PLACE 2026
PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

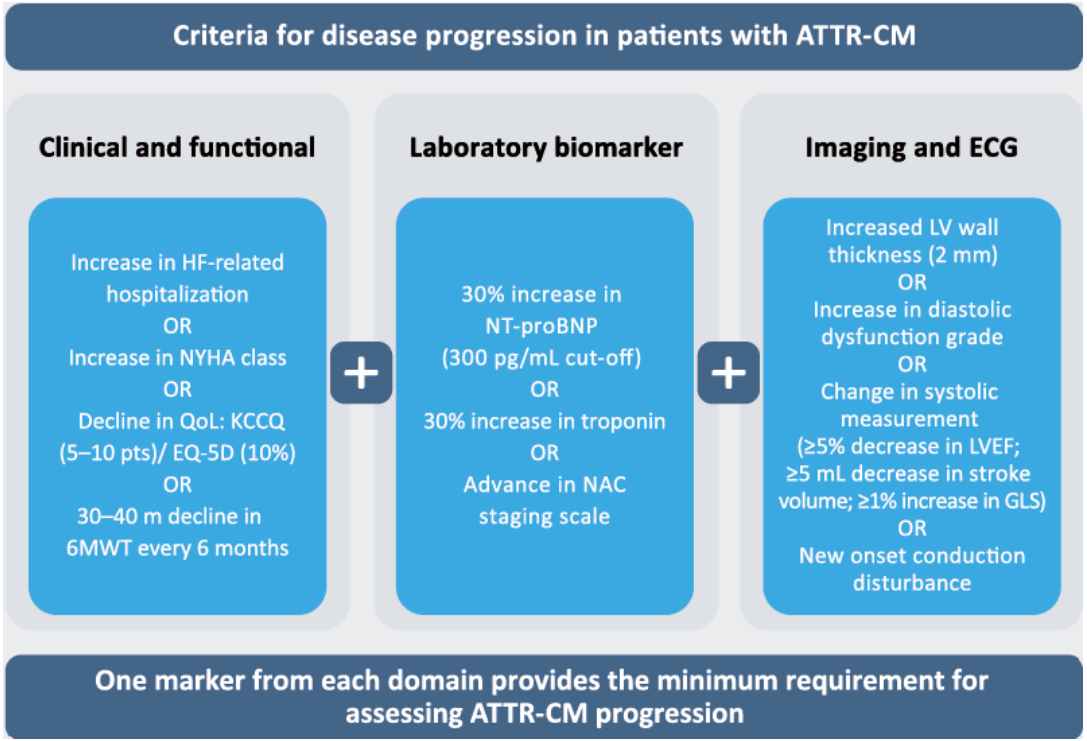
CONGRESSO
ROMA, 25 - 27 Giugno 2026

AMILOIDOSI CARDIACA

Stratificazione della progressione di malattia in ATTR-CA

S. Longhi
IRCCS – Azienda Ospedaliero Universitaria di Bologna, Policlinico di S.Orsola

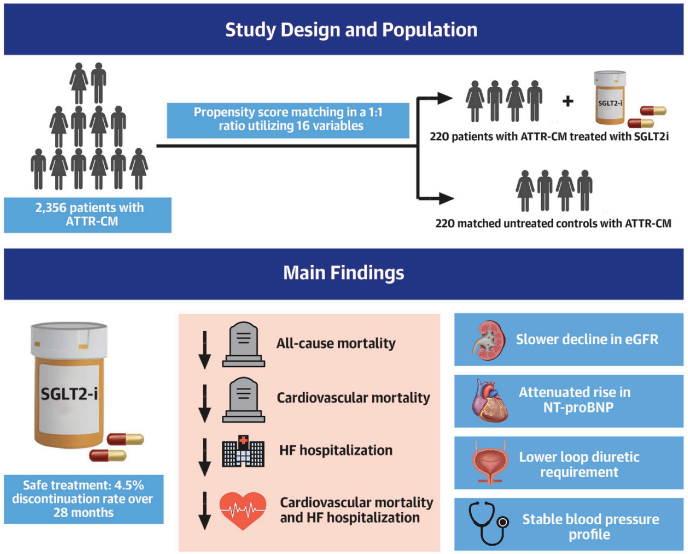
The first recommendation acknowledged the multifactorial nature of ATTR progression



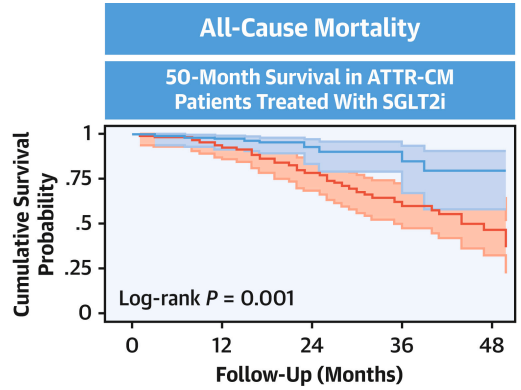
Based on expert opinion, not proven to be effective in real word practice

P. Garcia-Pavia et al. European Journal of Heart Failure (2021)

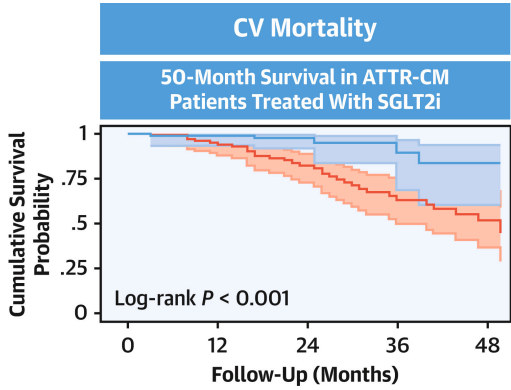
CENTRAL ILLUSTRATION: Sodium-Glucose Cotransporter 2 Inhibitors in Transthyretin Amyloid Cardiomyopathy



Porcari A, et al. J Am Coll Cardiol. 2024;83(24):2411-2422.



Number at risk						
No SGLT2i	109	104	70	43	26	14
SGLT2i	109	107	56	22	14	7



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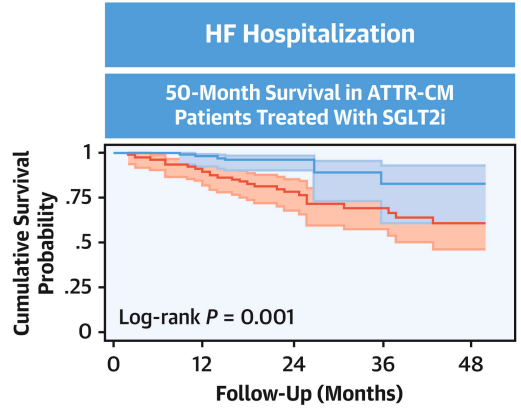
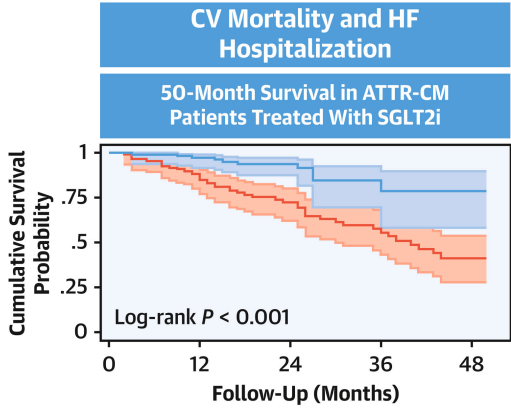


