Actualités sur la prise en charge de l'amylose cardiaque en Gériatrie

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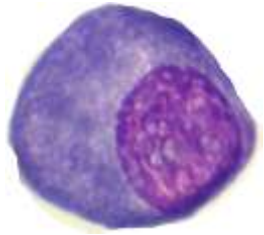
Liens d'intérêts

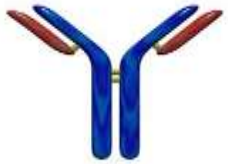
Société	Type d'affiliation	Période
Novartis	Consulting, Formations	En cours
Vifor	Consulting	2020-2022
Pfizer	Consulting, Formations, Boards	En cours
Astra Zeneca	Consulting, Formations, Boards	En cours
Boehringer	Formations	En cours

Différents types d'amyloses cardiaques



Clone lympho ou plasmocytaire

MGUS, myélome, lymphome…



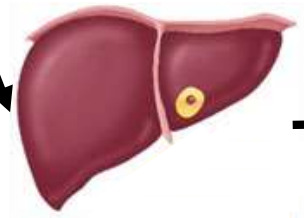
Chaînes légères d'Ig

Lambda > kappa

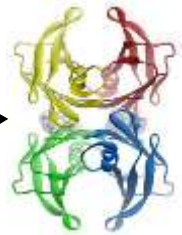
Apolipo

AL

Dépôts de fibrilles amyloïdes



Foie



TTR

Tétramérique

Dissociation

TTR

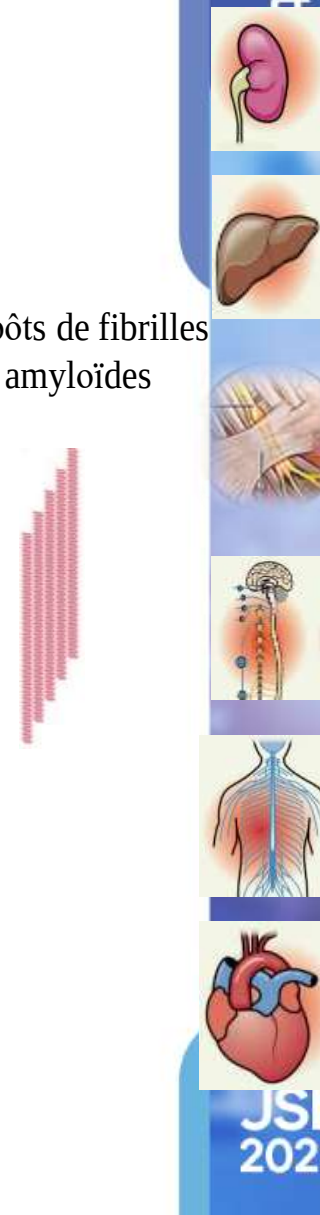
monomérique

Mutation TTR -

Mutation TTR +

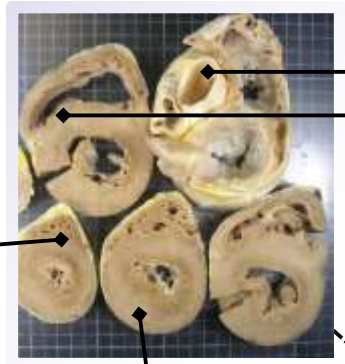
ATTR sauvage (sénile)

ATTR mutée



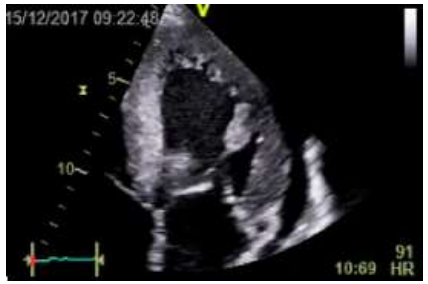
Conséquences cardiologiques

± Neuropathie périphérique sensitivo-motrice, symétrique et longueur dépendante



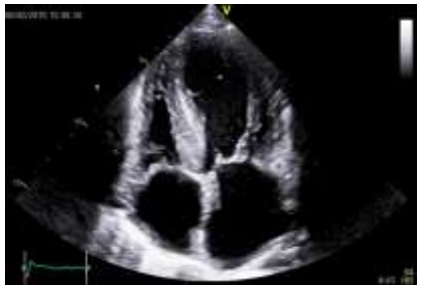
Myocarde

Ventriculaire



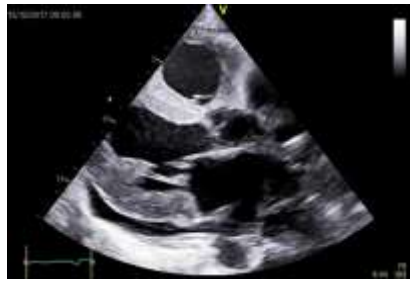
↗ Epaisseur
↗ Rigidité
Dysfct diastolique
Dysfct systolique
➔ **CMH** concentrique biventriculaire
➔ **CMR**
➔ **Insuffisance cardiaque**

Atrial



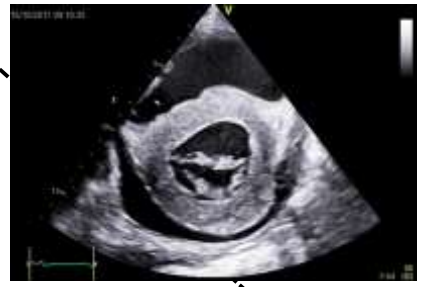
Dilatation bi-atriale
Infiltration SIA
↘ systole atriale
➔ **Emboles**, AVC ; AIT
➔ **TSV**

Péricarde



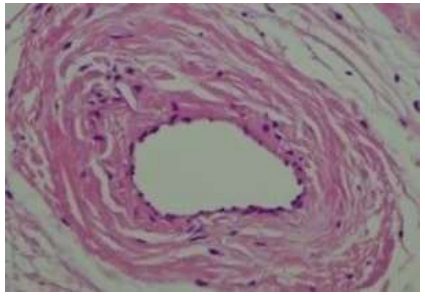
Ep. péricardique
Tamponnade

Endocarde



IM, IT
RAC

Vaisseaux



Ischémie
Nécrose
➔ DT atypique ; ↗ troponine

Tissus conductif

BAV, BSA, BB
➔ **Syncope**

SNA

↘ FC
hTOS
➔ Insuffisance chronotrope
➔ **Malaises** à l'orthostatisme

Conséquences cardiologiques

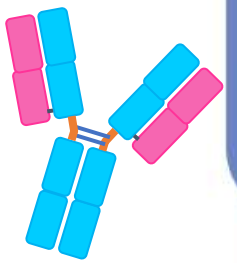
Examens morphologiques à la recherche d'arguments en faveur : ECG, ETT, IRM

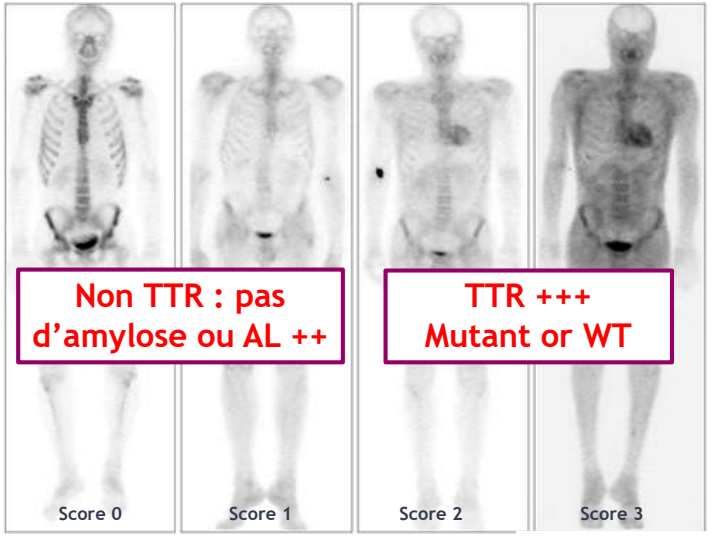
↓

Scintigraphie osseuse
(HMDP, DPD, PYP)

&

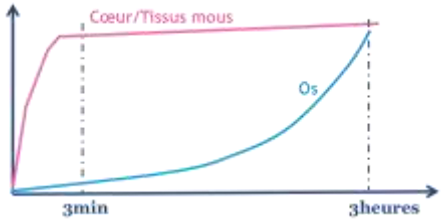
Bilan de gammapathie monoclonal complet
- EPP, IF
- EPU, IEPU (= Bence Jones)
- Dosage des chaînes légères libres circulantes



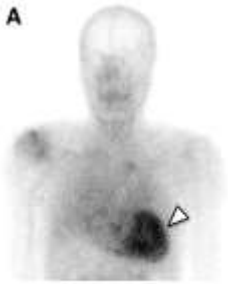


Pas de fixation cardiaque & fixation osseuse normale

Score visuel de Perugini : en faveur d'une ATTR si ≥ 2



ou



Forte fixation cardiaque & extinction de la fixation osseuse

Ratio (précoce) cœur / mediastin : en faveur d'une ATTR > 1,2

Electrophorèse des protides sériques : pic, hypogamma, normale

Immunofixation : plus sensible que l'électrophorèse

Dosage des chaines légères libres sériques : plus sensible que l'immunofixation. Dépend du niveau de production (plasmocyte) et d'élimination (rein)

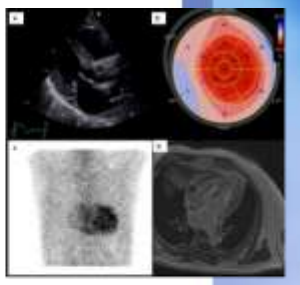
Recherche d'une protéinurie de Bence Jones

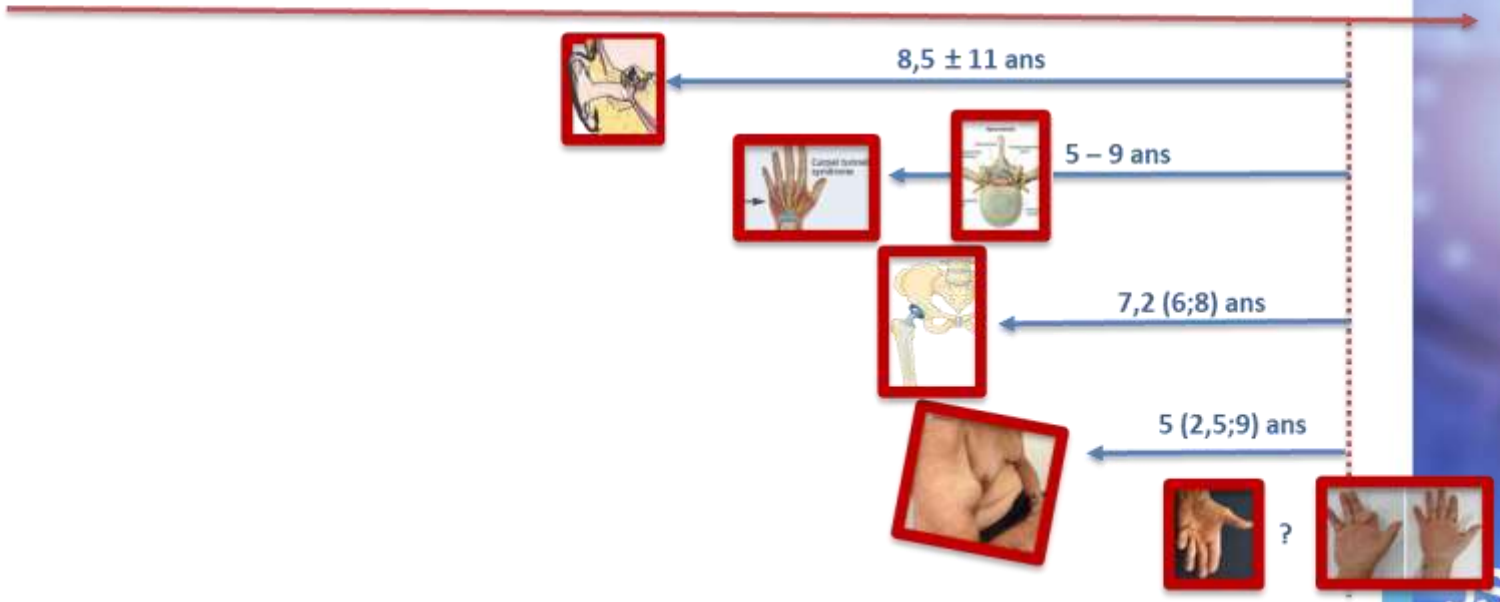
Perugini et al., JACC 2005 Sep 20;46(6):1076-84 ; Galat A et al JACCardioVasc Imaging 2016

Amylose à transthyrétine sauvage

- Age d'apparition des symptomes cardiaques : 78 ans
- Symptômes extra-cardiaques (canal carpien ++) 5 à 10 ans avant
- Hommes 90%

- Prévalence sous-estimée
  - Dépôts d'amylose TTR sauvage ≈ 25% des plus de 80 ans (séries autopsiques)





- Mais de plus en plus reconnue

Tanskanen et al., Ann Med. 2008;40(3):232-9

Spécificités du traitement non spécifique

CHADS-TOP

Conduction

Mort subite : très fréquente quelque soit le type d'amylose : dissociation électro-mécanique, parfois TV/FV

Prévalence élevée des **troubles conductifs**

➔ **Discussion implantation PM / DAI sur troubles conductifs de bas degré / sévérité**

Haute FC

Débit cardiaque = FC x VES

Cardiopathie restrictive donc VES constant : fréquence dependance pour augmenter le débit

➔ **Pas de bradycardisant (sauf amiodarone), PM pour insuffisance chronotrope**

Anticoagulation

Risque cardio-embolique élevé (même en rythme sinusal) ➔ **rechercher les indication à une anticoagulation (sd néphrotique, ATCD cardioembolique, profil mitral restrictif)**

Dosage facteur X pour pondérer le risque hémorragique

Diurétiques

Nécessaire pour la congestion mais marge thérapeutique étroite compte tenu du risque de dysautonomie

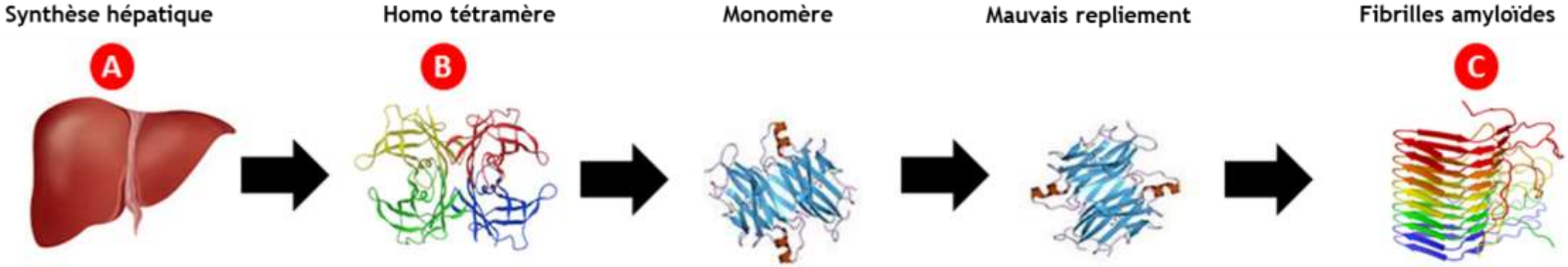
S-TOP BB, IEC, ….

