XII Meeting. State of the Art in
HEART FAILURE
CLINICAL PRACTICE AND ORGANIZATIONAL MODELS

Venue: Hotel Meliá María Pita, A Coruña

A Coruña 26-27 September 2025

A Coruña Heart Failure Academy

#ACORUÑAHF2025

Tafamidis in ATTR-CM. Scientific and Real-Life Evidence Update

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Complexo Hospitalario Universitario A Coruña

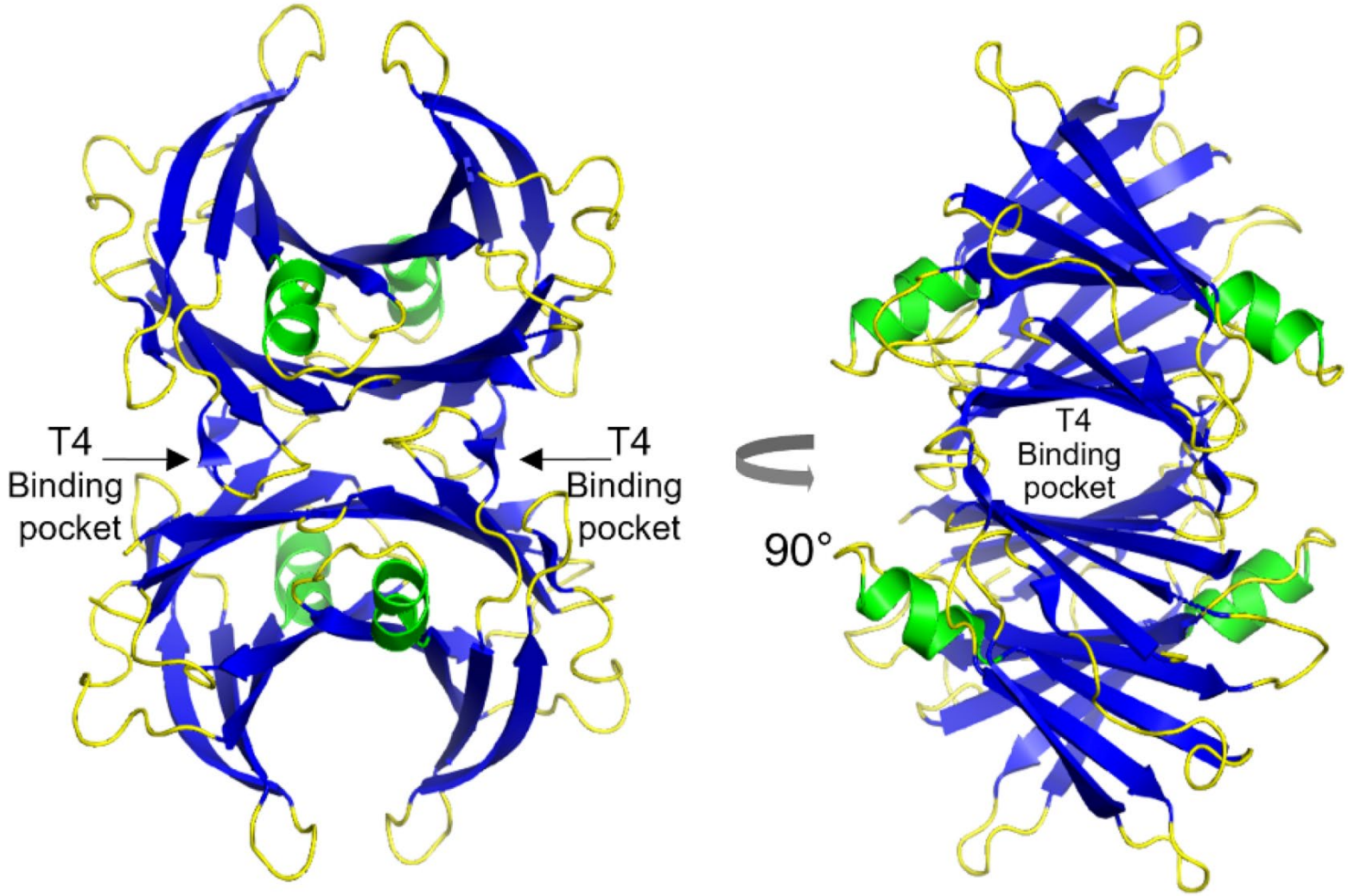
CIBER-CV

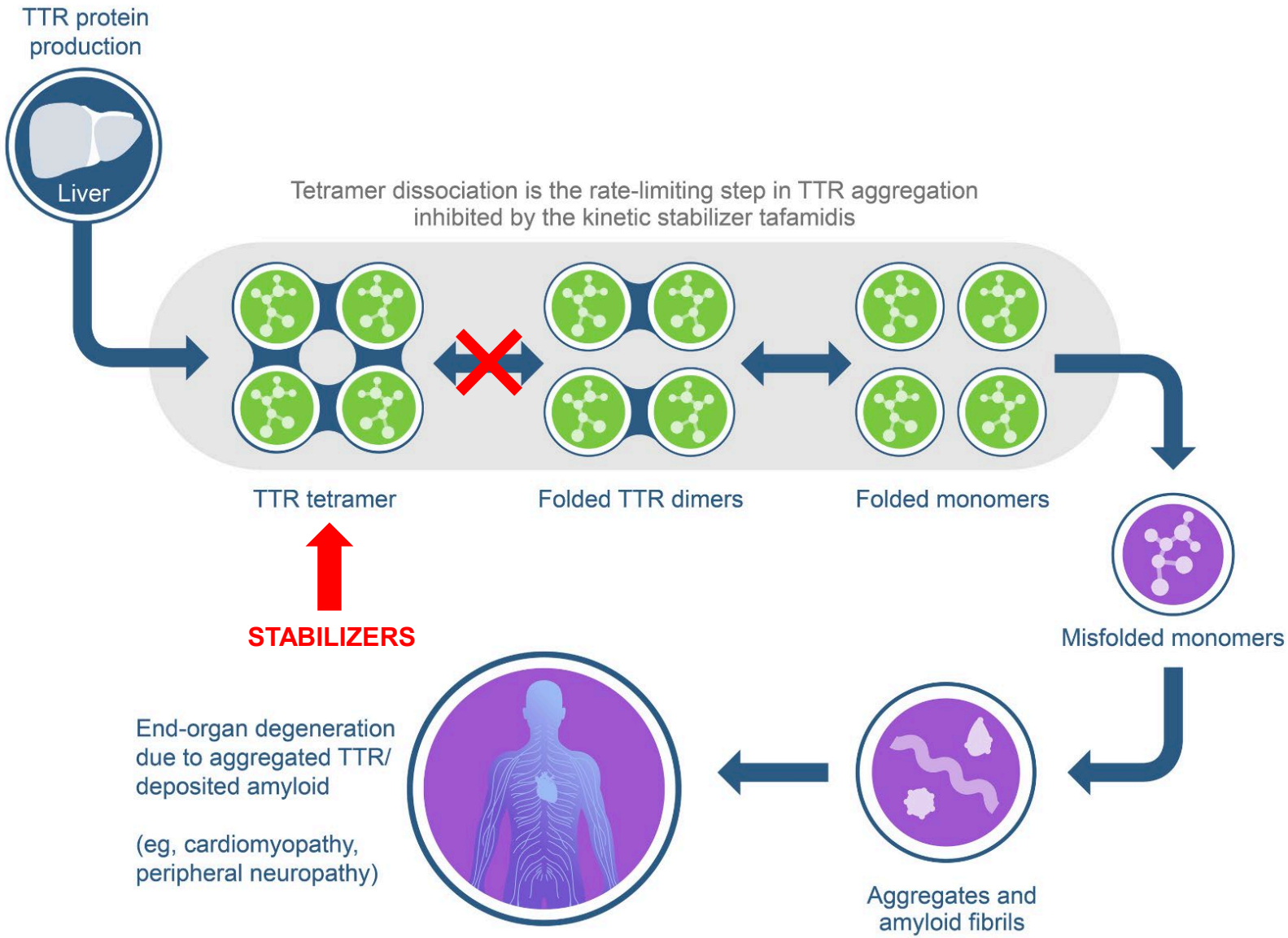
SERVIZO GALEGO DE SAÚDE · ÁREA SANITARIA DA CORUÑA E CEE · inibic · SOCIEDADE GALEGA DE CARDIOLOXÍA · UNIVERSIDADE DA CORUÑA · ciber | CV · UNIÓN EUROPEA Fondo Europeo de Desarrollo Regional · XUNTA DE GALICIA · galicia

DISCLOSURES

I received travel grants, speaker fees and two research grants from Pfizer

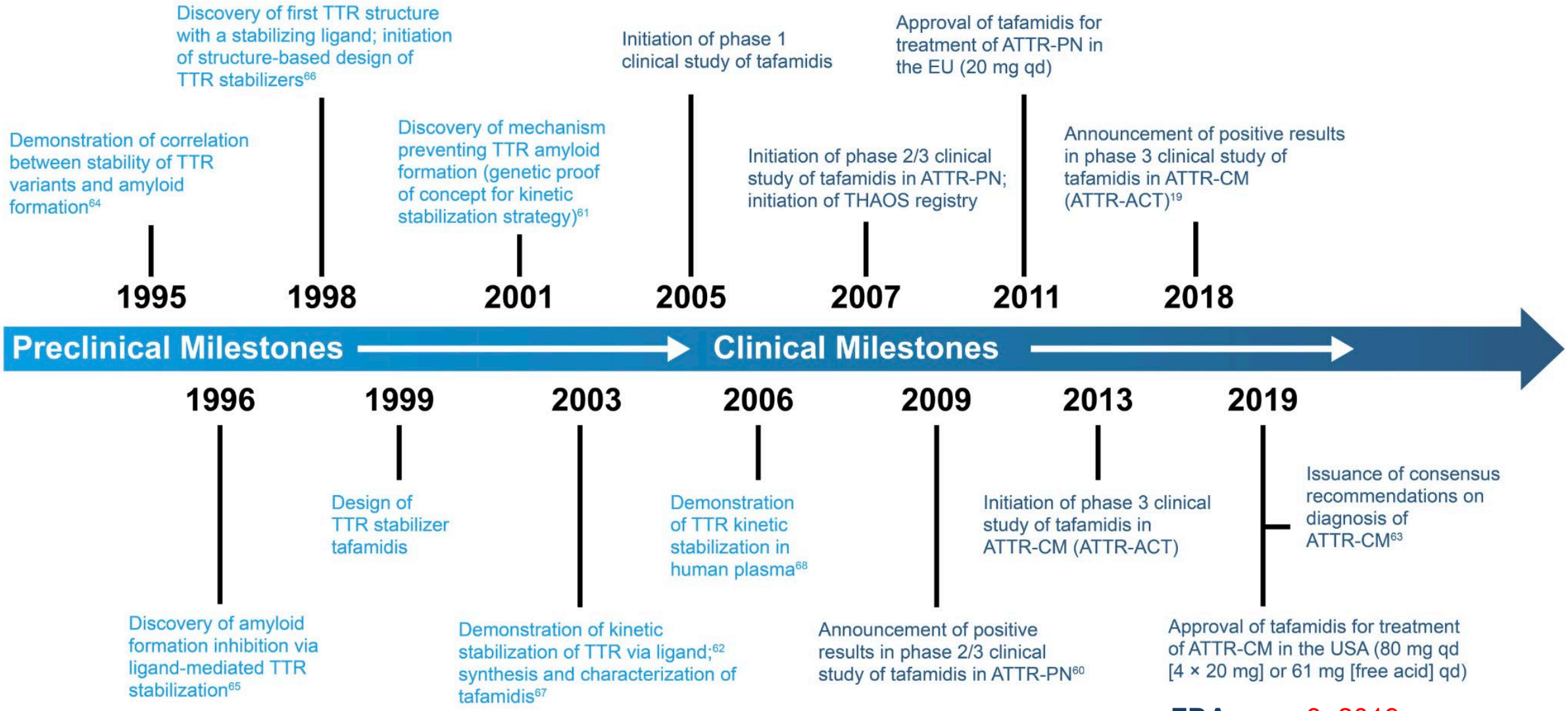
TRANSTHYRETIN: transports THYroxine (T4) and RETINol (vitamin A)