Number at risk						
No SGLT2i	109	98	60	39	22	10
SGLT2i	109	105	52	19	12	5

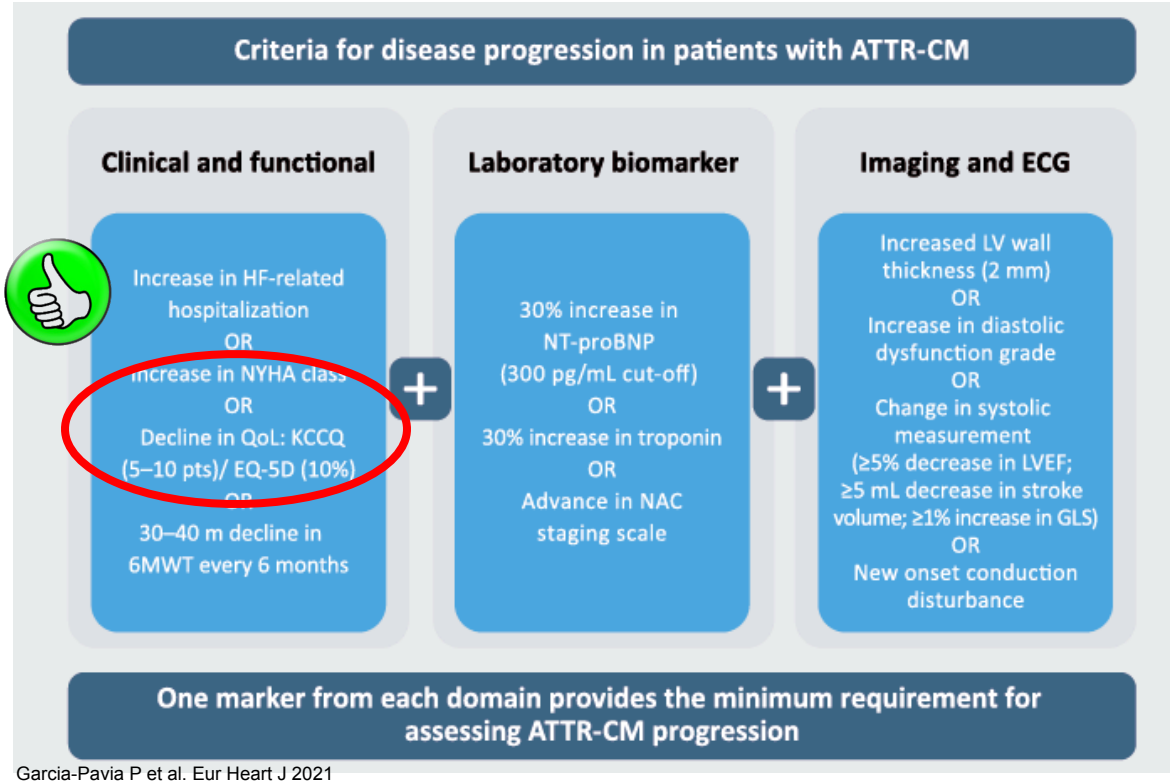


Number at risk						
No SGLT2i	109	98	60	39	22	10
SGLT2i	109	105	52	19	12	5

95% CI — No SGLT2i — 95% CI — SGLT2i

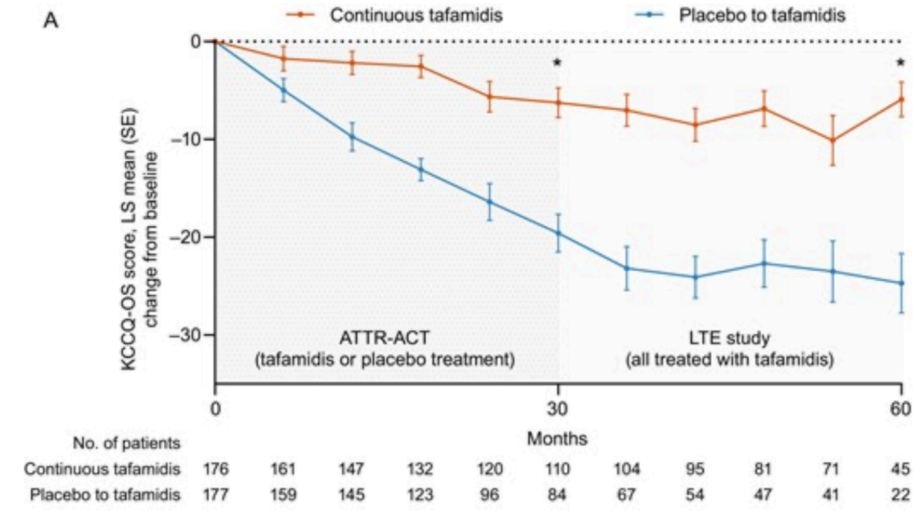
1 ATTRibute-CM
2 ATTR-ACT
3 Zeldin 2024

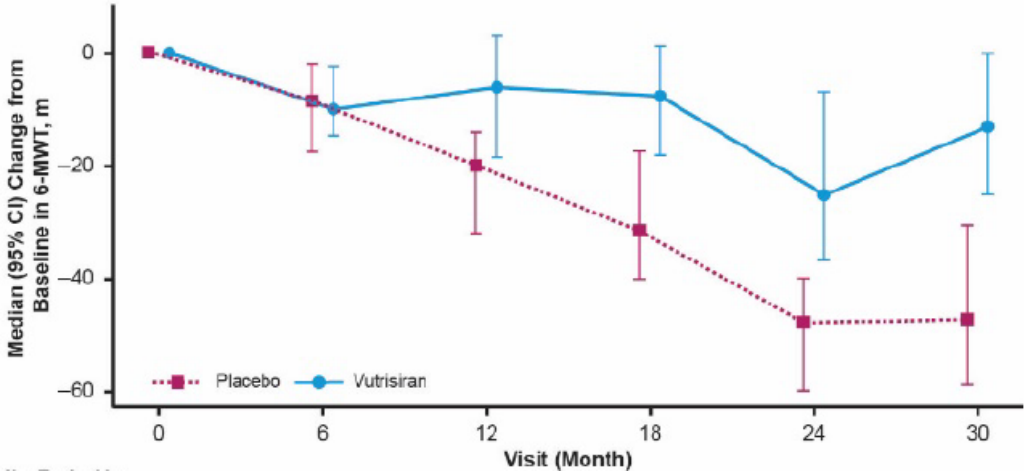
4 ATTR-ACT
5 Levy
6 Law
7 Cheng

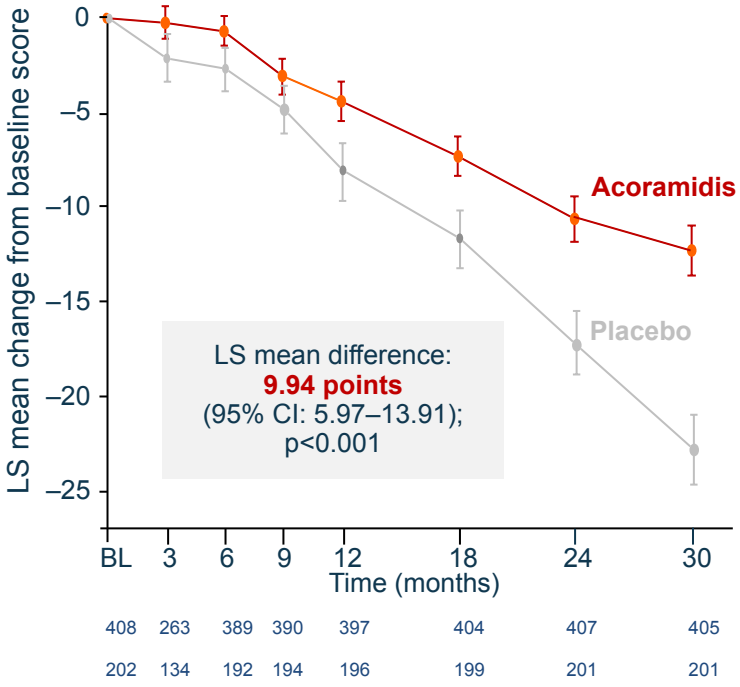


Garcia-Pavia P et al. Eur Heart J 2021

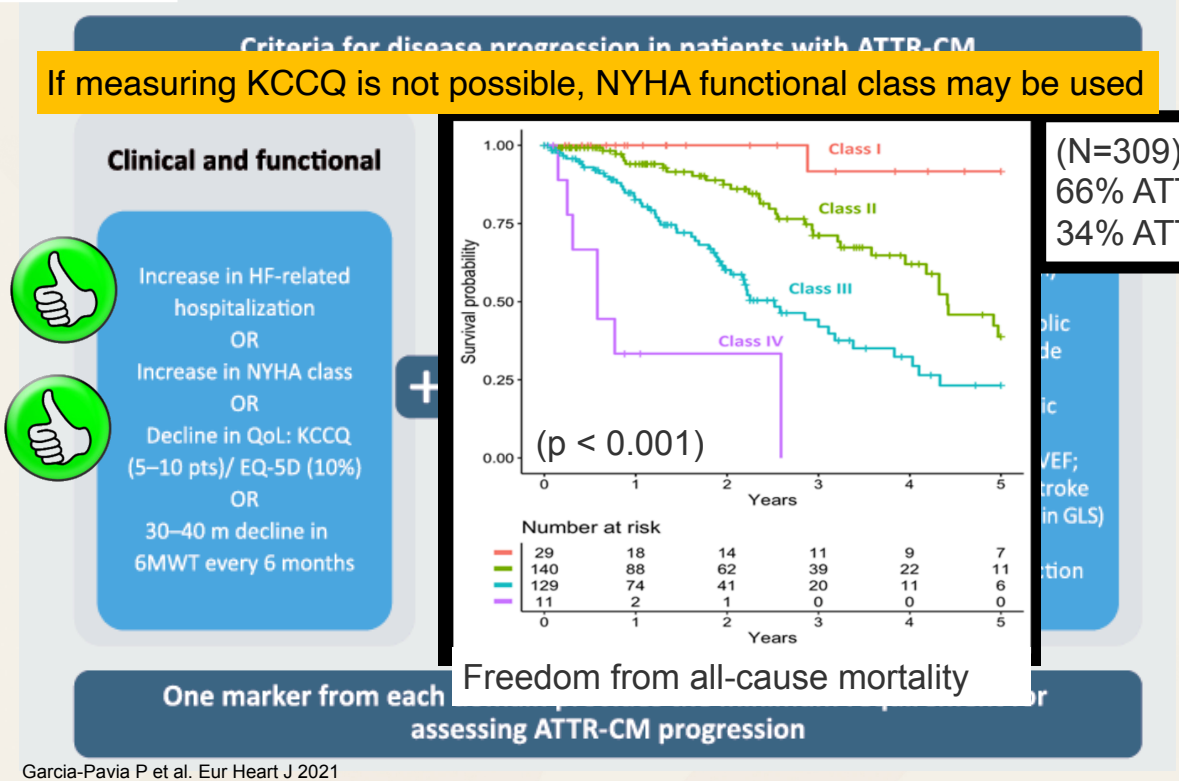
4Grogan M, Effect of long-term tafamidis treatment on health-related quality of life in patients with transthyretin amyloid cardiomyopathy. Eur J Heart Fail.
5Levy JC. Worsening quality of life, captured by change in KCCQ-OS, a heart failure-specific PRO, is predictive of outcomes in ATTR-CM. Paper presented at: American College of Cardiology Annual Scientific Session 2025.
6Law S. Change in N- terminal pro-B-type natriuretic peptide at 1 year predicts mortality in wild-type transthyretin amyloid cardiomyopathy. Heart.
7 RK Cheng. Diuretic Dose and NYHA Functional Class Are Independent Predictors of Mortality in Patients With Transthyretin Cardiac Amyloidosis. JACC CardioOncol 2020.


A
Continuous tafamidis
Placebo to tafamidis
KCCQ-OS score, LS mean (SE) change from baseline
0
−10
−20
−30
ATTR-ACT
(tafamidis or placebo treatment)
LTE study
(all treated with tafamidis)
0
30
60
Months
No. of patients
Continuous tafamidis 176 161 147 132 120 110 104 95 81 71 45
Placebo to tafamidis 177 159 145 123 96 84 67 54 47 41 22


Median (95% CI) Change from Baseline in 6-MWT, m
0
−20
−40
−60
Placebo
Vutrisiran
0
6
12
18
24
30
Visit (Month)


LS mean change from baseline score
0
−5
−10
−15
