XI Reunión. Estado del Arte en
INSUFICIENCIA CARDIACA
PRÁCTICA CLÍNICA Y MODELOS ORGANIZATIVOS
Sede: Hotel Meliá MaríaPita, A Coruña
A CORUÑA 27-28 SEPTIEMBRE 2024

XI Meeting. State of the Art in
HEART FAILURE
CLINICAL PRACTICE AND ORGANIZATIONAL MODELS
Venue: Hotel Meliá MaríaPita, A Coruña
ACoruñaHF2024
A CORUÑA 27-28 SEPTEMBER 2024

UPDATE ON AMYLOIDOSIS

Diagnosis and treatment. What do the guidelines say and what issues are under discussion?

Gonzalo Barge Caballero, MD, PhD

Heart Failure and Heart Transplant Unit. Cardiology Department, CHUAC

Centro de Investigación Biomédica en Red, Enfermedades Cardiovasculares

DISCLOSURES

Travel grants, speaker fees, and two research grants from **Pfizer**

DIAGNOSIS OF CARDIAC AMYLOIDOSIS

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS

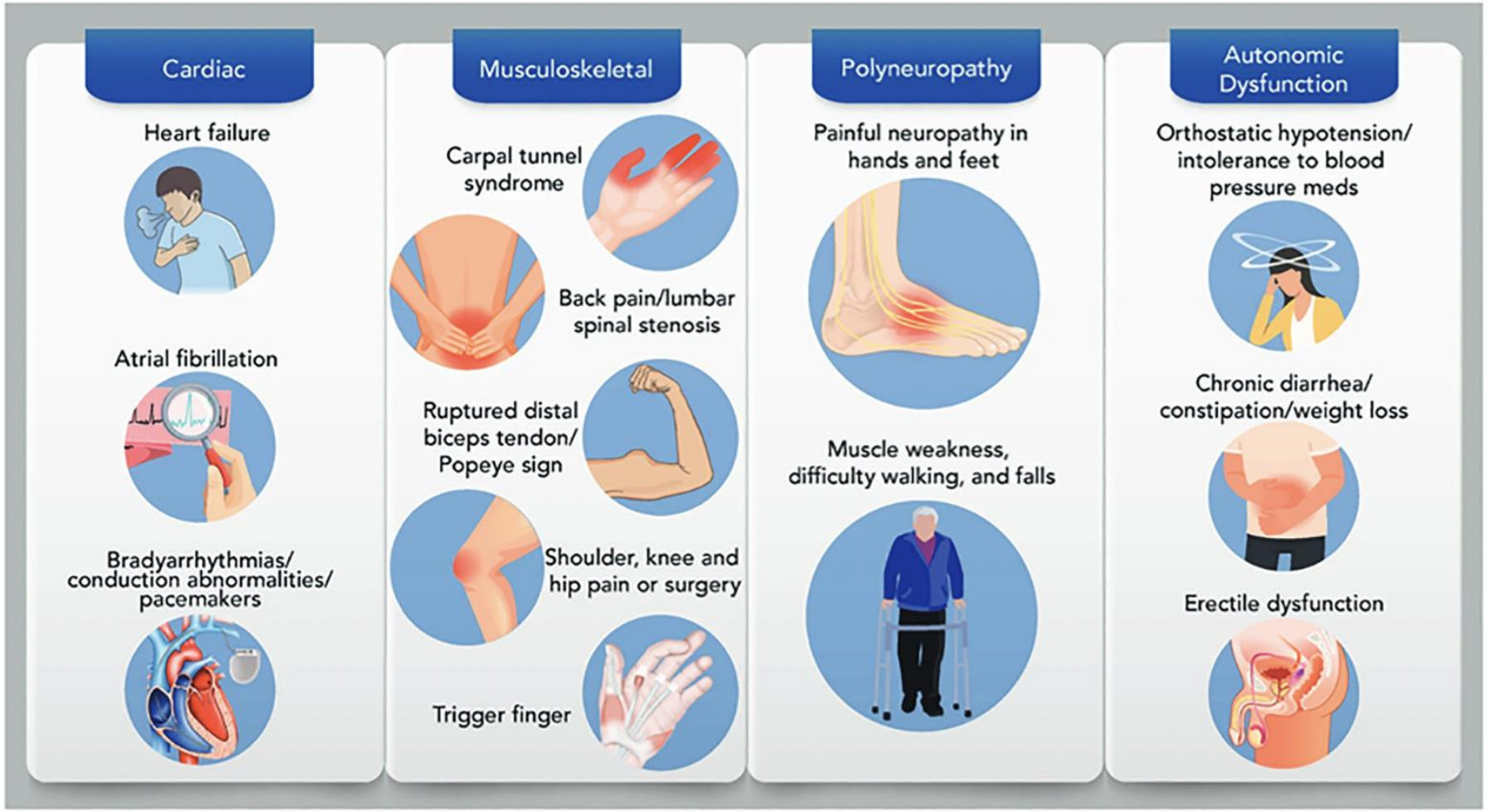
SPECIFIC TREATMENT OF ATTR CARDIAC AMYLOIDOSIS: TAFAMIDIS

DIAGNOSIS OF CARDIAC AMYLOIDOSIS

SUSPICION → Signs & symptoms, ECG, echo or CMR suggestive of cardiac amyloidosis

García-Pavía P, et al. Eur Heart J. 2021; 42:1554-1568.

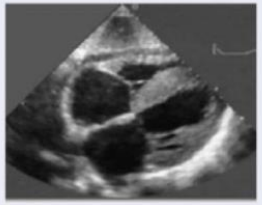
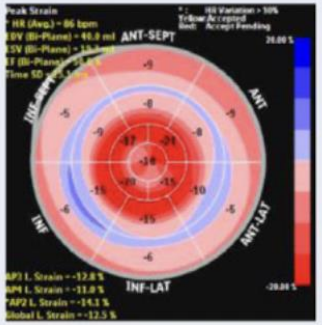
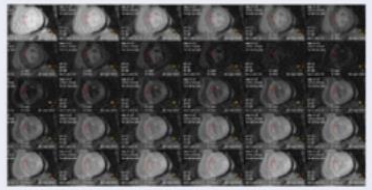
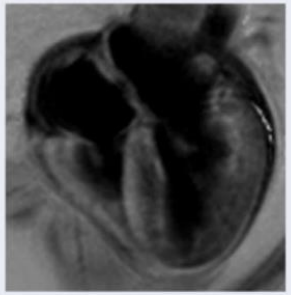
SUSPICION OF CARDIAC AMYLOIDOSIS: CLINICAL FINDIGS