Burton A, et al. Drug Des Devel Ther. 2021;15:1225-1243

TAFAMIDIS



FDA: may 3, 2019
EMA: february 17, 2020

Burton A, et al. Drug Des Devel Ther. 2021;15:1225-1243

TAFAMIDIS is available in Spain since june 2023 for the treatment of ATTRwt/ATTRv-CM

TAFAMIDIS was the first specific treatment for ATTR-CM and continues to be the only one available in Spain

TAFAMIDIS is administered orally and is available as free acid 61mg (CM) and meglumine 20mg (PN) capsules

SERVIZO GALEGO DE SAÚDE

TAFAMIDIS

Na indicación do tratamento da amiloidose por transtiretina nativa ou hereditaria en pacientes adultos con miocardiopatía (ATTR-CM).

O tratamento deberase iniciar baixo a supervisión dun médico con experiencia no manexo de pacientes con amiloidose ou miocardiopatía.

Os pacientes deben cumprir os seguintes criterios:

1. -Diagnóstico de insuficiencia cardíaca :
   - A lo menos unha hospitalización previa ou ter clínica de sobrecarga de volume que precise tratamento diurético para a melloría (sen hospitalización) -indicar data
   - Clase I-II* da NYHA -indicar clase
   - FEVI ≥ 50% -indicar FEVI
   - Grosor da parede do septo interventricular telediastólico >12 mm na ecocardiografía .- indicar data ecocardiografía e dato del grosor do septo.
2. -Gammagrafía nuclear confirmatoria da TTR (intensidade de captación grao 2-3, segundo gradación visual)- indicar data e grao de captación.
3. -Estudo xenético que confirme fenotipo cardíaco da amiloidose.
   - si ATTRwt-CM poderase iniciar tratamento si idade ≥ 60 e ≤ 90 anos
   - si ATTRh-CM poderase iniciar tratamento si idade ≥ 45 e ≤ 90 años
     -indicar data e mutación en caso de ATTRh-CM
4. -FG ≥ 30mL/min
5. -Test da marcha de 6 minutos (TM6M) >100 m- indicar datas e metros percorridos
6. -Valor do pro-B de tipo N-terminal (NT-proBNP) ≥ 600 pg/mL.-indicar valor e data do último valor analítico
7. -Non ter recibido transplante de corazón ou de fígado.
8. -Non levar un dispositivo de asistencia ventricular.
9. -Non estar recibindo outros tratamentos modificadores da enfermidade para a ATTR.

*NYHA III: a ficha técnica contempla o uso en pacientes NYHA I e II quedando os pacientes NYHA III a criterio dun médico con experiencia no manexo de pacientes con amiloidose.

CRITERIOS DE RETIRADA DO TRATAMENTO:

- NYHA IV
- recibir transplante de corazón ou fígado
- implantación de dispositivos de asistencia ventricular

ANEXO I

Formulario Solicitude inicio do tratamento con Tafamidis

Deberan cumprimentarse todos os datos deste anexo asi como a data, para ser valorado o financiamento do tratamento polos Servizos de Farmacia correspondentes.

	Data	Dato
Idade		
Hospitalización previa por IC		**SI**/NON
Utilización ambulatoria de diuréticos para síntomas de IC		**SI**/NON
Clase de la NYHA		
FEVI		
Ecocardiograma *		
Biopsia confirmatoria en tecido cardíaco ou extracardíaco ou Gammagrafía confirmatoria da transtirretina**		
Estudio xenético de transtirretina ***		
Test da marcha de 6 minutos		
Valor do NT-proBNP ****		
Filtrado glomerular(FG)		
No haber recibido un transplante de corazón ou de fígado No ter implantado un dispositivo de asistencia ventricular No estar recibindo outros tratamentos modificadores da enfermidade		

* indicar grosor da parede do septo interventricular telediastólico da última medición
** indicar grado de captación (gradación visual)
*** si hereditaria indicar mutación
**** valor última medición de NT-prBNP

ATTR-ACT

- Phase III clinical trial in patients with ATTRwt/ATTRv-CM
- **441** patients randomized to **tafamidis meglumine (80mg or 20mg)** vs **placebo** for 30 months
- Patients were enrolled between **2013-2015**
- **Primary outcome**: hierarchical analysis of all-cause mortality followed by CDV-hospitalizations
- **Secondary outcomes**:

  - Change from baseline to month 30 for the 6-minute walk test
  - Change from baseline to month 30 on the KCCQ-OS score

Maurer MS, et al. N Engl J Med. 2018;379:1007-1016

ATTR-ACT: BASELINE CHARACTERISTICS

Characteristic	Tafamidis (N=264)	Placebo (N=177)
Age — yr		
Mean	74.5±7.2	74.1±6.7
Median (range)	75 (46–88)	74 (51–89)
Sex — no. (%)		
Male	241 (91.3)	157 (88.7)
Female	23 (8.7)	20 (11.3)
Race — no. (%)		
White	211 (79.9)	146 (82.5)
Black	37 (14.0)	26 (14.7)
Asian	13 (4.9)	5 (2.8)
Other	3 (1.1)	0
TTR genotype — no. (%)		
ATTRm	63 (23.9)	43 (24.3)
ATTRwt	201 (76.1)	134 (75.7)
Blood pressure — mm Hg		
Supine		
Systolic	115.4±15.4	115.1±15.7
Diastolic	70.4±10.3	70.2±9.5
Standing		
Systolic	115.5±15.5	115.9±15.9
Diastolic	70.6±9.9	71.0±10.3
Heart rate, mean — beats per minute		
Supine	70.7±12.3	69.9±11.7
Standing	72.9±12.9	73.8±12.2
NYHA Class — no. (%)		
Class I	24 (9.1)	13 (7.3)
Class II	162 (61.4)	101 (57.1)
Class III	78 (29.5)	63 (35.6)
Modified BMI†	1058.8±173.8	1066.4±194.4
NT-proBNP level — pg/ml		
Median	2995.9	3161.0
Interquartile range	1751.5–4861.5	1864.4–4825.0

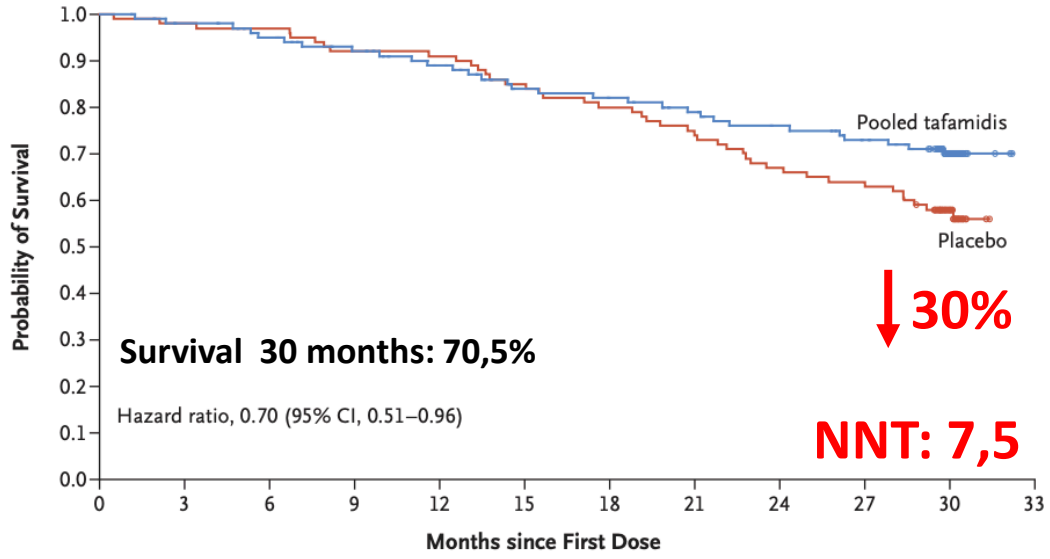
Maurer MS, et al. N Engl J Med. 2018;379:1007-1016

ATTR-ACT: primary outcome

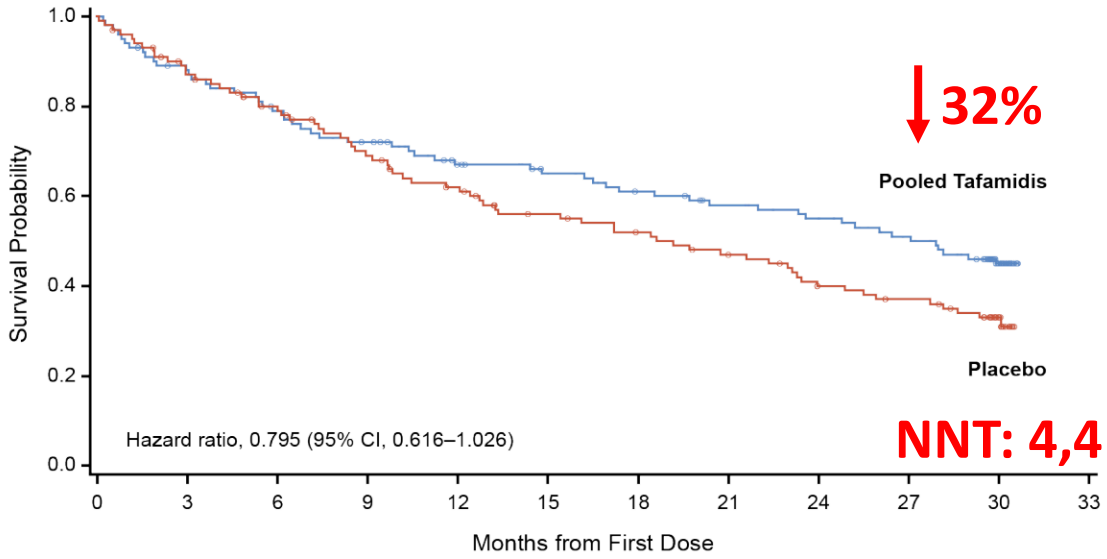
A Primary Analysis, with Finkelstein–Schoenfeld Method