−20
−25
Acoramidis
Placebo
LS mean difference:
9.94 points
(95% CI: 5.97–13.91);
p<0.001
BL 3 6 9 12 18 24 30
Time (months)
408 263 389 390 397 404 407 405
202 134 192 194 196 199 201 201

If measuring KCCQ is not possible, NYHA functional class may be used



Garcia-Pavia P et al. Eur Heart J 2021

4Grogan M, Effect of long-term tafamidis treatment on health-related quality of life in patients with transthyretin amyloid cardiomyopathy. Eur J Heart Fail.
5Levy JC. Worsening quality of life, captured by change in KCCQ-OS, a heart failure-specific PRO, is predictive of outcomes in ATTR-CM. Paper presented at: American College of Cardiology Annual Scientific Session 2025.
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1 ATTRibute-CM
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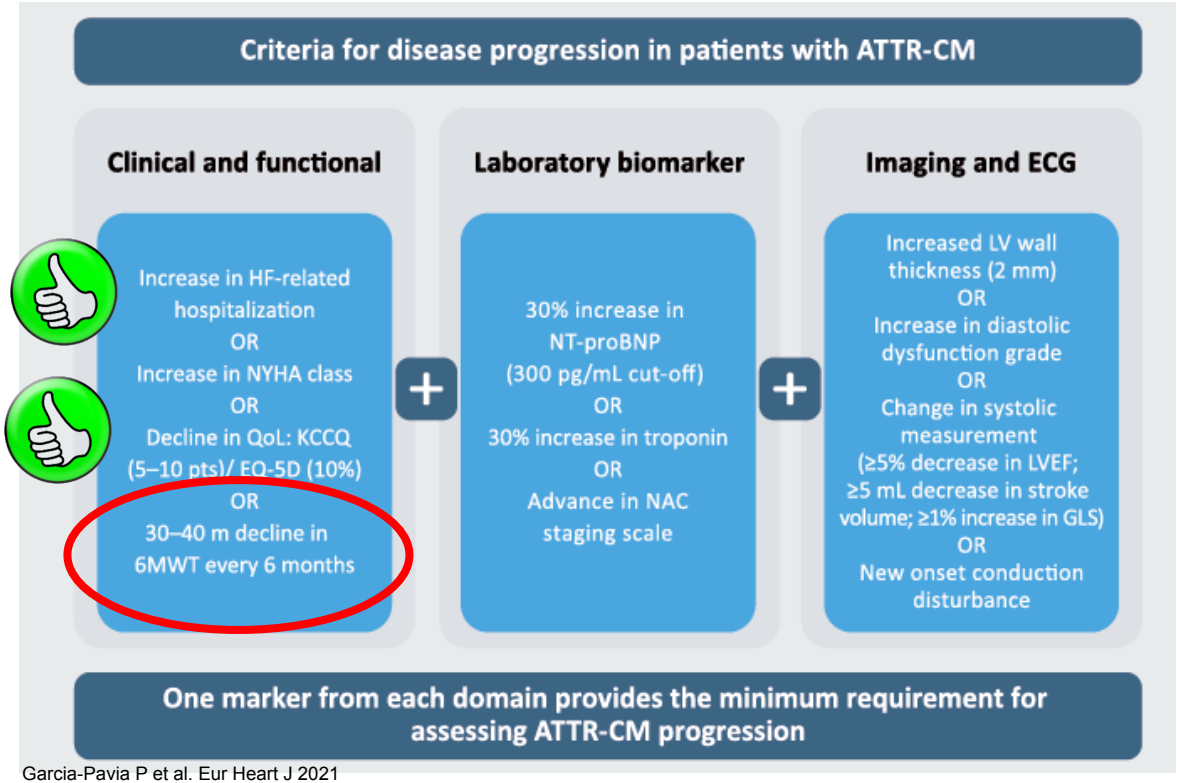


Garcia-Pavia P et al. Eur Heart J 2021

8Ioannou A. Prognostic value of a 6-minute walk test in patients with transthyretin cardiac amyloidosis. J Am Coll Cardiol. 2024

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 84, NO. 1, 2024

Prognostic Value of a 6-Minute Walk Test in Patients With Transthyretin Cardiac Amyloidosis

Adam Ioannou, MBBS, BSc,[a,*] Carlo Fumagalli, MD,[a,b,*] Yousuf Razvi, MBChB,[a] Aldostefano Porcari, MD,[a,c]

The median 6MWT distance was 347 m (Q1-Q3: 250- 428 m)

In a multivariable model with the covariates age, NAC disease stage, and baseline 6MWT distance of <350 m, NT-proBNP progression (HR: 1.65; 95% CI: 1.38-1.97; P < 0.001), ODI (HR: 1.58; 95% CI: 1.32-1.89; P < 0.001), and absolute reduction in 6MWT of >35 m (HR: 1.70; 95% CI: 1.43-2.03; P < 0.001) remained independently associated with an increased risk of mortality.