ATTRwt **ATTRv AL** **ATTRv AL**

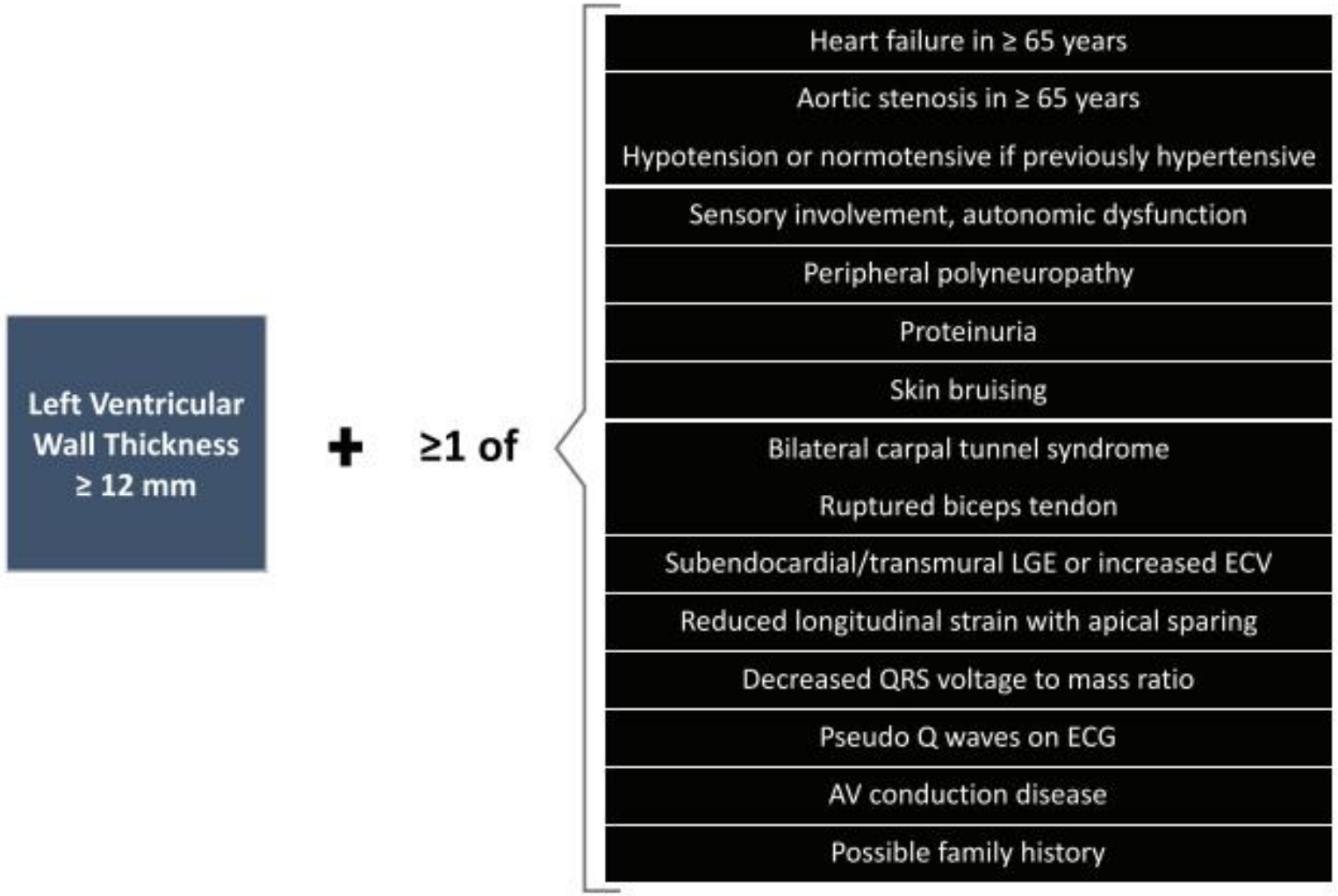
Kittleson MM, et al. J Am Coll Cardiol. 2023;81:1076-1126.

SUSPICION OF CARDIAC AMYLOIDOSIS: COMPLEMENTARY TESTS FINDINGS

Electrocardiográficas	Ecocardiográficas	RMC
• **Patrón de seudoinfarto (70%)**  • Patrón de bajos voltajes (28-43%)  • Índice de Sokolow-Lyon ≤ 1,5mV	• Hipertrofia biventricular  • Engrosamiento de las válvulas AV y del septo interauricular • Derrame pericárdico • Reducción del *strain* longitudinal global, con patrón segmentario *cherry-on-top* 	• Alteración de la cinética de gadolinio  • Realce tardío transmural o subendocárdico global  • T1 nativo elevado • Volumen extracelular aumentado

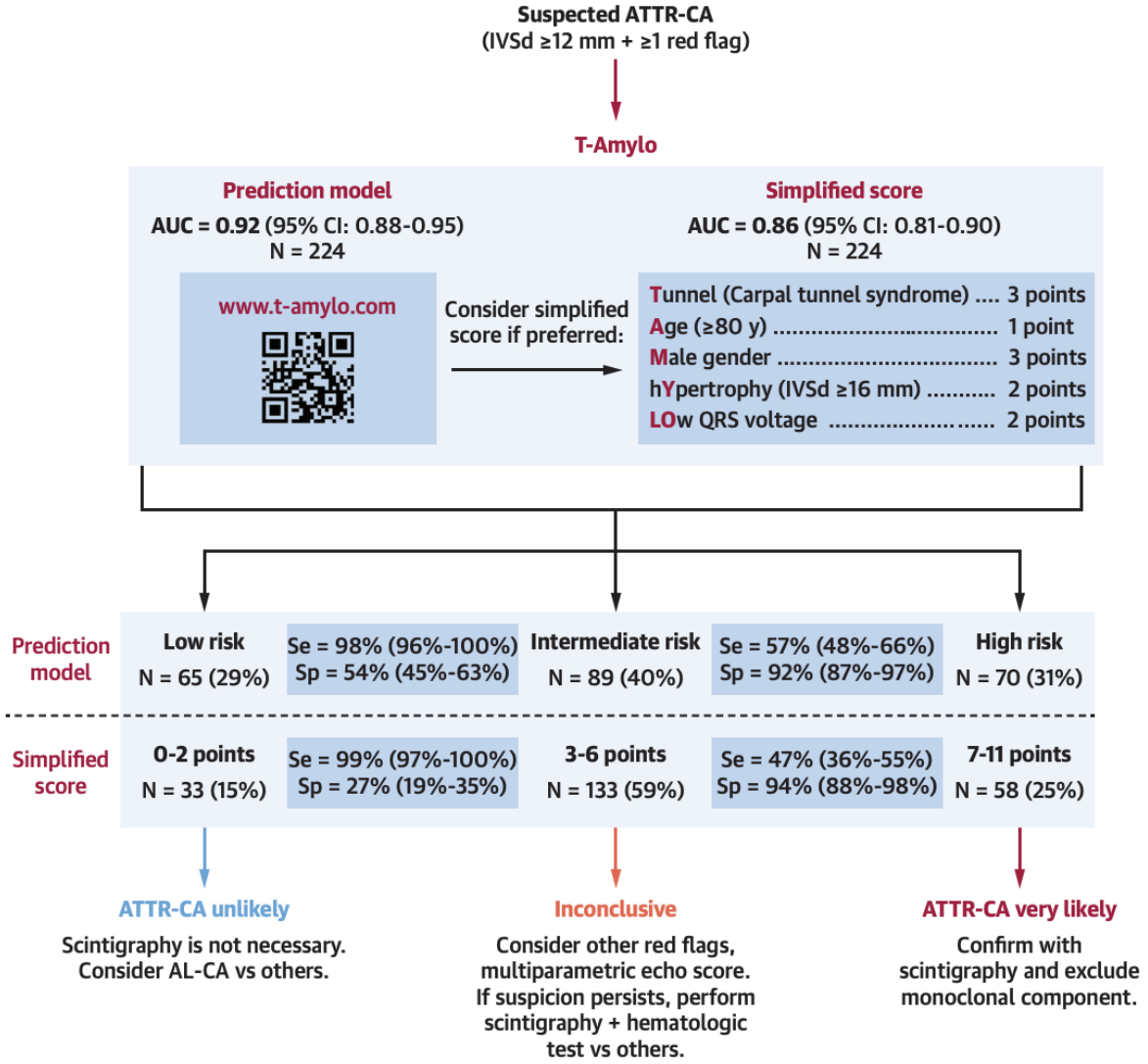
Combarro-Eiriz M, et al. REC Cardioclinics. 2022;57:s19-s27.

SUSPICION OF CARDIAC AMYLOIDOSIS



García-Pavía P, et al. Eur Heart J. 2021; 42:1554-1568.