Arrêt des traitements potentiellement délétères :

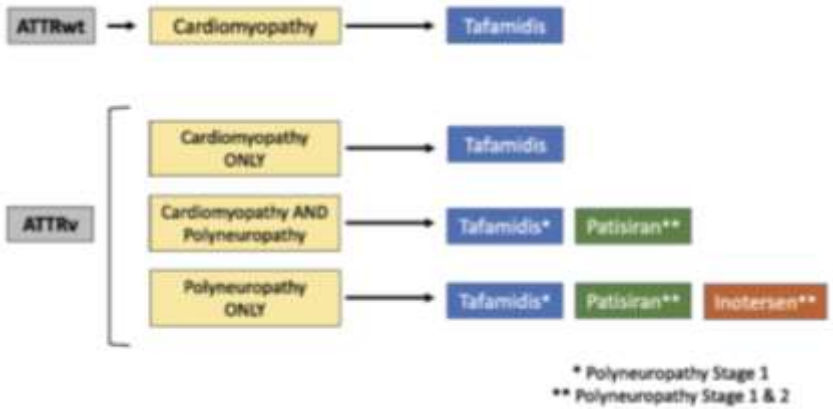
BB (bradycardie, inotrope -), Hypotenseurs (dysautonomie),

Digoxine (accumulation dans les fibrilles amyloïdes), Sacub/Valsartan

Traitement spécifique - amylose ATTR



- **A** **Supprimer la TTR amyloidogénique** → siRNA : ARN interférant (ATTRwt et ATTRv) : APPOLLO B
- **B** **Stabiliser le tétramère** → Stabilisateur du tétramère : tafamidis RTU initiale, AMM 06/2021
- **C** **Dégrader les fibrilles amyloïdes** → AC anti TTR : études en cours



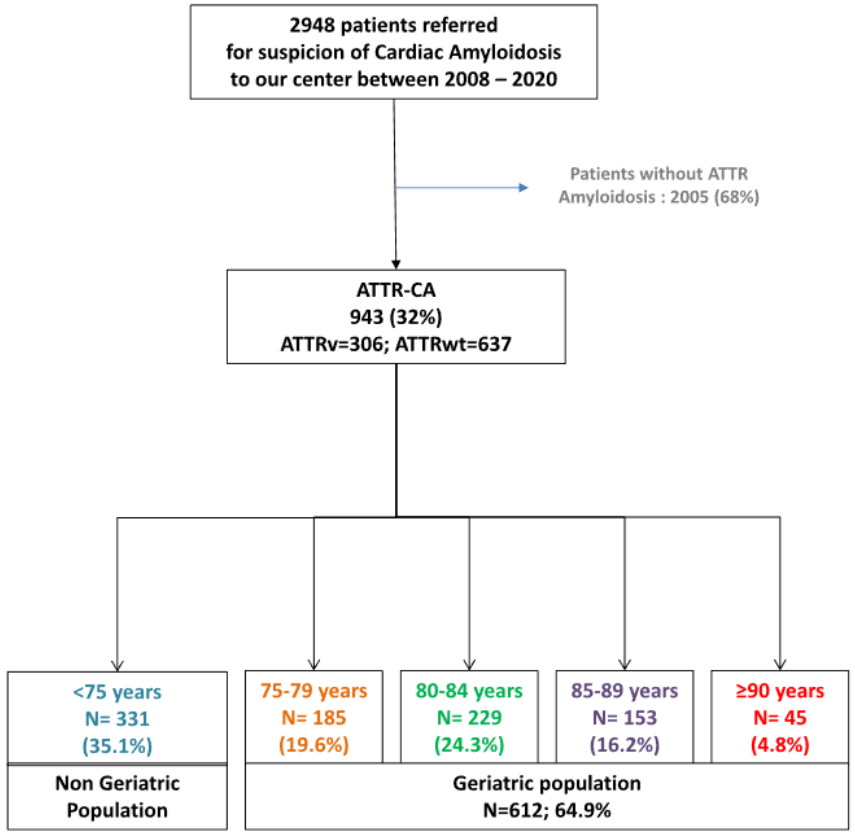
Garcia Pavia et al. Eur Heart J. 2021 Apr 21;42(16):1554-1568.

ESC HEART FAILURE
ESC Heart Failure (2024)
Published online in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/ehf2.14793

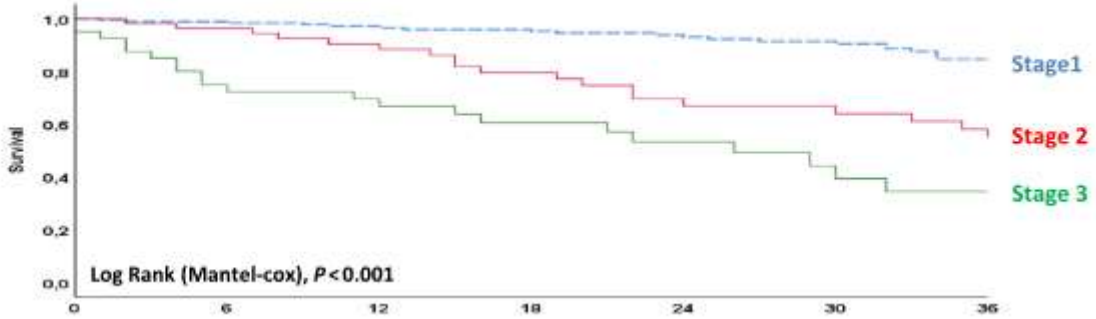
ORIGINAL ARTICLE

Phenotype and prognostic factors in geriatric and non-geriatric patients with transthyretin cardiomyopathy

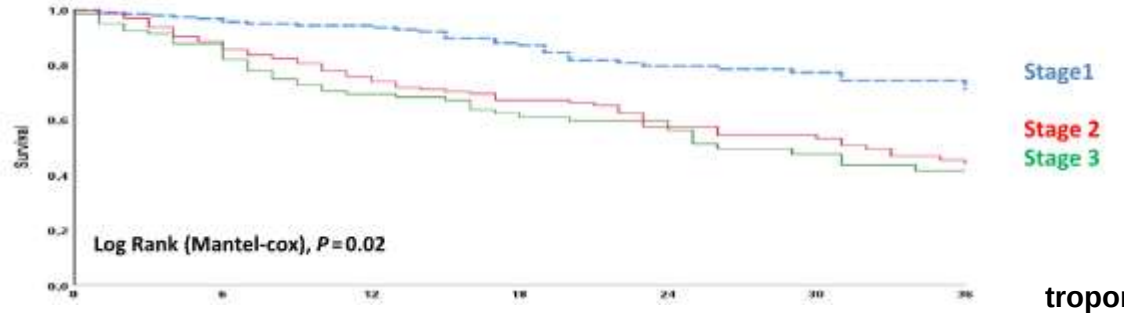
Eugenia Volpentesta[1,2], Mounira Kharoubi[3,4,5,6], Cristiano Donadio[2], Kahina Rebia[3,4], Pascale Fanen[7], Benoit Funalot[5,7], Thierry Gendre[8,9], Vincent Audard[8,10], Florence Canoui-Poitrine[6,11,12], Emmanuel Itti[8,12,13], Emmanuel Teiger[3,4,5,6], Violaine Planté-Bordeneuve[8,9], Silvia Oghina[3,4], Denis Tixier[3,4], Sophie Mallet[3,4], Amaury Broussier[11,15], Thibaud Damy[3,4,5,6,11]* and Amira Zaroui[3,4,5,6,11]



(A-i) NAC - Non Geriatric population

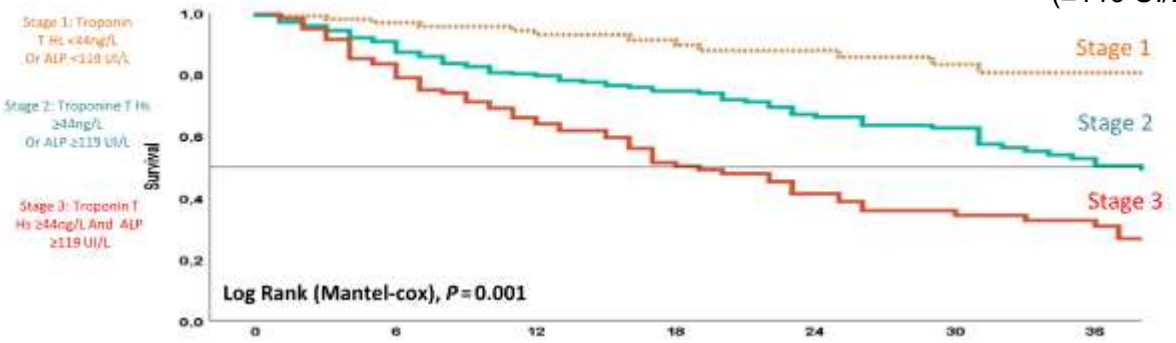


(A-ii) NAC - Geriatric population



troponin T hs (≥44 ng/L) and **ALP levels** (≥119 UI/L)

(B) New Geriatric cardiac amyloidosis staging (GCA) : for Geriatric pulation



Volpentesta et al. 2024

Journal of Clinical Medicine
MDPI

Article

Estimating the Prevalence of Cardiac Amyloidosis in Old Patients with Heart Failure—Barriers and Opportunities for Improvement: The PREVAMIC Study

Revista Española de Geriatría y Gerontología

ORIGINAL ARTICLE

Prevalence of transthyretin cardiac amyloidosis in elderly patients diagnosed with heart failure

- A total of 453 patients ≥ 65 years with HF and an interventricular septum or posterior wall thickness > 12 mm were included.
- All patients underwent a 99mTc-DPD/PYP/HMDP scintigraphy and monoclonal bands were studied, following the current criteria for non-invasive diagnosis.