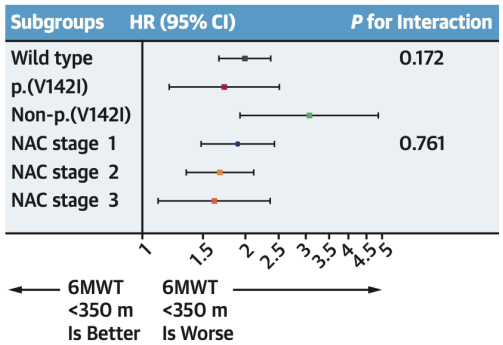
CENTRAL ILLUSTRATION Prognostic Importance of the 6-Minute Walk Test According to Subgroups

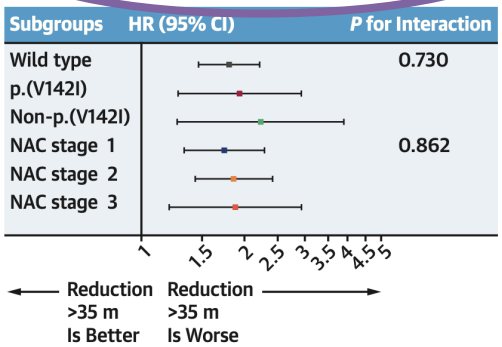
Baseline 6MWT Distance

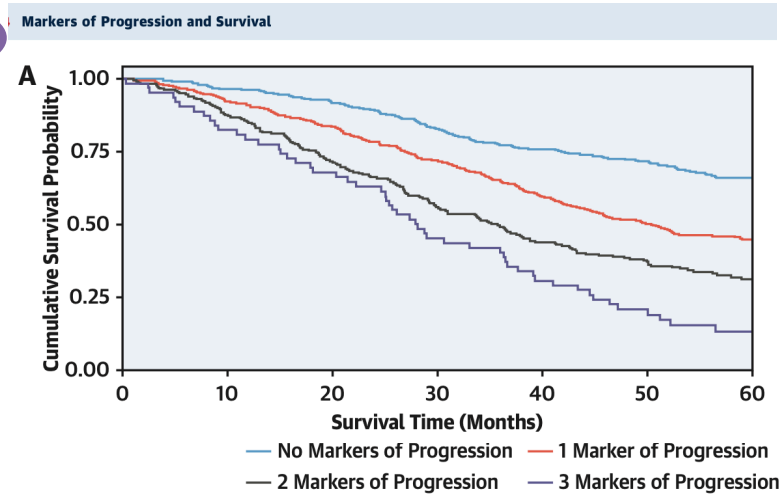
- 2,141 patients underwent a baseline 6MWT
- A shorter 6MWT distance was associated with a more severe cardiac phenotype
- A distance of <350 m was associated with a 2.2-fold higher risk of mortality in the overall population

Change in 6MWT Distance

- 1,118 patients underwent a follow-up 6MWT at 1 year
- Absolute worsening of the 6MWT defined as a reduction >35 m was associated with NT-proBNP progression and outpatient diuretic intensification
- Absolute worsening of the 6MWT was associated with a 1.8-fold higher risk of mortality in the overall population







9 Ioannou

1 ATTRibute-CM
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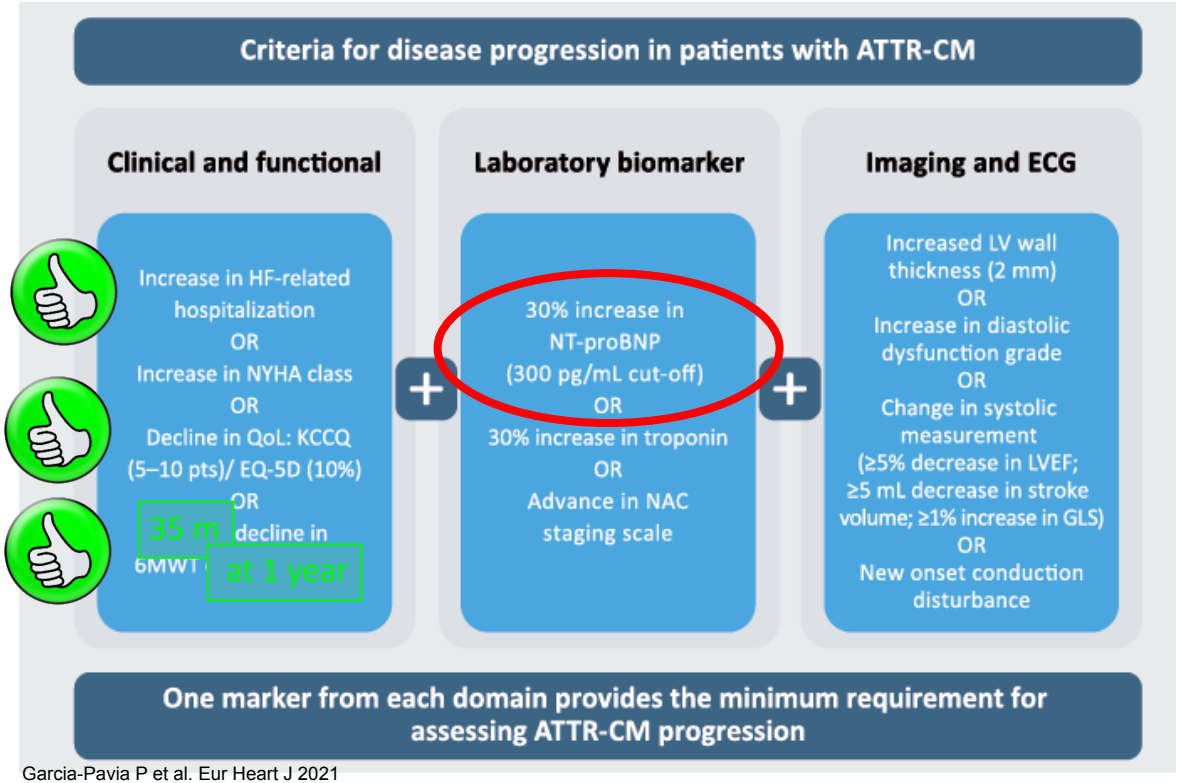
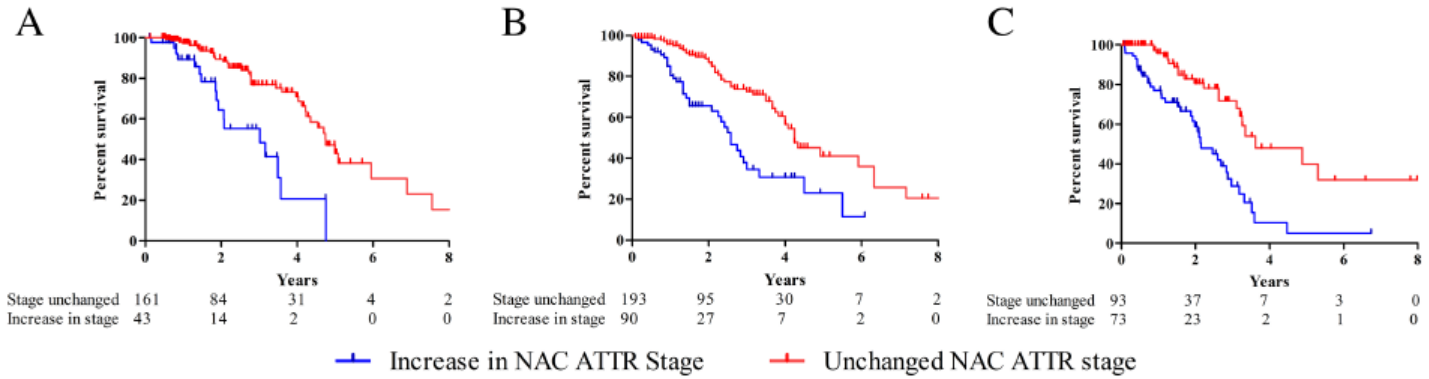


Garcia-Pavia P et al. Eur Heart J 2021

9Ioannou A. Stratifying disease progression in patients with cardiac ATTR amyloidosis. *J Am Coll Cardiol.* 2024.

