effects
Stabilizers							
Diflunisal	Stabilizes TTR to prevent dissociation	Approved as an NSAID, off-license use for ATTR-CA and ATTR-PN	Oral	250 mg twice daily	NA	Small retrospective studies have demonstrated an	Fluid retention Bleeding
Tafamidis	Stabilizes TTR to prevent dissociation	Approved for ATTR-CA		max 61 mg or Vy mg once daily			
Acoramidis	Stabilizes TTR to prevent dissociation	Due to be reviewed by the FDA					
Silencers							
Patisiran	siRNA targeting TTR mRNA	Approved for ATTR-PN, but not for ATTR-CA	Intravenous infusion	80-min infusion based weight every 3 wks <100 kg = 0.3 mg >100 kg = 30 mg			
Vutrisiran	siRNA targeting TTR mRNA	App... CA		...ion every 3			
Eplontersen	ASO inhibitor of TTR production	Approved for ATTR-PN, but not for ATTR-CA	Subcutaneous injection	45 mg monthly	CARDIO-TTRansform	CARDIO-TTRansform is a phase 3 RCT designed to assess the efficacy of eplontersen in patients with ATTR-CA	Headache Vitamin A deficiency

TABLE 3 Continued

	Mechanism of Action	Stage of Approval	Route of Administration	Dose	Phase 3 Clinical Trial	Cardiovascular Trial Outcomes	Side Effects
Gene Editors							
NTLA-2001	CRISP-Cas9 editing of the TTR gene	Under investigation	Intravenous infusion	0.1 mg/kg or 0.3 mg/kg given once	NA	A small phase 1 trial has demonstrated that NTLA-2001 is safe and results in a sustained TTR knockdown	Headache Vitamin A deficiency
Depleters							
NI006	Recombinant human anti-ATTR monoclonal IgG1 antibody that binds ATTR-amyloid	Under investigation	Intravenous infusion	4 weekly infusions with doses ranging from 0.3-60 mg/kg	NA	A small phase 1 trial has demonstrated that NI006 is safe and at higher doses appeared to reduce NT-proBNP, troponin I, and myocardial extracellular volume. A phase 3 trial will assess efficacy in ATTR-CA.	Arthralgia Thrombocytopenia
PX004	Humanized IgG antibody that binds ATTR-amyloid	Under investigation	Intravenous infusion	4 weekly infusions with doses ranging from 0.1-3.0 mg/kg	NA	A small phase 1 trial has demonstrated that PX004 is safe	Unknown
AT-02	Pan amyloid removal technology using a single-chain fusion protein to stimulate immunological removal of amyloid	Under investigation	Intravenous infusion	Dosing not available	NA	A small phase 1 trial is currently ongoing	Unknown

6MWT = 6-minute walk test; ASO = antisense oligonucleotide; CA = cardiac amyloidosis; FDA = U.S. Food and Drug Administration; IgG = immunoglobulin G; mRNA = messenger RNA; NA = not available; NSAID = nonsteroidal anti-inflammatory drug; PN = polyneuropathy; RCT = Randomized controlled trial; siRNA = small interfering RNA; TTR = Transthyretin; other abbreviations as in Tables 1 and 2.

Continued on the next page

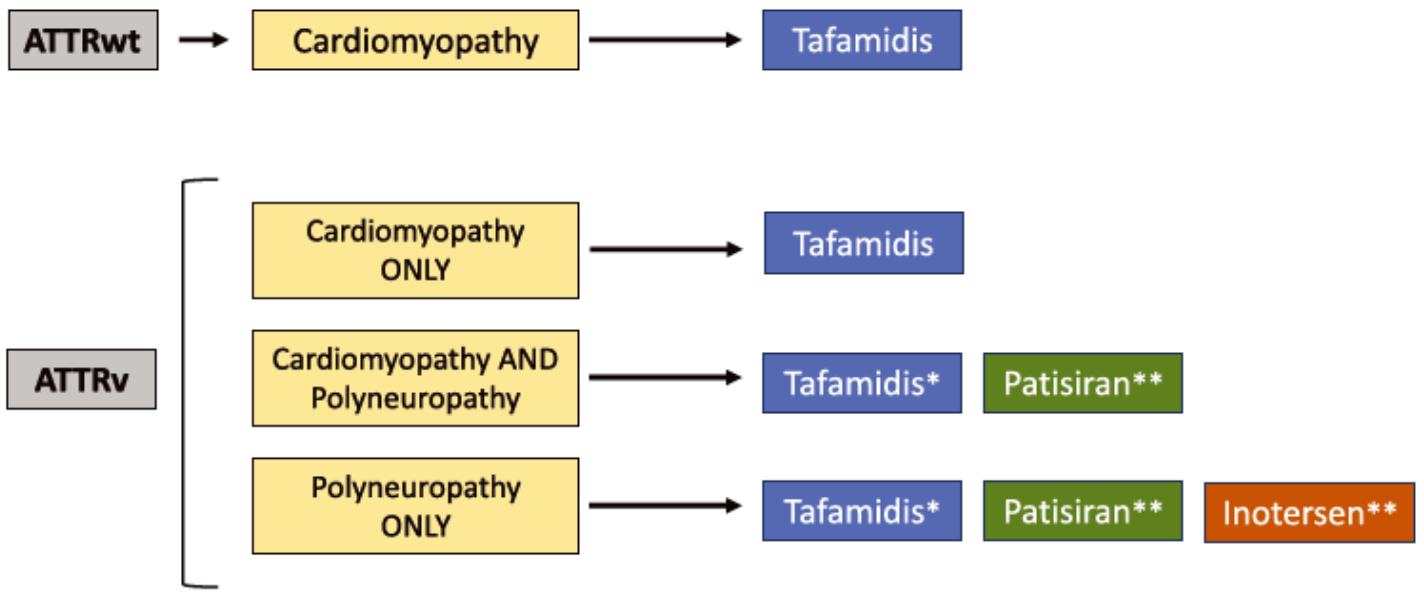
Fontana et al. JACC CV Img 2025, in press

ESC European Society of Cardiology
European Journal of Heart Failure (2021)
doi:10.1002/ejhf.2140

POSITION PAPER

Diagnosis and treatment of cardiac amyloidosis. A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases

Cardiac amyloidosis is "treatable" !



* Polyneuropathy Stage 1
** Polyneuropathy Stage 1 & 2

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy

Mathew S. Maurer, M.D., Jeffrey H. Schwartz, Ph.D., Balarama Gundapaneni, M.S., Perry M. Elliott, M.D., Giampaolo Merlini, M.D., Ph.D., Marcia Waddington-Cruz, M.D., Arnt V. Kristen, M.D., Martha Grogan, M.D., Ronald Witteles, M.D., Thibaud Damy, M.D., Ph.D., Brian M. Drachman, M.D., Sanjiv J. Shah, M.D., Mazen Hanna, M.D., Daniel P. Judge, M.D., Alexandra I. Barsdorf, Ph.D., Peter Huber, R.Ph., Terrell A. Patterson, Ph.D., Steven Riley, Pharm.D., Ph.D., Jennifer Schumacher, Ph.D., Michelle Stewart, Ph.D., Marla B. Sultan, M.D., M.B.A., and Claudio Rapezzi, M.D., for the ATTR-ACT Study Investigators*

ATTR-ACT[1]

ATTR-ACT LTE[2]

MDedge LATEST QUIZZES VIDEOS

ATTR-ACT shows treatment breakthrough in amyloid cardiomyopathy

September 4, 2018 | CARDIOLOGY NEWS

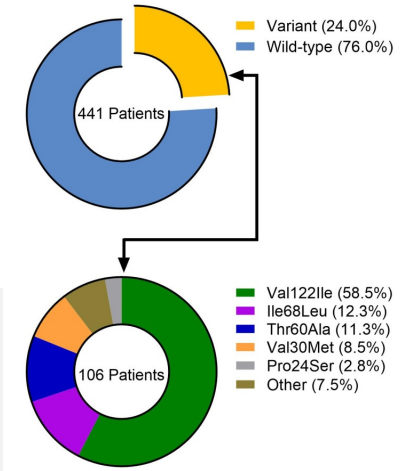
Bruce Jancin

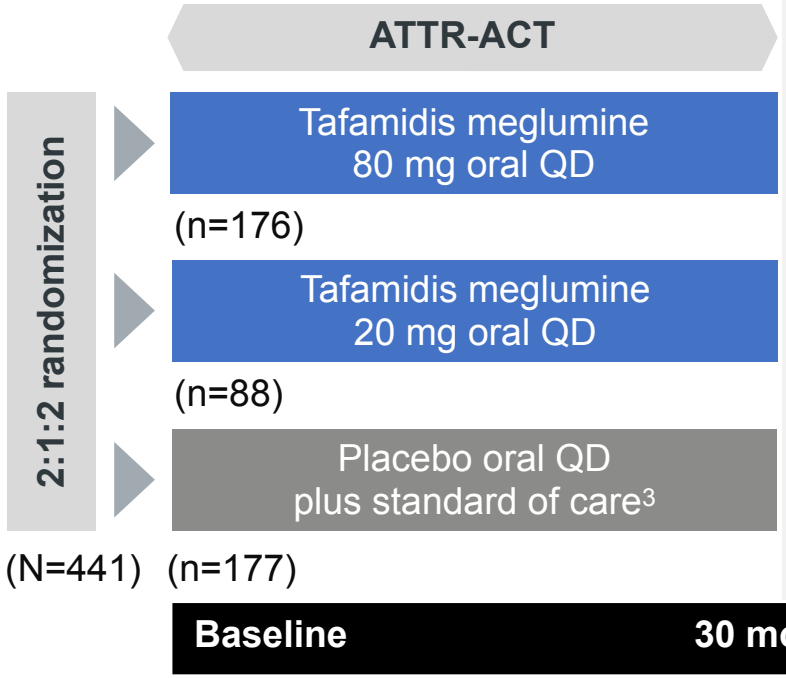
- **NYHA class (I/II and III)**[3]
- **LVEF status**[4]
- **Atrial fibrillation**[5]
- **Octogenarian (aged <80 and ≥80 years)**[6]
- **CKD**[7]

ATTR-ACT: Tafamidis in Transthyretin Cardiomyopathy Clinical Trial; CKD: chronic kidney disease; LTE: long-term extension; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

1. Maurer MS, et al. *N Engl J Med* 2018;379(11):1007–16; 2. Elliott P, et al. *Circ Heart Fail* 2022;15(1):e008193; 3. Elliott P, et al. *Eur J Heart Fail* 2023;25(11):2060–4; 4. Drachman B, et al. *Eur J Heart Fail* 2024;26(9):2038–46; 5. Witteles R, et al. *JACC CardioOncol* 2024;6(4):592–8; 6. Garcia-Pavia P, et al. *JACC Heart Fail* 2024;12(1):150–60; 7. Sperry BW, et al. *JACC CardioOncol* 2024;6(2):300–6.

ATTR-ACT and LTE:* study design[1]

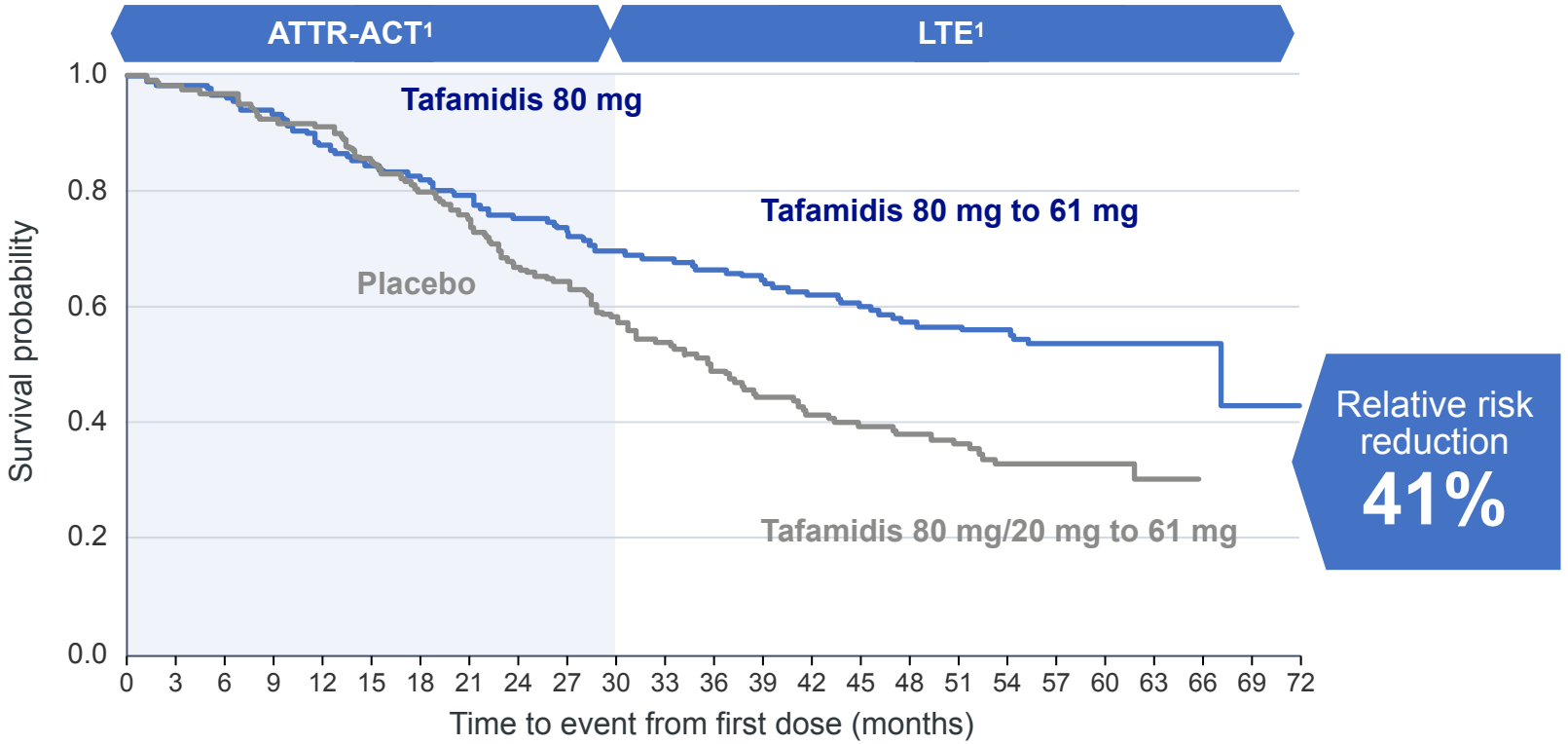




Tafamidis is the only treatment for ATTR cardiomyopathy with 5 years of clinical data
Prolonged survival was observed throughout ATTR-ACT and the LTE[1]