SUSPICION OF CARDIAC AMYLOIDOSIS: T-AMYLO SCORE



Development and Validation of a Prediction Model and Score for Transthyretin Cardiac Amyloidosis Diagnosis

T-Amylo

Xabier Arana-Achaga, MD,[a,b,*] Cristina Goena-Vives, MD,[a,b,c,*] Iñaki Villanueva-Benito, PhD,[a,b] Itziar Solla-Ruiz, MD,[a,b] Ainhoa Rengel Jimenez, MD,[a,b] Teresa Iglesias Gaspar, MD,[d] Iratxe Urreta-Barallobre, MD,[b,d] Gonzalo Barge-Caballero, PhD,[e,f] Sara Seijas-Marcos, PhD,[e] Eva Cabrera, MD,[g] Pablo Garcia-Pavía, PhD,[g,h] María Teresa Basurte Elorz, MD,[i,j] Nerea Mora Ayestarán, MD,[j] Lucas Tojal Sierra, MD,[k] Maria Robledo Iñarritu, MD,[k] Ainara Lozano-Bahamonde, PhD,[l] Vanesa Escolar-Perez, PhD,[l] Cristina Gómez-Ramírez, MD,[m] Elisabete Alzola, MD,[m] Rubén Natividad Andrés, MD,[n] Jose Luis Francisco Matias, MD,[n] Javier Limeres Freire, MD,[o,p,q] Arola Armengou Arxe, PhD,[r] Montserrat Negre Busó, PhD,[s] Jesus Piqueras-Flores, PhD,[t,u] Jorge Martínez-del Río, MD,[t] Jose Juan Onaindia Gandarias, MD,[v] Ibon Rodriguez Sanchez, MD,[v] Ramón Querejeta Iraola, PhD[a,d]

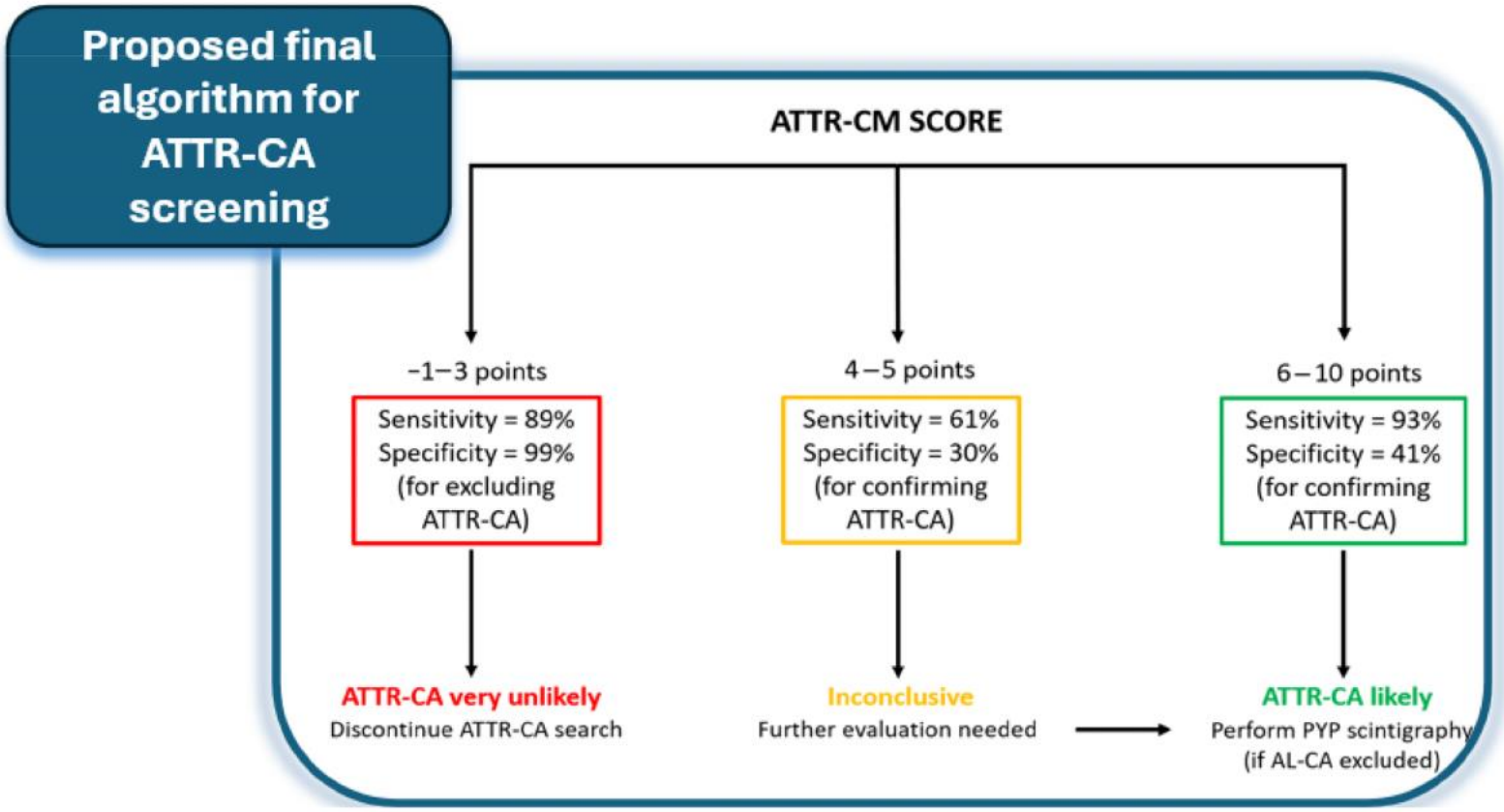
A Coruña Heart Failure Academy

Arana-Achaga X, et al. JACC Cardiovasc Imaging. 2023;16:1567-1580.

SUSPICION OF CARDIAC AMYLOIDOSIS: ATTR-CM SCORE

ATTR-CM score

Clinical variable	Value	Points
Age, years	60–69	+2
	70–79	+3
	≥80	+4
Sex	Male	+2
Hypertension	Yes	–1
LVEF	<60%	+1
Posterior wall thickness	≥12 mm	+1
Relative wall thickness	>0.57	+2



Bonfioli GB, et al. Eur J Heart Fail. 2024 Sep 9. Online ahead of print.

DIAGNOSIS OF CARDIAC AMYLOIDOSIS

SUSPICION → Signs & symptoms, ECG, echo or CMR suggestive of cardiac amyloidosis

García-Pavía P, et al. Eur Heart J. 2021; 42:1554-1568.

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS

- Heart Failure
- Atrial Fibrillation – Embolic risk
- Conduction disorders
- Ventricular arrhythmias
- Aortic stenosis

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS: HEART FAILURE

- **Nowadays, heart failure is the most common clinical manifestation of cardiac amyloidosis (~60%)**

Presentación clínica al diagnóstico				
Insuficiencia cardiaca/disnea	101 (57,1)	51 (44,4)	50 (80,7)	<0,001
Fibrilación auricular	29 (16,4)	24 (20,9)	5 (8,1)	0,028
BAV	11 (6,2)	10 (8,7)	1 (1,6)	0,100
ACV	9 (5,1)	6 (5,2)	3 (4,8)	0,100
Síncope	6 (3,4)	5 (4,4)	1 (1,6)	0,667
Dolor torácico	5 (2,8)	5 (4,4)	0	0,164
Alteraciones en el ECG	6 (3,4)	5 (4,4)	1 (1,6)	0,667
Incidental	10 (5,6)	9 (7,8)	1 (1,6)	0,168

57,1%

López-Sainz A, et al. Rev Esp Cardiol. 2021;74:149-158

Características clínicas basales de los pacientes en el momento de la inclusión en el registro

	AC-ATTR (n = 128)	AC-AL (n = 15)	Total (N = 143)	p
Edad (años)	81,0 ± 6,0	67,9 ± 10,8	79,6 ± 7,7	<0,0001
Sexo femenino	28 (21,9)	6 (40,0)	34 (23,8)	0,119
Motivo de consulta que llevó al diagnóstico				
Síntomas de insuficiencia cardiaca	77 (60,2)	8 (53,3)	85 (59,4)	0,29
Síncope o episodio arrítmico	15 (11,7)	1 (6,7)	16 (11,2)	
Diagnóstico diferencial de HVI	24 (18,7)	2 (13,3)	26 (18,2)	
Dolor torácico	5 (3,9)	1 (6,7)	6 (4,2)	
Otros	7 (5,5)	3 (20,0)	10 (7,0)	

59,4%

Barge-Caballero G, et al. Med Clin (Barc). 2021;156:369-378.

- **A reduced left ventricular ejection fraction (≤40%) is not uncommon at diagnosis (15-40%)[a-d]**

(a) Shah SJ, et al. JAMA Cardiol. 2024;9:25-34 (b) AMIGAL registry data 31/12/2023 (c) Bhattacharya PT, et al. HFSA Meeting 2021 (d) Ioannou A, et al. Eur Heart J. 2023;44:2893-2907.