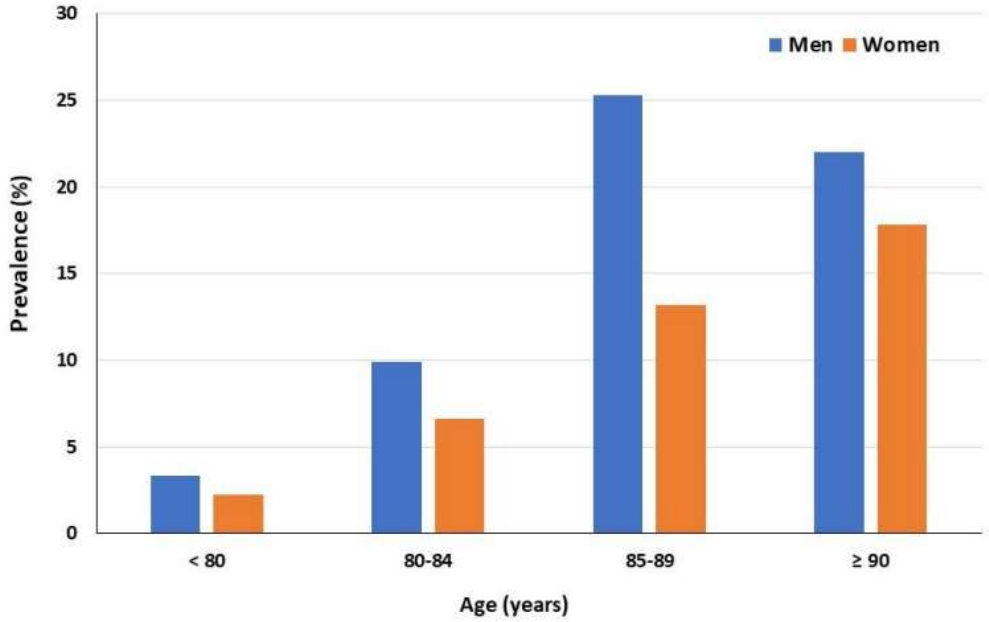
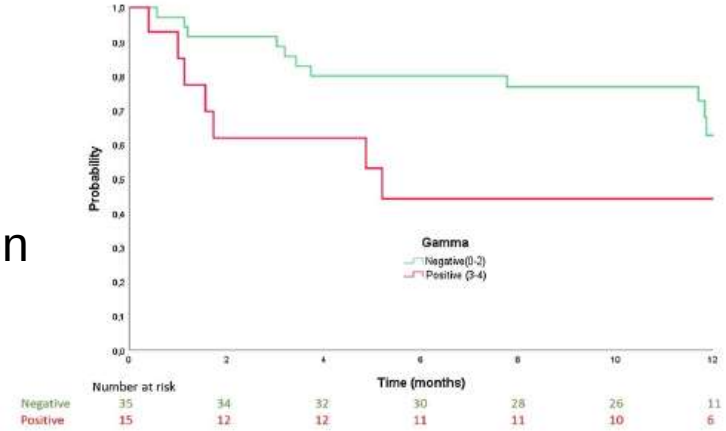


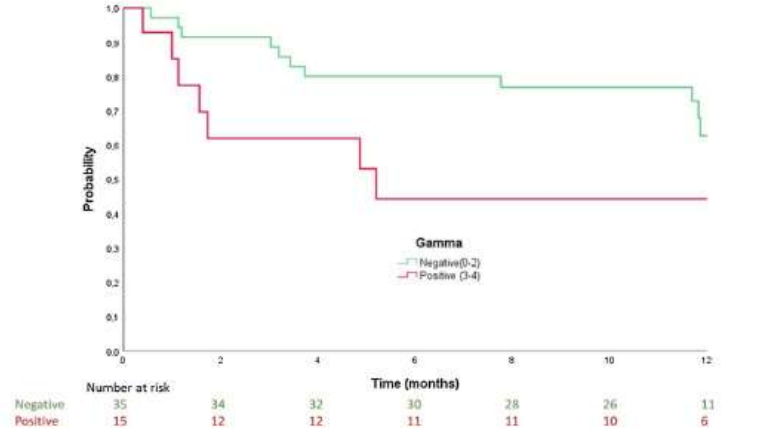
Figure 2. Cardiac amyloidosis prevalence according to age and sex.

The prevalence was **20.1%.** Most of the CA were transthyretin (**ATTR-CM**, 84.6%), with a minority of cardiac light-chain amyloidosis (AL-CM, 2.2%).

Death and HF Readmission



HF Readmission



Ruiz-Hueso, JCM 2023

Jaramillo-Hidalgo et al. Revista Española de Geriatría y Gerontología 2023

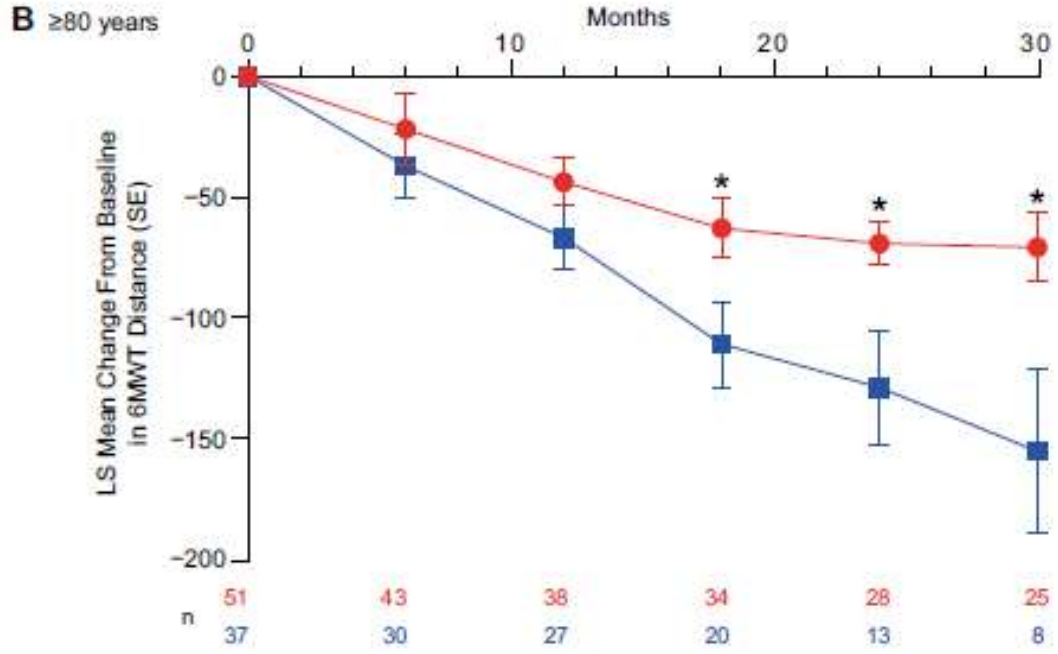
JSB 2025

JACC: HEART FAILURE VOL. ■, NO. ■, 2023

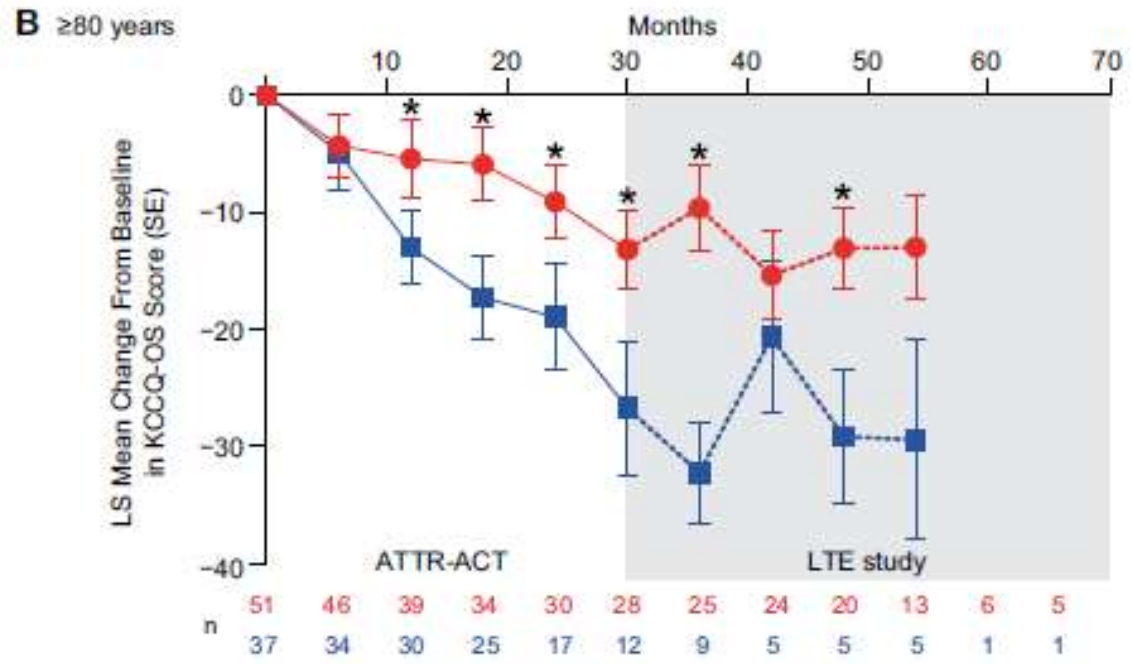
Tafamidis Efficacy Among Octogenarian Patients in the Phase 3 ATTR-ACT and Ongoing Long-Term Extension Study

Pablo Garcia-Pavia, MD, PhD,[a,b,c] Marla B. Sultan, MD, MBA,[d] Balarama Gundapaneni, MS,[e] Yoshiki Sekijima, MD,[f] Federico Perfetto, MD,[g] Mazen Hanna, MD,[h] Ronald Witteles, MD[i]

Patients aged ≥80 years
51 received tafamidis and 37 received placebo



6-MWT



Quality of life

Garcia Pavia et al. JACC HF 2023

12e édition

JSB 2025

JACC: HEART FAILURE
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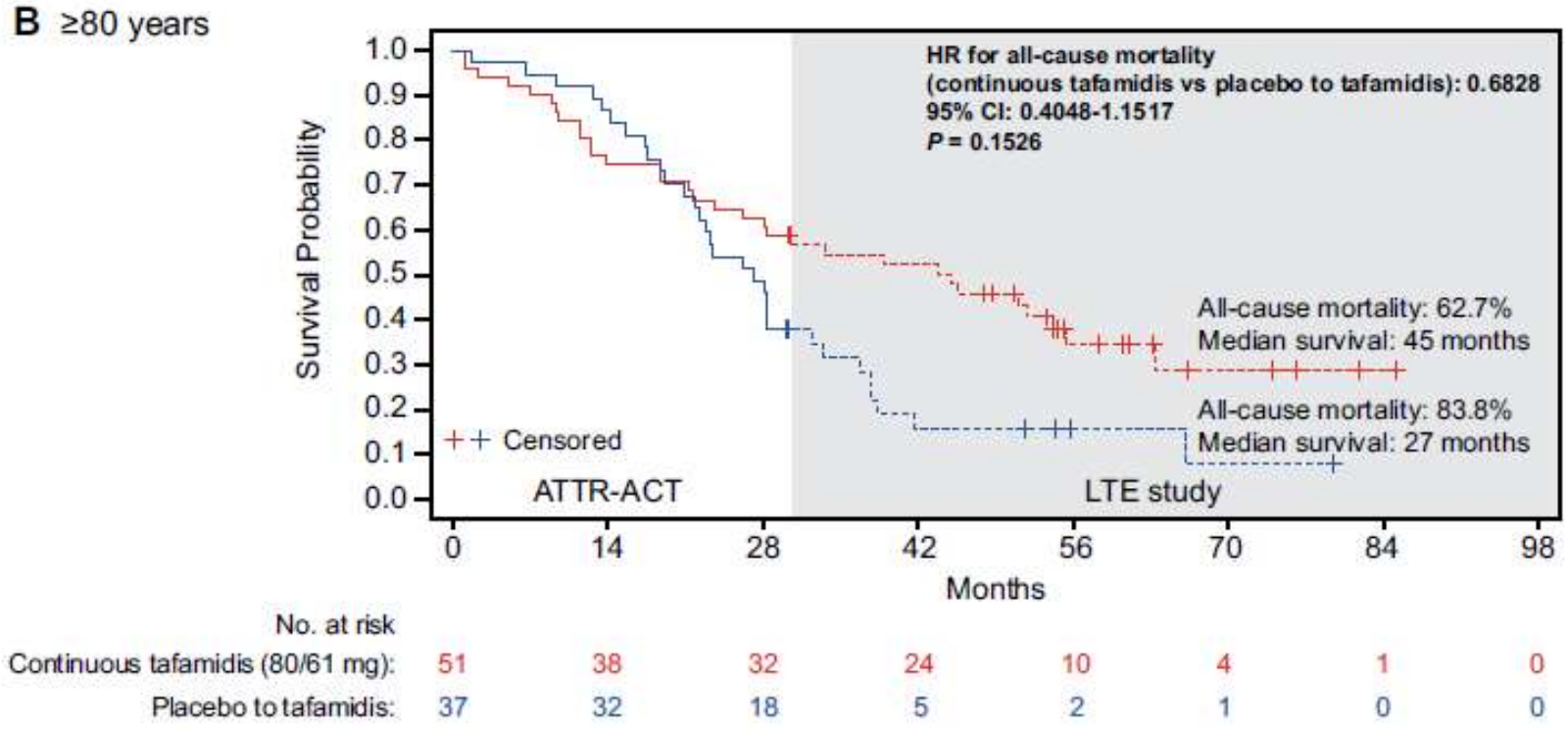


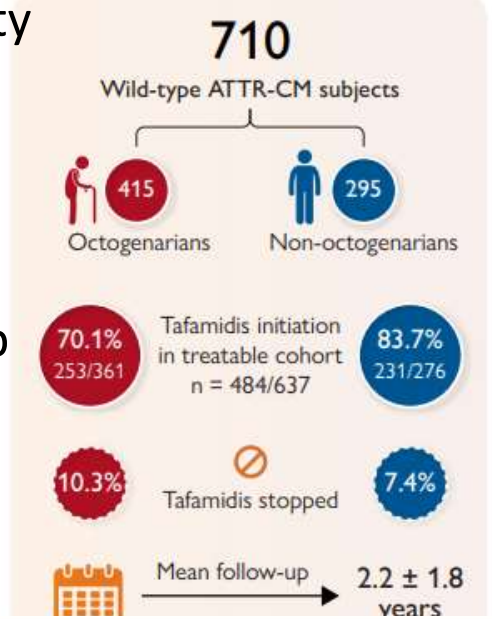
Garcia Pavia et al. JACC HF 2023

ESC European Heart Journal (2025) 46, 1057–1070 https://doi.org/10.1093/eurheartj/ehae923
CLINICAL RESEARCH Heart failure and cardiomyopathies

Tafamidis in octogenarians with wild-type transthyretin cardiac amyloidosis: an international cohort study

	Overall cohort $n = 710$	Non-octogenarians $n = 295$	Octogenarians $n = 415$	*P*-value
Demographics				
Age, years	[710] 81 ± 7	[295] 74 ± 5	[415] 85 ± 4	<.001
Male	566/710 (79.7%)	258/295 (87.5%)	308/415 (74.2%)	<.001