	No. of Patients	P Value from Finkelstein–Schoenfeld Method	Win Ratio (95% CI)	Patients Alive at Mo 30 *no. (%)*	Average Cardiovascular-Related Hospitalizations during 30 Mo among Those Alive at Mo 30 *per patient per yr*
Pooled Tafamidis	264	<0.001	1.70 (1.26–2.29)	186 (70.5)	0.30
Placebo	177			101 (57.1)	0.46

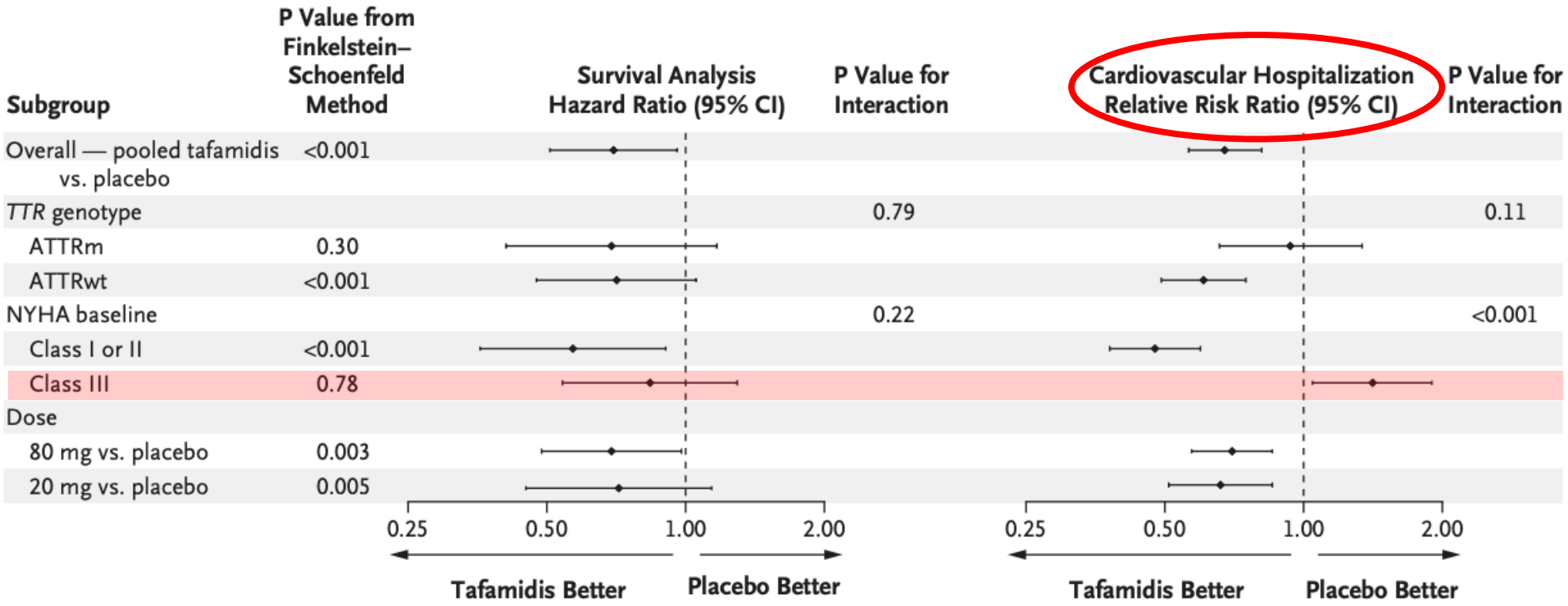
B Analysis of All-Cause Mortality



Analysis of CDV-related hospitalizations



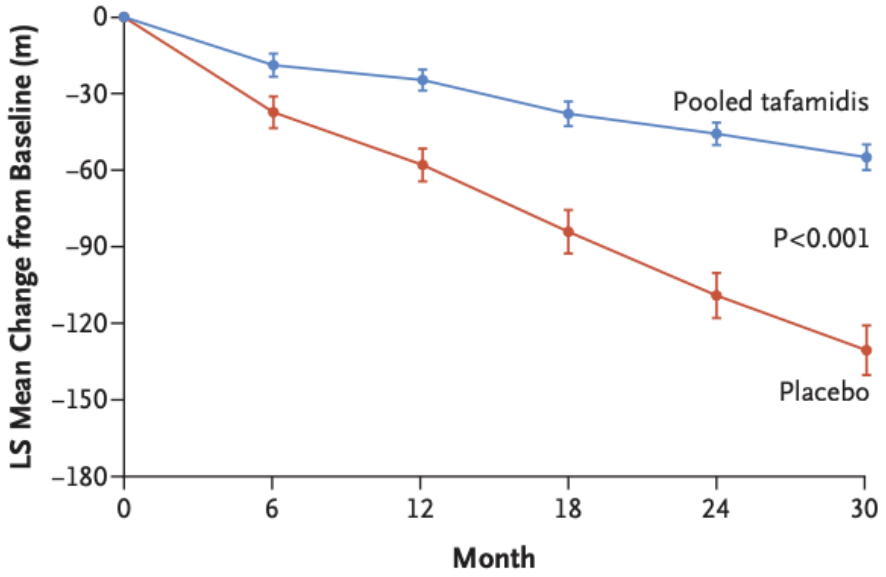
Maurer MS, et al. N Engl J Med. 2018;379:1007-1016



Maurer MS, et al. N Engl J Med. 2018;379:1007-1016

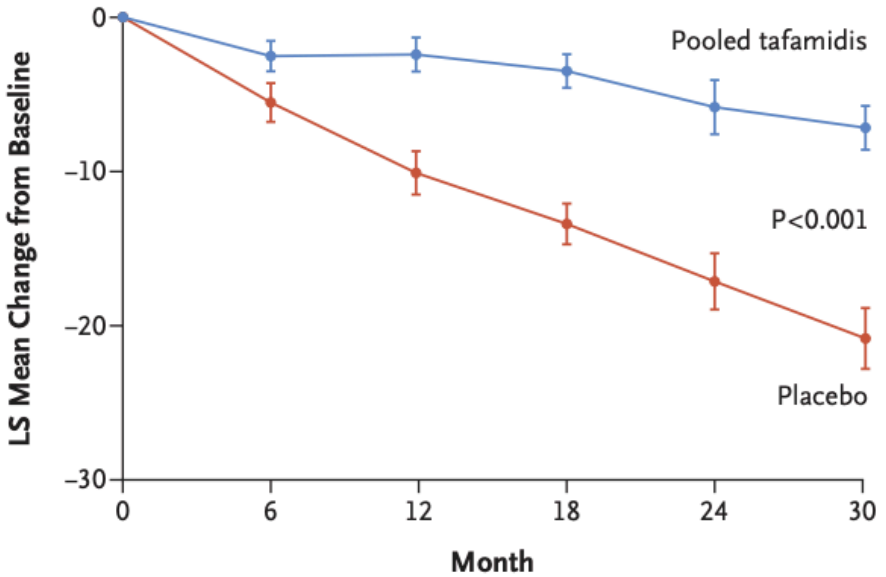
ATTR-ACT: secondary outcomes

A Change from Baseline in 6-Minute Walk Test



No. of Patients						
Tafamidis	264	233	216	193	163	155
Placebo	177	147	136	111	85	70

B Change from Baseline in KCCQ-OS



No. of Patients						
Tafamidis	264	241	221	201	181	170
Placebo	177	159	145	123	96	84

TAFAMIDIS demonstrated to be a safe drug, with an ocurrence of adverse events similar to placebo

Dose reduction or discontinuation of the drug due to adverse events was greater with placebo

Maurer MS, et al. N Engl J Med. 2018;379:1007-1016

TAFAMIDIS in HF guidelines

(1)

Recommendations for the treatment of transthyretin amyloidosis-cardiac amyloidosis

Recommendations	Class[a]	Level[b]
Tafamidis is recommended in patients with genetic testing proven hTTR-CA and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.[980]	I	B
Tafamidis is recommended in patients with wtTTR-CA and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.[980]	I	B

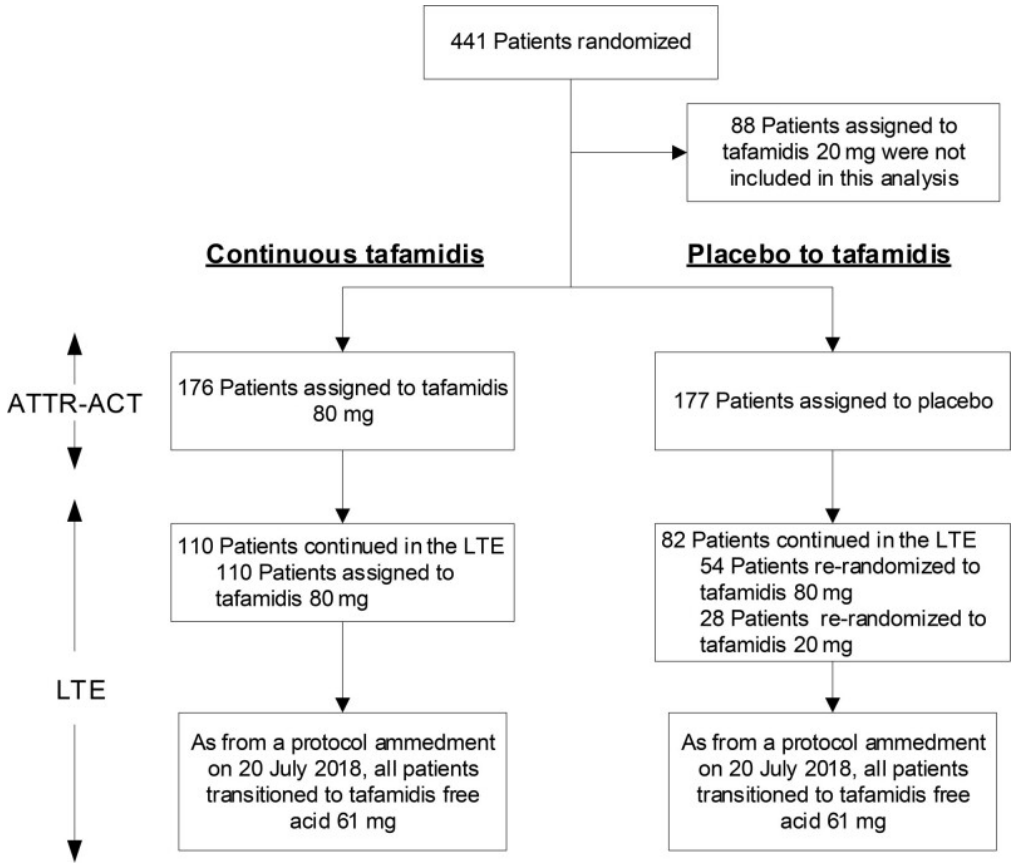
(2)