Tafamidis 61 mg is indicated to treat adult wild-type and hereditary ATTR cardiomyopathy patients.[3] All patients on tafamidis meglumine (20 or 80 mg QD) were analyzed in a combined approach. Tafamidis 61 mg corresponds to 80 mg tafamidis meglumine. Tafamidis and tafamidis meglumine are not interchangeable on a per-mg basis.[2,3]
*Upon completion of ATTR-ACT, patients could enroll in the ongoing LTE study for up to 60 months. Patients receiving tafamidis in ATTR-ACT continued to receive the same dose uninterrupted, while those in the placebo group were randomized 2:1 to tafamidis 80 mg or 20 mg. Patients were treated with tafamidis 80 mg or 20 mg (up to the protocol amendment) for a median of 39 months. Median LTE follow-up was 58.5 months in the continuous tafamidis 80 mg to 61 mg group and 57.1 months in the placebo to tafamidis 80 mg/20 mg to 61 mg group. For both groups, time zero for survival analyses was the time of enrollment in ATTR-ACT;[1,4] †A single tafamidis 61 mg capsule is bioequivalent to tafamidis 80 mg (four 20-mg capsules) and is not interchangeable on a per-mg basis.[2,3]
ATTR-ACT: Tafamidis in Transthyretin Cardiomyopathy Clinical Trial; ATTR cardiomyopathy: transthyretin amyloid cardiomyopathy; LTE: long-term extension; QD, once daily.
1. Elliott P, et al. *Circ Heart Fail* 2022;15(1):e008193; 2. Lockwood PA, et al. *Clin Pharmacol Drug Dev* 2020;9(7):849–54; 3. Vyndaqel (tafamidis), Summary of Product Characteristics, EMA. Available at: https://www.ema.europa.eu/documents/product-informaton/vyndaqel-epar-product-information_en.pdf (Accessed April 2025); 4. Maurer MS, et al. *N Engl J Med* 2018;379(11):1007–16.

ATTR-ACT and LTE *post hoc* analysis: 5-year all-cause mortality data

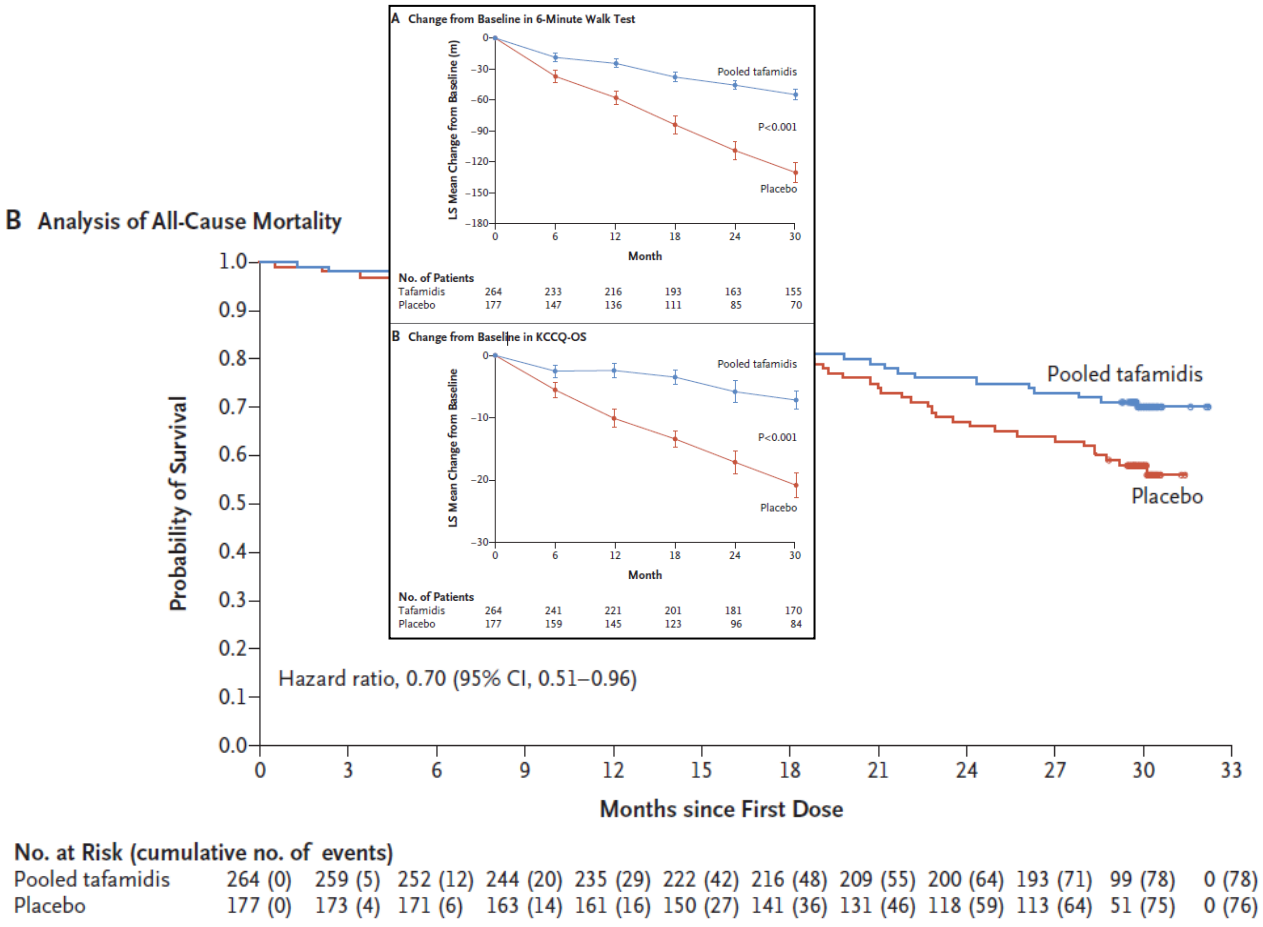


Patients taking continuous tafamidis meglumine 80 mg to tafamidis free acid 61 mg showed a **clinically significant improvement** in **survival** at **5 years** versus those first treated with placebo*,†

The preliminary 5-year **survival rate** with continuous tafamidis was **53% versus 32%** in patients who first received placebo (P<0.001)

Figure adapted from Elliott P, et al. *Circ Heart Fail* 2022;15(1):e008193.[1]

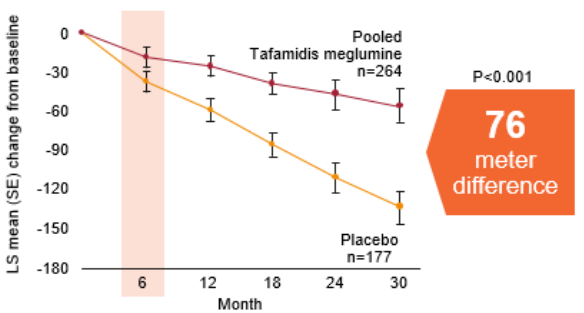
Tafamidis 61 mg is indicated to treat adult wild-type and hereditary ATTR cardiomyopathy patients.[2] All patients on tafamidis meglumine (20 or 80 mg QD) were analyzed in a combined approach. Tafamidis 61 mg corresponds to 80 mg tafamidis meglumine. Tafamidis and tafamidis meglumine are not interchangeable on a per-mg basis.[2,3]
*Upon completion of ATTR-ACT, patients could enroll in the ongoing LTE *post hoc* analysis for up to 60 months. In the LTE study, patients treated with tafamidis meglumine 80 mg in ATTR-ACT continued with tafamidis 80 mg, then transitioned to tafamidis free acid 61 mg, and were compared with those treated with placebo in ATTR-ACT, who were randomized to tafamidis meglumine 80 mg or tafamidis meglumine 20 mg (2:1), then transitioned to tafamidis free acid 61 mg. Median LTE follow-up was 58.5 months in the continuous tafamidis meglumine 80 mg to tafamidis free acid 61 mg group and 57.1 months in the placebo to tafamidis meglumine 80 mg/20 mg to tafamidis free acid 61 mg group. For both groups, time zero for survival analyses was the time of enrolment in ATTR-ACT.[1] †The primary efficacy endpoint in the LTE study was all-cause mortality, with heart transplantation and implantation of a cardiac mechanical assist device treated as death. Differential all-cause mortality in the two groups was assessed by a Cox proportional hazards model with treatment, genotype, and NYHA baseline classification in the model.[1]
ATTR-ACT: Tafamidis in Transthyretin Cardiomyopathy Clinical Trial; ATTR cardiomyopathy: transthyretin amyloid cardiomyopathy; LTE: long-term extension; NYHA: New York Heart Association; QD: once daily.
1. Elliott P, et al. *Circ Heart Fail* 2022;15(1):e008193; 2. Vyndaqel (tafamidis), Summary of Product Characteristics. Available at: https://www.ema.europa.eu/documents/product-information/vyndaqel-epar-product-information_en.pdf (Accessed April 25, 2025); 3. Lockwood PA, et al. *Clin Pharmacol Drug Dev* 2020;9(7):849–54.



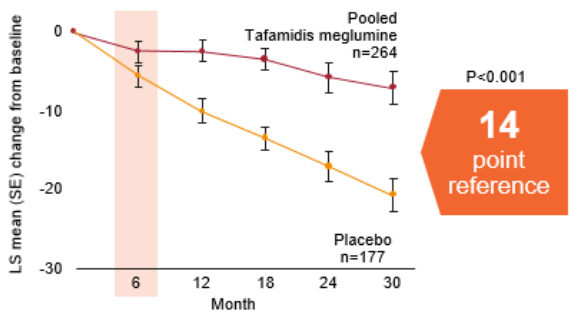
ATTR-ACT: change in functional capacity and quality of life vs placebo

A significant effect favoring tafamidis was first observed at Month 6 and remained consistent through Month 30 on both 6MWT distance and KCCQ-OS score[1]

Functional capacity:
6MWT change from baseline at Month 30*[1]



QoL:
KCCQ-OS score change from baseline at Month 30†[1]



Images reproduced from Maurer MS, et al. *N Engl J Med* 2018;379:1007–16.

*The 6-minute walk test (6MWT) evaluated patients' functional capacity by measuring their distance walked in 6 minutes.[1] †The Kansas City Cardiomyopathy Questionnaire-Overall Summary (KCCQ-OS) score assesses patients' quality of life using the follow domains: total symptoms (symptom frequency, symptom burden), physical limitation, quality of life, and social limitation. Score range from 0 to 100, with higher scores reflecting better health status. Vital status at month 30 was assessed for all enrolled patients.[1,2]

6MWT, 6-minute walk test; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire Overall Summary; LS, least squares; SE, standard error.