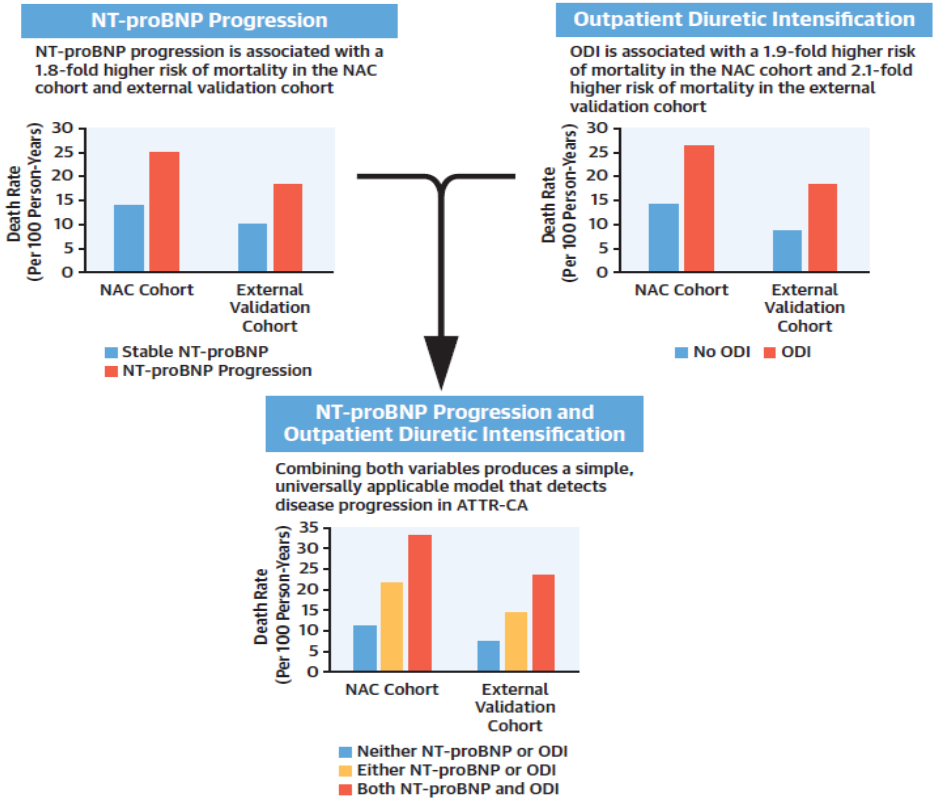
Biomarkers and laboratory markers

Biomarkers and laboratory markers	NT-proBNP	30% increase with 300 pg/mL cut-off To be measured during a 30-day period of clinical stability and under same atrial rhythm	6 months
	Troponin (high-sensitivity) assay	30% increase	6 months
	Clinical staging system	Advance in NAC staging score	6 months



Garcia Pavia P et al. Eur J Heart Failure (2021) 23, 895-905
Law S et al. ESC Heart Failure (2020);7:3942-3949

CENTRAL ILLUSTRATION N-Terminal Pro-B-Type Natriuretic Peptide Progression and Outpatient Diuretic Intensification Detect Disease Progression



Ioannou A, et al. J Am Coll Cardiol. 2024;83(14):1276–1291.

N-terminal pro-B-type natriuretic peptide (NT-proBNP) progression and outpatient diuretic intensification (ODI) are associated with an increased risk of mortality. Combining both variables produces a simple, universally applicable model that detects disease progression in the National Amyloidosis Centre (NAC) and external validation cohorts.

Ioannou A et al. JACC Vol.83, n.14, 2024

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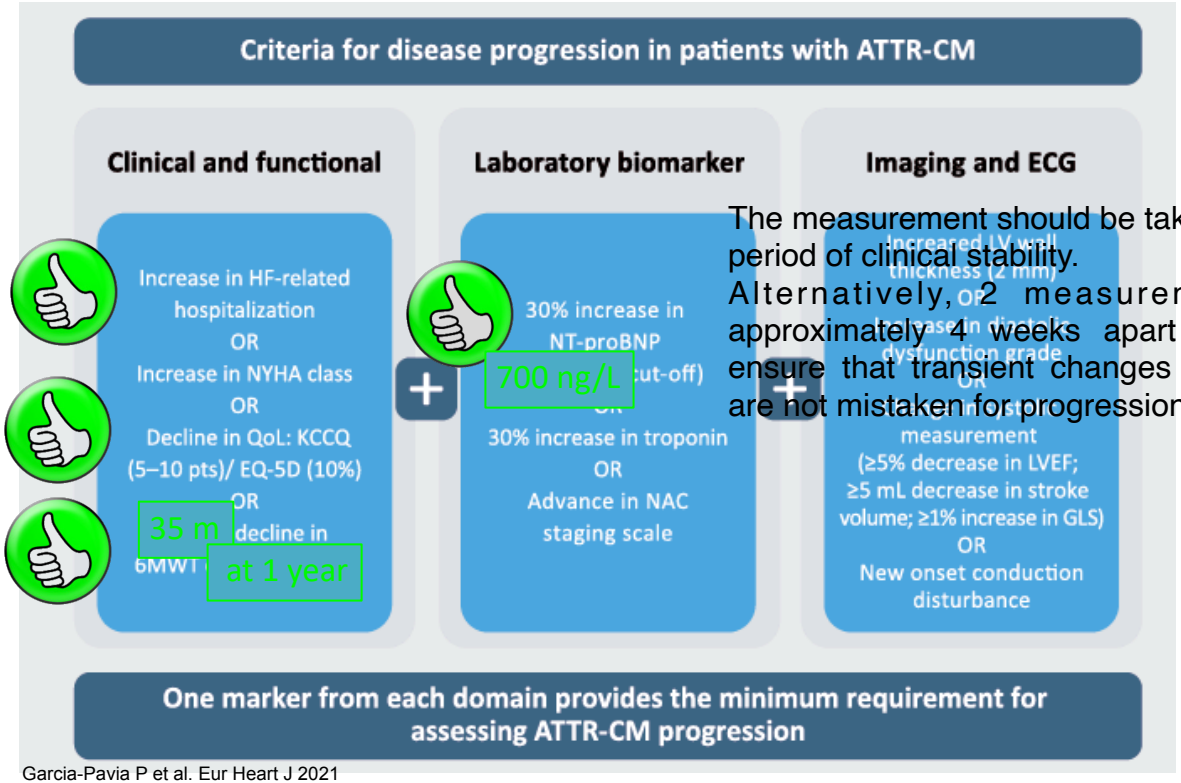
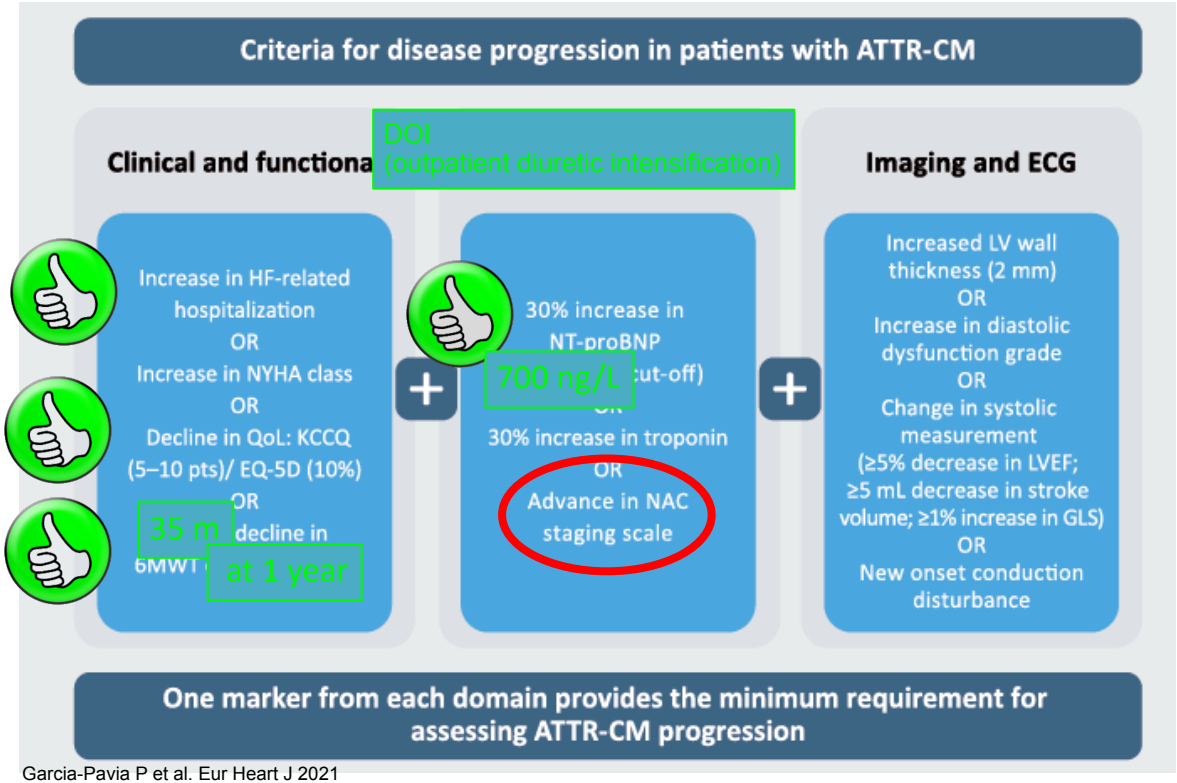