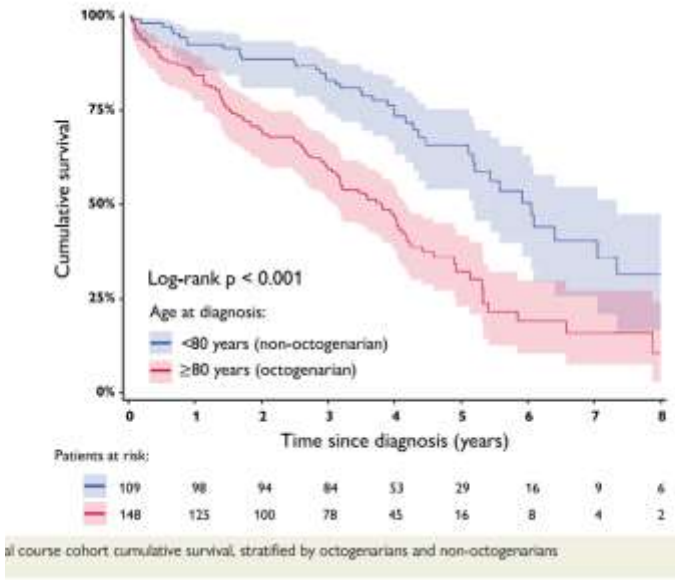
- The impact of tafamidis treatment on mortality in real-world wild-type transthyretin cardiomyopathy octogenarians was studied.
- An international, multicentre cohort study of 710 consecutive wild-type transthyretin cardiomyopathy patients with mean follow-up of 2.2 ± 1.8 years for all-cause mortality endpoint was performed.
- 58.5% (415/710) octogenarians (85 ± 4 years, 74.2% male)



We demonstrated **poor overall survival** in untreated octogenarians with high 1- and 5-year mortality rates of 16% and 71%, respectively, and a median survival of 3.8 years

Table 3 Reasons for tafamidis discontinuation in treated patients

Principal reason	Overall $n = 43$	Non-octogenarians $n = 17$	Octogenarians $n = 26$
Progressive disease, advanced heart failure	17 (39.5%)	7 (41.2%)	10 (38.5%)
Undefined reason	8 (18.6%)	2 (11.8%)	6 (23.1%)
Comorbidities, cognitive decline and/or frailty	5 (11.6%)	2 (11.8%)	3 (11.5%)
Advanced age, presumed futility	3 (7.0%)	0 (0.0%)	3 (11.5%)
Side-effects	7 (16.3%)	4 (23.5%)	3 (11.5%)
Patient preference	2 (4.7%)	2 (11.8%)	0 (0%)
Early disease stage, no heart failure	1 (2.3%)	0 (0.0%)	1 (3.8%)



l course cohort cumulative survival, stratified by octogenarians and non-octogenarians

Debonnaire et al. EHJ 2025

ESC European Society of Cardiology
CLINICAL RESEARCH
Heart failure and cardiomyopathies

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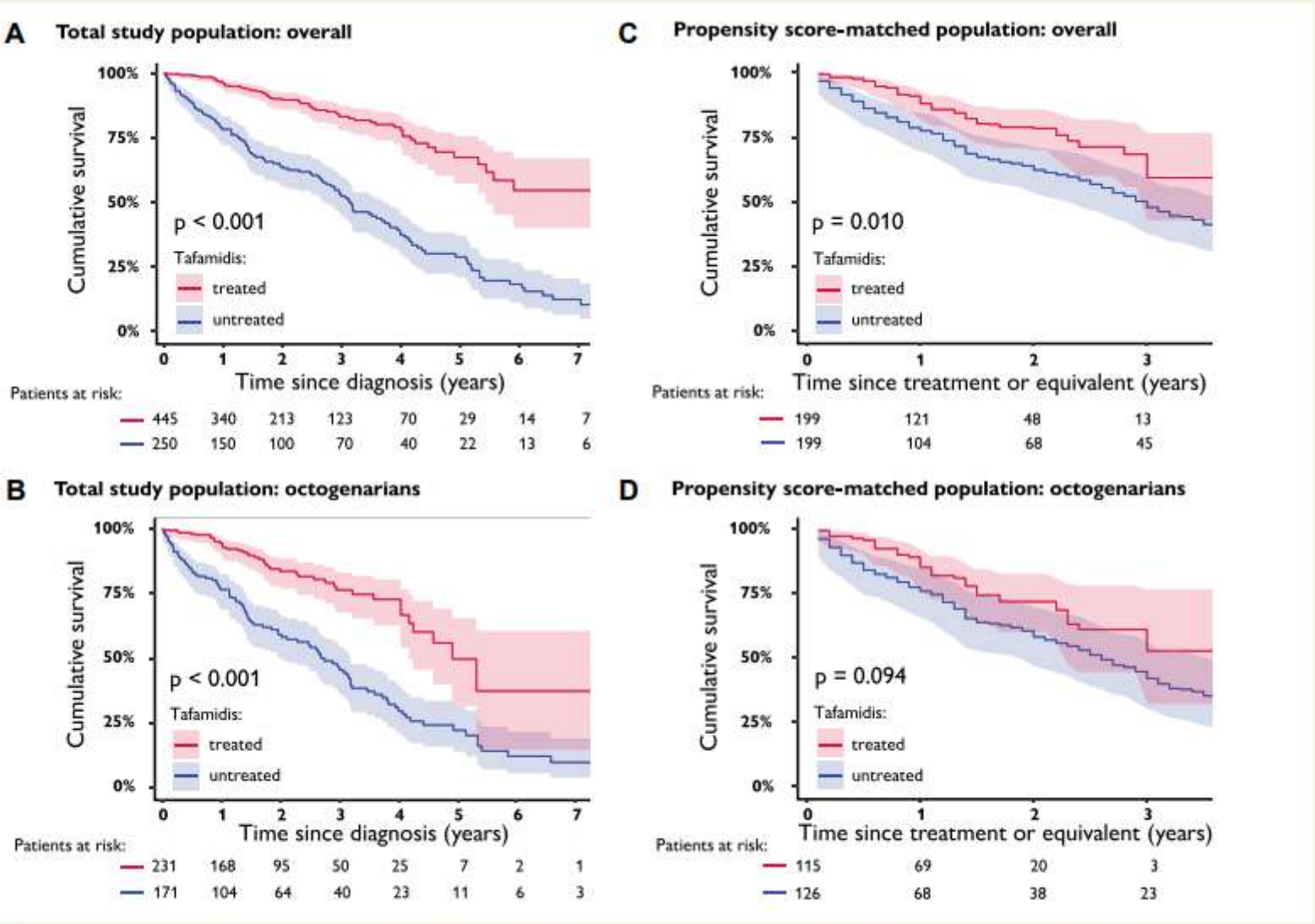

Figure 3 Cumulative survival in tafamidis treated vs. untreated patients. Total patient population. (*A*) Overall cohort. (*B*) Octogenarian cohort. Propensity score-matched population, with patients at risk from the first imputation. (*C*) Overall cohort. (*D*) Octogenarian cohort

Propensity score matching on baseline variables, including **age, National Amyloidosis Centre stage, and New York Heart Association class**

Debonnaire et al. EHJ 2025

ESC European Society of Cardiology European Heart Journal (2025) 46, 1057–1070 https://doi.org/10.1093/eurheartj/ehae923

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Heart failure and cardiomyopathies

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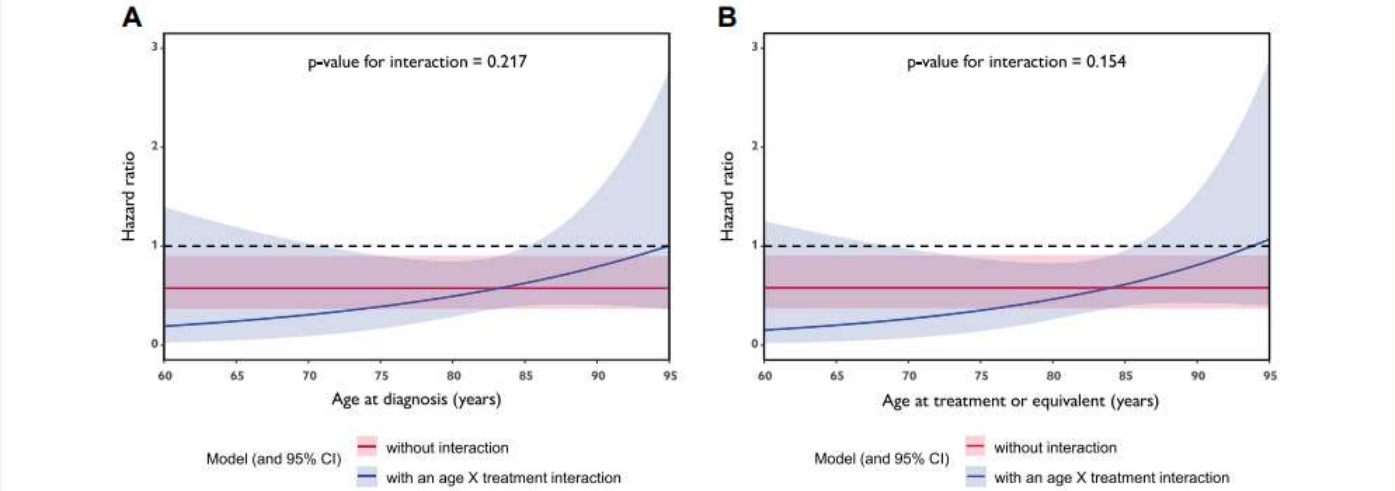

Figure 4 Age interaction with tafamidis treatment efficacy (mortality). (*A*) Interaction with age at diagnosis. (*B*) Interaction with age at start treatment (or equivalent). CI, confidence interval

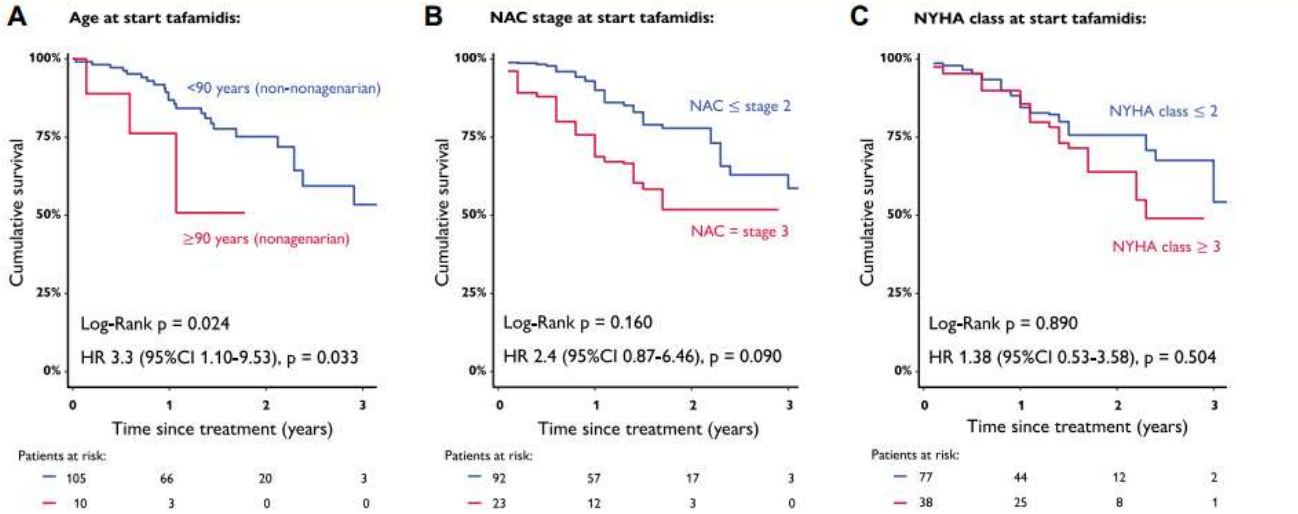

Figure 5 Cumulative survival in tafamidis treated octogenarians, since treatment. (*A*) Stratified by nonagenarian and non-nonagenarian. (*B*) Stratified by National Amyloidosis Centre prognostic stage category. (*C*) Stratified by New York Heart Association functional class category. CI, confidence interval; HR, hazard ratio; NAC, National Amyloidosis Centre; NYHA, New York Heart Association

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Impact of Tafamidis on survival in elderly patients: Insights from the Healthcare European Amyloidosis Registry

- **Our aim** was to analyze clinical characteristics and survival of patients with ATTR-CM aged ≥80 years diagnosed after November 2018, treated with tafamidis 80/61 mg, and compare them with a non-treated group diagnosed before that date.
- Data from the two groups were extracted from the **Healthcare European Amyloidosis Registry (HEAR).** Propensity score matching was used to adjust for baseline differences between the groups

- Between June 2021 and June 2024, the HEAR cohort included 6051 patients with amyloidosis, of whom 4310 were diagnosed with ATTR-CM. Among these, **1380 patients were over 80 years old**. Of the patients over 80 years old, **1194 were diagnosed after November 2018 and treated with tafamidis 80/61 mg, while 186 patients were diagnosed before November 2018 and were not treated.**
- Treated patients were older (**86 vs. 83 years**, $p < 0.001$) and significantly **less severe at baseline**, with a significantly lower occurrence of NYHA class III-IV compared to the untreated group (23.5 % vs. 45.5 %, $p < 0.001$).