1. Maurer MS, et al. *N Engl J Med* 2018;379:1007–16; 2. Hanna M, et al. *Am J Cardiol* 2021;141:98–105.

Mean baseline KCCQ-OS

- **67.12** (SD 21.29) for the **continuous tafamidis group***
- **65.90** (SD 21.74) for the **placebo to tafamidis group**

Comparison of treatment groups

- **At both Months 30 and 60**, the **continuous tafamidis group** had a **significantly smaller decline in KCCQ-OS** compared with the placebo to tafamidis group
  - **At Month 30:** LS mean difference in change between groups was 13.38 (95% CI, 9.21–17.54; P<0.0001)
  - **At Month 60:** LS mean difference in change between groups was 18.83 (95% CI, 12.64–25.03; P<0.0001)
- The **continuous tafamidis group** had a **6-point reduction** in LS mean (SE) KCCQ-OS **at Month 30**, with **no further decline over the next 30 months**
- The **placebo to tafamidis group** had a **20-point reduction** in LS mean KCCQ-OS **at Month 30**, but the **decline slowed after initiating tafamidis** during the LTE

LS mean change from baseline in KCCQ-OS

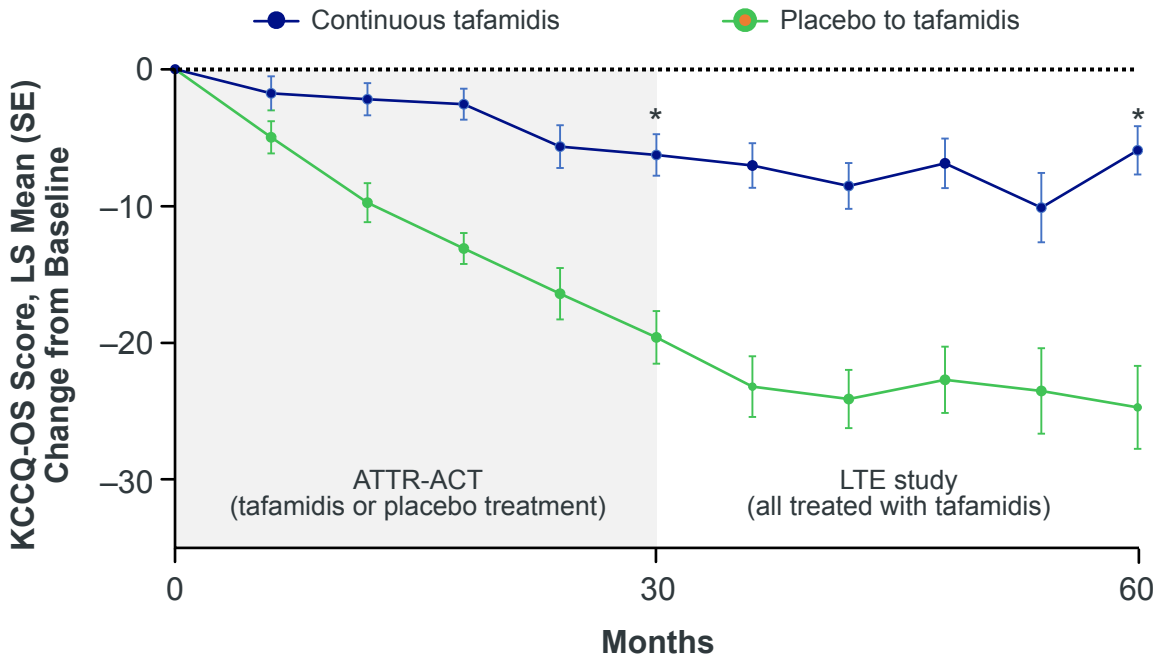


Figure adapted from Grogan M, et al. *Eur J Heart Fail* 2024;26(3):612–5.

*Patients receiving tafamidis 20 mg in ATTR-ACT were excluded from this analysis because this dose is not approved for the treatment of ATTR cardiomyopathy.
ATTR-ACT: Tafamidis in Transthyretin Cardiomyopathy Clinical Trial; ATTR cardiomyopathy: transthyretin amyloid cardiomyopathy CI: confidence interval; KCCQ-OS: Kansas City Cardiomyopathy Questionnaire Overall Summary score; LS: least squares; LTE: long-term extension; SD: standard deviation; SE: standard error.
Grogan M, et al. *Eur J Heart Fail* 2024;26(3):612–5.

Tafamidis has a similar and comparable safety profile to placebo

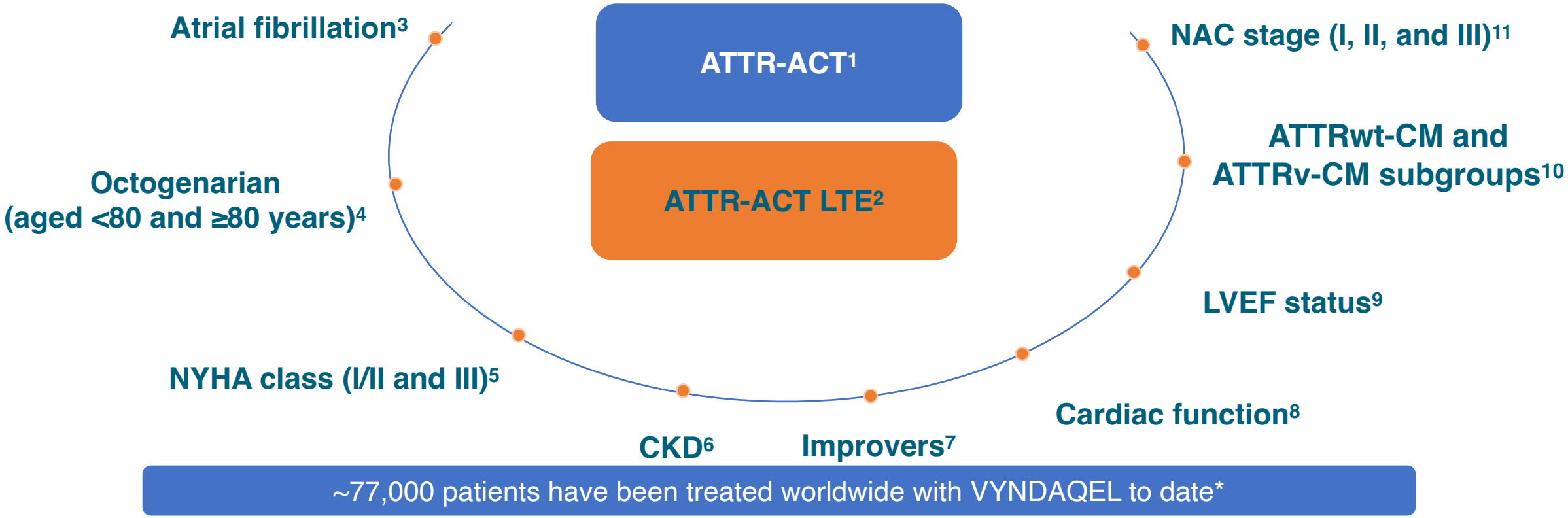
	Tafamidis meglumine 80 mg	Tafamidis meglumine 20 mg*	Placebo (ATTR-ACT only)
ATTR-ACT[1]			
N	176	88	177
Patients with serious TEAEs	75.6%	75.0%	79.1%
Patients with severe TEAEs	62.5%	61.4%	64.4%
ATTR-ACT + LTE[1]			
N	227	115	
Patients with serious TEAEs	69.6%	72.2%	
Patients with severe TEAEs	53.3%	53.0%	

In the ATTR-ACT study, the frequency of **adverse events in patients treated with tafamidis meglumine 80 mg†** was generally **similar** and **comparable** to that of the placebo group[1,2]

No new safety concerns were identified throughout the LTE, and the **frequency of adverse events remained similar** to that with placebo (median follow-up across both studies: ~58 months)[3]

Tafamidis 61 mg is indicated to treat adult wild-type and hereditary ATTR cardiomyopathy patients.[2]
*Tafamidis meglumine 20 mg is not indicated for use in ATTR-CM.[2] †All patients on tafamidis meglumine (20 or 80 mg QD) were analyzed in a combined approach. Tafamidis 61 mg corresponds to 80 mg tafamidis meglumine. Tafamidis and tafamidis meglumine are not interchangeable on a per-mg basis.[2,4]
ATTR-ACT: Tafamidis in Transthyretin Cardiomyopathy Clinical Trial; ATTR cardiomyopathy: transthyretin amyloid cardiomyopathy; LTE: long-term extension; QD: once daily; TEAE: treatment-emergent adverse event.
1. Damy T, et al. *Eur J Heart Fail* 2021;23(2):277–85; 2. Vyndaqel (tafamidis), Summary of Product Characteristics, EMA. Available at: https://www.ema.europa.eu/documents/product-information/vyndaqel-epar-product-information_en.pdf (Accessed April 25, 2025); 3. Elliott P, et al. *Circ Heart Fail* 2022;15(1):e008193; 4. Lockwood PA, et al. *Clin Pharmacol Drug Dev* 2020;9(7):849–54.

Tafamidis has 7+ years of efficacy data, including data across multiple patient populations and parameters[1–11]



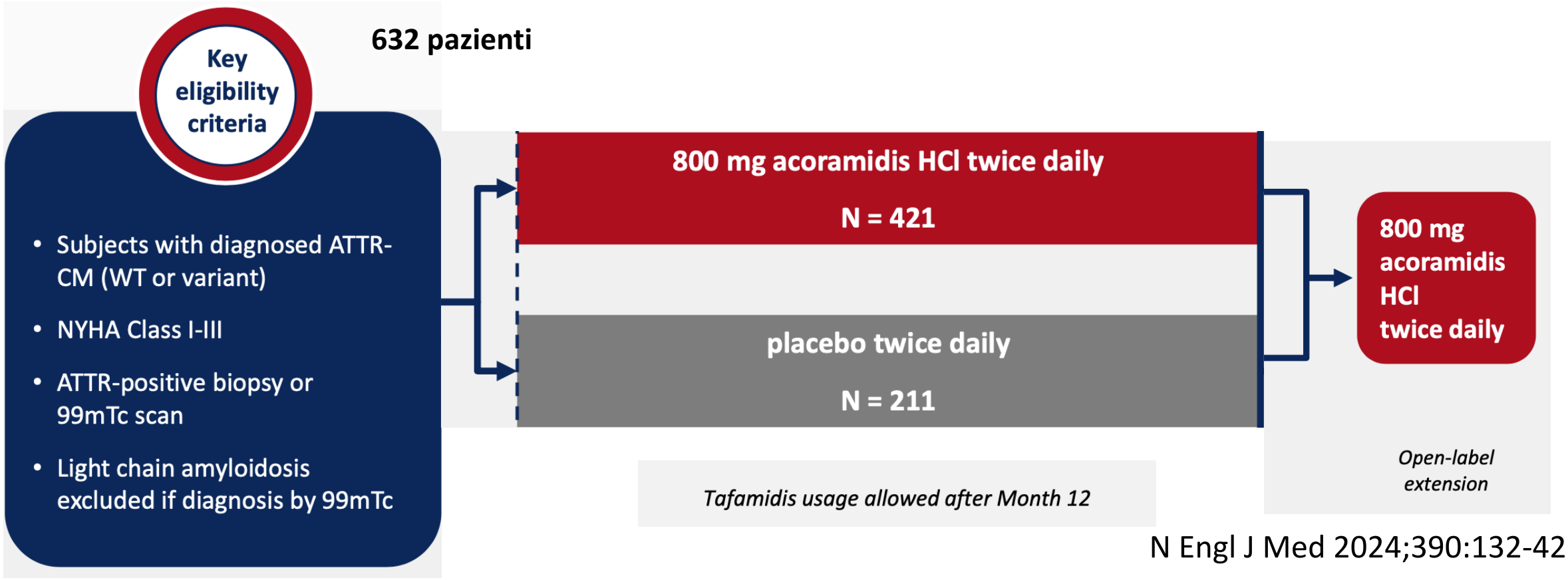
*76,888 from May 2019 to January 2026. Data obtained from multiple sources, such as IQVIA reports, national registry data, distribution reports, and finance data.

ATTR-ACT, Tafamidis in Transthyretin Cardiomyopathy Clinical Trial; ATTRv-CM, hereditary transthyretin amyloid cardiomyopathy; ATTRwt-CM, wild-type transthyretin amyloid cardiomyopathy; CKD, chronic kidney disease; LTE, long-term extension; LVEF, left ventricular ejection fraction; NAC, National Amyloidosis Centre; NYHA, New York Heart Association.

1. Maurer MS, et al. Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy. *N Engl J Med*. 2018;379(11):1007–16; 2. Elliott P, et al. Long-term survival with tafamidis in patients with transthyretin amyloid cardiomyopathy. *Circ Heart Fail*. 2022;15(1):e008193; 3. Witteles R, et al. Atrial fibrillation as a prognostic factor for all-cause mortality in patients with transthyretin amyloid cardiomyopathy. *JACC CardioOncol*. 2024;6(4):592–8; 4. Garcia-Pavia P, et al. Tafamidis efficacy among octogenarian patients in the Phase 3 ATTR-ACT and ongoing long-term extension study. *JACC Heart Fail*. 2024;12(1):150–60; 5. Elliott P, et al. Improved long-term survival with tafamidis treatment in patients with transthyretin amyloid cardiomyopathy and severe heart failure symptoms. *Eur J Heart Fail*. 2023;25(11):2060–4; 6. Sperry BW, et al. Effect of tafamidis on renal function in patients with transthyretin amyloid cardiomyopathy in ATTR-ACT. *JACC CardioOncol*. 2024;6(2):300–6; 7. Hanna M, et al. Improvements in Efficacy Measures With Tafamidis in the Tafamidis in Transthyretin Cardiomyopathy Clinical Trial. *JACC Adv*. 2022;1(5):100148; 8. Shah SJ, et al. Effect of tafamidis on cardiac function in patients with transthyretin amyloid cardiomyopathy: a post hoc analysis of the ATTR-ACT randomized clinical trial. *JAMA Cardiol*. 2024;9(1):25–34; 9. Drachman B, et al. Long-term tafamidis efficacy in patients with transthyretin amyloid cardiomyopathy by baseline left ventricular ejection fraction. *Eur J Heart Fail*. 2024;26(9):2038–46; 10. Rapezzi C, et al. Efficacy of tafamidis in patients with hereditary and wild-type transthyretin amyloid cardiomyopathy: further analyses from ATTR-ACT. *JACC Heart Fail*. 2021;9(2):115–23; 11. Damy T, et al. Long-term efficacy of tafamidis in patients with transthyretin amyloid cardiomyopathy by National Amyloidosis Centre stage. *Eur J Heart Fail*. 2025;27(12):2998–3009.