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS: HEART FAILURE

- Data from observational (most retrospective) studies, absence of clinical trials
- Most studies with ATTR-CA (especially ATTRwt-CA) patients; data with AL-CA patients is scarce
- Very heterogeneous studies
- Inclusion of patients with multiple indications for treatment, not only heart failure
- Contradictory results

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS: HEART FAILURE

DRUGS: *Expert Recommendations*

Drug	ESC[1]	DGK[2]	CCS/CHFS[3]	AHA[5]	JCS[6]
HF setting					
Loop or thiazide diuretics	Recommended[a]	Recommended[a]	Recommended[a]	Recommended, but avoid underfilling and worsening renal function from restrictive physiology[a]	Recommended[a]
Nitrates or carperitide (AHF)	No recommendation	No recommendation	No recommendation	No recommendation	Might be considered[a]
Catecholamines, PDE inhibitor (AHF)	No recommendation	No recommendation	No recommendation	No recommendation	Might be considered[a]
Beta-blockers	Not recommended, deprescribe (should be avoided)[a]	Avoid or very cautious use[a]	Avoid or very cautious use[a]	No data for benefit; may not be tolerated given fixed stroke volume (should be avoided)[a]	Tolerated dosing might be considered[a]
ACE inhibitor/ARB	Not recommended (should be avoided)[a]	Avoid or very cautious use[a]	Avoid or very cautious use[a]	No data for benefit; may exacerbate amyloid-related hypotension from autonomic dysfunction (should be avoided)[a]	Tolerated dosing might be considered[a]
Sacubitril/valsartan	No recommendation	No recommendation	No recommendation	No data for benefit; may exacerbate amyloid-related hypotension from autonomic dysfunction (should be avoided)[a]	No recommendation
MRA	No recommendation	No recommendation	Recommended[a]	Might be considered in conjunction with loop diuretics if adequate blood pressure and renal function[a]	Tolerated dosing might be considered[a]

Rapezzi C, et al. J Am Coll Cardiol 2022;79:1288–1303.

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS: HEART FAILURE

DRUGS: *Published Data on 27/09/2024*

- **AMIGAL:** 128 ATTR (89,8% ATTRwt), FEVIr: 23%
- **LONDON:** 2371 ATTR (77,6% ATTRwt), FEVIr: 22,4%
- **COLUMBIA:** 309 ATTR (66% ATTRwt), FEVIr: 34%
- **MIAMI:** 84 AC (37 ATTRwt, 31 ATTRv, 16 AL)

	ACEi/ARBs/ARNI	BETABLOCKERS	MRAs
(a) AMIGAL (2022)	-	↓ All cause mortality	-
(b) LONDON (2023)	No benefit	↓ All cause mortality in LVEF ≤40	↓ All cause mortality
(c) COLUMBIA (2022)	No benefit	No benefit	No benefit
(d) MIAMI (2023)	No benefit	No benefit	No benefit

(a) Barge-Caballero G, et al. Mayo Clin Proc. 2022;97(2):261-273.
(b) Ioannou A, et al. Eur Heart J. 2023;44:2893-2907.
(c) Cheng RK, et al. J Am Heart Assoc. 2021;10:e022859.
(d) Yan CL, et al. Am J Cardiol. 2023;204:360-365.

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS: HEART FAILURE

DRUGS: *Published Data on 27/09/2024*

- **AMIGAL:** 128 ATTR (89,8% ATTRwt), FEVIr: 23%
- **LONDON:** 2371 ATTR (77,6% ATTRwt), FEVIr: 22,4%
- **PISA:** 99 CA (63 ATTRwt, 33 AL, 3 ATTRv), FEVIr: 16%
- **MIAMI:** 84 AC (37 ATTRwt, 31 ATTRv, 16 AL)
- **ATHENS:** 236 AL

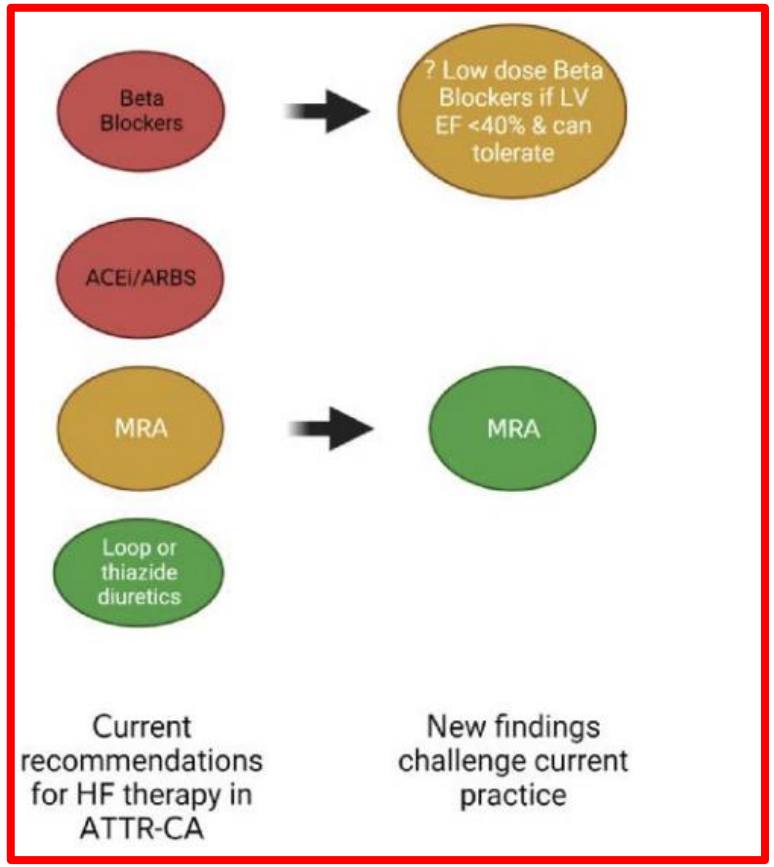
	ACEi/ARBs/ARNI	BETABLOCKERS	MRAs
(a) AMIGAL (2022)	-	75%	-
(b) LONDON (2023)	67%	78%	92%
(c) PISA (2020)	100%	93%	100%
(d) MIAMI (2023)	78%	79%	84%
(e) ATHENS (2022)	-	53%	-

% of patients who continued treatment (low-intermediate doses)

(a) Barge-Caballero G, et al. Mayo Clin Proc. 2022;97(2):261-273.
(b) Ioannou A, et al. Eur Heart J. 2023;44:2893-2907.
(c) Aimo A, et al. Eur J Intern Med. 2020;80:66-72.
(d) Yan CL, et al. Am J Cardiol. 2023;204:360-365.
(e) Briasoulis A, et al. Amyloid. 2022;29:31-37.

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS: HEART FAILURE

DRUGS: *Expert Recommendations*



	ACEi/ARBs/ARNI	BETABLOCKERS	MRAs
(a) AMIGAL (2022)	-	↓ All cause mortality	-
(b) LONDON (2023)	No benefit	↓ All cause mortality in LVEF ≤40	↓ All cause mortality
(c) COLUMBIA (2022)	No benefit	No benefit	No benefit
(d) MIAMI (2023)	No benefit	No benefit	No benefit

(c) Cheng RK, et al. J Am Heart Assoc. 2021;10:e022859.

Cheng RK, et al. Eur Heart J. 2023;44:2908-2910.