Garcia-Pavia P et al. Eur Heart J 2021

The measurement should be taken during a period of clinical stability. Alternatively, 2 measurements taken approximately 4 weeks apart may help to ensure that transient changes in NT-proBNP are not mistaken for progression.

9Ioannou A. Stratifying disease progression in patients with cardiac ATTR amyloidosis. *J Am Coll Cardiol.* 2024.

9 Ioannou
10 HELIOS-B



Garcia-Pavia P et al. Eur Heart J 2021

9Ioannou A. Stratifying disease progression in patients with cardiac ATTR amyloidosis. J Am Coll Cardiol. 2024.
10Fontana M. Outpatient worsening heart failure in patients with transthyretin amyloidosis with cardiomyopathy in the HELIOS-B trial. J Am Coll Cardiol. 2025

JAMA Cardiology | Original Investigation

Kidney Outcomes in Transthyretin Amyloid Cardiomyopathy

Adam Ioannou, MBBS, BSc, PhD; Yousuf Razvi, MBChB; Aldostefano Porcari, MD; Muhammad U. Rauf, MBBS; Ana Martinez-Naharro, PhD; Lucia Venneri, MD, PhD; Salsabeel Kazi, MBBS, BSc; Ali Pasyar, MBBS, BSc;

MAIN OUTCOMES AND MEASURES The primary outcome was the risk of all-cause mortality associated with decline in kidney function (defined as a decrease in eGFR >20%).

(N=2001, 69% ATTRwt, 15% V142I, 16% non-V142I)

Patients who experienced decline in kidney function more often had the p.(V142I) genotype (20.6% vs 13.3%; $P < .001$) and had a more severe cardiac phenotype at baseline (NT-proBNP: 2949 pg/mL vs 2309 pg/mL; $P < .001$)

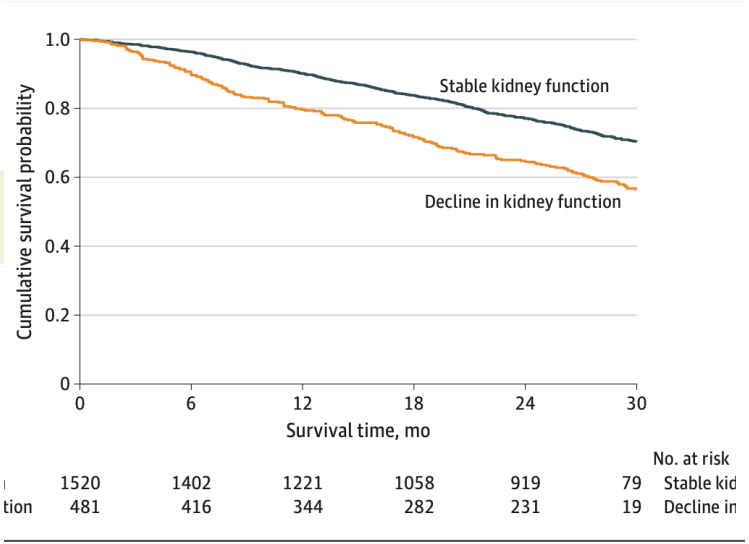
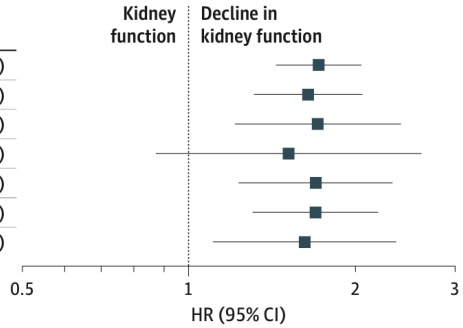


Figure 2. Risk of Mortality Associated With Decline in Kidney Function in Transthyretin Amyloid Cardiomyopathy

Subgroups	No. of patients	HR (95% CI)	*P* for interaction
Overall population	2001	1.71 (1.43-2.04)	
Wild type	1385	1.64 (1.31-2.04)	.93
p.(V142I)	301	1.70 (1.21-2.39)	
Non-p.(V142I)	315	1.51 (0.87-2.61)	
NAC stage 1	1078	1.69 (1.11-2.35)	.97
NAC stage 2	687	1.69 (1.30-2.18)	
NAC stage 3	236	1.61 (1.11-2.35)	



Decline in kidney function remained independently associated with mortality after adjusting for increases in NT-proBNP and outpatient diuretic intensification (HR, 1.48; 95% CI, 1.23-2.76; $P < .001$).

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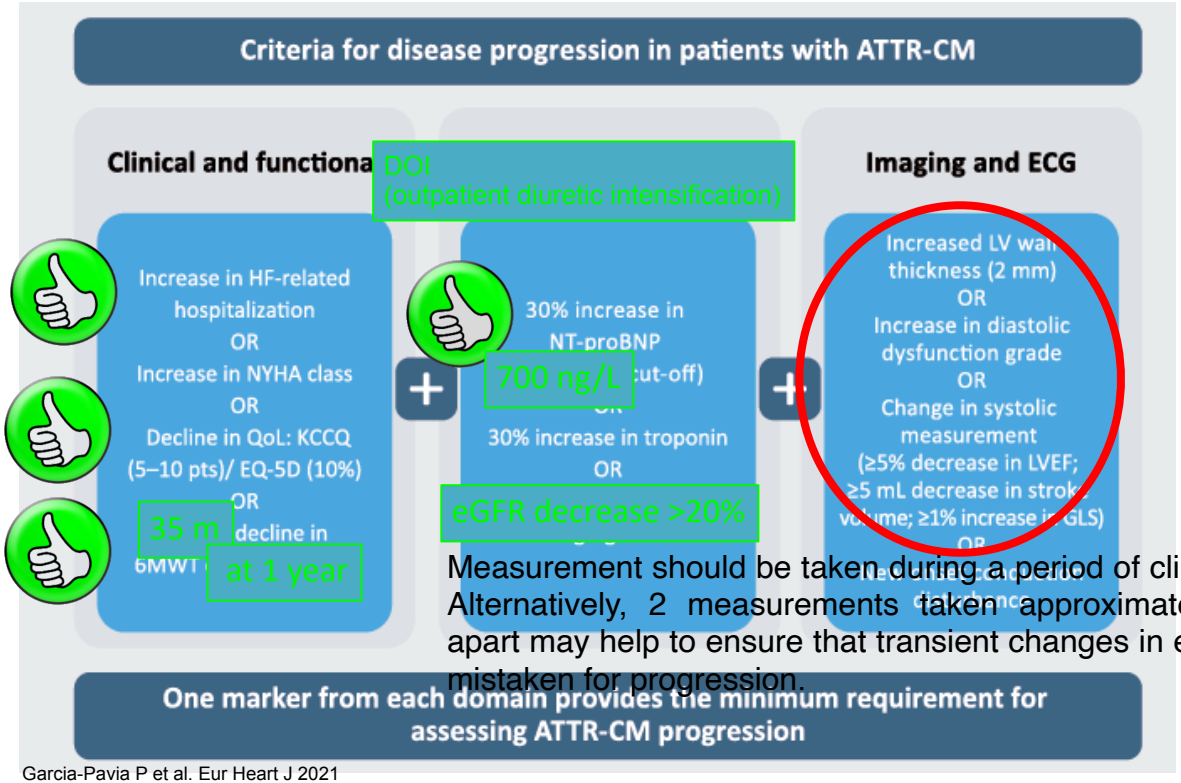


Garcia-Pavia P et al. Eur Heart J 2021

Measurement should be taken during a period of clinical stability. Alternatively, 2 measurements taken approximately 4 weeks apart may help to ensure that transient changes in eGFR are not mistaken for progression.