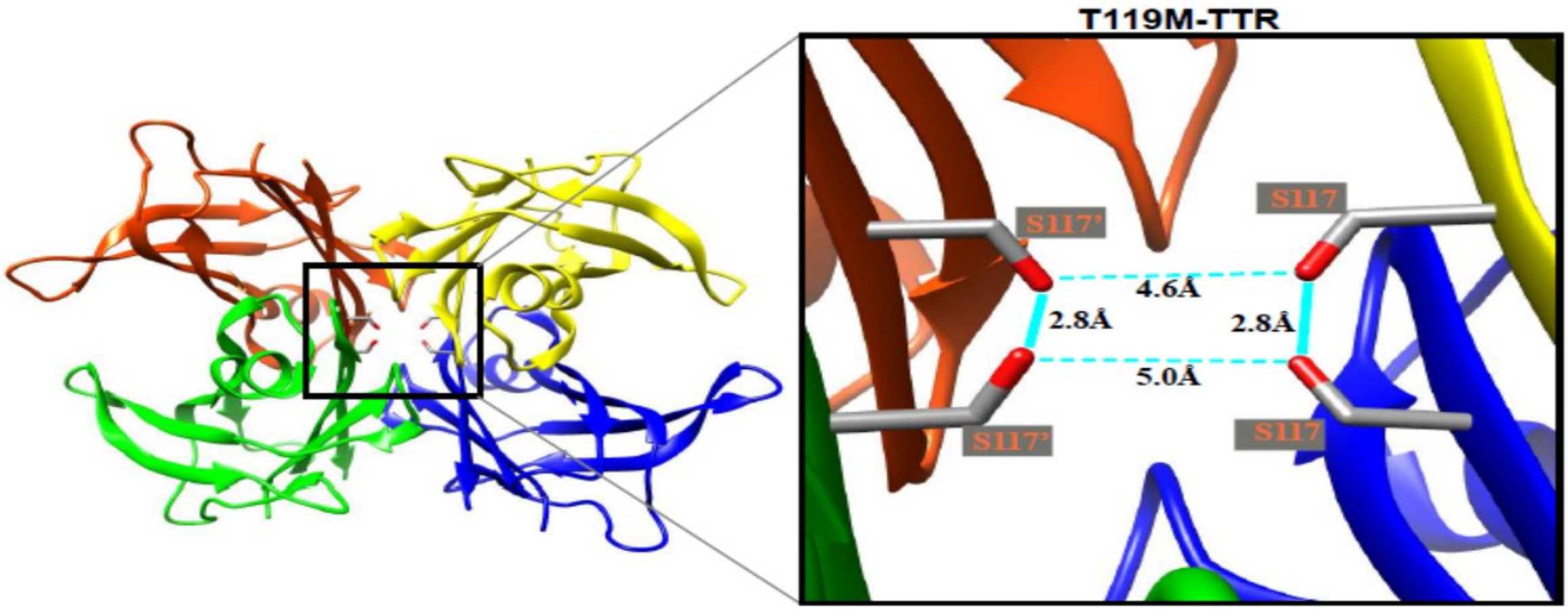
Efficacy and Safety of Acoramidis in Transthyretin Amyloid Cardiomyopathy

Results of the ATTRibute-CM Trial

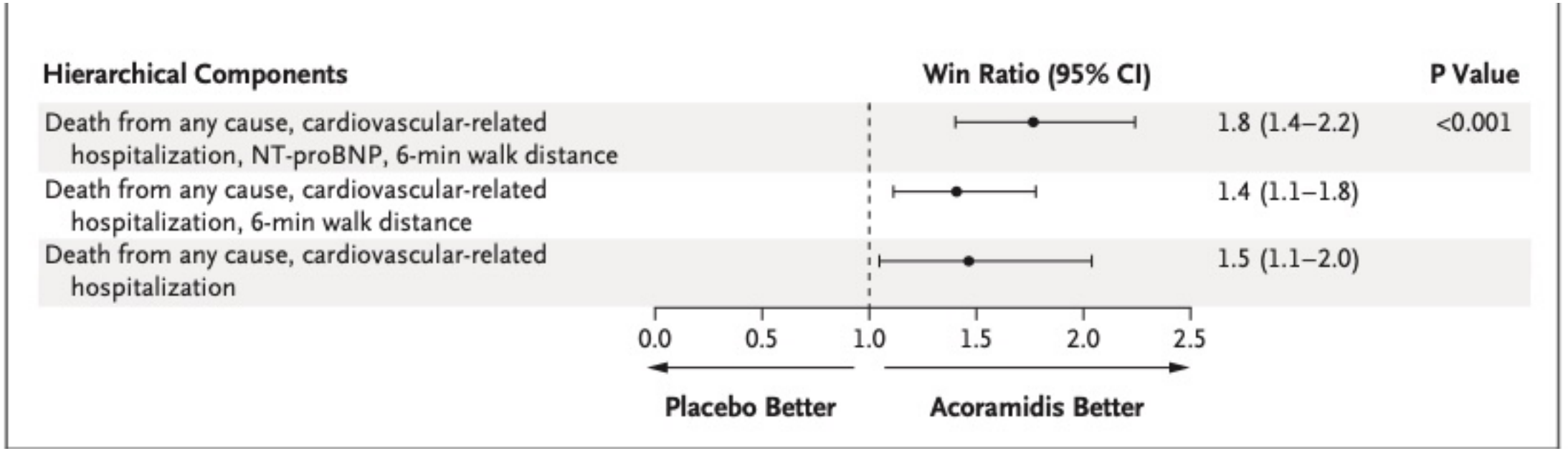


N Engl J Med 2024;390:132-42

Acoramidis tetrameric stabilization mimic T119M mutation



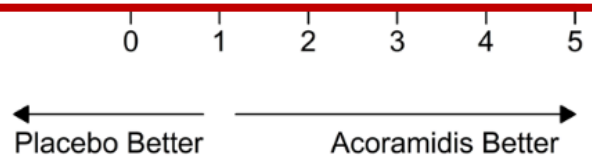
PRIMARY ENDPOINT – overall and subgroups



N Engl J Med 2024;390:132-42

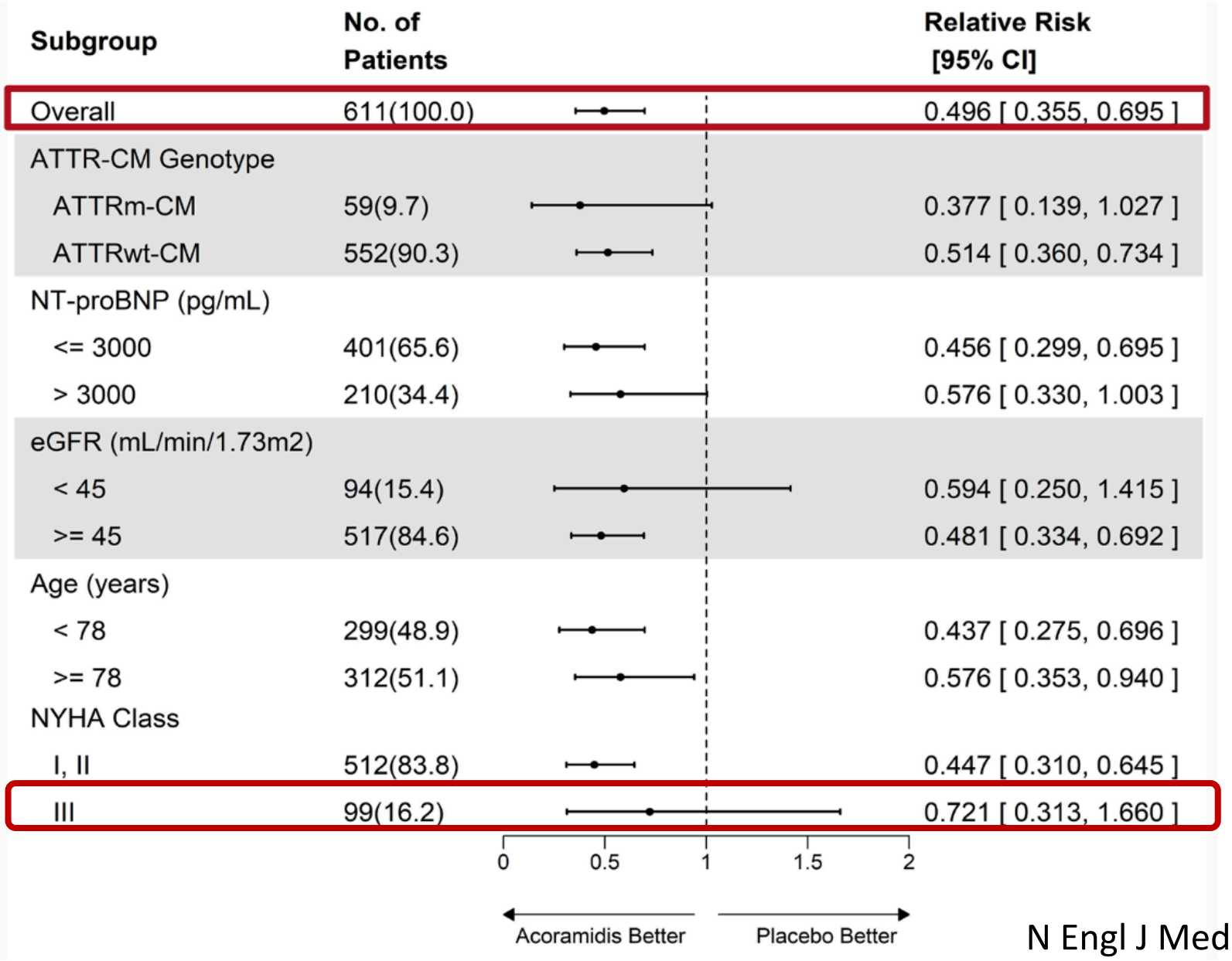
PRIMARY ENDPOINT – overall and subgroups

Subgroup	No. of Patients	Win Ratio [95% CI]	FS test P-value
Overall	611(100.0)	1.772 [1.417, 2.217]	<0.0001
ATTR-CM Genotype			
ATTRm-CM	59(9.7)	2.529 [1.303, 4.911]	0.0061
ATTRwt-CM	552(90.3)	1.756 [1.396, 2.208]	<0.0001
NT-proBNP (pg/mL)			
<= 3000	401(65.6)	1.787 [1.373, 2.325]	<0.0001
> 3000	210(34.4)	1.678 [1.160, 2.426]	0.0060
eGFR (mL/min/1.73m2)			
< 45	94(15.4)	1.410 [0.849, 2.341]	0.1841
>= 45	517(84.6)	1.797 [1.452, 2.226]	<0.0001
Age (years)			
< 78	299(48.9)	2.052 [1.489, 2.829]	<0.0001
>= 78	312(51.1)	1.499 [1.098, 2.045]	0.0107
NYHA Class			
I, II	512(83.8)	1.892 [1.479, 2.419]	<0.0001
III	99(16.2)	1.150 [0.652, 2.030]	0.6292