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS: HEART FAILURE

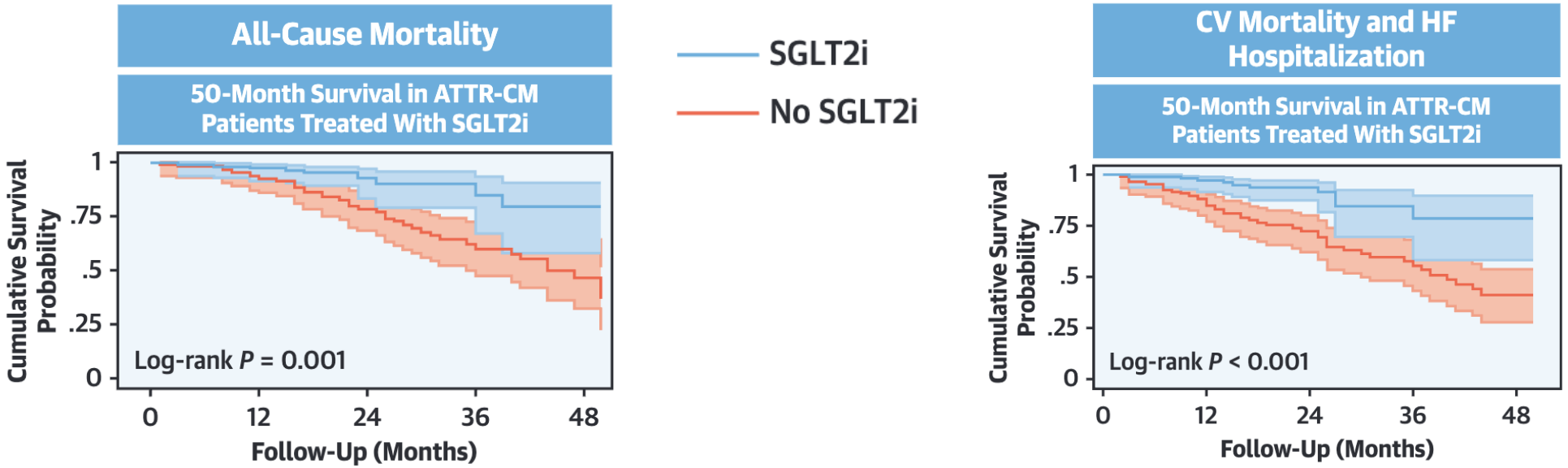
DRUGS: *Published Data on 27/09/2024*

440 patients with ATTR-CA (80,7% ATTRwt)

220 with SGLT2i (dapagliflozin 67,3%) **vs 220 propensity-matched controls**

Mean age: 77 years / **Mean LVEF:** 46% / **HFrEF:** 34%

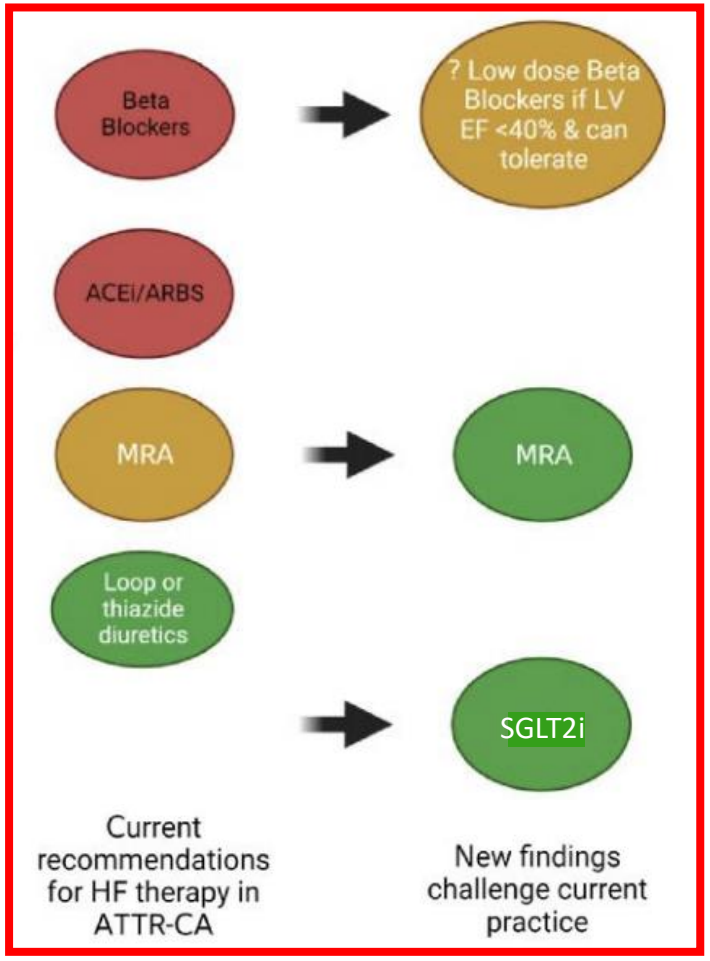
95.5% patients continued treatment



Porcari A, et al. J Am Coll Cardiol. 2024;83:2411-2422.

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS: HEART FAILURE

DRUGS: *Expert Recommendations*



Modified from Cheng RK, et al. Eur Heart J. 2023;44:2908-2910.

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS: HEART FAILURE

DRUGS: *A Coruña Heart Failure Unit Recommendation*

- Try to treat heart failure due to ATTR-CA (especially ATTRwt) with standard drugs (quadruple therapy in HFrEF)

- This strategy does not seem reasonable in AL-CA: lack of evidence and worse tolerability

- Slow titration, accept low-intermediate doses; maintain treatment if tolerated

- Close monitoring of side effects

- Remember: evidence in favor of using these drugs in cardiac amyloidosis is scarce, but evidence against it is weaker and there is no data that demonstrates their harm

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS: HEART FAILURE

Resultados

154 pacientes dx ATTR-CM entre 2018 y 2023 en CHUAC

127 (82,5%) FEVI > 40%

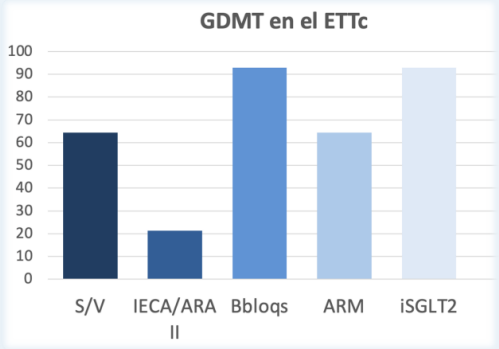
27 (17,5%) ATTR-CM-rEF

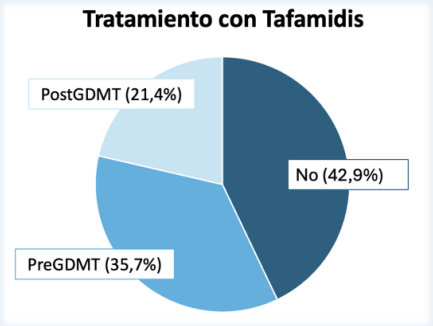
13 sin ETTc y/o GDMT

14 GDMT + ETTc en el seguimiento

Al diagnóstico…
Edad media: 81,9±4,5 años
13 (92,9%) varones.
Todos ATTRwt
FEVI media al dx 35 ± 4,7%
NTproBNP medio al dx 3671±2321pg/mL

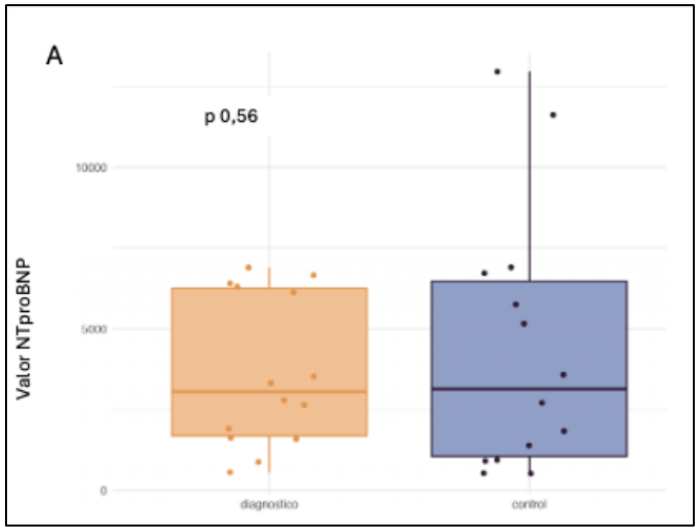
En el seguimiento…
11 (78,6%) mejoría FEVI
6 (42,9%) mejoría NT
5 (35,7%) hTA
6 (42,9%) hiperK+ leve
3 (21,4%) fallecidos
5 (35,7%) ingreso por IC
3 (21,4%) IC ambulatoria