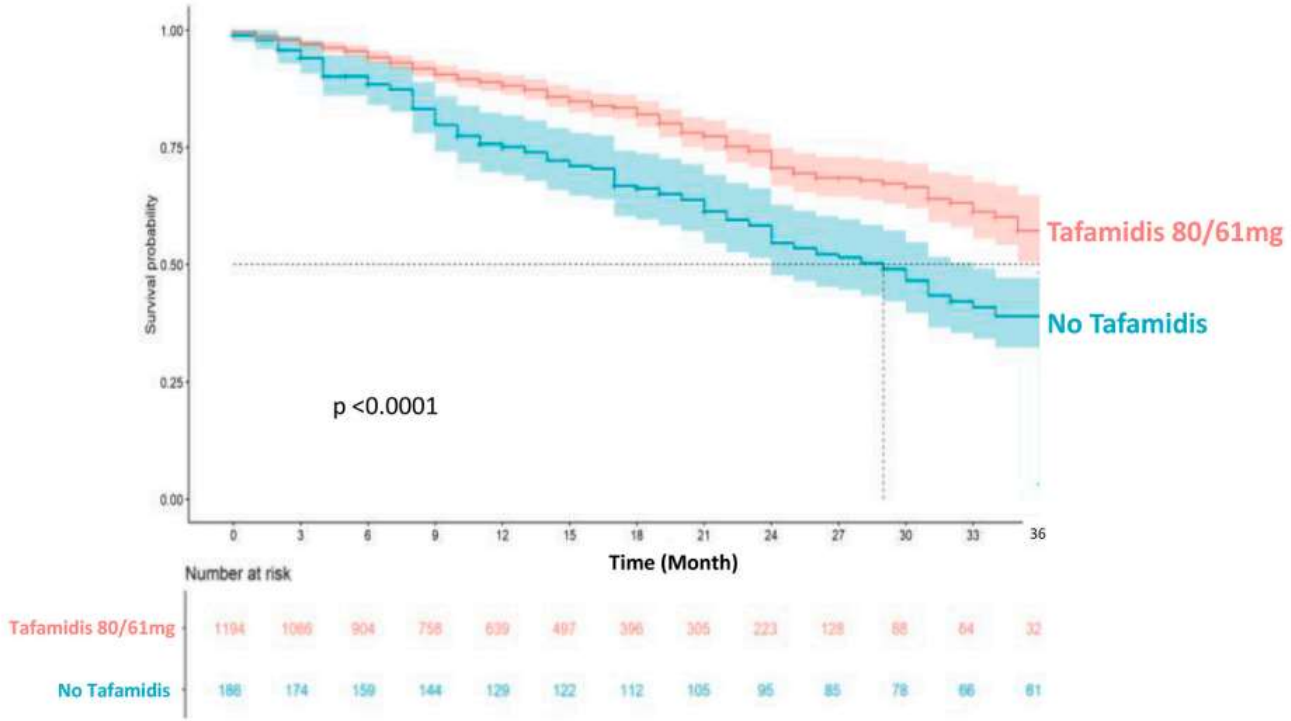

Fig. 1. Survival in patients over 80 years old treated with tafamidis 80/61mg versus no treatment: Kaplan-Meier curve.

Jobbe-Duval et al. IJC 2025

International Journal of Cardiology 437 (2025) 133522

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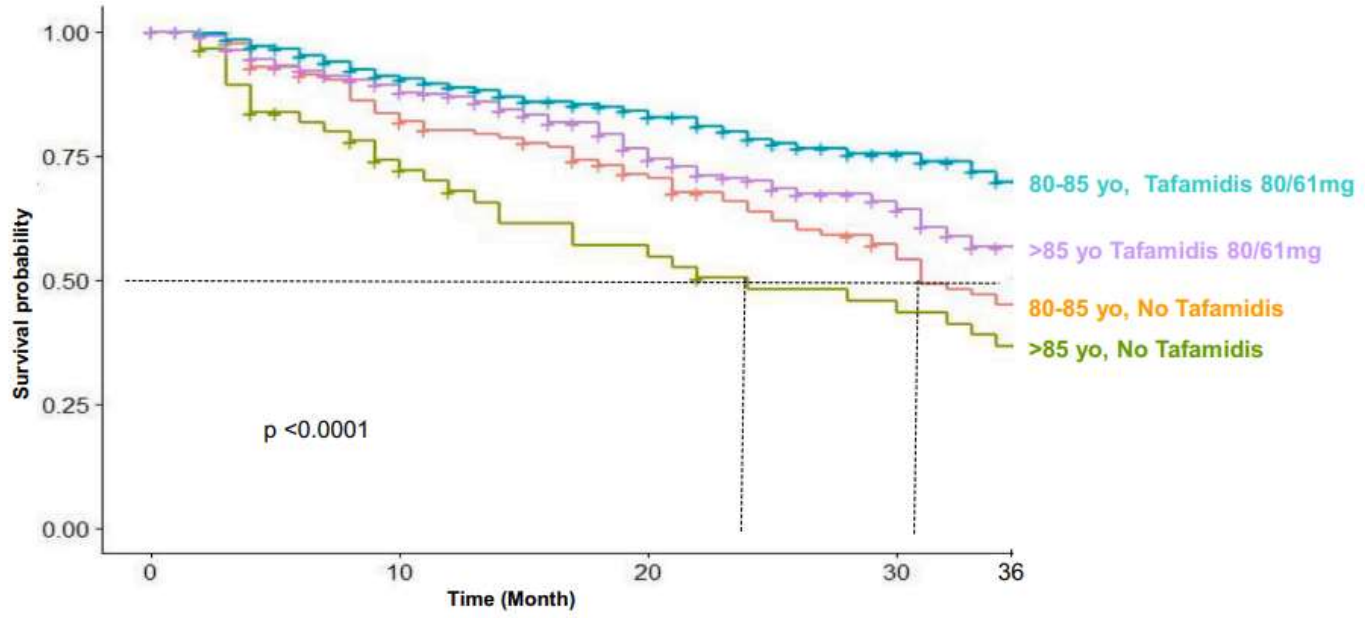
Impact of Tafamidis on survival in elderly patients: Insights from the Healthcare European Amyloidosis Registry

The **propensity score** was estimated based on the following parameters: age, NYHA, systolic blood pressure, troponin T HS, NT-proBNP, Interventricular Septal Thickness (IVST), LVEF, E/ e'ratio, Aspartate Aminotransferase (ASAT), and Alkaline Phosphatase (ALP).



Number at risk				
80-85 yo, Tafamidis 80/61mg	582	355	178	39
>85 yo Tafamidis 80/61mg	612	386	202	50
80-85 yo, No Tafamidis	130	99	77	57
>85 yo, No Tafamidis	56	37	26	20

Fig. 2. Survival in patients over 80 years old treated with tafamidis 80/61 mg versus no treatment based on age class (80–85 vs >85 years): Kaplan-Meier curve.

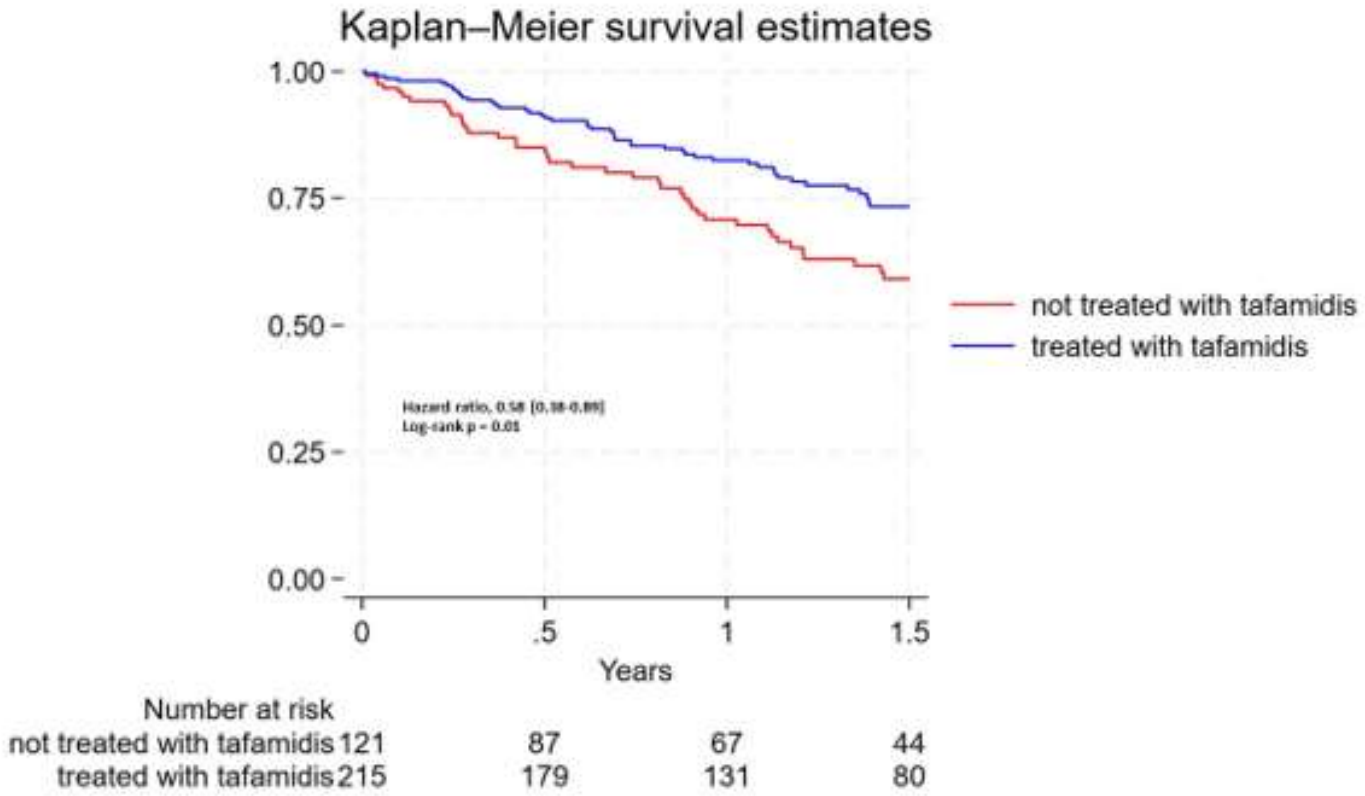
Jobbe-Duval et al. IJC 2025

ESC European Society of Cardiology
European Heart Journal (2025) 00, 1–2
https://doi.org/10.1093/eurheartj/ehaf482

Nonagenarian patients with ATTR cardiac amyloidosis: should they be treated with tafamidis?

Antoine Jobbé-Duval [1,*], Thibaud Damy [2,3,4], and Amaury Broussier [4,5]

- **336 patients over the age of 90**
- males: 69%; median hypertrophy: 16 mm, median ejection fraction: 55%; median ventricular strain: -11%; median serum level : median serum N-terminal prohormone of brain natriuretic peptide level: 3438 pg/ml; National Amyloidosis Centre (NAC) stage 2: 44%; NAC stage 3: 24%)

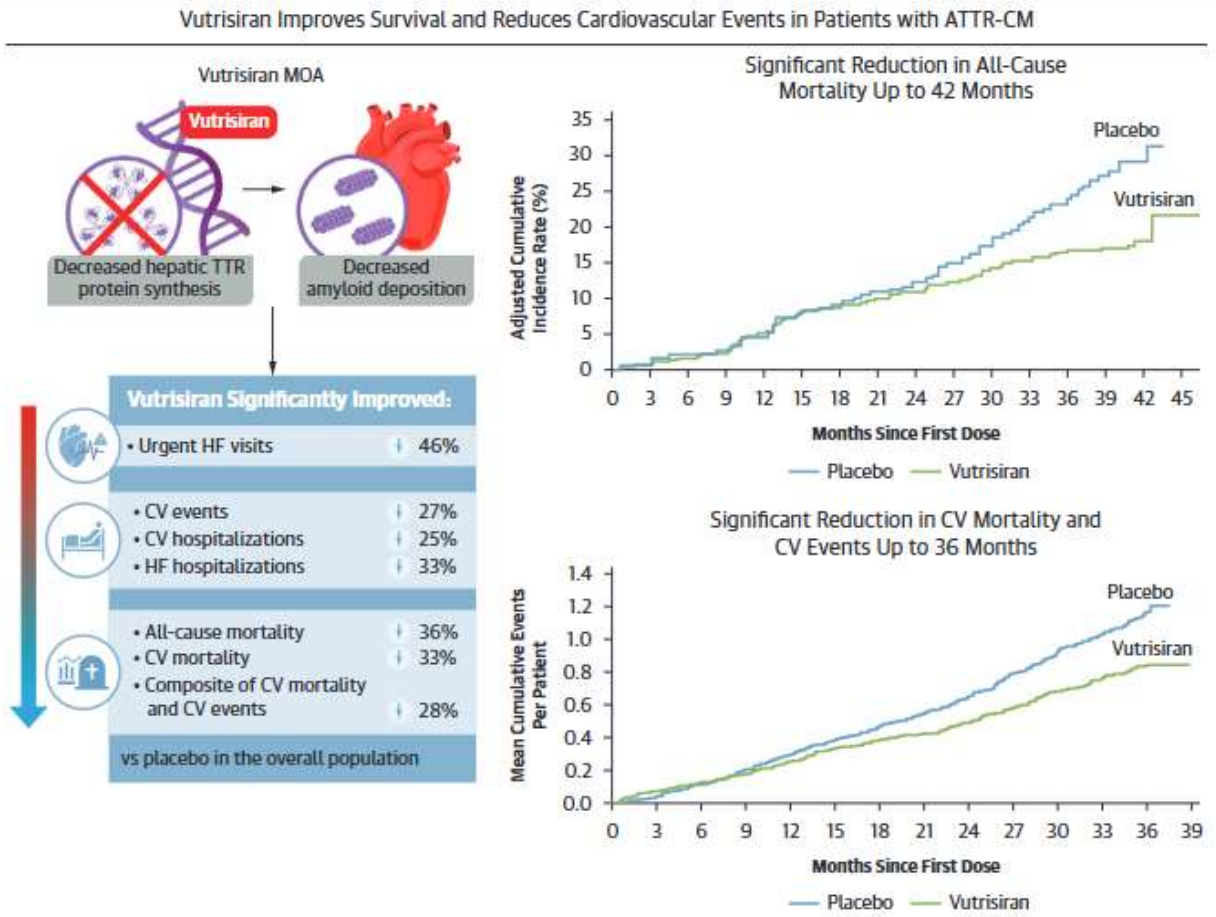


Jobbe-Duval et al. EHJ 2025

Vutrisiran Improves Survival and Reduces Cardiovascular Events in ATTR Amyloid Cardiomyopathy

HELIOS-B

CENTRAL ILLUSTRATION **Vutrisiran Reduces the Risk of Mortality and Cardiovascular Events Among Patients With Transthyretin Amyloidosis With Cardiomyopathy**



Witteles RM, et al. JACC. 2025;85(20):1959-1970.