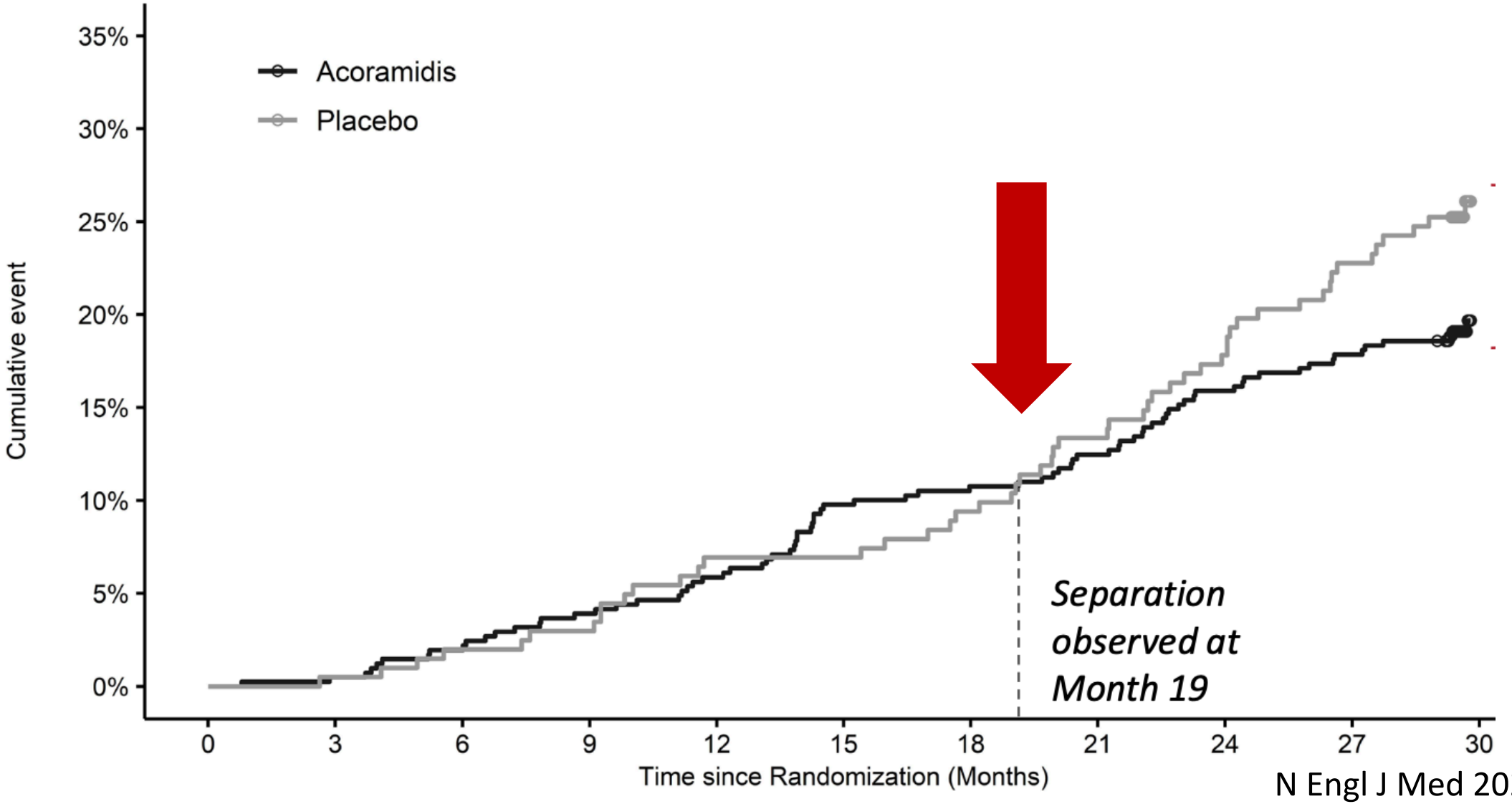
N Engl J Med 2024;390:132-42

Cardiovascular Hospitalization on overall analysis



N Engl J Med 2024;390:132-42

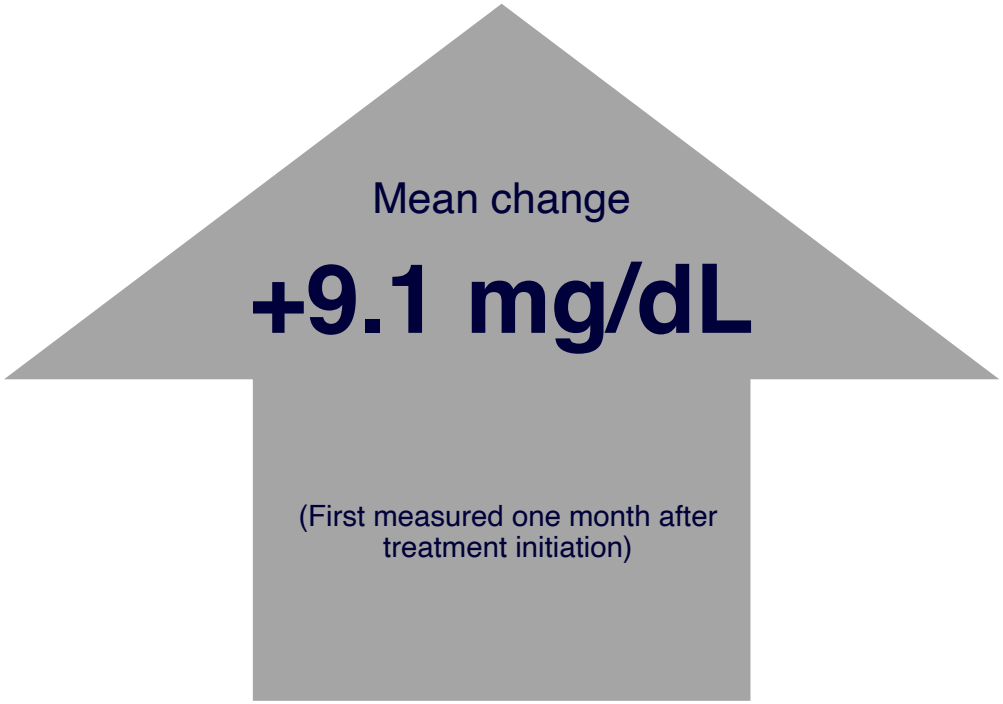
SECONDARY ENDPOINT – All cause Mortality



N Engl J Med 2024;390:132-42

Stabilization of TTR is associated with increases in serum TTR

Data from the ATTRibute-CM trial found elevated serum TTR levels following treatment with acoramidis

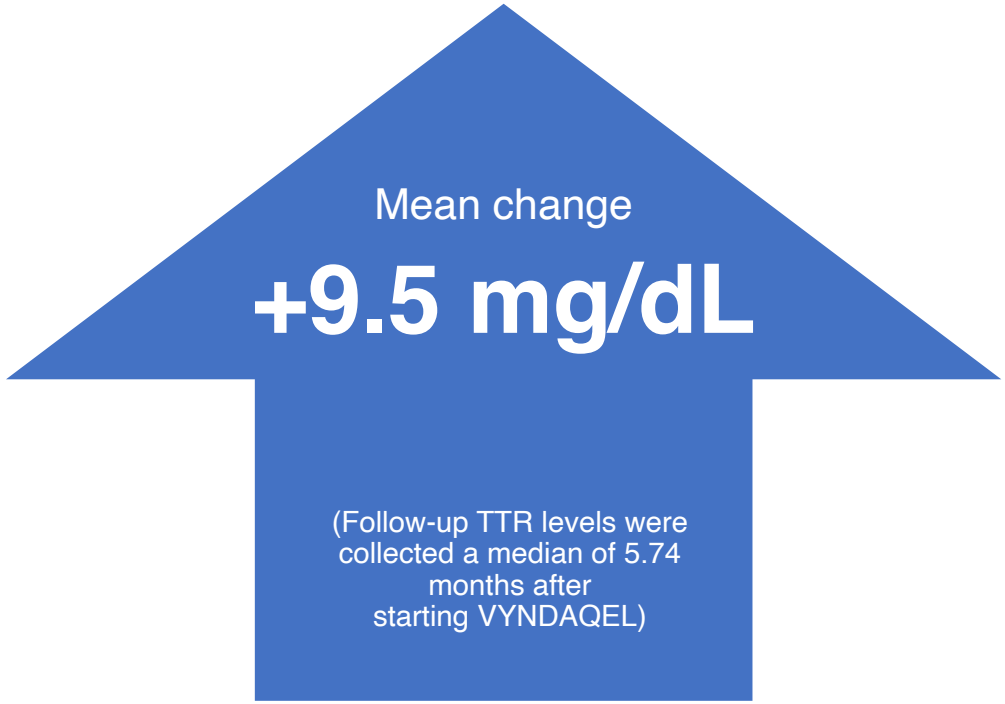


TTR, transthyretin.

Maurer MS, et al. Early Increase in Serum Transthyretin by Acoramidis Independently Predicts Improved Survival in TTR Amyloid Cardiomyopathy. *J Am Coll Cardiol.* 2025;85 (20):1911–1923.

The increase in serum TTR and correlation with survival outcomes represents a class effect for TTR kinetic stabilizers[1]

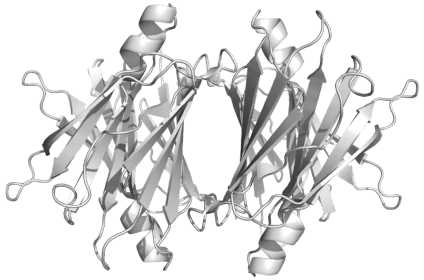
In a retrospective cohort of 185 **tafamidis-treated** patients, **serum TTR rose significantly**

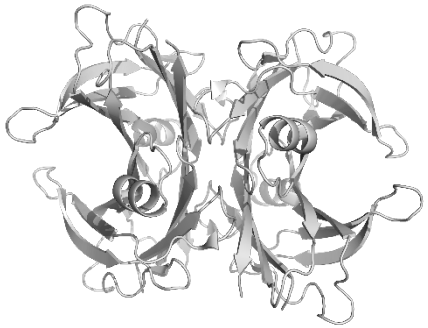


VYNDAQEL (tafamidis 61 mg) is indicated to treat adult wild-type and hereditary ATTR-CM patients. Tafamidis 61 mg corresponds to 80 mg tafamidis meglumine. Tafamidis and tafamidis meglumine are not interchangeable on a per-mg basis[2,3]

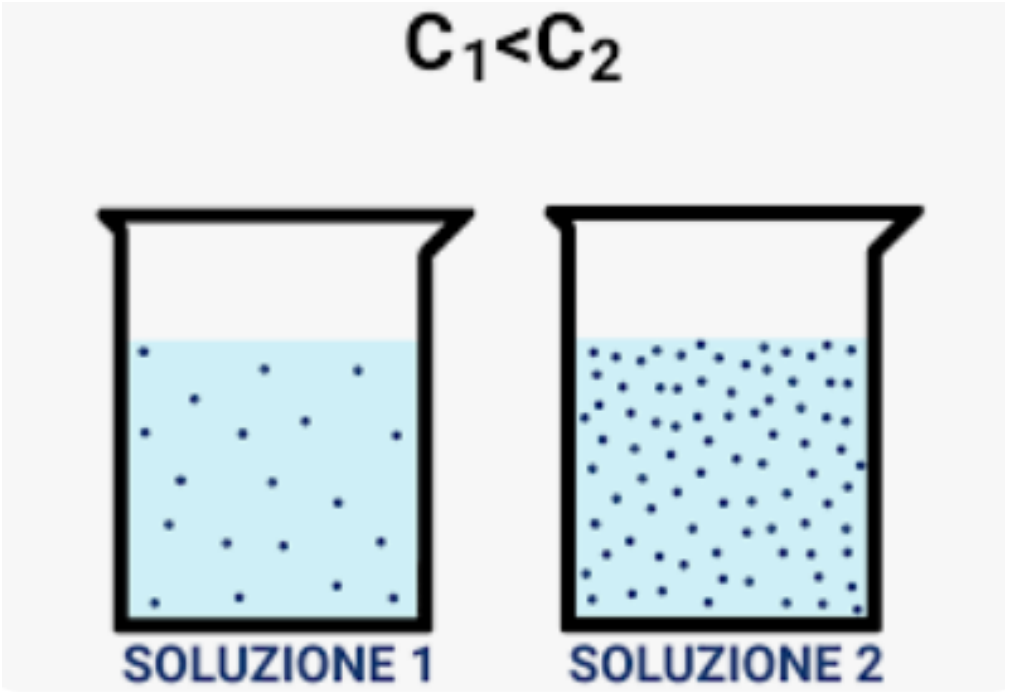
ATTR-CM, transthyretin amyloid cardiomyopathy; TTR, transthyretin.

1. Ansari B, et al. Increase in serum transthyretin after tafamidis is associated with improved survival in transthyretin amyloid cardiomyopathy. *J Am Coll Cardiol*. 2026; Epub ahead of print; 2. Pfizer Inc. Vyndaqel 20 mg (tafamidis meglumine) and 61 mg (tafamidis) summary of product characteristics. https://www.ema.europa.eu/documents/product-information/vyndaqel-epar-product-information_en.pdf (Accessed April 2026); 3. Lockwood PA, et al. The bioequivalence of tafamidis 61-mg free acid capsules and tafamidis meglumine 4× 20-mg capsules in healthy volunteers. *Clin Pharmacol Drug Dev*. 2020;9(7):849–54.





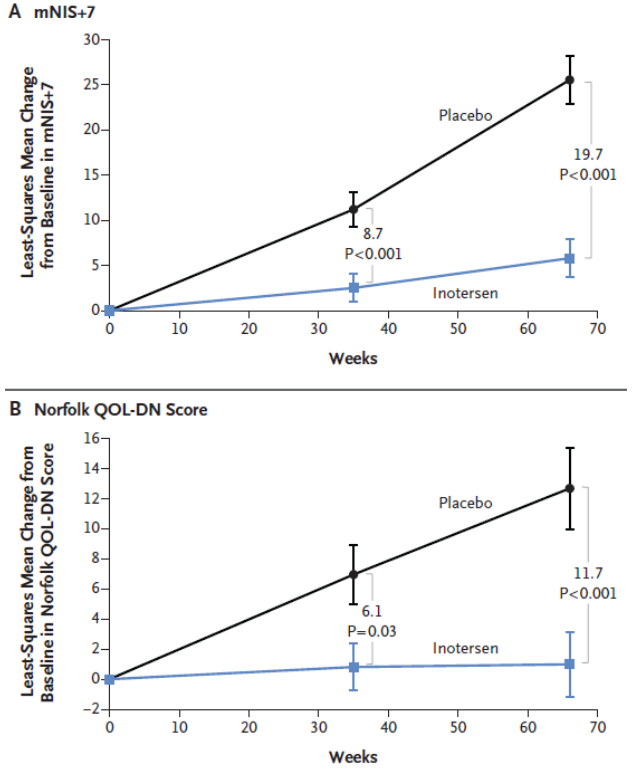
Concentration ….