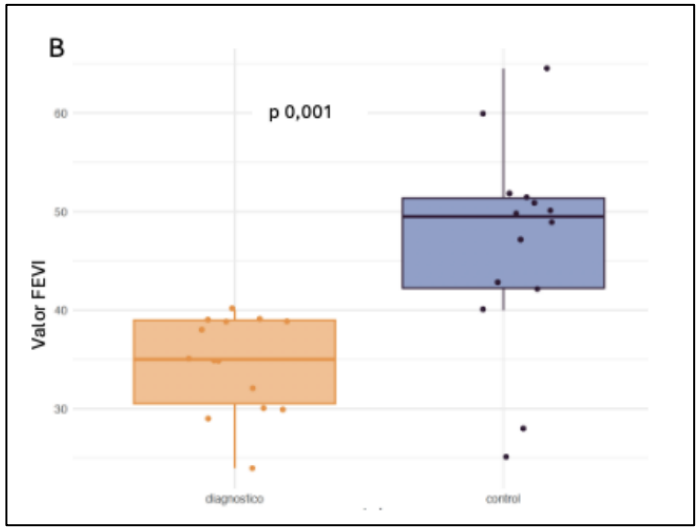




Discontinuation

- *ACEi/ARB/ARNI:* 33.3%
- *Betablockers:* 7.7%
- *MRA:* 33.3%
- *SGLT2i:* 0%





A Coruña Heart Failure Academy

Antúnez-Ballesteros M, et al. Abstract from SOGACAR 2024 Meeting

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS

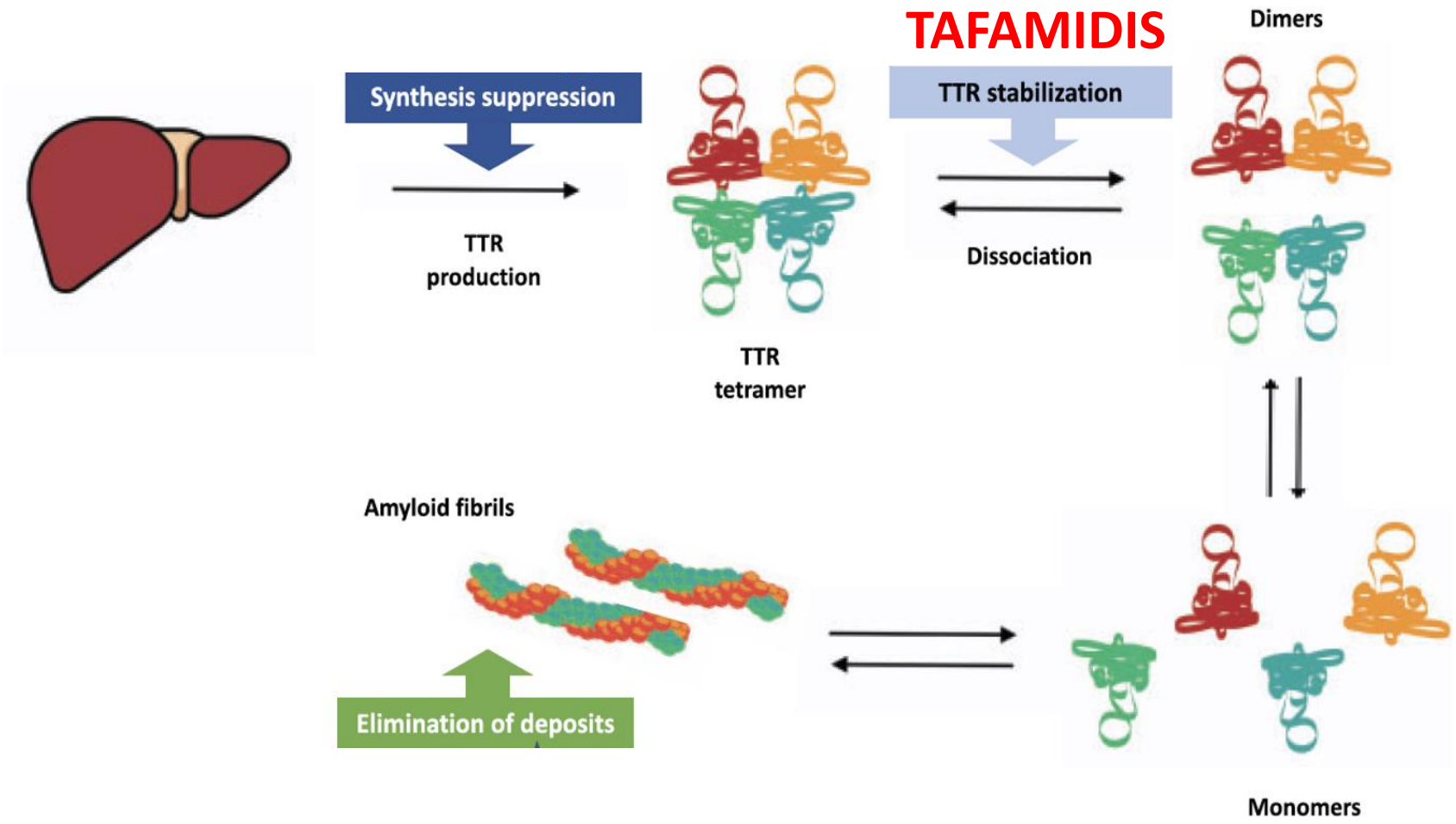
- Heart Failure
- Atrial Fibrillation – Embolic risk
- Conduction disorders
- Ventricular arrhythmias
- Aortic stenosis

GENERAL TREATMENT OF CARDIAC AMYLOIDOSIS: ATRIAL FIBRILLATION

2a	C-LD	2. In patients with cardiac amyloidosis and AF, anticoagulation is reasonable to reduce the risk of stroke regardless of the CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke or transient ischemic attack [TIA], vascular disease, age 65 to 74 years, sex category) score (103,104).

Rapezzi C, et al. J Am Coll Cardiol 2022;79:1288–1303/ Heidenreich PA, et al. J Am Coll Cardiol. 2022 May 3;79(17):1757-1780.