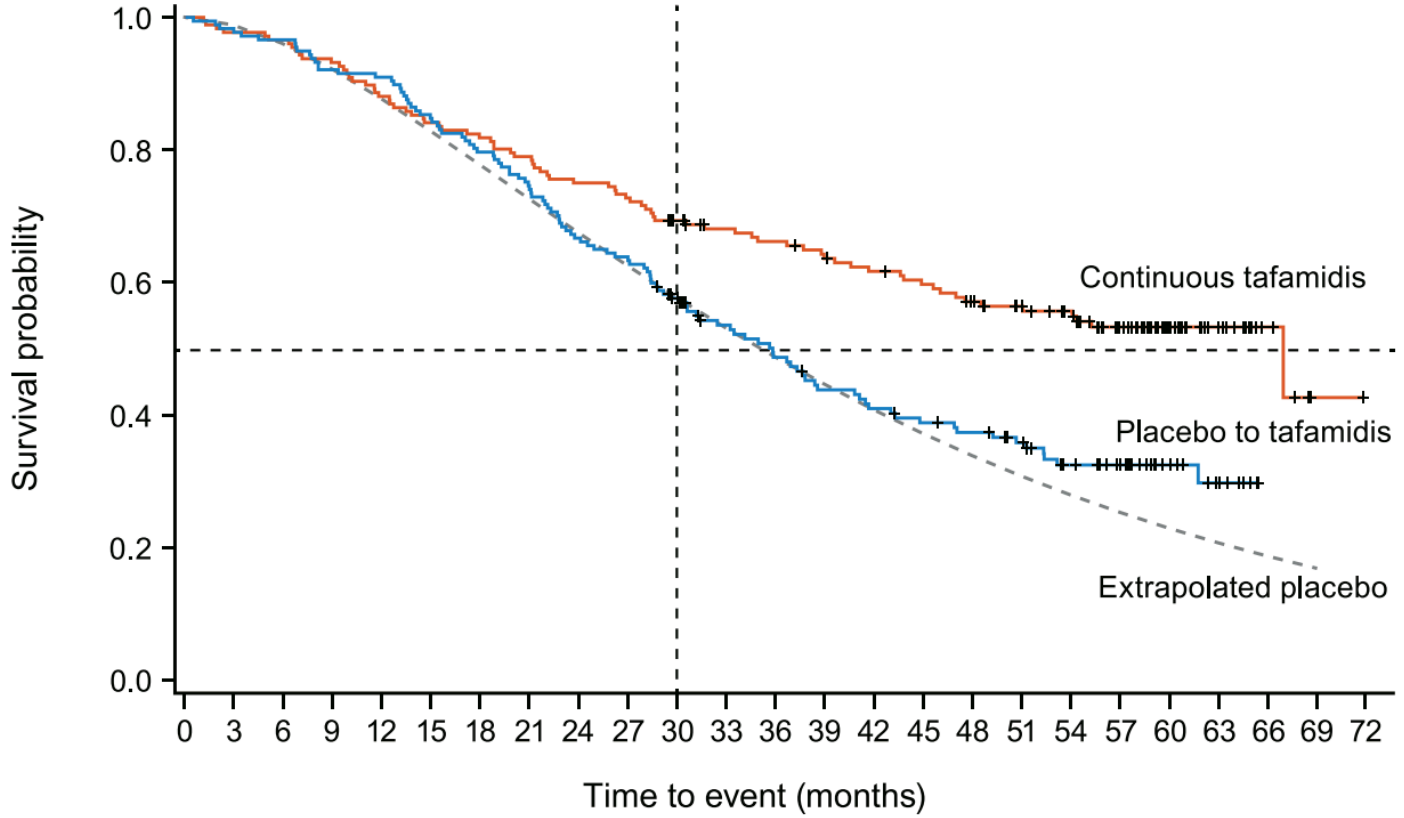
Recommendations for Treatment of Cardiac Amyloidosis
Referenced studies that support the recommendations are summarized in the Online Data Supplements.

COR	LOE	Recommendations
1	B-R	1. In select patients with wild-type or variant transthyretin cardiac amyloidosis and NYHA class I to III HF symptoms, transthyretin tetramer stabilizer therapy (tafamidis) is indicated to reduce cardiovascular morbidity and mortality.[1]

(1) McDonagh TA, et al. Eur Heart J. 2021;42:3599-3726 / (2) Heidenreich PA, et al. J Am Coll Cardiol. 2022;79:1757-1780

ATTR-ACT LTE (long-term extension)





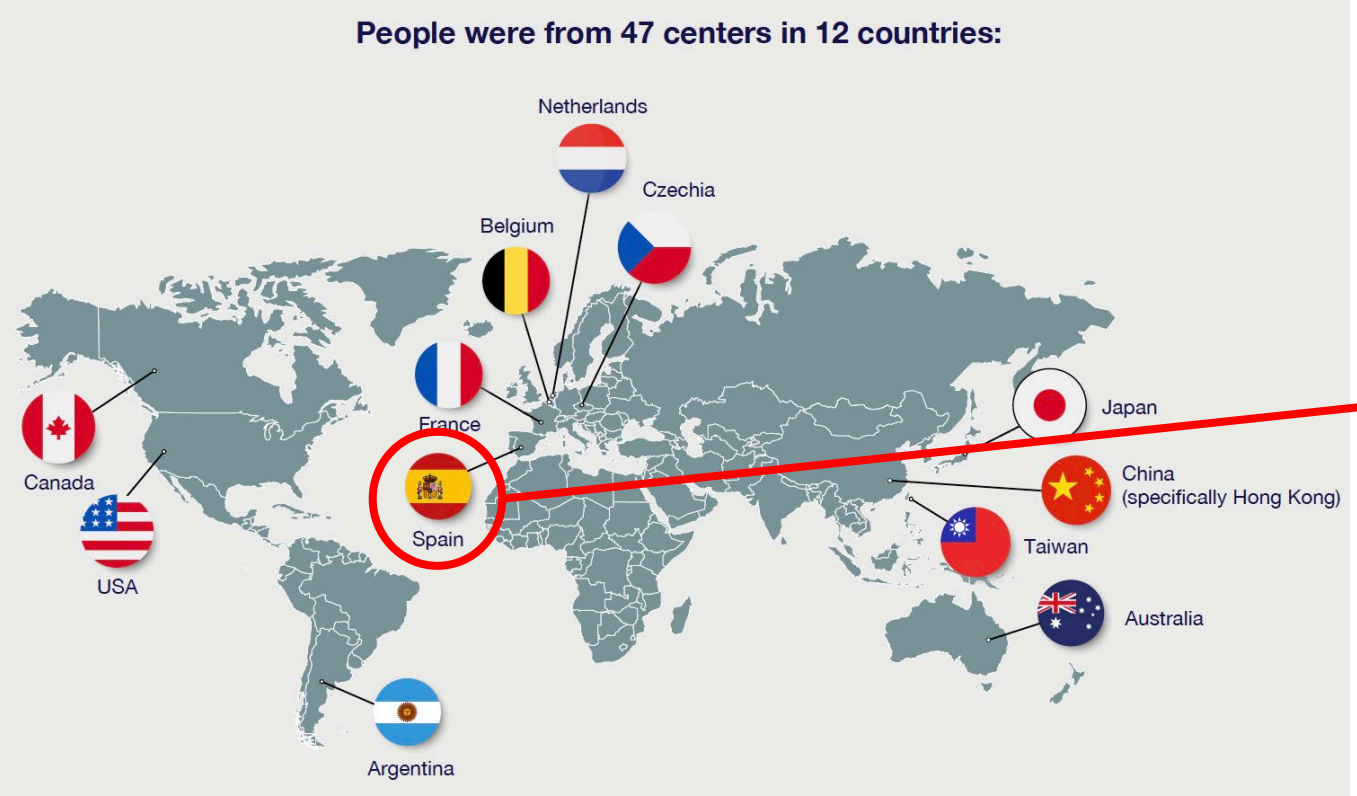
Elliott P, et al. Circ Heart Fail. 2022;15:e008193

ATTR-ACT LTE (long-term extension)

- Open-label study of tafamidis treatment in patients with ATTRwt/ATTRv-CM
- Patients who took part in ATTR-ACT were not included
- **1476** patientes received tafamidis for up to 60 months, until it became commercially available in their region
- Patients were enrolled between **2018-2023**
- Median exposure: 1 year
- Longest treatment duration: 4,5 years

Crespo-Leiro MG, et al. JACC Adv. 2025;4:102122

ATTR-ACT LTE (long-term extension)



2 centers in Spain

Crespo-Leiro MG, et al. JACC Adv. 2025;4:102122

ATTR-ACT LTE (long-term extension)

1,476 patients with ATTR-CM

- Treated with tafamidis free acid 61 mg in an early access cohort with minimal enrollment criteria
- Treatment could continue for up to 60 months, or until commercially approved in their region