ATTR-CM = transthyretin amyloidosis with cardiomyopathy; CV = cardiovascular; HF = heart failure; MOA = mechanism of action; TTR = transthyretin.

Witteles et al. JACC 2025

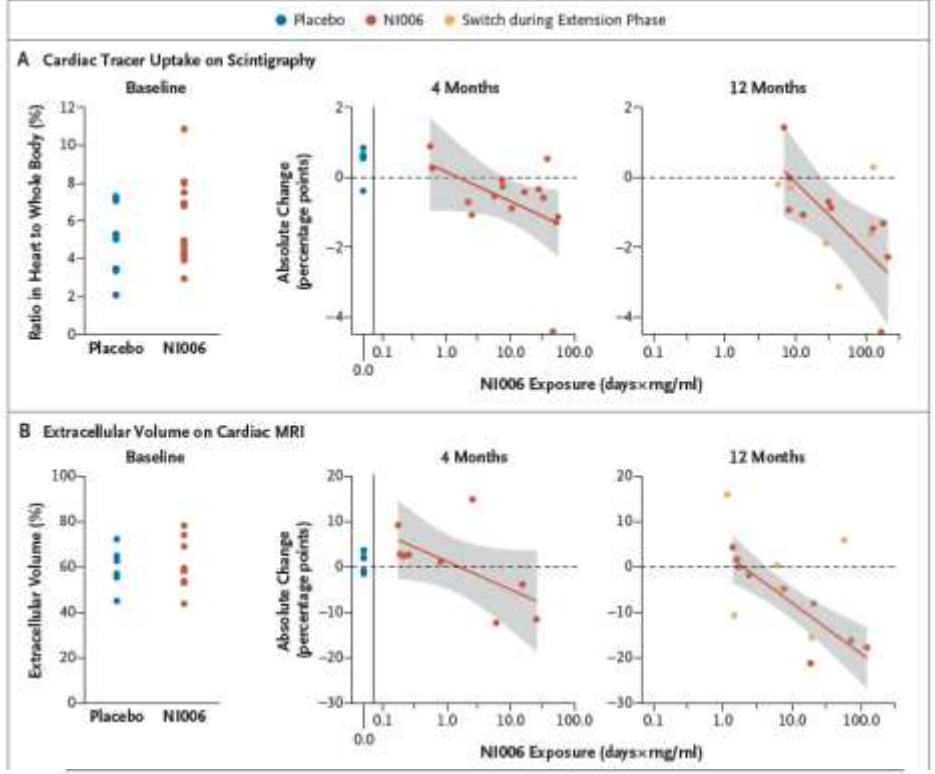
The NEW ENGLAND JOURNAL of MEDICINE

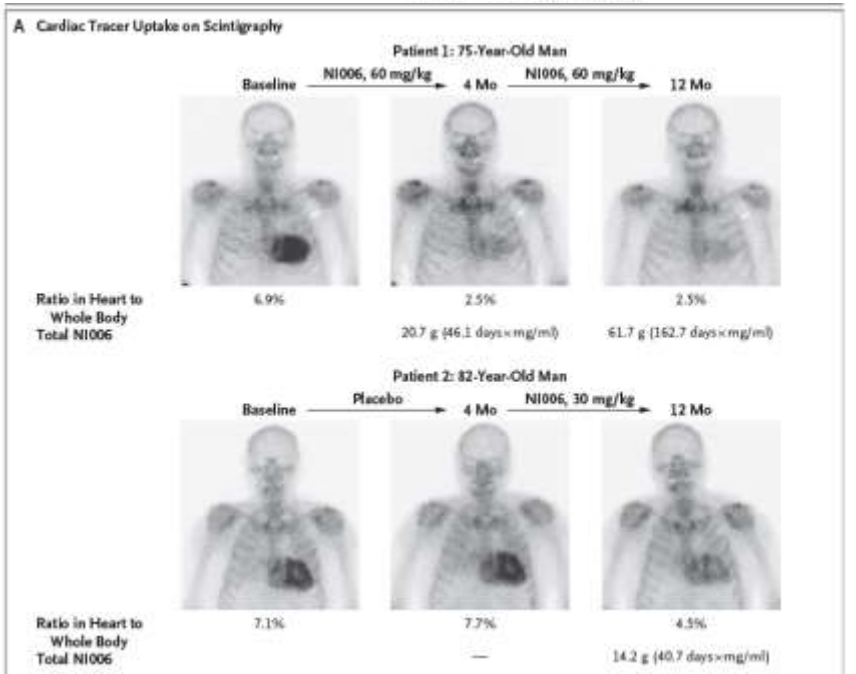
ORIGINAL ARTICLE

Phase 1 Trial of Antibody NI006 for Depletion of Cardiac Transthyretin Amyloid

Pablo Garcia-Pavia, M.D., Ph.D., Fabian aus dem Siepen, M.D., Erwan Donal, M.D., Ph.D., Olivier Lairez, M.D., Peter van der Meer, M.D., Ph.D., Arnt V. Kristen, M.D., Michele F. Mercuri, M.D., Ph.D., Aubin Michalon, Ph.D., Robert J.A. Frost, M.D., Ph.D., Jan Grimm, Ph.D., Roger M. Nitsch, M.D., Christoph Hock, M.D., Peter C. Kahr, M.D., and Thibaud Damy, M.D., Ph.D.

- In this **phase 1**, double-blind trial, we randomly assigned (in a 2:1 ratio) 40 patients with wild-type or variant ATTR cardiomyopathy and chronic heart failure
- Intravenous infusions of either **NI006 or placebo** every 4 weeks for 4 months (ranging from 0.3 to 60 mg per kilogram of body weight).
- After four infusions, patients were enrolled in **an open-label extension phase** in which they received eight infusions of NI006 with stepwise increases in the dose.
- **The safety and pharmacokinetic profiles** of NI006 were assessed, and cardiac imaging studies were performed.





Garcia-Pavia et al., NEJM 2023.

Clinical Phenotype and Prognostic Significance of Frailty in Transthyretin Cardiac Amyloidosis

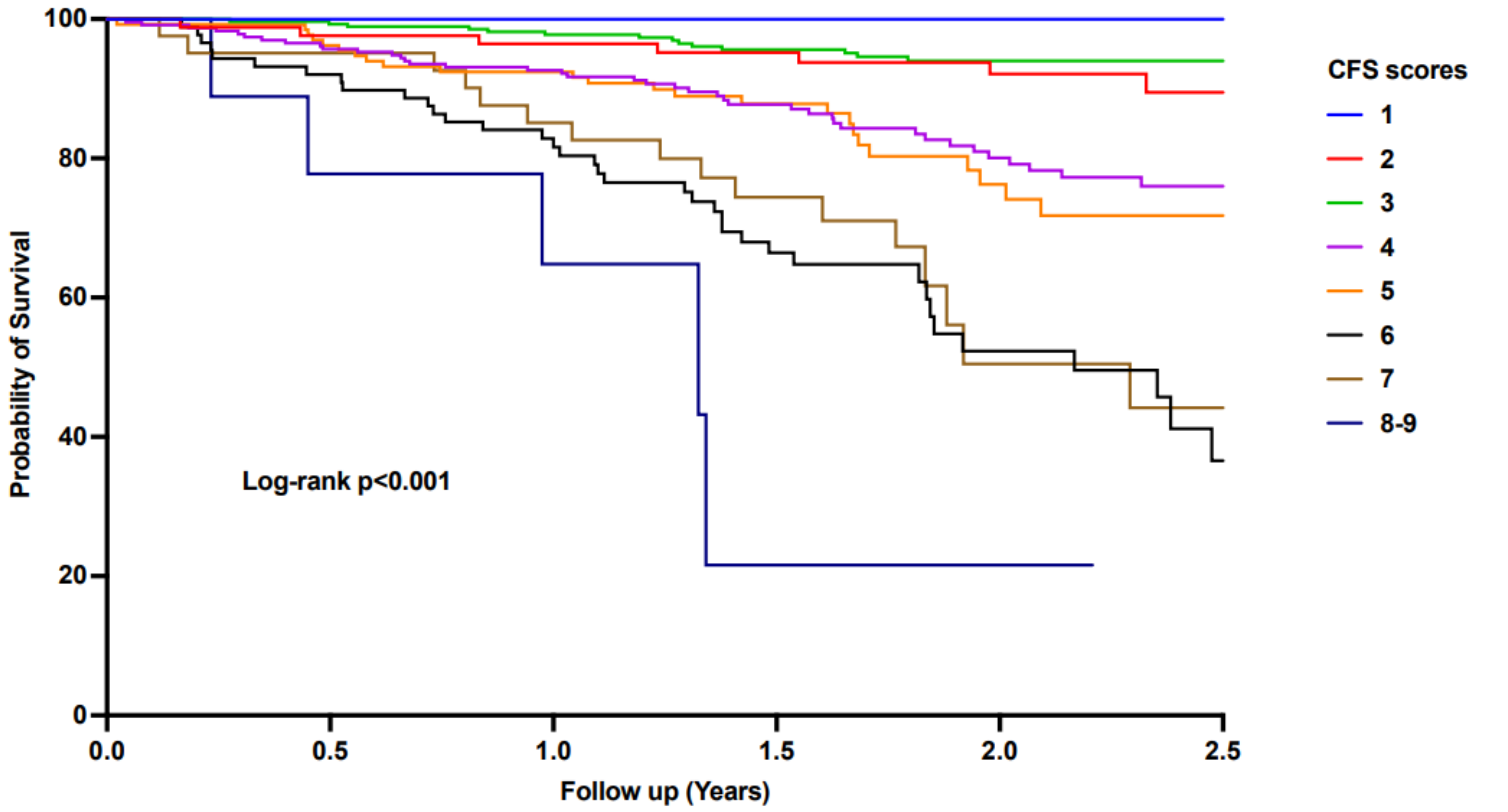
TABLE 1 Clinical and Imaging Characteristics of Patients Diagnosed With ATTR-CM at CFS Assessment

57.1 %

	CFS 1-3 (n = 378, 43.0%)	CFS 4 or 5 (n = 364, 41.4%)	CFS 6 or 7 (n = 129, 14.7%)	CFS 8 or 9 (n = 9, 1.0%)	*P* Value
Demographics					
Age, y	78 (74-82)	82 (77-85)	83 (78-88)	87 (84-90)	<0.001
>80 y	130 (34.3)	200 (55.2)	74 (57.4)	9 (100.0)	<0.001

- To evaluate the prevalence, clinical determinants, and prognostic significance of frailty in a large cohort of patients with ATTR-CA.
- Frailty was assessed in **880 patients with ATTR-CA** (median age 80 years [Q1-Q3: 75-84 years], 719 [81.7%] male) using the Clinical Frailty Scale (CFS).