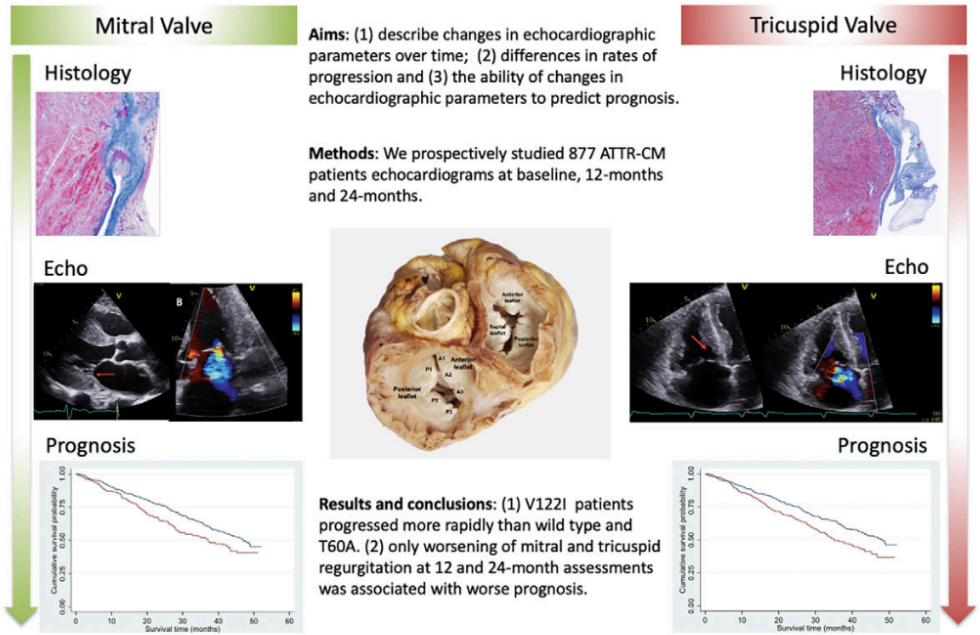
11Ioannou A. Kidney outcomes in transthyretin amyloid cardiomyopa- thy. JAMA Cardiol. 2025.

Echocardiographic variables

IVSd (mm)
PWTd (mm)
LVM (g)
LVEDD (mm)
LVEDDi (mm/m^2)
MWT (mm)
LVEDV (ml)
LVEDVi (ml/m^2)
LVESV (ml)
LVESVi (ml/m^2)
SV (ml)
SV index (ml/m^2)
EF (%)
LAA (cm^2)
LAA index (cm^2/m^2)
RAA (cm^2)
RAA index (cm^2/m^2)
E/A
DT (ms)
e′ lateral (cm/s)
e′ septal (cm/s)
E/e′ lateral
E/e′ average
MAPSE (mm)
TAPSE (mm)
TAPSE/PASP
S′ tricuspid (cm/s)
RWT
MCF (%)
LV LS (%)
RV LS (%)
SABr
RALS
PASP (mmHg)
LA strain reservoir
LA strain contraction

Methods and results

We prospectively studied 877 ATTR-CM patients attending our centre between 2000 and 2020. Serial echocardiography findings at baseline, 12 months and 24 months were compared with survival. Overall, 565 patients had wild-type ATTR-CM and 312 hereditary ATTR-CM (201 with V122I; 90 with T60A). There was progressive worsening of structural and functional parameters over time, patients with V122I ATTR-CM showing more rapid worsening of left and right ventricular structural and functional parameters compared to both wild-type and T60A ATTR-CM. Among



Conclusion

In ATTR-CM, echocardiographic parameters progressively worsen over time. Patients with V122I ATTR-CM demonstrate the most rapid deterioration. Worsening of MR and TR were the only parameters associated with mortality, MR remaining independent after adjusting for known predictors.

Liza Chacko et al. European Journal of Heart Failure (2022)

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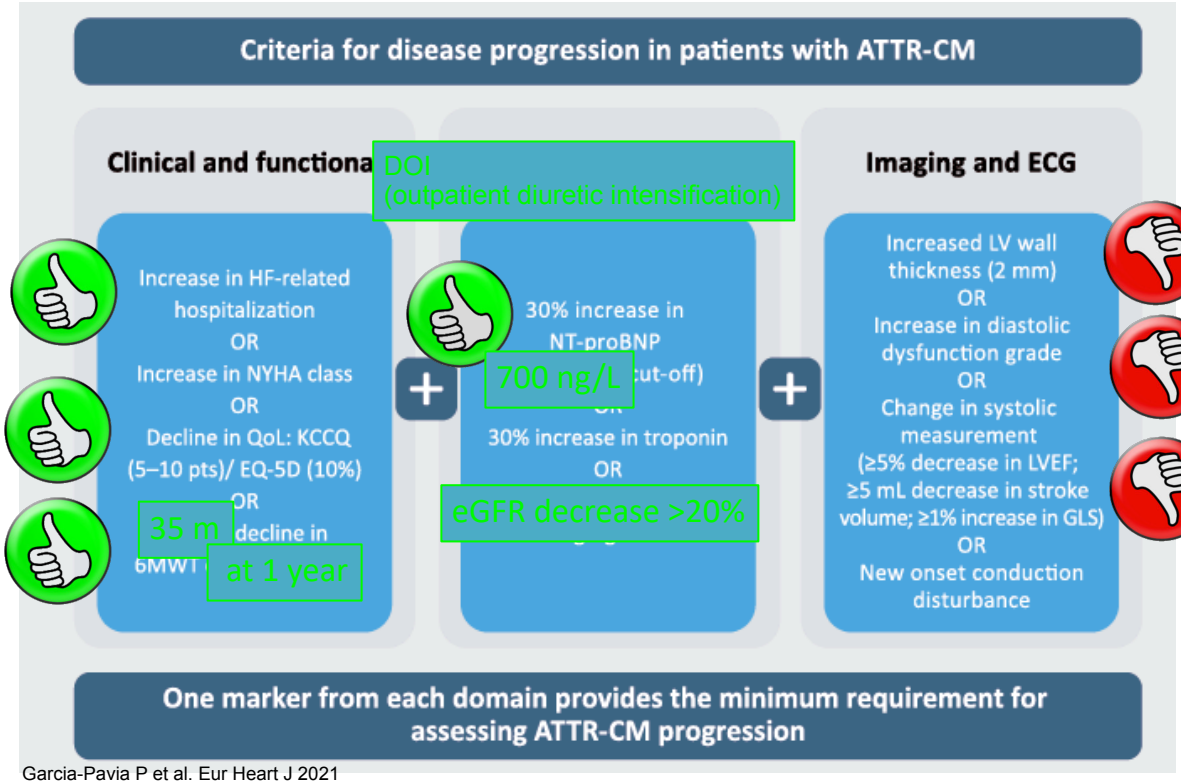

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Worsening of MR and TR

Garcia-Pavia P et al. Eur Heart J 2021

12Liza Chacko et al. European Journal of Heart Failure (2022)