… or stabilization?

Gene silencing in ATTR Amyloidosis

Inotersen (antisense oligonucleotide)



Most frequent SAEs
glomerulonephritis (3%)
thrombocytopenia (3%)

Benson, et al. NEJM 2018

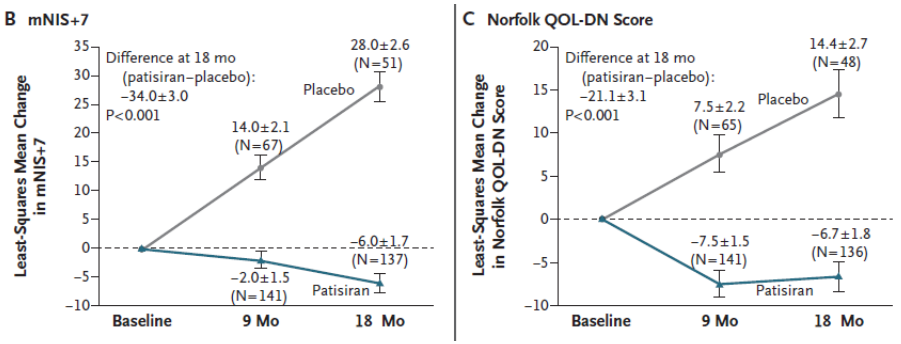
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis

M.D. Benson, M. Waddington-Cruz, J.L. Berk, M. Polydefkis, P.J. Dyck, A.K. Wang, V. Planté-Bordeneuve, F.A. Barroso, G. Merlini, L. Obici, M. Scheinberg, T.H. Brannagan III, W.J. Litchy, C. Whelan, B.M. Drachman, D. Adams, S.B. Heitner, I. Conceição, H.H. Schmidt, G. Vita, J.M. Campistol, J. Gamez, P.D. Gorevic, E. Gane, A.M. Shah, S.D. Solomon, B.P. Monia, S.G. Hughes, T.J. Kwoh, B.W. McEvoy, S.W. Jung, B.F. Baker, E.J. Ackermann, M.A. Gertz, and T. Coelho

Patisiran (small interfering RNA)



Exploratory end points in the cardiac subpopulation**	placebo	patisiran	
No. of patients	36	90	
Left ventricular wall thickness — mm			
Mean (±SD) baseline value	16.4±2.1	16.8±2.6	
Least-squares mean (±SE) change from baseline at 18 mo	−0.1±0.3	−1.0±0.2	0.02
Left ventricular longitudinal strain — %			
Mean (±SD) baseline value	−15.66±3.51	−15.13±3.41	
Least-squares mean (±SE) change from baseline at 18 mo	1.46±0.48	0.08±0.28	0.02
NT-proBNP††			
Baseline value			
Geometric mean — pg/ml	711.1	726.9	
Coefficient of variation — %	190.8	220.3	
Ratio to baseline at 18 mo‡‡	1.97	0.89	<0.001

Adams, et al. NEJM 2018

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 5, 2018 VOL. 379 NO. 1

Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis

D. Adams, A. Gonzalez-Duarte, W.D. O'Riordan, C.-C. Yang, M. Ueda, A.V. Kristen, I. Tournev, H.H. Schmidt, T. Coelho, J.L. Berk, K.-P. Lin, G. Vita, S. Attarian, V. Planté-Bordeneuve, M.M. Mezei, J.M. Campistol, J. Buades, T.H. Brannagan III, B.J. Kim, J. Oh, Y. Parman, Y. Sekijima, P.N. Hawkins, S.D. Solomon, M. Polydefkis, P.J. Dyck, P.J. Gandhi, S. Goyal, J. Chen, A.L. Strahs, S.V. Nochur, M.T. Sweetser, P.P. Garg, A.K. Vaishnaw, J.A. Gollob, and O.B. Suhr

Death from Any Cause and Recurrent Cardiovascular Events

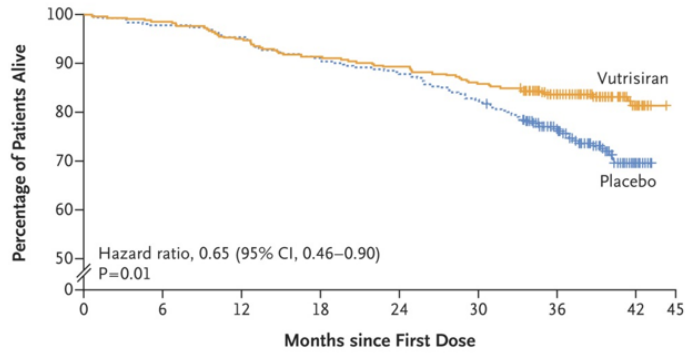
ORIGINAL ARTICLE

Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy

M. Fontana, J.L. Berk, J.D. Gillmore, R.M. Witteles, M. Grogan, B. Drachman, T. Damy, P. Garcia-Pavia, J. Taubel, S.D. Solomon, F.H. Sheikh, N. Tahara, J. González-Costello, K. Tsujita, C. Morbach, Z. Pozsonyi, M.C. Petrie, D. Delgado, P. Van der Meer, A. Jabbour, A. Bondue, D. Kim, O. Azevedo, S. Hvitfeldt Poulsen, A. Yilmaz, E.A. Jankowska, V. Algalarrondo, A. Slugg, P.P. Garg, K.L. Boyle, E. Yureneva, N. Silliman, L. Yang, J. Chen, S.A. Eraly, J. Vest, and M.S. Maurer, for the HELIOS-B Trial Investigators*

N Engl J Med 2025; 392:33-44

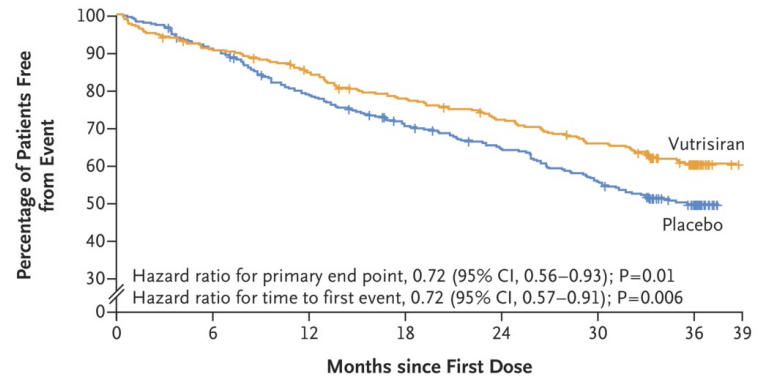
A Death from Any Cause in the Overall Population



No. at Risk (cumulative no. of events)

Vutrisiran	326 (0)	321 (5)	308 (18)	296 (30)	289 (37)	277 (49)	198 (56)	33 (60) 0 (60)
Placebo	328 (0)	321 (7)	314 (14)	299 (29)	290 (38)	271 (57)	180 (74)	24 (85) 0 (85)

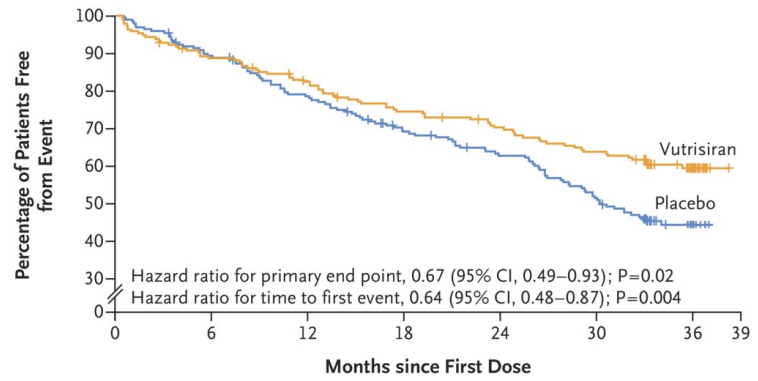
A Time to First Event in the Overall Population



No. at Risk (cumulative no. of events)

Vutrisiran	326 (0)	294 (30)	271 (50)	247 (72)	227 (90)	206 (110)	62 (125) 0 (125)
Placebo	328 (0)	295 (31)	253 (70)	221 (96)	199 (115)	172 (142)	52 (159) 0 (159)

B Time to First Event in the Monotherapy Population

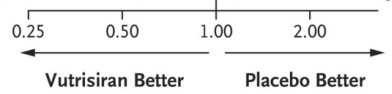


No. at Risk (cumulative no. of events)

Vutrisiran	196 (0)	172 (22)	157 (34)	141 (49)	131 (57)	119 (69)	32 (76) 0 (76)
Placebo	199 (0)	175 (22)	152 (43)	130 (60)	116 (72)	95 (93)	26 (105) 0 (105)

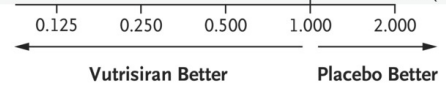
C Subgroup Analyses of the Primary End Point (overall population)

Subgroup	No. of Patients	Hazard Ratio (95% CI)
Overall	654	0.72 (0.56–0.93)
Age		
<75 yr	257	0.55 (0.35–0.85)
≥75 yr	397	0.81 (0.58–1.11)
Tafamidis use at baseline		
No	395	0.67 (0.49–0.93)
Yes	259	0.79 (0.51–1.21)
ATTR disease type		
Variant	76	0.92 (0.49–1.72)
Wild type	578	0.67 (0.51–0.90)
NYHA class		
I or II	592	0.73 (0.55–0.96)
III	62	0.68 (0.33–1.41)
Baseline NT-proBNP level		
≤2000 pg/ml	342	0.53 (0.35–0.79)
>2000 pg/ml	312	0.80 (0.56–1.13)

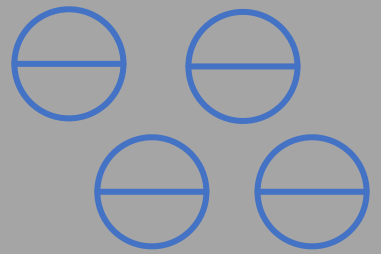


D Subgroup Analyses of the Primary End Point (monotherapy population)

Subgroup	No. of Patients	Hazard Ratio (95% CI)
Overall	395	0.67 (0.49–0.93)
Age		
<75 yr	153	0.53 (0.32–0.88)
≥75 yr	242	0.72 (0.47–1.10)
ATTR disease type		
Variant	48	0.67 (0.31–1.44)
Wild type	347	0.66 (0.45–0.95)
NYHA class		
I or II	368	0.73 (0.53–1.02)
III	27	0.31 (0.09–1.02)
Baseline NT-proBNP level		
≤2000 pg/ml	188	0.50 (0.28–0.92)
>2000 pg/ml	207	0.71 (0.47–1.07)



	Tafamidis (Pfizer Inc.)	Acoramidis[2] (Beyonttra®, BridgeBio/Bayer AG)	Vutrisiran▼[3] (Amvuttra®, Alnylam Pharmaceuticals)
Mechanism of action	TTR stabilizer	TTR stabilizer	siRNA *TTR* gene silencer
Approved dose	One capsule of VYNDAQEL 61 mg orally once daily	Two 356-mg tablets orally twice daily	25 mg subcutaneously every 3 months **Vitamin A supplementation at ~≤2,500–3,000 IU/day is advised**