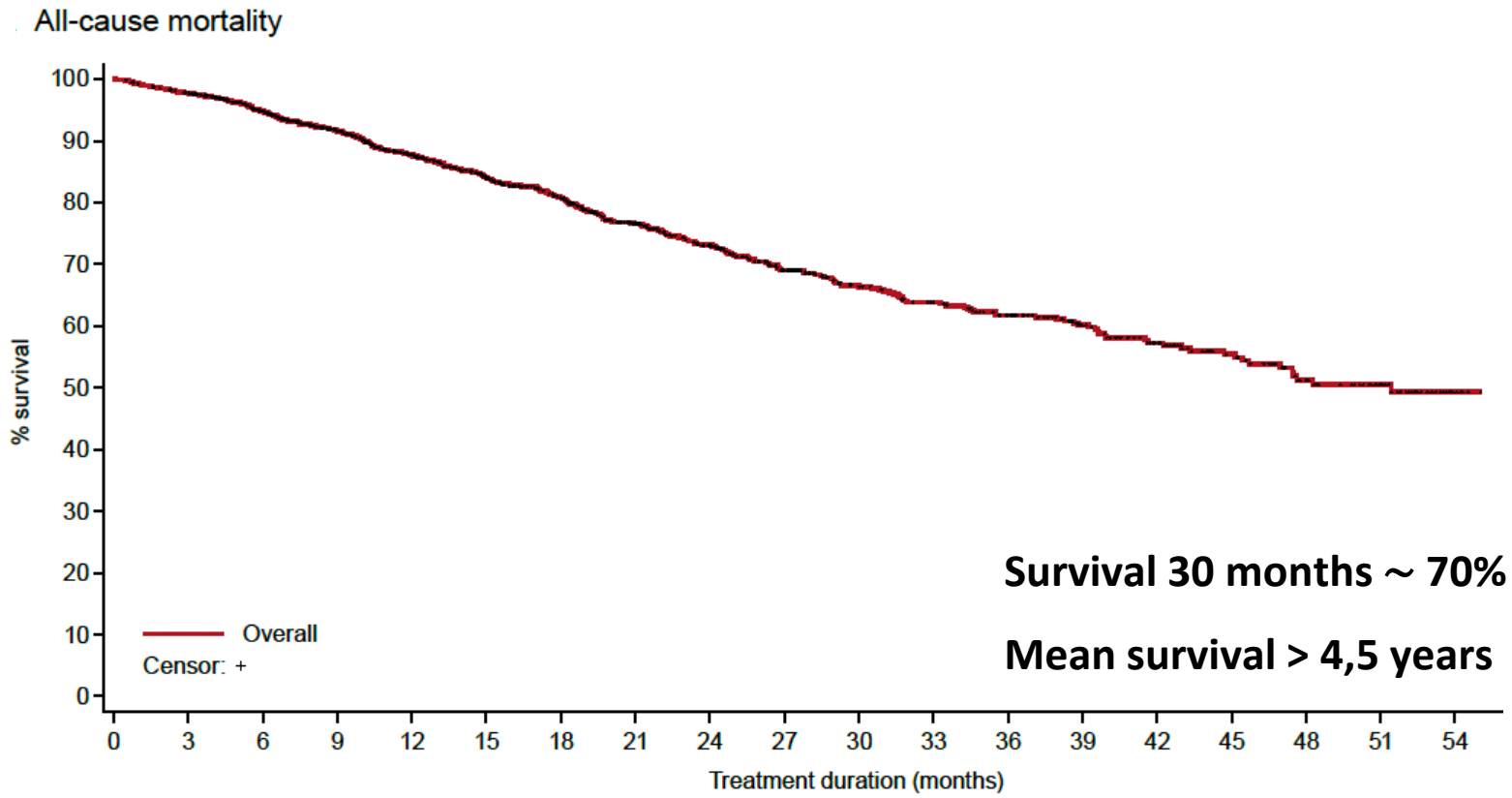
- Median exposure was 1 year
- The longest treatment duration was 4.5 years

	Treated Patients (N = 1,476)
Age, y	
Mean (SD)	76.5 (7.8)
Median (range)	77 (32-96)
Sex, n (%)	
Male	1,311 (88.8)
Female	165 (11.2)
Race, n (%)	
White	1,252 (84.8)
Black	139 (9.4)
Asian	66 (4.5)
Other	19 (1.3)

	Treated Patients (N = 1,476)
NYHA classification, n (%)	
I	220 (14.9)
II	781 (52.9)
III	455 (30.8)
IV	19 (1.3)
Missing	1 (<0.1)
TTR genotype, n (%)	
Wild-type	1,264 (85.6)
Variant	212 (14.4)
V122I (p. V142I)	132 (8.9)
A97S (p. A117S)	25 (1.7)
V30M (p. V50M)	13 (0.9)
T60A (p. T80A)	11 (0.7)
Others[b]	31 (2.1)
Most common medical history,[c] n (%)	
Hypertension	907 (61.4)
Atrial fibrillation	854 (57.9)
Carpal tunnel syndrome	695 (47.1)
Osteoarthritis	384 (26.0)
Benign prostatic hyperplasia	372 (25.2)
Hyperlipidemia	366 (24.8)
Coronary artery disease	339 (23.0)
Dyslipidemia	324 (22.0)
NT-proBNP, ng/L	n = 124
Mean (SD)	2,832 (4,036)
Median (range)	1,669 (51, 28,061)

Crespo-Leiro MG, et al. JACC Adv. 2025;4:102122

ATTR-ACT LTE (long-term extension)



Crespo-Leiro MG, et al. JACC Adv. 2025;4:102122

ATTR-ACT LTE (long-term extension)

TABLE 4 Incidence of Treatment-Related Adverse Events (N = 1,476)

Any treatment-related adverse event	112 (7.6)
Serious	9 (0.6)
Severe	4 (0.3)
Caused study discontinuation	9 (0.6)
Caused treatment discontinuation (patient remained in the study)	0 (0.0)
Caused a dose reduction	5 (0.3)

The most common tafamidis-related side effects were:

Diarrhea - reported in 26 people

Fatigue - reported in 10 people.
Fatigue is a feeling of exhaustion, both mentally and physically

Other tafamidis-related side effects:
reported in fewer than 10 people

Crespo-Leiro MG, et al. JACC Adv. 2025;4:102122

TAFAMIDIS: real world evidence

- Retrospective observational multicenter (5 centers in USA) study
- **624** patients received tafamidis (early access program or commercial prescriptions)
- Patients were enrolled between january/2018-october/2021
- Median follow-up: 3,6 years

Masri A, et al. JACC CardioOncol. 2025;7:282-293.

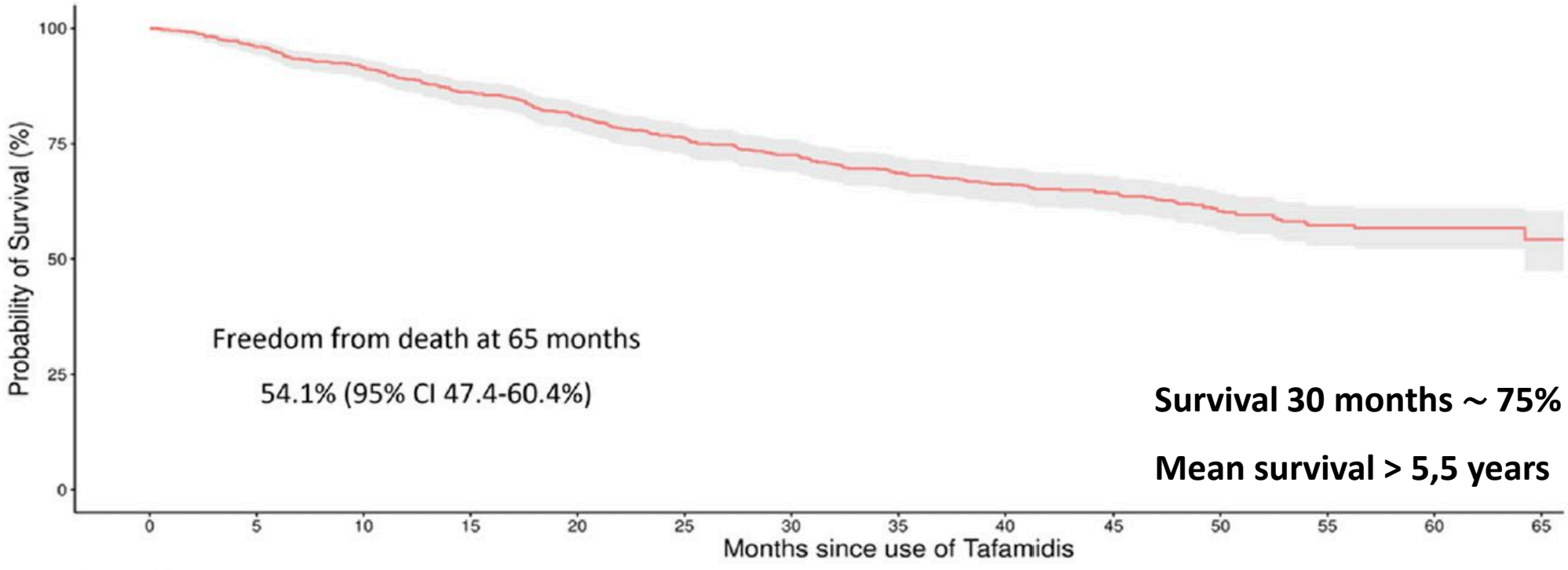
TAFAMIDIS: real world evidence

82,5%

	Total (N = 624)	wtATTR (n = 515)	vATTR (n = 109)	*P* Value
Age, y	78.0 (72.0-83.0)	79.0 (73.1-84.0)	71.0 (65.0-76.0)	
Male	546 (87.5)	469 (91.1)	77 (70.6)	
Race				<0.001
White	507 (81.3)	472 (91.7)	35 (32.1)	<0.001
Black	109 (17.5)	38 (7.4)	71 (65.1)	
Other	8 (1.3)	5 (1.0)	3 (2.8)	
TTR variant		–		
V122I			77 (70.6)	
T60A			15 (13.8)	
V30M			5 (4.6)	
Other			12 (11.0)	
NYHA functional class				
I	84 (13.5)	65 (12.6)	19 (17.4)	0.16
II	324 (51.9)	276 (53.6)	48 (44.0)	
III	210 (33.7)	168 (32.6)	42 (38.5)	
IV	6 (1.0)	6 (1.2)	0 (0.0)	
Diagnosis method				0.090
Endomyocardial biopsy	92 (14.7)	82 (15.9)	10 (9.2)	
Scintigraphy	498 (79.8)	408 (79.2)	90 (82.6)	
Others	34 (5.4)	25 (4.9)	9 (8.3)	
NT-proBNP, pg/mL	1,911.0 (960.5-3,909.0)	2,080.0 (1,007.0-3,859.0)	1,495.0 (705.0-4,034.5)	0.11

Masri A, et al. JACC CardioOncol. 2025;7:282-293.