SPECIFIC TREATMENT OF ATTR CARDIAC AMYLOIDOSIS



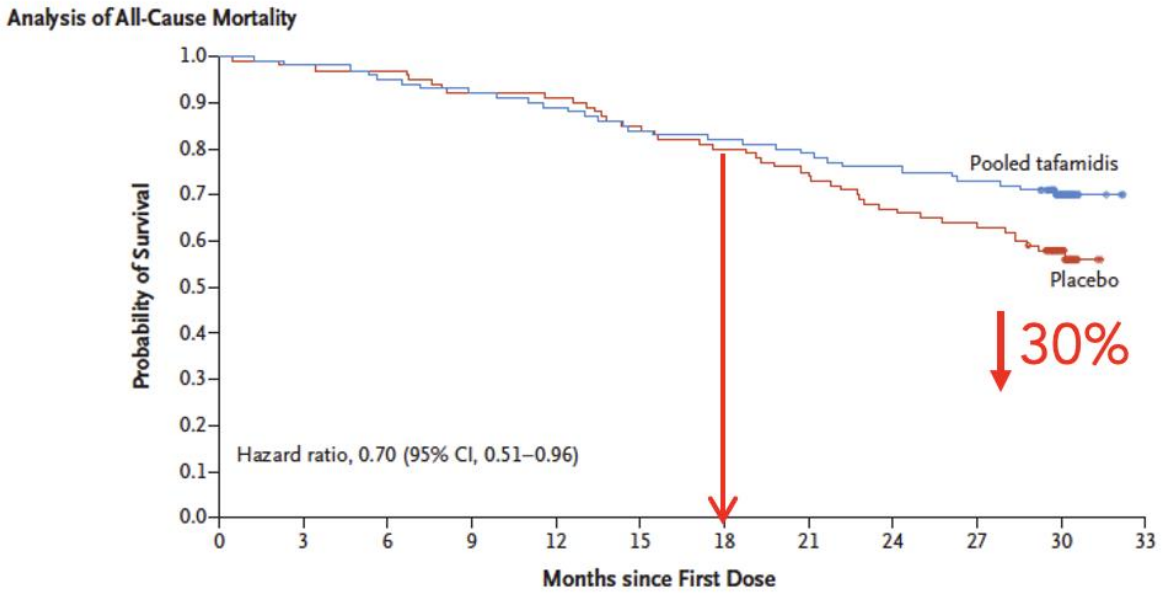
SPECIFIC TREATMENT OF ATTR CARDIAC AMYLOIDOSIS: TAFAMIDIS

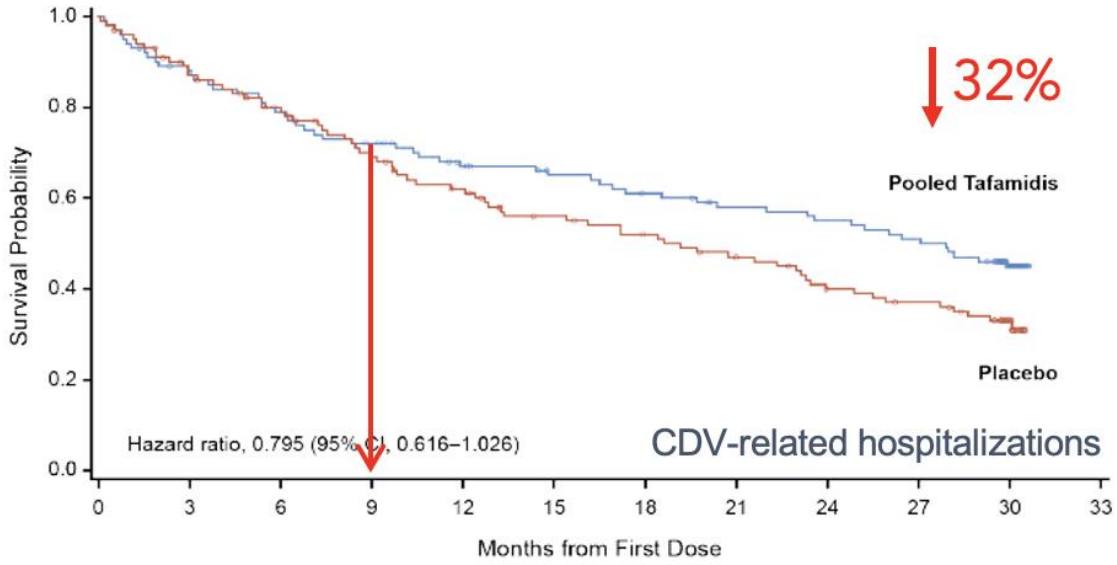
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy

* n=441 ATTRwt-CA (76%) – ATTRv-CA (24%)
* Tafamidis meglumine 80mg vs 20 mg vs placebo
* 30 months
* Mean age: 74 yo
* NYHA I-III (60% NYHA II)



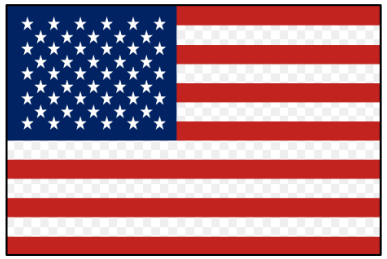


A Coruña Heart Failure Academy

Maurer MS, et al. N Engl J Med. 2018;379(11):1007-1016.

SPECIFIC TREATMENT OF ATTR CARDIAC AMYLOIDOSIS: TAFAMIDIS

HEART FAILURE GUIDELINES RECOMMENDATIONS

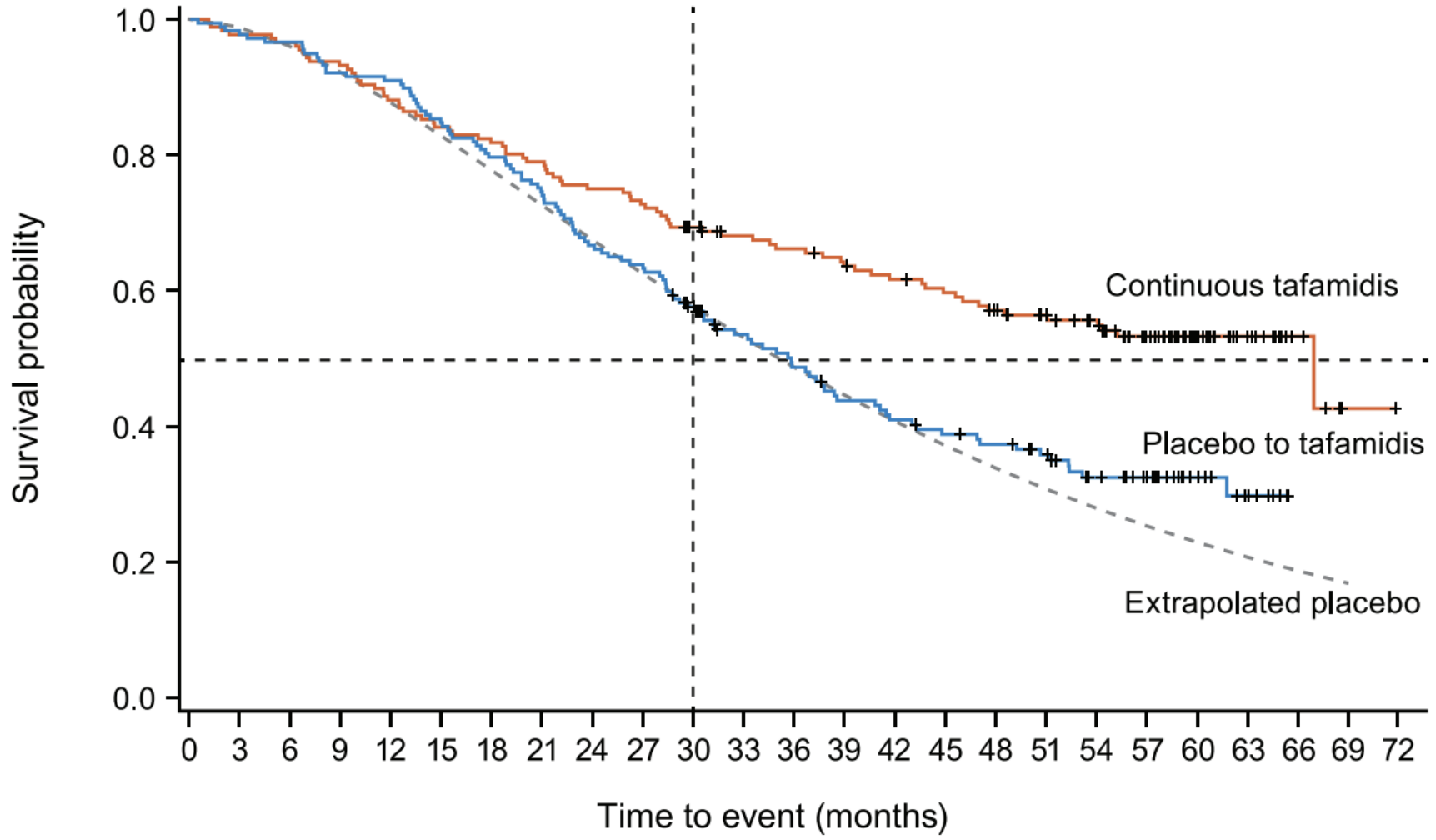


1	B-R	1. In select patients with wild-type or variant transthyretin cardiac amyloidosis and NYHA class I to III HF symptoms, transthyretin tetramer stabilizer therapy (tafamidis) is indicated to reduce cardiovascular morbidity and mortality (102).

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.	I	B
Tafamidis is recommended in patients with wtTTR-CA and NYHA class I or II symptoms to reduce symptoms, CV hospitalization and mortality.	I	B

Heidenreich PA, et al. J Am Coll Cardiol. 2022 May 3;79(17):1757-1780 / McDonagh TA, et al. Eur Heart J. 2021;42:3599-3726.