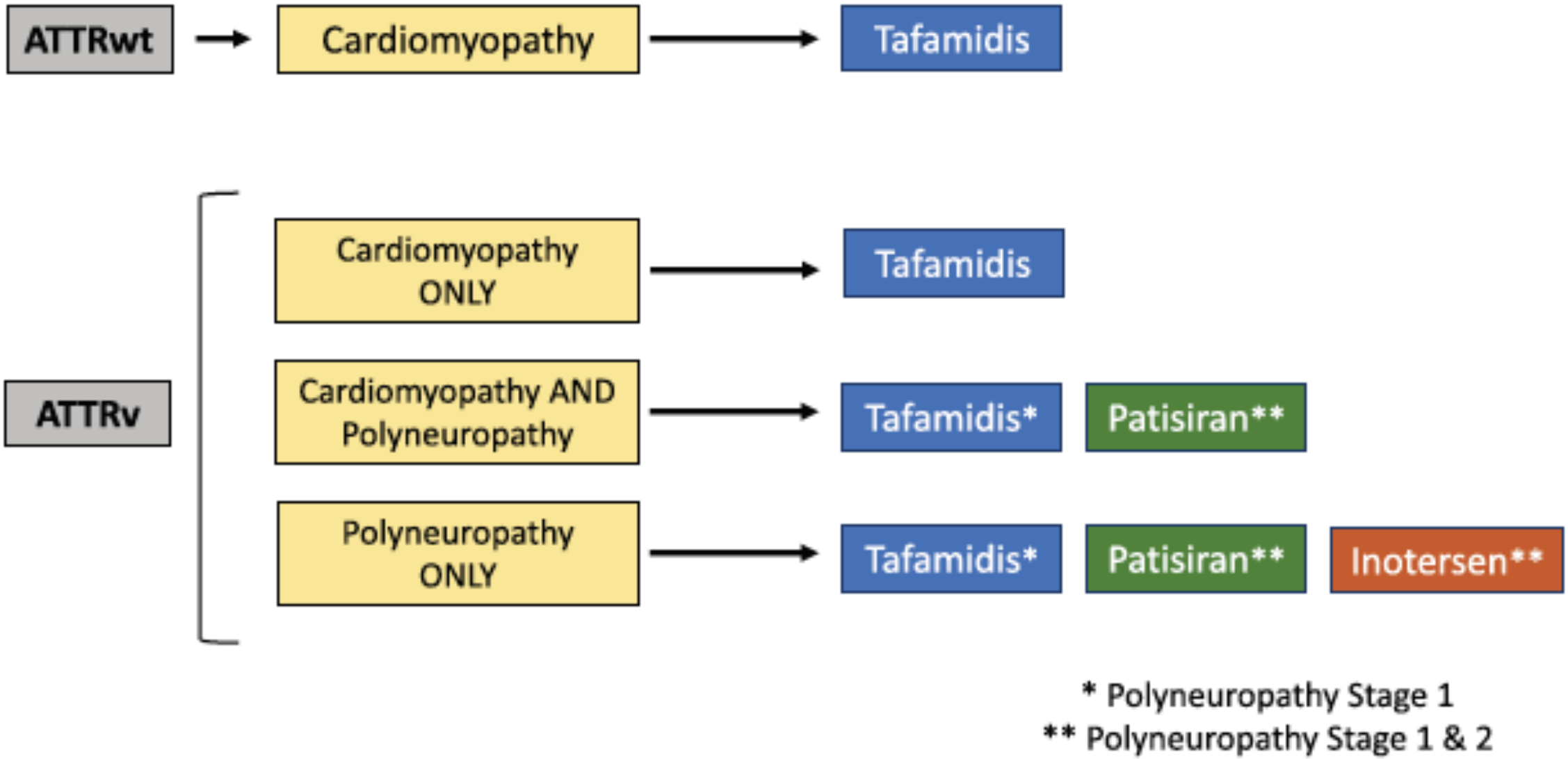
▼ This drug is subject to additional follow-up. It is a priority to report suspected adverse reactions associated with this medicinal product.

▼ Este medicamento está sujeto a seguimiento adicional, es prioritaria la notificación de sospechas de reacciones adversas asociadas a este medicamento.

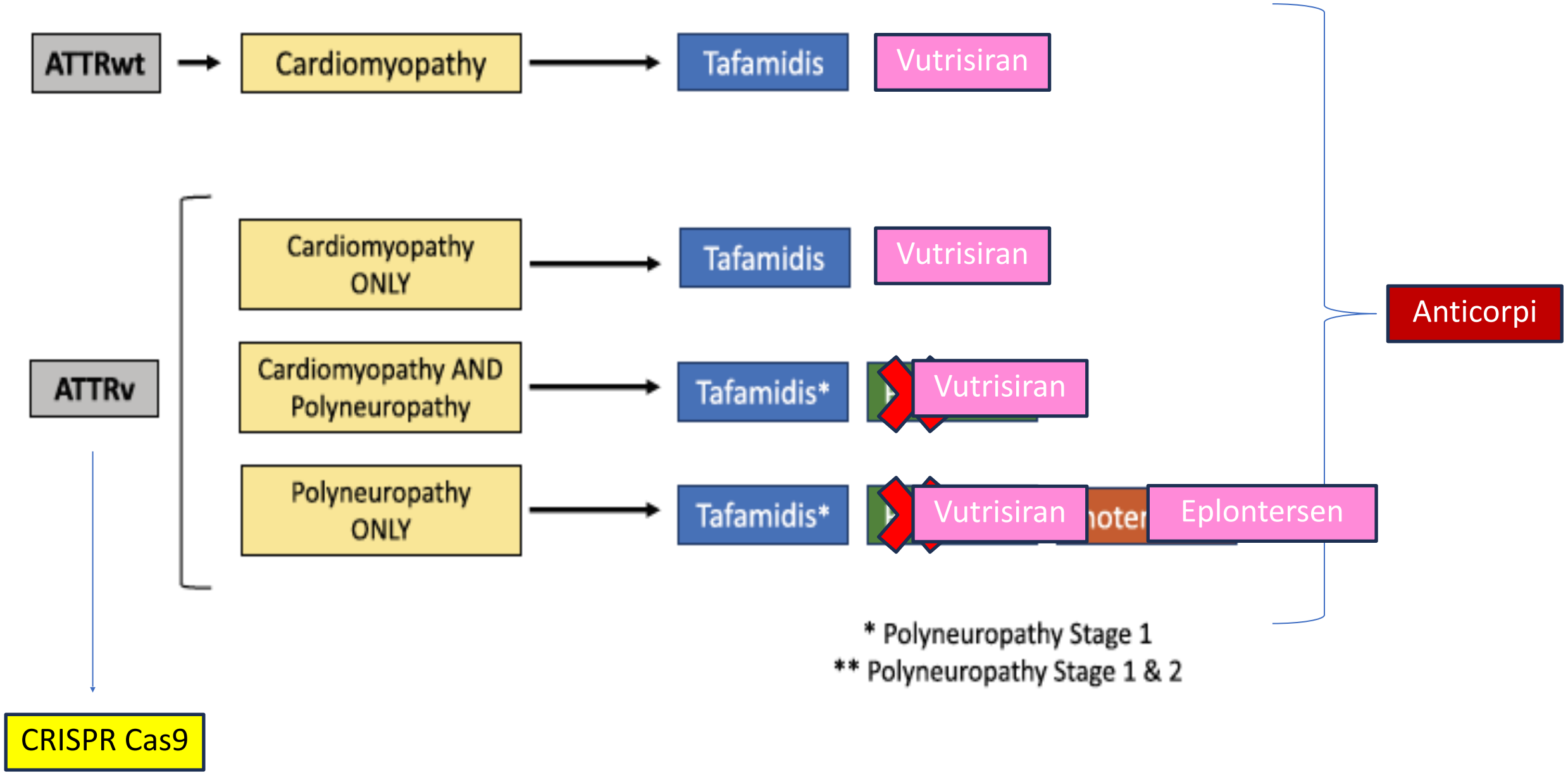
VYNDAQEL (tafamidis 61 mg) is indicated to treat adult wild-type and hereditary ATTR-CM patients.[1] VYNDAQEL (tafamidis 61 mg) está indicado para el tratamiento de pacientes adultos con ATTR-CM de tipo silvestre y hereditario.[1] A single tafamidis 61 mg capsule is bioequivalent to tafamidis 80 mg (four 20-mg capsules) and is not interchangeable on a per-mg basis.[1,4] Una sola cápsula de ácido libre de tafamidis de 61 mg es bioequivalente a tafamidis meglumina de 80 mg (cuatro cápsulas de 20 mg) y no es intercambiable por mg.[1,4]

ATTR-CM, transthyretin amyloid cardiomyopathy; IU, international units; siRNA, small interfering RNA; TTR, transthyretin.

1. Pfizer Inc. Vyndaqel 20 mg (tafamidis meglumine) and 61 mg (tafamidis) summary of product characteristics. https://www.ema.europa.eu/documents/product-information/vyndaqel-epar-product-information_en.pdf (Accessed April 2026); 2. Bayer AG. Beyonttra (acoramidis) summary of product characteristics. https://www.ema.europa.eu/en/documents/product-information/beyonttra-epar-product-information_en.pdf (Accessed April 2026); 3. Alnylam. Amvuttra (vutrisiran) summary of product characteristics. https://www.ema.europa.eu/en/documents/product-information/amvuttra-epar-product-information_en.pdf (Accessed April 2026); 4. Lockwood PA, et al. The bioequivalence of tafamidis 61-mg free acid capsules and tafamidis meglumine 4 × 20-mg capsules in healthy volunteers. *Clin Pharmacol Drug Dev.* 2020;9(7):849–54.



Garcia-Pavia P et al Eur Heart Journal 2021


ATTRwt
Cardiomyopathy
Tafamidis
Vutrisiran
ATTRv
Cardiomyopathy ONLY
Tafamidis
Vutrisiran
Cardiomyopathy AND Polyneuropathy
Tafamidis*
Vutrisiran
Polyneuropathy ONLY
Tafamidis*
Vutrisiran
Eplontersen
Anticorpi
CRISPR Cas9
* Polyneuropathy Stage 1
** Polyneuropathy Stage 1 & 2

A 2026 Position Statement provides recommendations on how to assess overall disease progression in patients with ATTR-CM

Published in JACC: Heart Failure

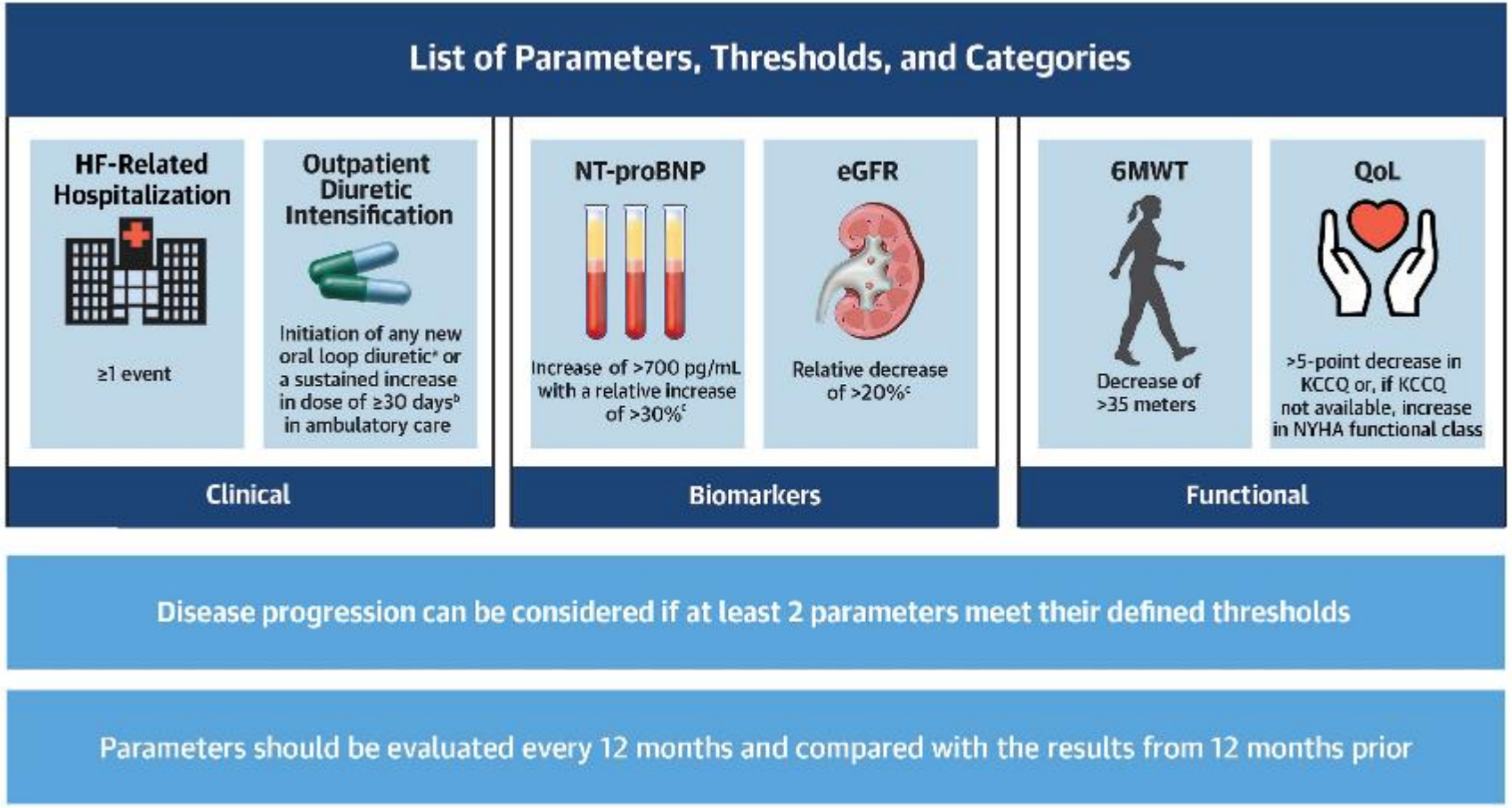


Figure extracted from Garcia-Pavia, P, et al. *JACC Heart Fail* 2026.

[a]Among those not taking loop diuretics; [b]Among those taking diuretics; [c]The measurement should be taken during a period of clinical stability. Alternatively, two measurements taken approximately 4 weeks apart may help to ensure that transient changes are not mistaken for progression.
6MWT, 6-minute walk test; ATTR-CM, transthyretin amyloid cardiomyopathy; eGFR, estimated glomerular filtration rate; HF, heart failure; KCCQ, Kansas City Cardiomyopathy Questionnaire; NT-proBNP, N-terminal pro B-type natriuretic peptide; NYHA, New York Heart Association; QoL, quality of life.