TAFAMIDIS: real world evidence



Survival 30 months ~ 75%

Mean survival > 5,5 years

A Coruña Heart Failure Academy

García-Pavía P, et al. J Card Fail. 2025;31:525-533

TAFAMIDIS: real world evidence

- Retrospective analisis from THAOS (TranstHyretin Amyloidosis Outcomes Survey) real-world registry
- **1441** patients (587 with tafamidis vs 854 without tafamidis) enrolled between 2007-2023
- **73,4%** of treated patients enrolled 2019-2023 / **54,8%** of untreated patients enrolled 2013-2018
- Median follow-up: 2,2 years

García-Pavía P, et al. J Card Fail. 2025;31:525-533

TAFAMIDIS: real world evidence

	Tafamidis-treated (n = 587)	Tafamidis-untreated (n = 854)	*P* Value
Sex, n (%)			0.25
Male	539 (91.8)	769 (90.0)	
Female	48 (8.2)	85 (10.0)	
Race/ethnicity,*n (%)	502	767	<0.001
Afro-Caribbean	1 (0.2)	8 (1.0)	
American Hispanic	1 (0.2)	0	
Asian	9 (1.8)	8 (1.0)	
Black or African American	28 (5.6)	72 (9.4)	
Latino American	0	12 (1.6)	
White	463 (92.2)	659 (85.9)	
Other	0	8 (1.0)	
Age at symptom onset (y), n	500	783	0.86
Median (10th, 90th percentile)	72.5 (59.5, 82.5)	72.5 (57.5, 82.5)	
Time from symptom onset to diagnosis (y), n	495	726	0.45
Median (10th, 90th percentile)	1.6 (0.0, 13.0)	1.4 (0.0, 10.7)	
Year of enrollment, n (%)			<0.001
2007–2012	13 (2.2)	147 (17.2)	
2013–2018	143 (24.4)	468 (54.8)	
2019–2023	431 (73.4)	239 (28.0)	
Age at enrollment (y), median (10th, 90th percentile)	77.7 (68.0, 85.9)	76.4 (65.2, 85.7)	0.02
Symptom duration at enrollment (y), n	500	783	0.30
Median (10th, 90th percentile)	3.0 (0.4, 13.7)	2.7 (0.3, 11.9)	
Follow-up time,† (y), median (10th, 90th percentile)	2.2 (0.5, 5.3)	2.3 (0.6, 5.7)	0.07
TTR genotype, n (%)			<0.001
Variant	48 (8.2)	138 (16.2)	
Wild-type	539 (91.8)	716 (83.8)	

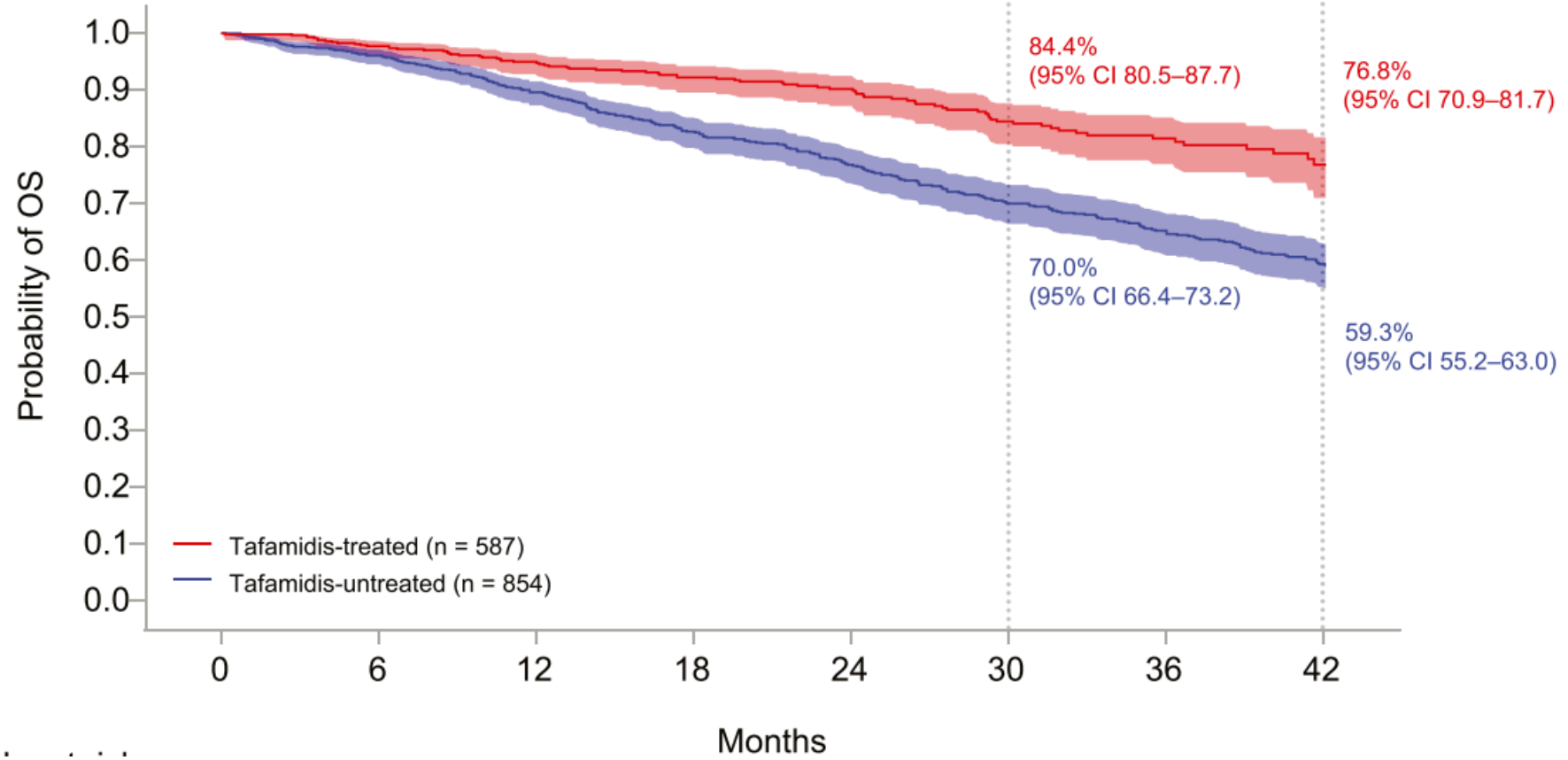
García-Pavía P, et al. J Card Fail. 2025;31:525-533

TAFAMIDIS: real world evidence

Most Common *TTR* Variants,[‡] n (%)			0.01
V122I (p. V142I)	21 (3.6)	69 (8.1)	
V30M (p.V50M)[§]	3 (0.5)	18 (2.1)	
I68L (p.I88L)	5 (0.9)	10 (1.2)	
Heart failure, n (%)	509 (86.7)	787 (92.2)	<0.001
NYHA functional class, n (%)	484	769	<0.001
I	76 (15.7)	80 (10.4)	
II	305 (63.0)	456 (59.3)	
III	102 (21.1)	207 (26.9)	
IV	1 (0.2)	26 (3.4)	
NT-proBNP (pg/mL), n	157	487	0.04
Median (10th, 90th percentile)	1883.0 (459.0, 6837.0)	2498.0 (466.0, 8256.0)	
LV septum thickness (mm), n	464	611	0.13
Median (10th, 90th percentile)	17.0 (13.0, 22.0)	17.0 (13.0, 22.0)	
LV ejection fraction (%), n	472	609	0.02
Median (10th, 90th percentile)	50.0 (33.0, 63.0)	49.0 (29.0, 62.0)	
mBMI, n	403	473	0.23
Median (10th, 90th percentile)	1077.6 (851.8, 1346.5)	1060.2 (806.4, 1344.1)	
Past or current clinical trial participation, [‖] n (%)	581	752	0.70
Yes	120 (20.7)	149 (19.8)	
Tafamidis trial	7 (1.2)	0	
Non-tafamidis trial	113 (19.4)	149 (19.8)	
No	461 (79.3)	603 (80.2)	
Diagnostic method,[¶] n (%)			-
Clinical symptoms	546 (93.0)	734 (85.9)	
Amyloid confirmed on tissue biopsy	244 (41.6)	460 (53.9)	
TTR confirmed as precursor protein on tissue biopsy	218 (37.1)	401 (47.0)	
Scintigraphy	352 (60.0)	228 (26.7)	
Other	66 (11.2)	34 (4.0)	

García-Pavía P, et al. J Card Fail. 2025;31:525-533

TAFAMIDIS: real world evidence



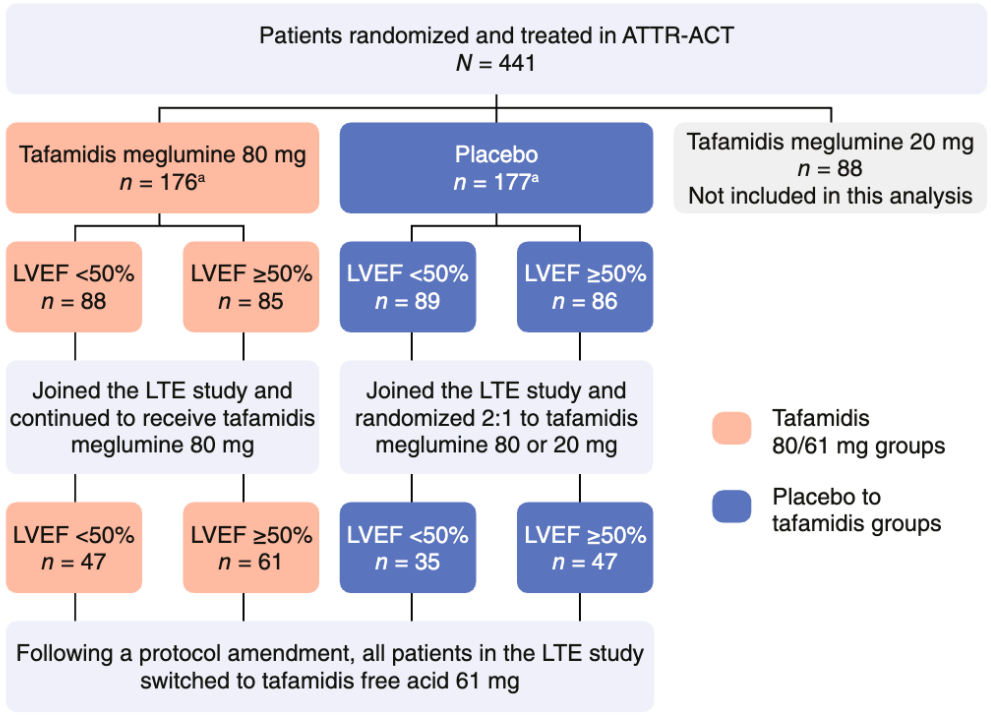
García-Pavía P, et al. J Card Fail. 2025;31:525-533