FIGURE 2 Survival Analysis of Patients With ATTR-CA by Clinical Frailty Status



Fumagalli et al. JACC cardiooncol 2025

Clinical Phenotype and Prognostic Significance of Frailty in Transthyretin Cardiac Amyloidosis

FIGURE 3 Survival Analysis of Patients With ATTR-CA by NAC Stage and CFS

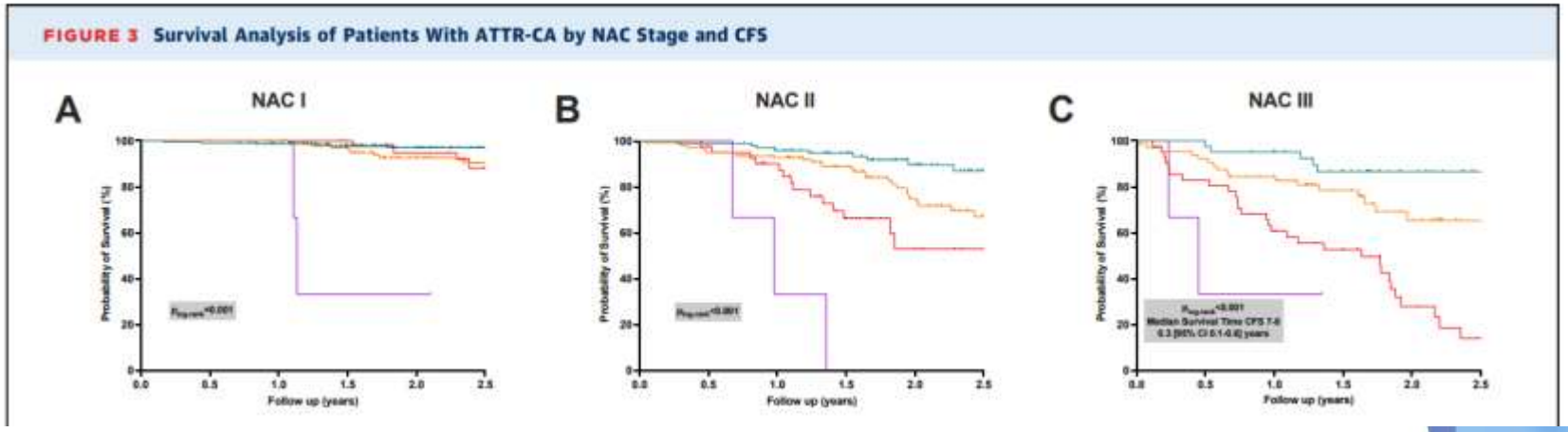
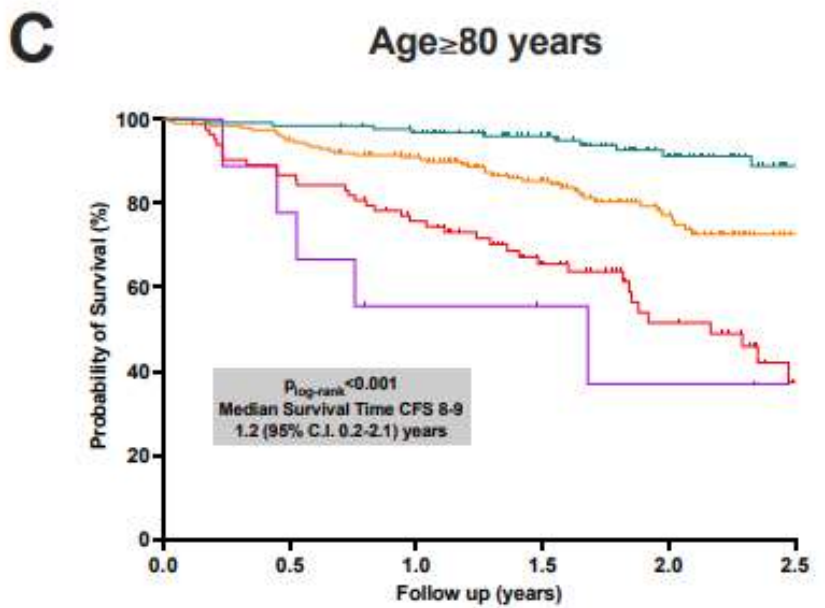


TABLE 3 Univariable and Multivariable Cox Regression Analysis to Determine Factors Associated With All-Cause Mortality

	Univariable			Multivariable		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Age at evaluation (Δ year)	1.102	1.071-1.134	<0.001	1.029	0.998-1.061	0.063
Men	1.244	0.728-2.125	0.41			
NYHA functional class (III/IV)	3.162	2.226-4.493	<0.001	1.501	1.038-2.171	0.031
CFS (vs 1-3)			<0.001			<0.001
4 or 5	3.125	2.085-4.971	<0.001	2.941	1.774-4.867	<0.001
6 or 7	4.799	2.666-8.348	<0.001	4.123	2.423-7.015	<0.001
8 or 9	8.038	2.761-19.719	<0.001	9.716	3.340-28.266	<0.001
Log NT-proBNP	2.121	1.428-2.054	<0.001	1.897	1.512-2.379	<0.001
Log eGFR	0.491	0.301-0.894	0.015	0.533	0.311-0.915	0.022
Ischemic heart disease[a]	1.428	0.966-2.110	0.07	1.385	0.932-2.056	0.11
Diabetes mellitus[a]	1.404	0.946-2.082	0.09	1.067	0.719-1.592	0.84
Hypertension[a]	1.061	0.761-1.479	0.73			
Atrial fibrillation	1.330	0.951-1.860	0.09	0.815	0.578-1.152	0.25
Stroke/TIA[a]	1.134	0.653-1.970	0.66			
LV wall thickness (Δ mm)	1.071	1.007-1.138	0.029	1.052	0.966-1.099	0.36
LVEF (Δ %)	0.973	0.958-0.988	0.001	0.998	0.986-1.014	0.81
Loop diuretics[a]	1.381	0.980-1.946	0.07	1.050	0.734-1.509	0.78

The model was performed in 861 individuals. [a]At the time of assessment.
Abbreviations as in Table 1.



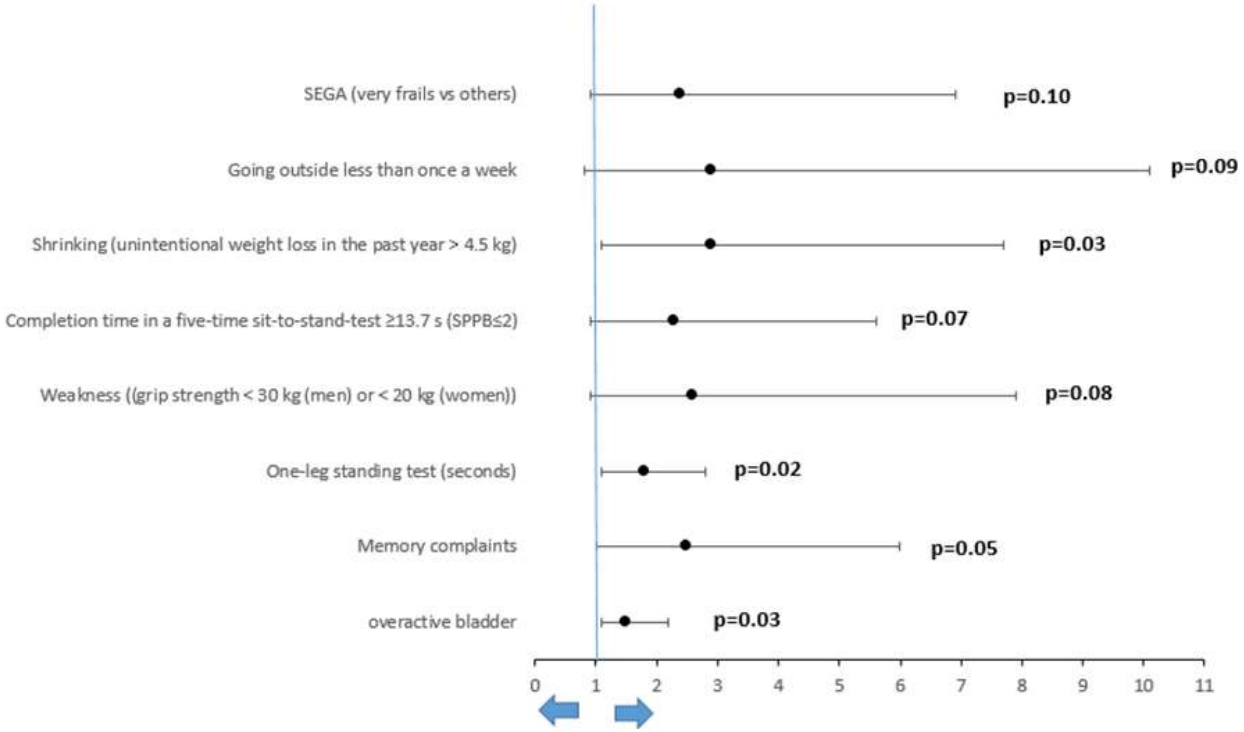
Fumagalli et al. JACC cardiooncol 2025

JSB 2025

ESC HEART FAILURE
ESC Heart Failure 2025; 12: 281–289
Published online 16 September 2024 in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/ehf2.15026

ORIGINAL ARTICLE

Frailty in heart failure according to the presence or absence of wild-type transthyretin cardiac amyloidosis

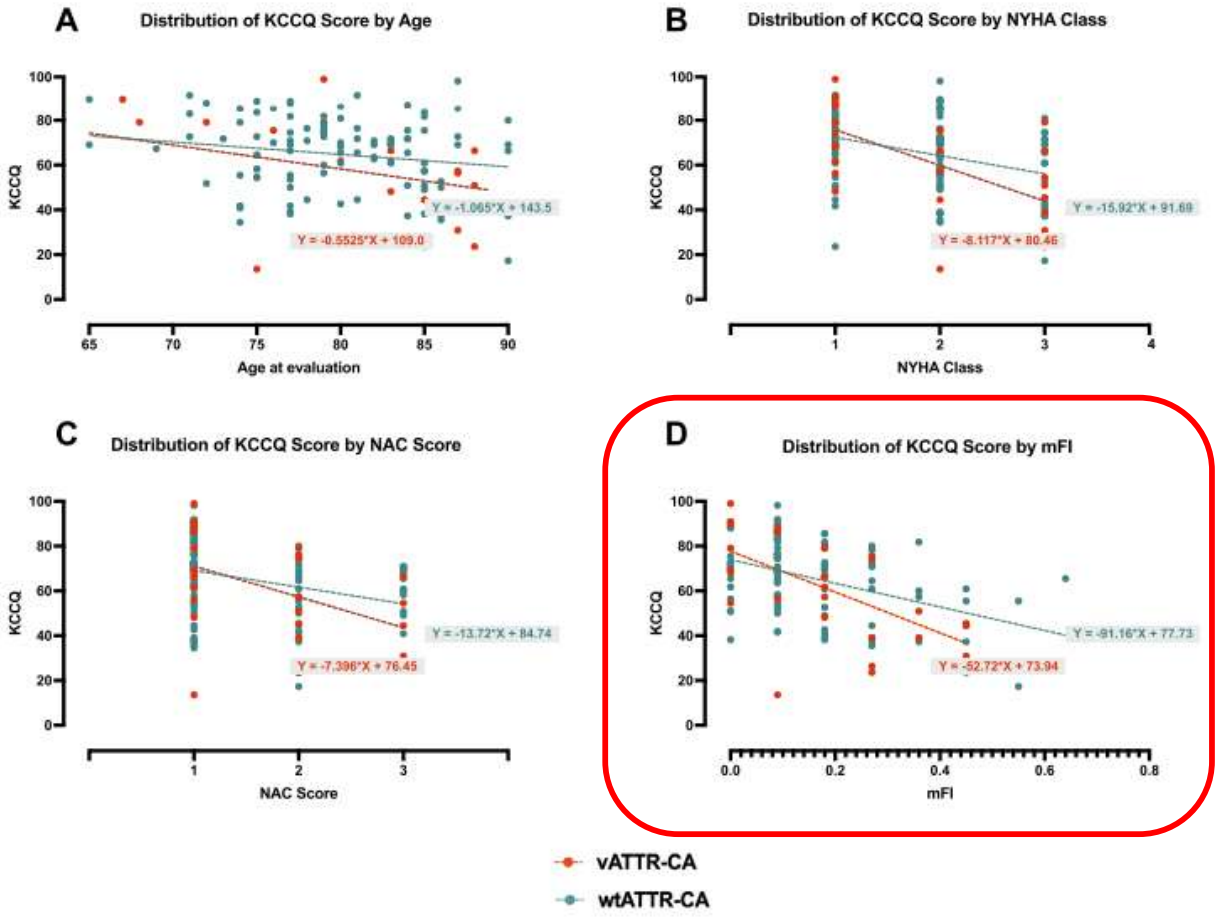


Aging Clinical and Experimental Research (2024) 36:89
https://doi.org/10.1007/s40520-024-02750-6

ORIGINAL ARTICLE

Determinants of health status in older patients with transthyretin cardiac amyloidosis: a prospective cohort study

Carlo Fumagalli[1,2,3] · Lucia Ponti[3,4] · Martina Smorti[5] · Francesca Pozza[3] · Alessia Argirò[2,3] · Mattia Zampieri[4] · Carlo Di Mario[3] · Raffaele Marfella[1] · Celestino Sardu[1] · Giuseppe Paolisso[1] · Iacopo Olivotto[2,6] · Federico Perfetto[3,6] · Andrea Ungar[10] · Niccolò Marchionni[8] · Francesco Cappelli[2,7,8]



Un phénotype particulier

Broussier et al., ESC-HF 2024
Fumagalli et al. Aging Clinical and Experimental Research 2024