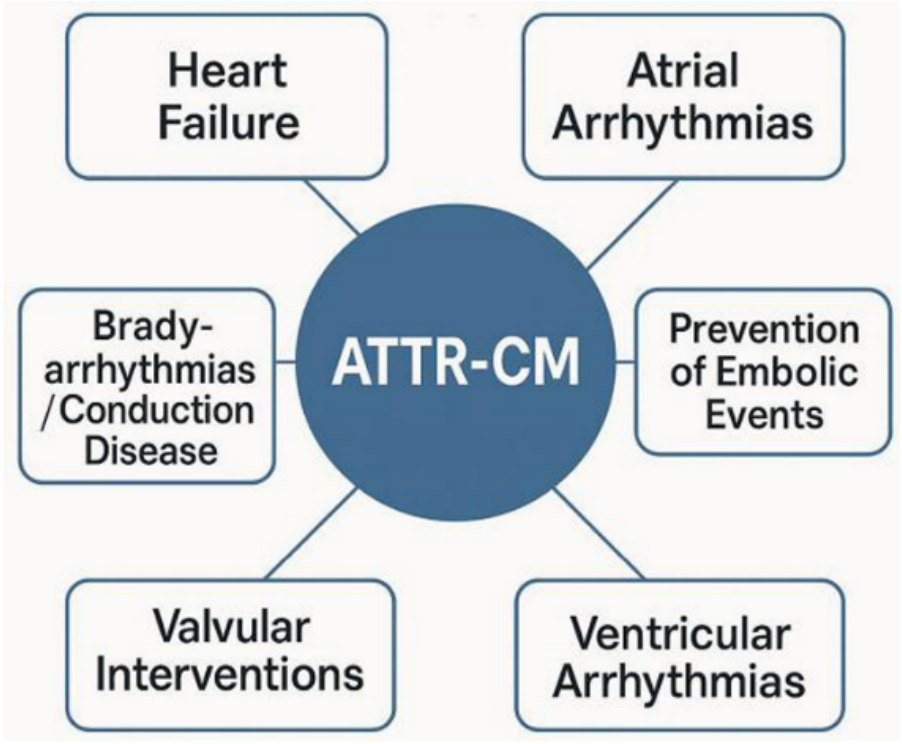
García-Pavía, P, et al. Monitoring disease progression in patients with transthyretin amyloid cardiomyopathy. *JACC Heart Fail* 2026;14(1):102766.

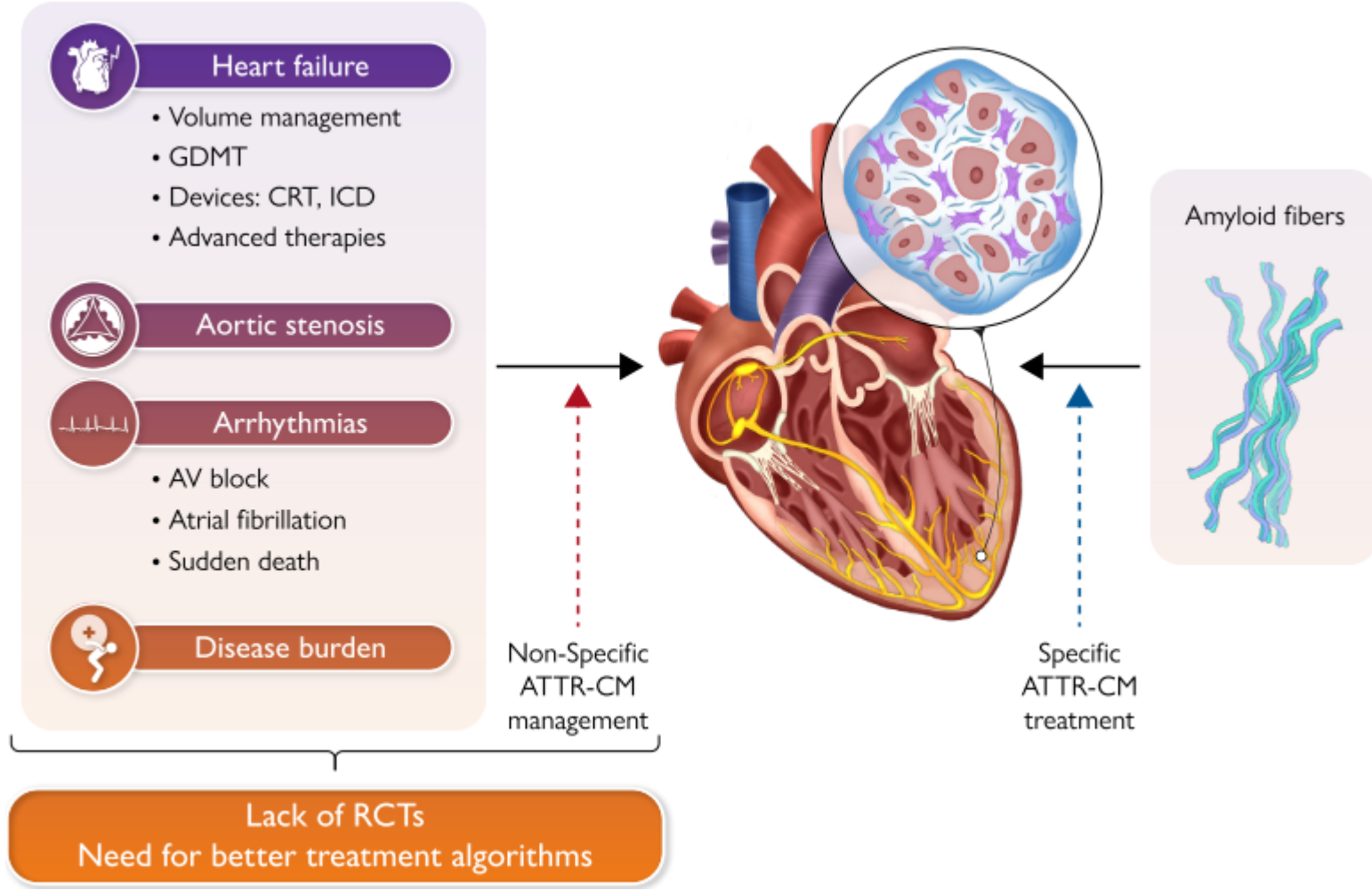
ESC European Society of Cardiology
European Heart Journal (2025) **00**, 1–15
https://doi.org/10.1093/eurheartj/ehaf710

SPECIAL ARTICLE
Heart failure and cardiomyopathies

Non-amyloid specific treatment for transthyretin cardiac amyloidosis: a clinical consensus statement of the ESC Heart Failure Association

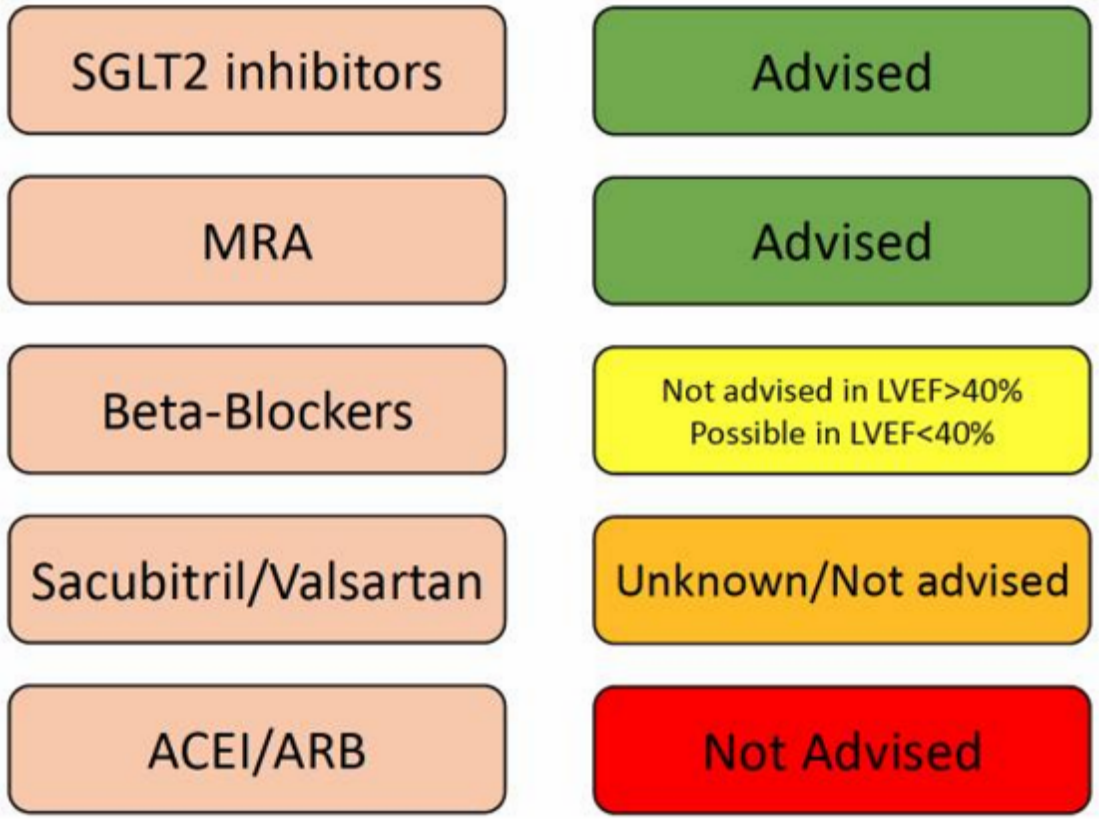
Pablo Garcia-Pavia [1,2,3,*†], Esther Gonzalez-Lopez[1,2,†], Lisa J. Anderson[4], Francesco Cappelli[5], Thibaud Damy [6], Marianna Fontana[7], Jose Gonzalez-Costello[8,9], Ruxandra Jurcut [10,11], Olivier Lairez[12], Peter van der Meer [13], Marco Merlo [14,15], Stefano Perlini[16], and Antoni Bayes-Genis [2,17,18,*]





Patients exhibiting disease progression may benefit from review and optimization of their non-ATTR-CM-specific therapies

Heart failure guideline-directed medical therapies in ATTR-CM



Additionally, the consensus advises the use of diuretics as part of a volume management plan for patients with ATTR-CM

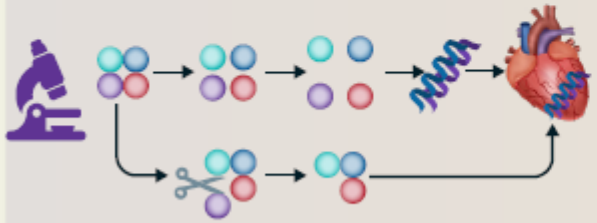
Figure extracted from García-Pavía P, et al. *Eur Heart J* 2026.

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ATTR-CM, transthyretin amyloid cardiomyopathy; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium-glucose co-transporter-2 inhibitor.

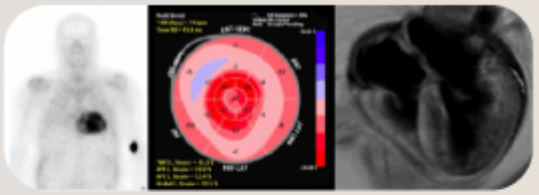
Garcia-Pavia P, et al. Non-amyloid specific treatment for transthyretin cardiac amyloidosis: a clinical consensus statement of the ESC Heart Failure Association. *Eur Heart J* 2026;47(1):22–36.

Transthyretin cardiac amyloidosis as an example of precision medicine in cardiology

Elucidation of underlying disease mechanisms



Advances in imaging techniques: **Non-invasive diagnosis possible**



Precise data of the epidemiology: **High prevalence of the disease in common clinical scenarios**

- Heart failure
- Aortic stenosis
- LVH/HCM

Gonzales-Lopez et al. EHJ 2024, 00, 1–15

Conclusion

What we know

CHALLENGES IN THE DIAGNOSIS OF AMYLOID IN 2024

Plenary Lecture
Diagnosis of Amyloid Session
Monday, May 27

STEFAN SCHÖNLAND

Amyloidosis Center
Medical Department V
Heidelberg University Hospital,
Germany

UNIVERSITÄTS KLINIKUM HEIDELBERG

AMYLOIDOSE ZENTRUM

Acknowledgments

Amyloidosis Research and Treatment Center

Giovanni Palladini
Giampaolo Merlini
Marco Basset
Claudia Bellofiore
Serena Caminito
Anna Carnevale
Simona Casarini
Valeria Di Simone
Andrea Foli
Margherita Massa
Giulia Mazzini
Martina Nanci
Roberta Mussinelli
Alice Nevone
Mario Nuvolone
Laura Obici
Paola Rognoni
Giuseppe Damiano Sanna
Study Coordinators and data managers

Emergency Medicine
Stefano Perlini
Francesco Salinaro

Nuclear Medicine Department
Giorgio Cavenaghi
Giulia Manfrinato
Giovanna Pepe

Radiology Unit
Emilio Bassi
Lorenzo Preda
Adele Valentini
Michela Zacchino

Cardiology Unit
Leonardo De Luca
Stefano Ghio
Laura Scelsi
Annalisa Turco

Hematology Unit
Luca Arcaini
Claudio Cartia
Silvia Mangiacavalli
Marzia Varettoni

Clinical Chemistry Laboratory
Riccardo Albertini
Tiziana Bosoni

Founding/support

FC AECC and AIRC under the Accelerator Award Program

Cancer Research UK