TAFAMIDIS: real world evidence

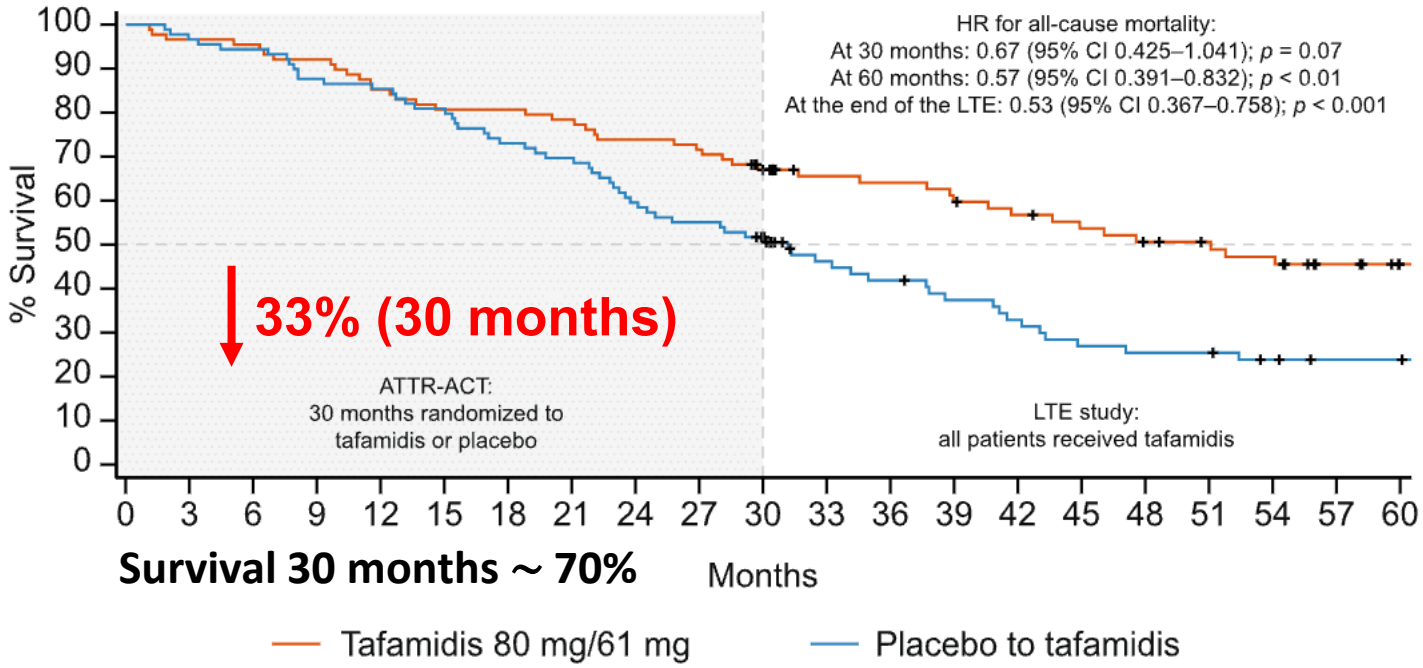
	Tafamidis dose				
	20 mg (n = 52)	80/61 mg (n = 455)	20 to 80/61 mg (n = 73)	Other doses (n = 7)	All doses (n = 587)
Number of AEs, n	22	258	61	11	352
Patients with AEs, n (%)	11 (21.2)	120 (26.4)	28 (38.4)	2 (28.6)	161 (27.4)
Patients with serious AEs, n (%)	10 (19.2)	91 (20.0)	20 (27.4)	2 (28.6)	123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

García-Pavía P, et al. J Card Fail. 2025;31:525-533

TAFAMIDIS and LVEF



FEVI <50% (50% of the cohort)



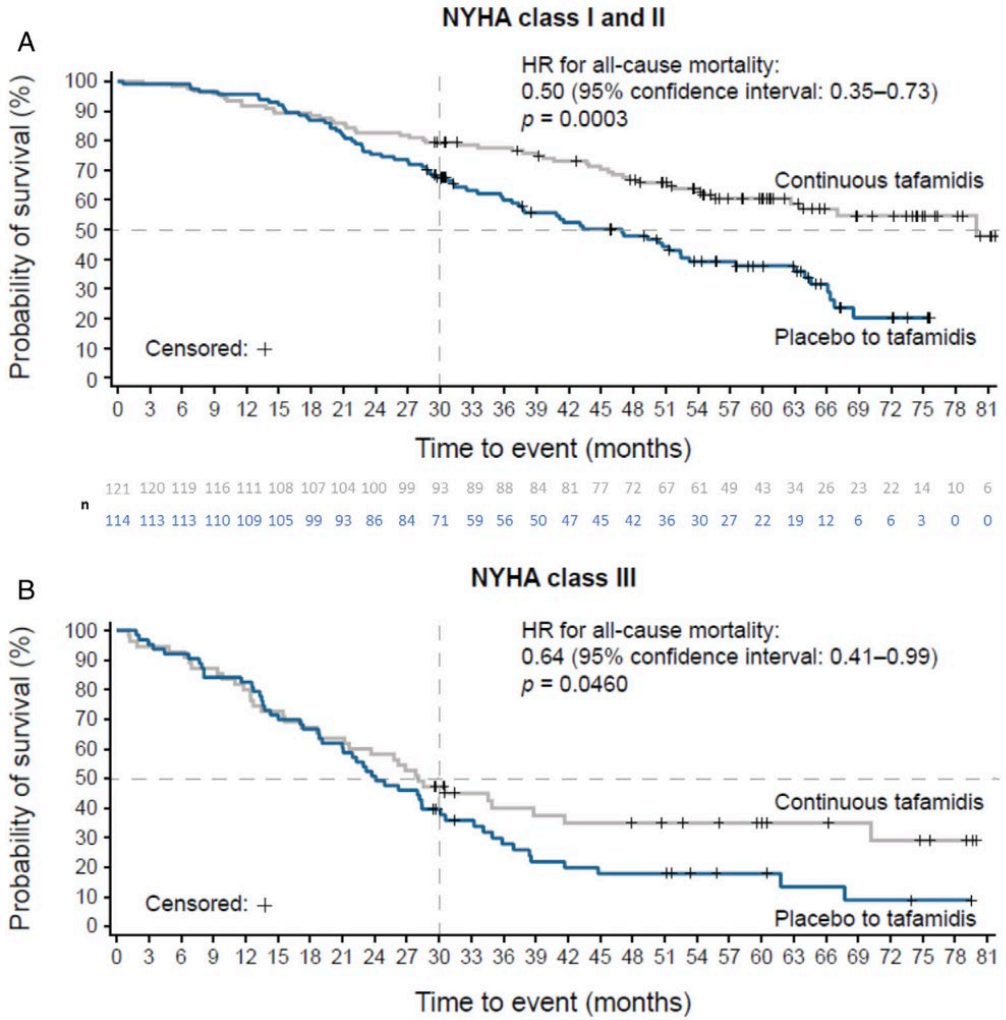
Drachman B, et al. Eur J Heart Fail. 2024;26:2038-2046

Os pacientes deben cumprir os seguintes criterios:

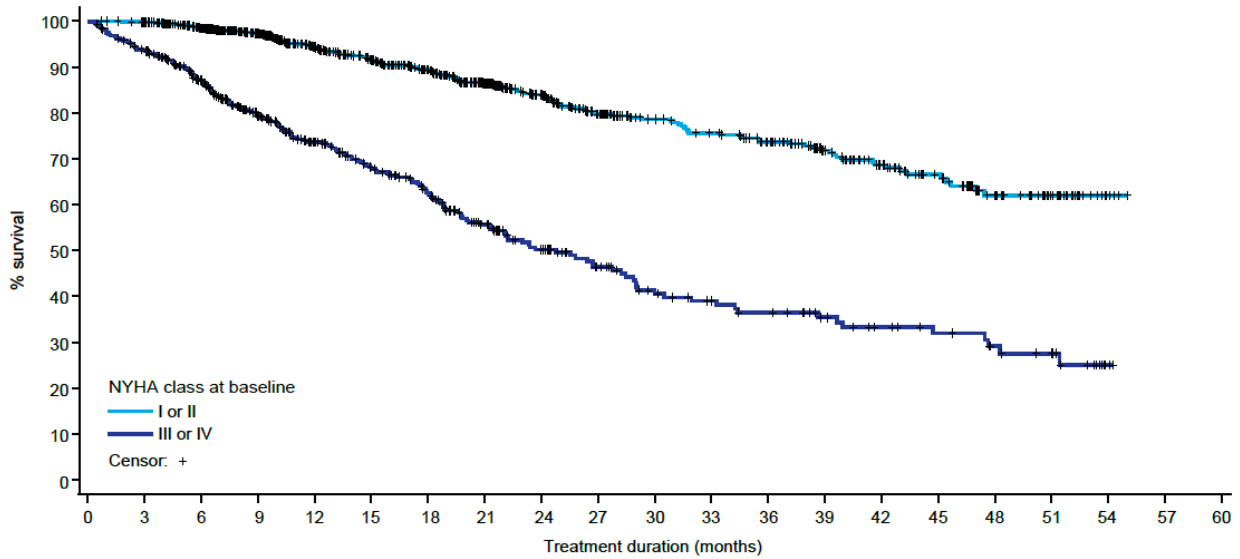
1. -Diagnóstico de insuficiencia cardíaca :
   - A lo menos unha hospitalización previa ou ter clínica de sobrecarga de volume que precise tratamento diurético para a melloría (sen hospitalización) -indicar data
   - Clase I-II* da NYHA -indicar clase
   - FEVI ≥ 50% -indicar FEVI
   - Grosor da parede do septo interventricular telediastólico >12 mm na ecocardiografía .- indicar data ecocardiografía e dato del grosor do septo.

TAFAMIDIS and NYHA functional class

(1)



(2)

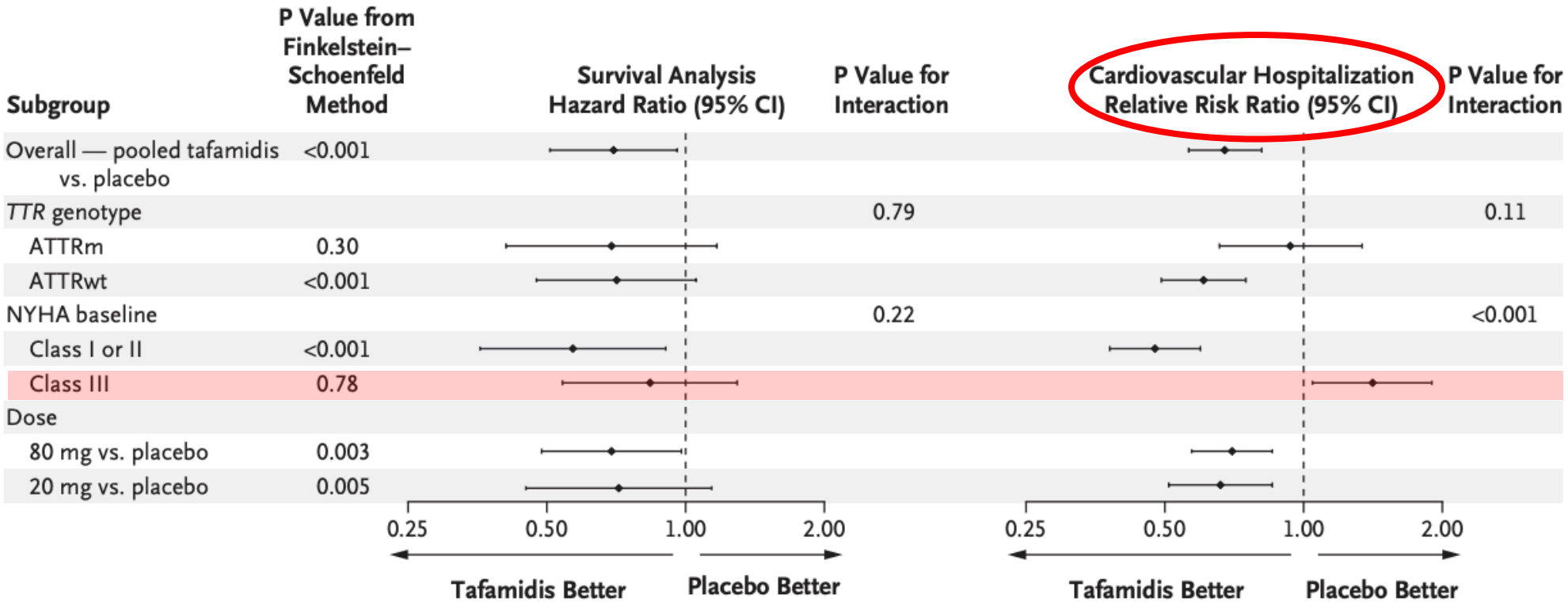


NYHA I-II survival 30 months ~ 80%

NYHA III Survival 30 months ~ 40%

NYHA III mean survival ~ 2 years

(1) Elliott P, et al. Eur J Heart Fail. 2023;25:2060-2064 / (2) Crespo-Leiro MG, et al. JACC Adv. 2025;4:102122