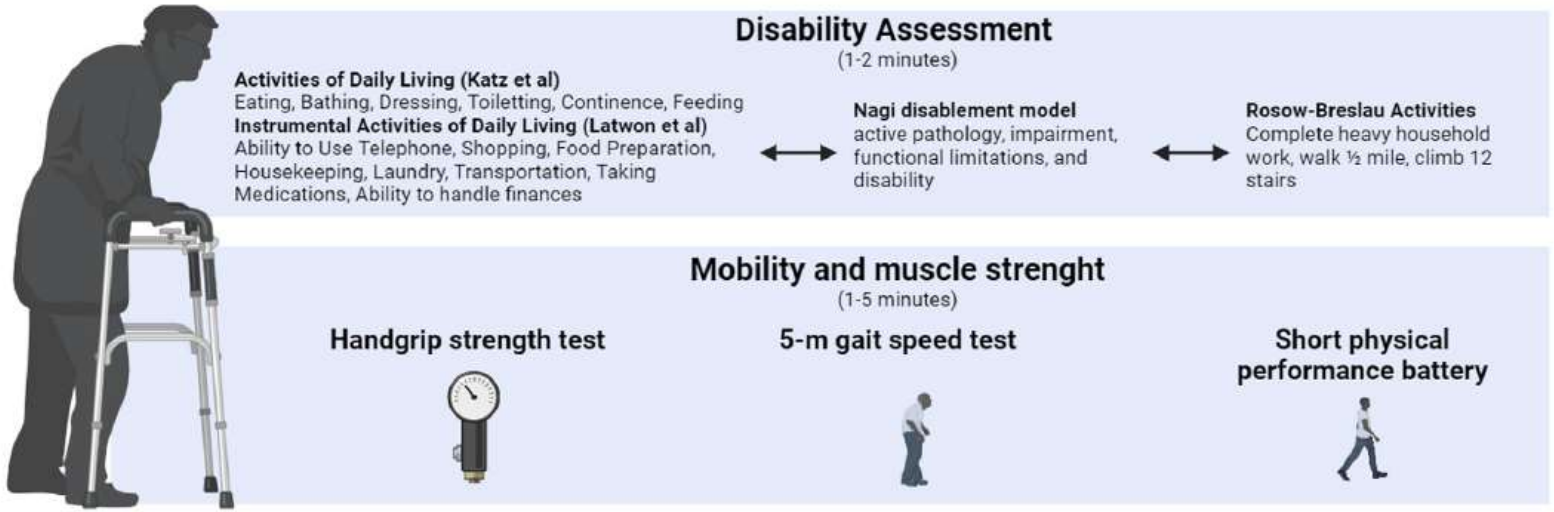
JSB 2025

JACC: ADVANCES VOL. 3, NO. 9, 2024

EXPERT PANEL

Comprehensive Geriatric Assessment to Optimize the Management of Older Patients With Transthyretin Cardiac Amyloidosis

FIGURE 1 Functional and Disability Assessment in Older Patients Diagnosed With ATTR-CA



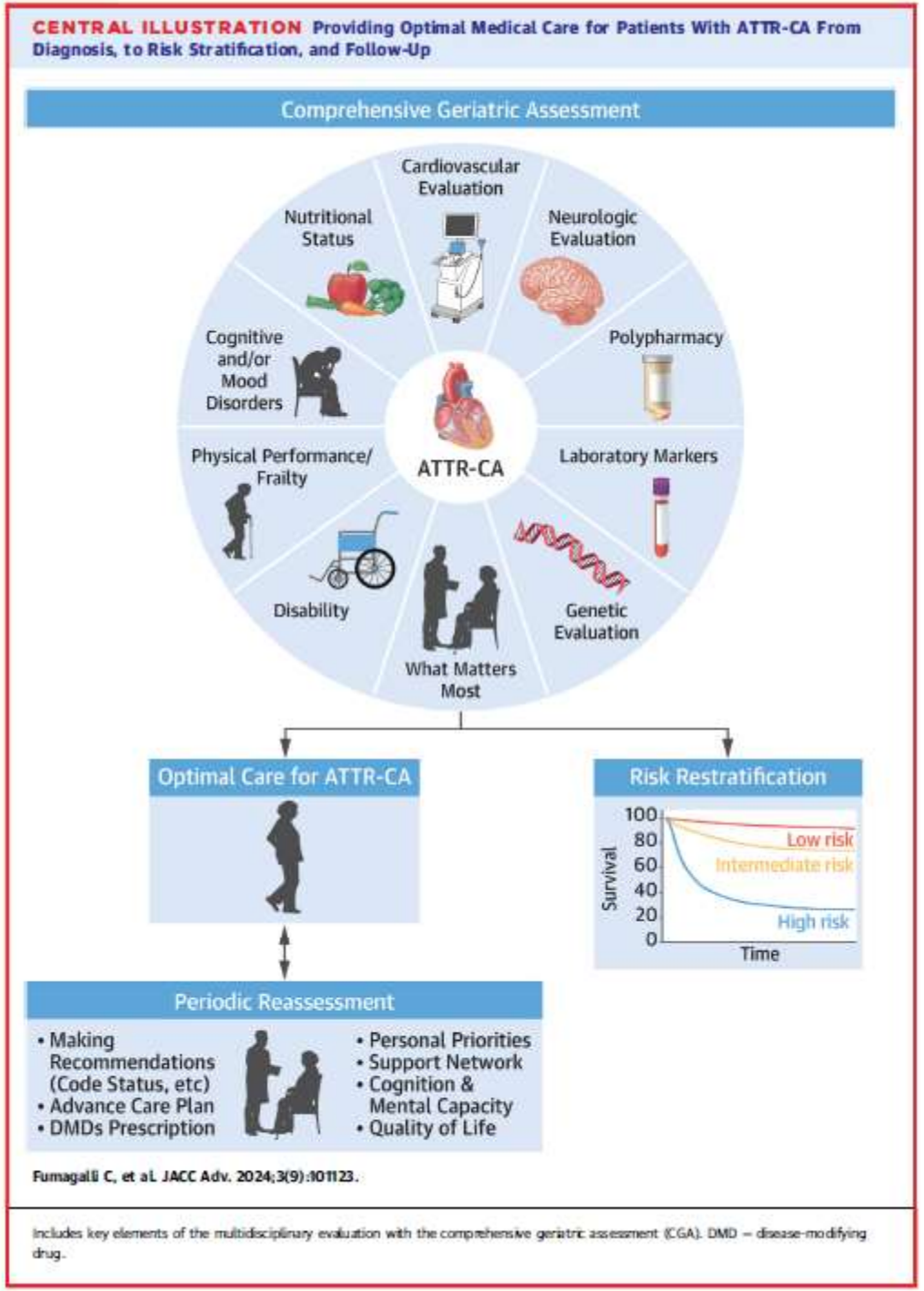
The figure illustrates the components of functional and disability assessment for older patients diagnosed with transthyretin cardiac amyloidosis (ATTR-CA). The assessment is divided into 2 main categories: disability assessment and physical performance. Created with BioRender.com.

HIGHLIGHTS

- Patients with ATTR-CA are almost exclusively older adults at diagnosis with multiple chronic conditions.
- A routine CGA is useful to delineate the clinical complexity (ie geriatric syndromes) of older ATTR-CA patients.
- A CGA that incorporates the expertise of geriatricians, cardiologists, neurologists, palliative care specialists, and others may help reduce ageism and futility and could be integrated in future clinical trials.

Fumagalli et al. JACC 2024

CENTRAL ILLUSTRATION Providing Optimal Medical Care for Patients With ATTR-CA From Diagnosis, to Risk Stratification, and Follow-Up



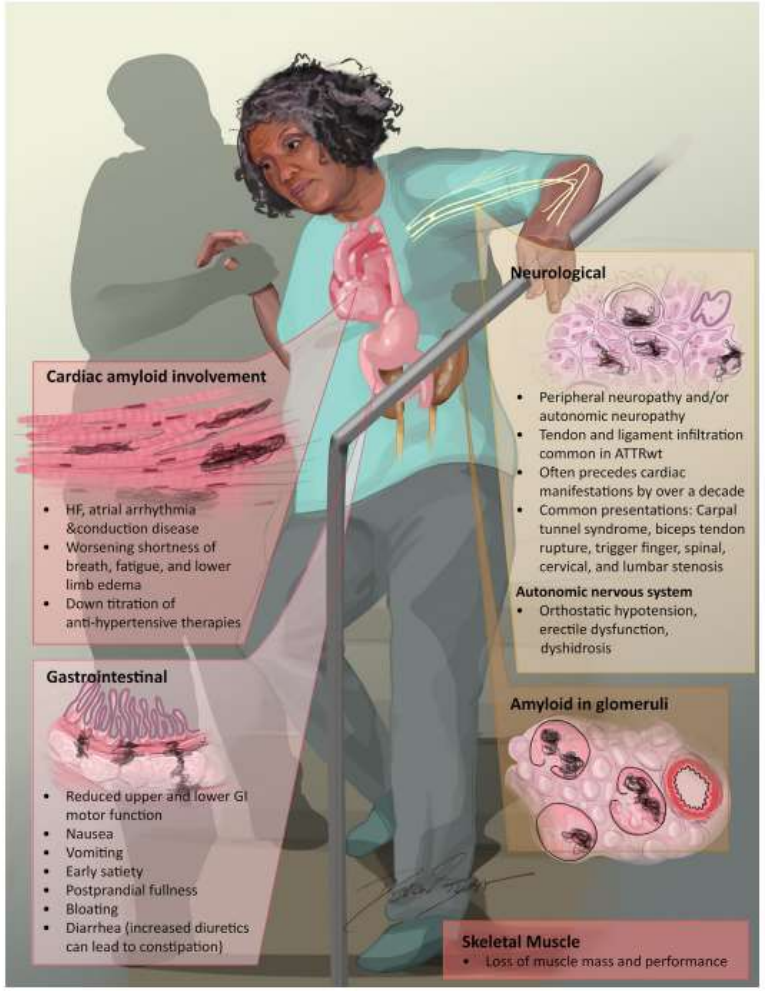
Fumagalli C, et al. JACC Adv. 2024;3(9):101123.

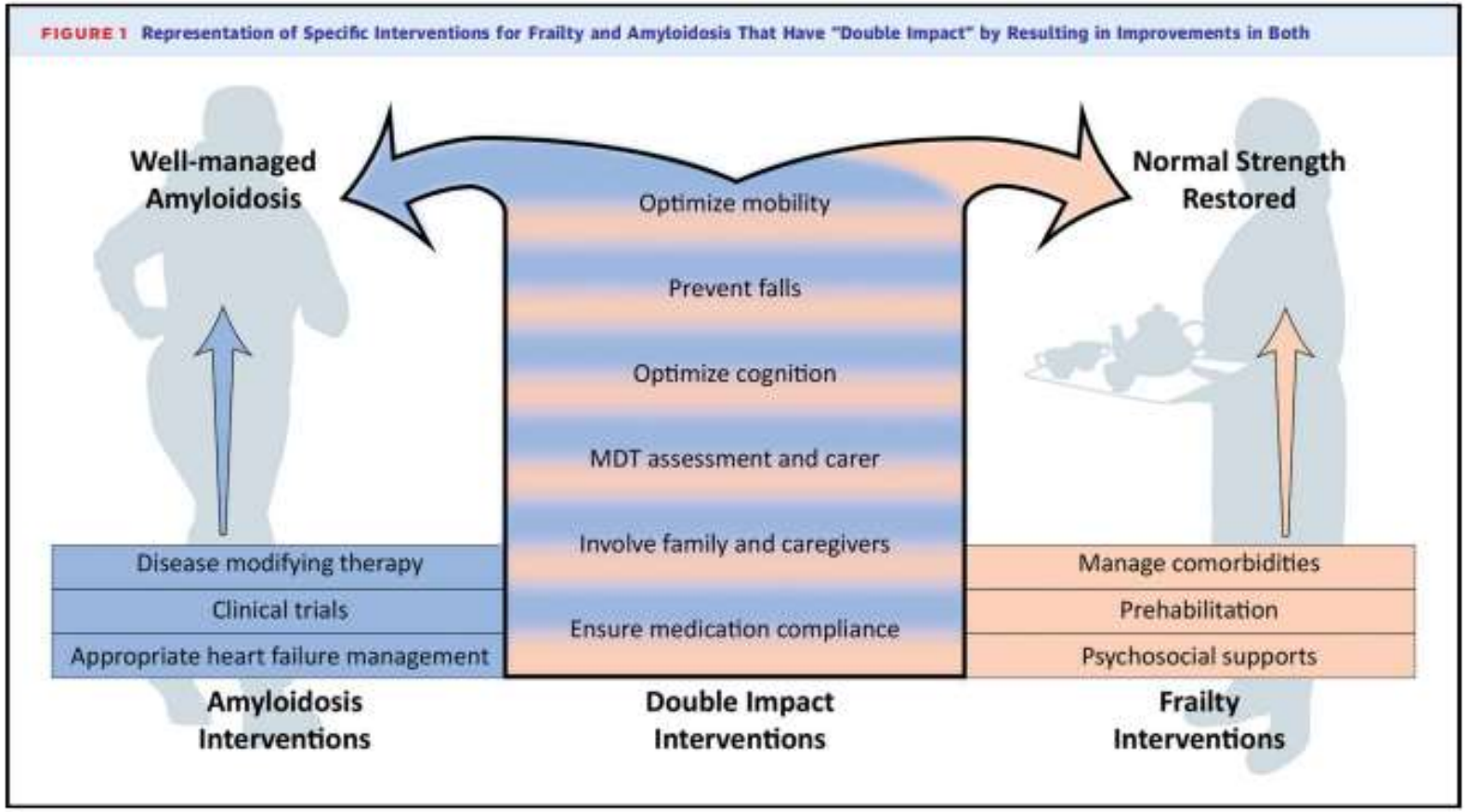
Includes key elements of the multidisciplinary evaluation with the comprehensive geriatric assessment (CGA). DMD = disease-modifying drug.

Fumagalli et al. JACC 2024

Cardiac Amyloidosis in Older Adults With a Focus on Frailty

JACC: Advances Expert Consensus





Bart et al. JACC Advances 2025

Take home messages

- Une prévalence significative dans l'IC du sujet âgé
- Une explosion thérapeutique avec différentes voies, différentes molécules
- Des données de vraie vie chez le sujet âgé
- Place grandissante de l'EGA chez ces patients : aide à la décision thérapeutique, management des comorbidités / fragilités / Syndromes gériatriques

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Merci de votre attention

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