SPECIFIC TREATMENT OF ATTR CARDIAC AMYLOIDOSIS: TAFAMIDIS



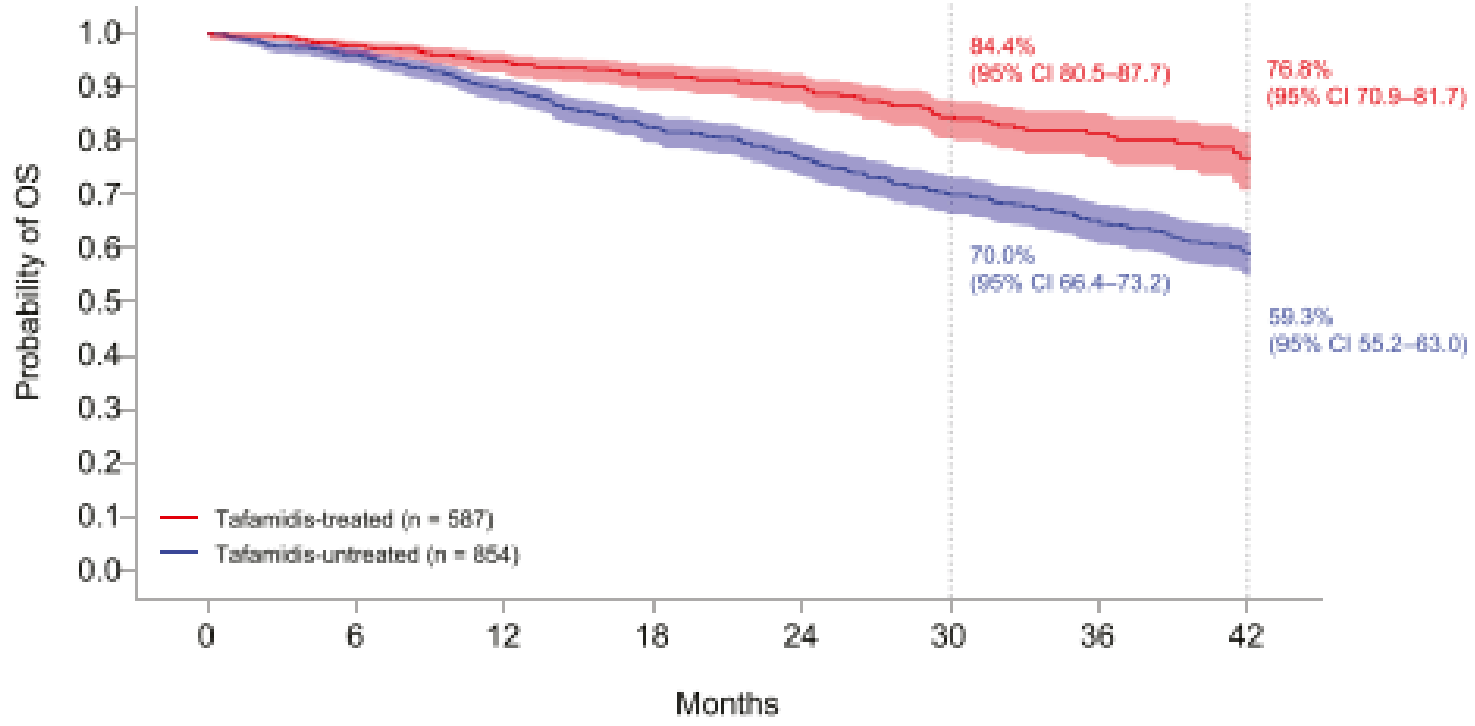
Elliott P, et al. Circ Heart Fail. 2022;15:e008193.

SPECIFIC TREATMENT OF ATTR CARDIAC AMYLOIDOSIS: TAFAMIDIS

Data from THAOS (TranstHyretin Amyloidosis Outcomes Survey) **real-world registry**

587 with tafamidis **vs 854** without tafamidis

Median age: 77 years **/** 87.8% **ATTRwt**



García-Pavía P, et al. J Card Fail. 2024:S1071-9164(24)00222-7.

SPECIFIC TREATMENT OF ATTR CARDIAC AMYLOIDOSIS: TAFAMIDIS

Available in Spain from june 2023 for the treatment of ATTRwt/ATTRv-CA

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-III 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
   - si ATTRh-CM poderase iniciar tratamento si idade ≥ 45
     -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

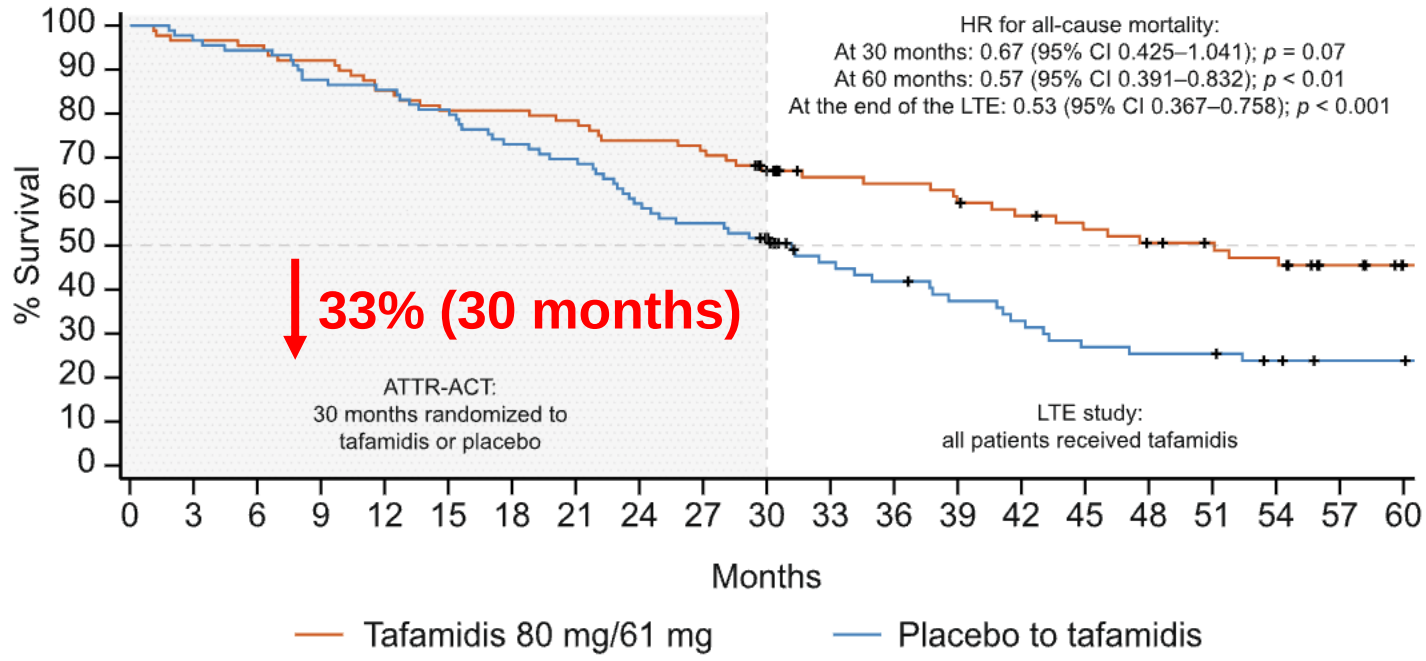
Deberan cumprimentarse todos os datos deste anexo asi como a data, para ser valorado o financiamento do tratamento polos Servizos de Farmacia correspondentes.

	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

SPECIFIC TREATMENT OF ATTR CARDIAC AMYLOIDOSIS: TAFAMIDIS

Long-term tafamidis efficacy in patients with transthyretin amyloid cardiomyopathy by baseline left ventricular ejection fraction



FEVI <50%

Drachman B, et al. Eur J Heart Fail. 2024 Jun 26. doi: 10.1002/ejhf.3330. Online ahead of print.

TAKE-HOME MESSAGES

- ✓ If cardiac amyloidosis (CA) is **suspected**, a **scintigraphy** and **haematologic tests** to assessment for a monoclonal protein are recomended
- ✓ Results of these tests can reasonably **rule out CA**, **diagnose ATTR-CA** or suggest **histological exams**
- ✓ General treament of CA focuses on management of clinical manifestations due to cardiac involvement
- ✓ How to treat heart failure due to CA is currently the most controversial issue of its treament. **We** recommend trying to use standard drugs in patients with ATTR-CA (especially ATTRwt-CA) as in other heart diseases
- ✓ **Tafamidis** is currently the only drug approved for the specific treatment of ATTR-CA