Maurer MS, et al. N Engl J Med. 2018;379:1007-1016

TAFAMIDIS and NYHA functional class

Os pacientes deben cumprir os seguintes criterios:

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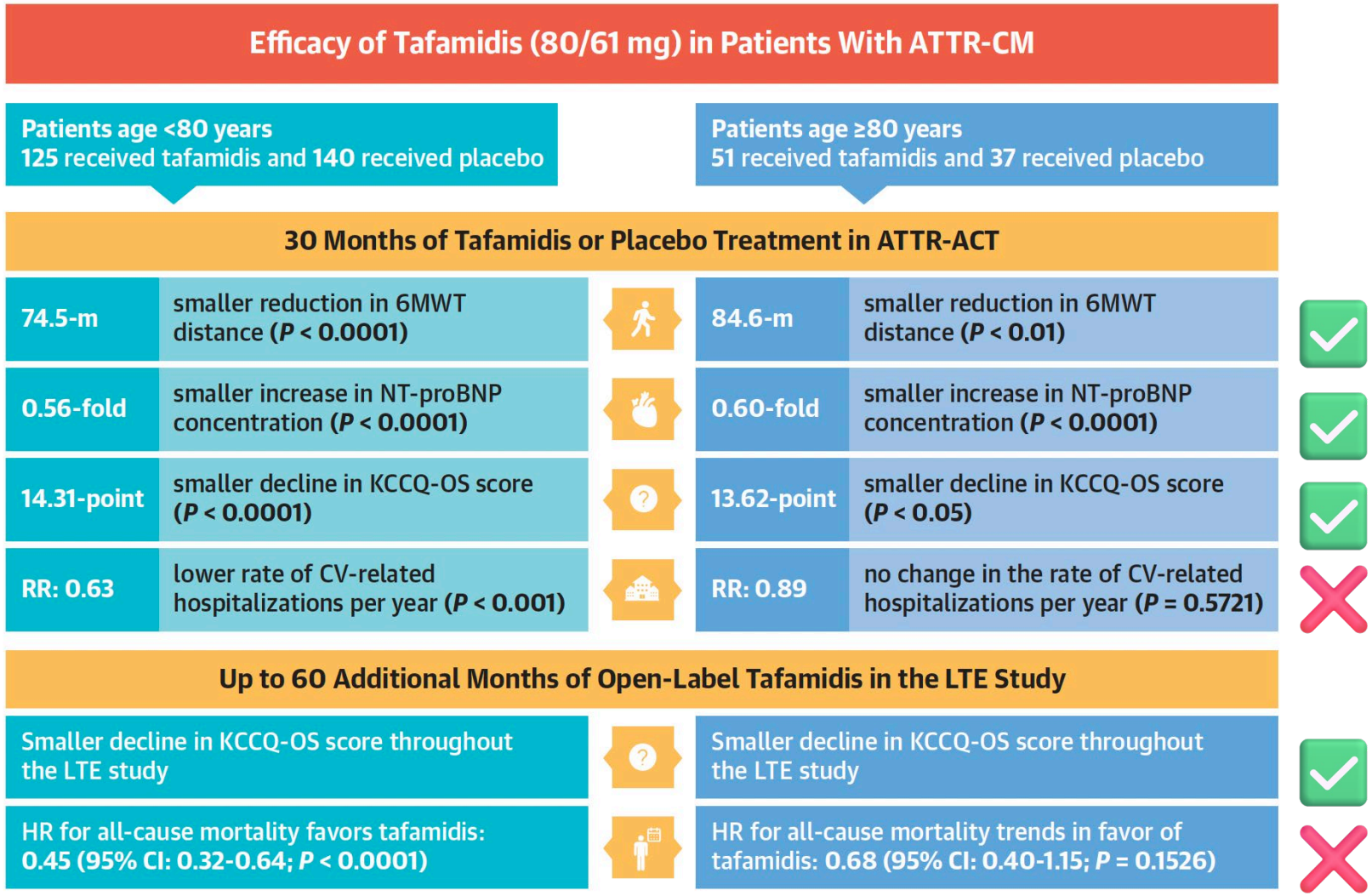
   - A lo menos unha hospitalización previa ou ter clínica de sobrecarga de volume que precise tratamento diurético para a melloría (sen hospitalización) -indicar data
   - Clase I-II* da NYHA -indicar clase
   - FEVI ≥ 50% -indicar FEVI
   - Grosor da parede do septo interventricular telediastólico >12 mm na ecocardiografía .- indicar data ecocardiografía e dato del grosor do septo.

*NYHA III: a ficha técnica contempla o uso en pacientes NYHA I e II quedando os pacientes NYHA III a criterio dun médico con experiencia no manexo de pacientes con amiloidose.

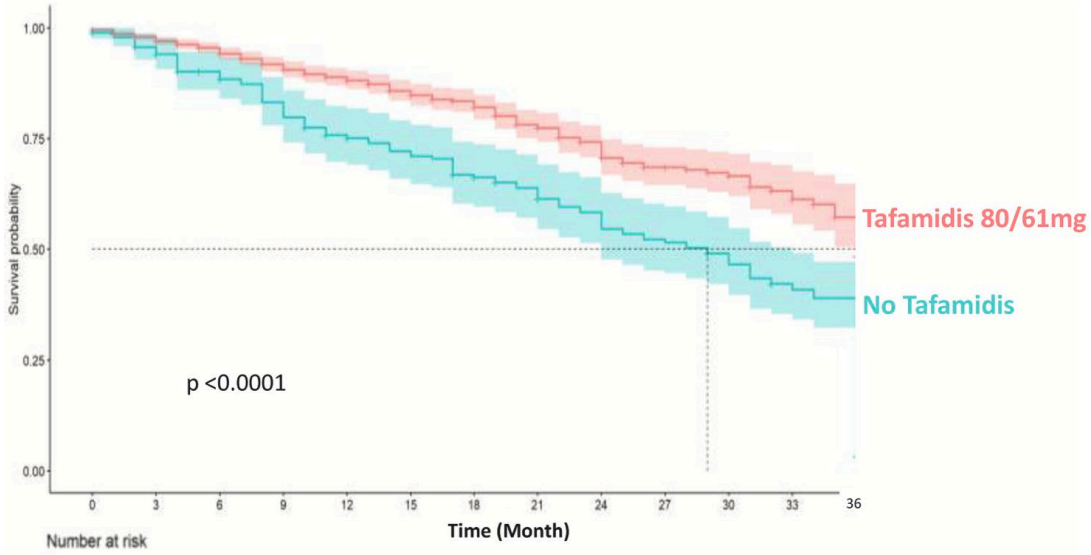
TAFAMIDIS and AGE



García-Pavía P, et al. JACC Heart Fail. 2024;12:150-160

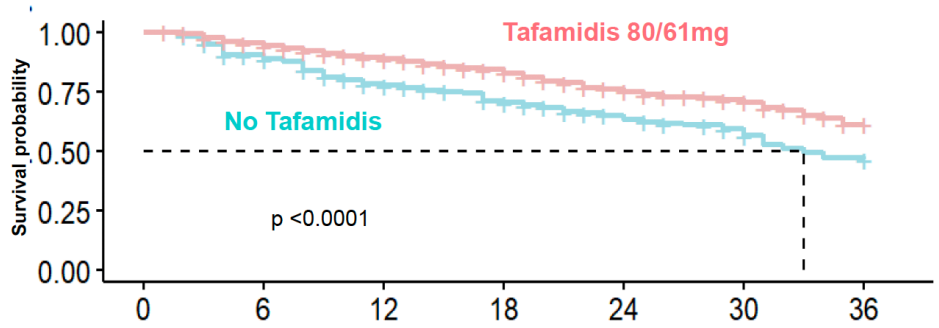
TAFAMIDIS and AGE

- Retrospective observational multicenter study in France (Healthcare European Amyloidosis Registry)
- **1380** patients ≥ 80 yo (1194 with tafamidis vs 186 without tafamidis)



Propensity score

Age
NYHA
SBP
Troponin T
NTproBNP
IVST
LVEF
E/e´
ASAT
ALP



Jobbé-Duval A, et al. Int J Cardiol. 2025;437:133522

CONCLUSIONS

1. Tafamidis is a transthyretin stabilizer available in Spain since june 2023. It was the first specific drug to treat patients with ATTRwt/ATTRv-CM, and continues to be the only available in our country

2. In the ATTR-ACT clinical trial, tafamidis was associated with reductions in all-cause mortality and cardiovascular-related hospitalizations and reduced the decline in functional capacity and quality of life compared with placebo. Furthermore, it proved to be a safe and well-tolerated drug

3. The results of the ATTR-ACT long-term extension study and the evidence obtained from the use of tafamidis in real life confirm its usefulness and safety

CONCLUSIONS

4. Patients with ATTR-CM and a reduced LVEF <50% benefit from tafamidis, similar to those with a preserved LVEF

5. In patients with ATTR-CM and an advanced functional class, tafamidis was also associated with a reduction in all-cause mortality compared with placebo. However, the poor prognosis of these patients may determine the prescription of the drug

6. In octogenarians with ATTR-CM, treatment with tafamidis is associated with less deterioration in quality of life and functional capacity, and seems to reduce all-cause mortality. In these patients, a comprehensive assessment beyond age should guide the treatment decision