Imaging parameters and ECG			
Echocardiography	LV measures wall thickness/mass	≥2-mm increase in LV wall thickness	6–12 months
	Systolic function measurements	≥5% decrease in LV ejection fraction decrease; ≥5 mL decrease in stroke volume and ≥1% increase in LV global longitudinal strain	12 months
	Diastolic dysfunction worsening, e.g. using diastolic functioning grade	Stepwise increase in diastolic functioning grade; consistent deterioration in diastolic function	12 months
ECG/Holter ECG	New-onset of arrhythmic/conduction disturbances	New-onset bundle branch block New-onset AV block (of any degree) Sinus pauses, sinus node dysfunction, AF with a very slow ventricular response without pharmacologic treatment (<50 bpm)	6 months

Garcia Pavia P et al. Eur J Heart Failure (2021) 23, 895-905

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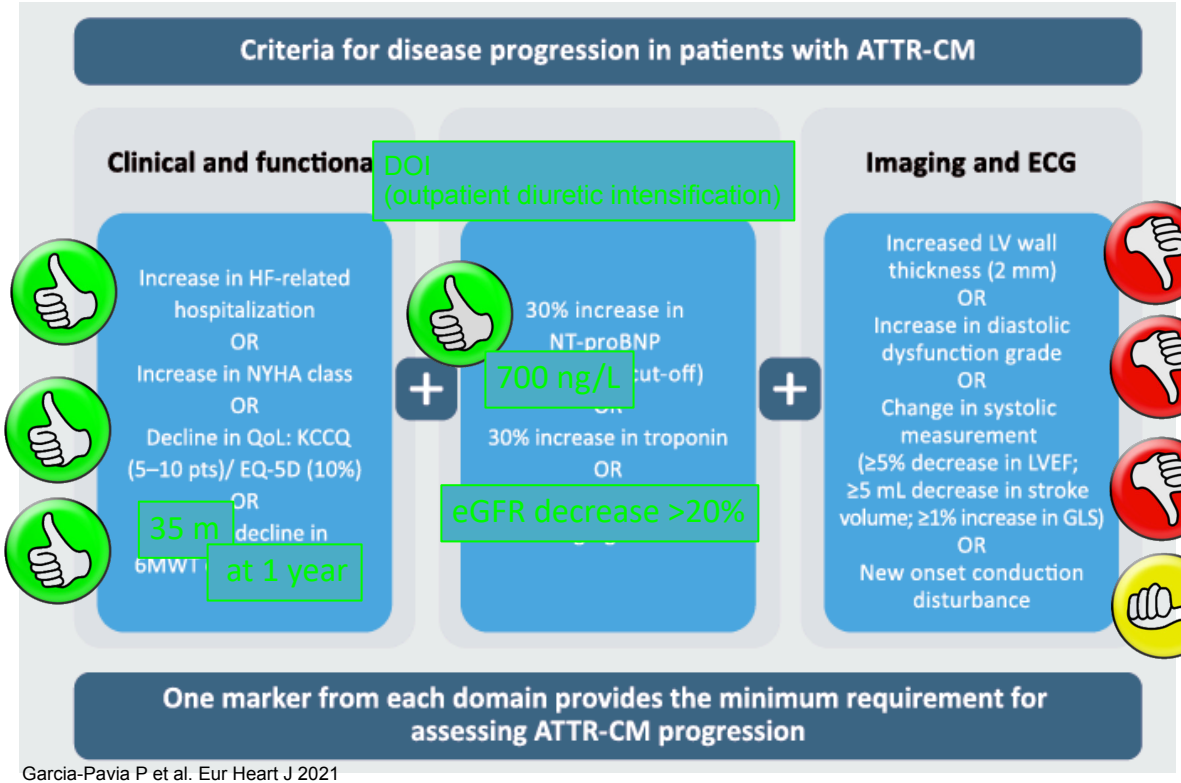

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Worsening of MR and TR

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Other considerations when assessing disease progression

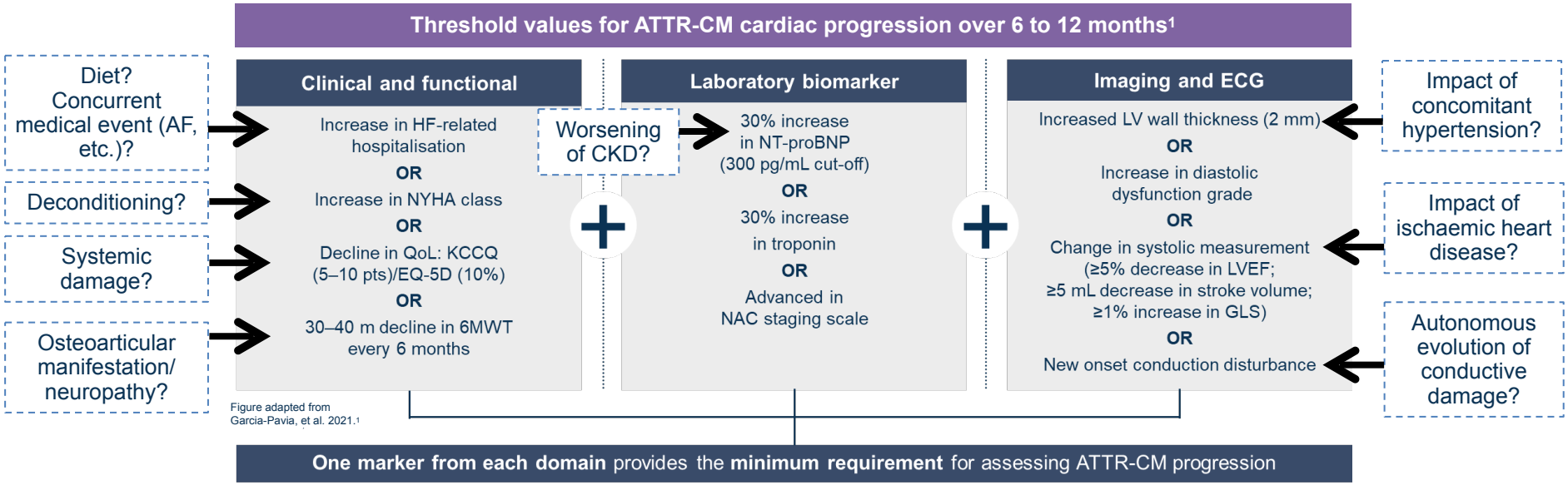
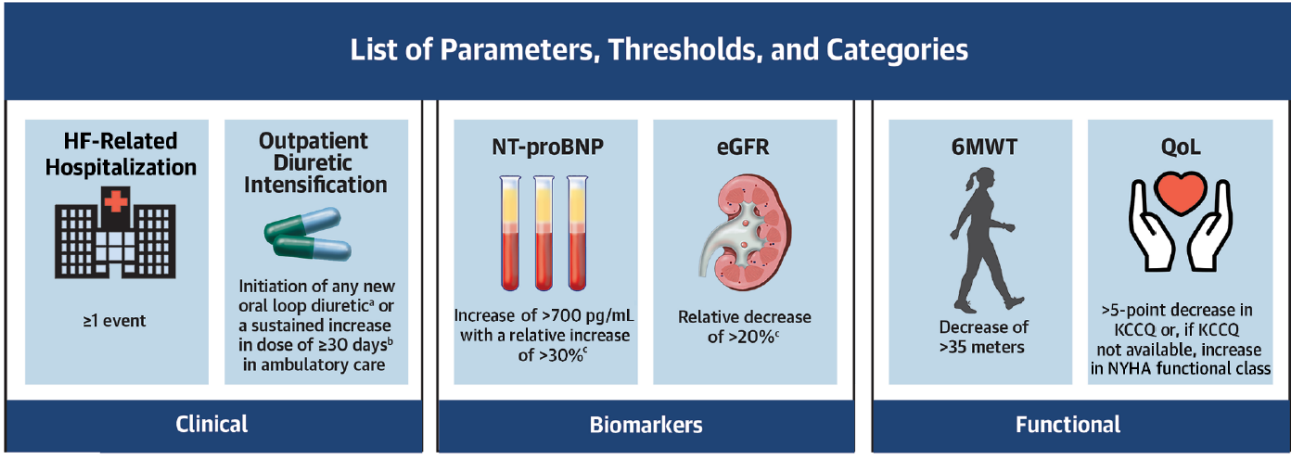


Figure adapted from Garcia-Pavia, et al. 2021.[1]

Criteria for Evaluating Disease Progression in Patients With ATTR-CM: update

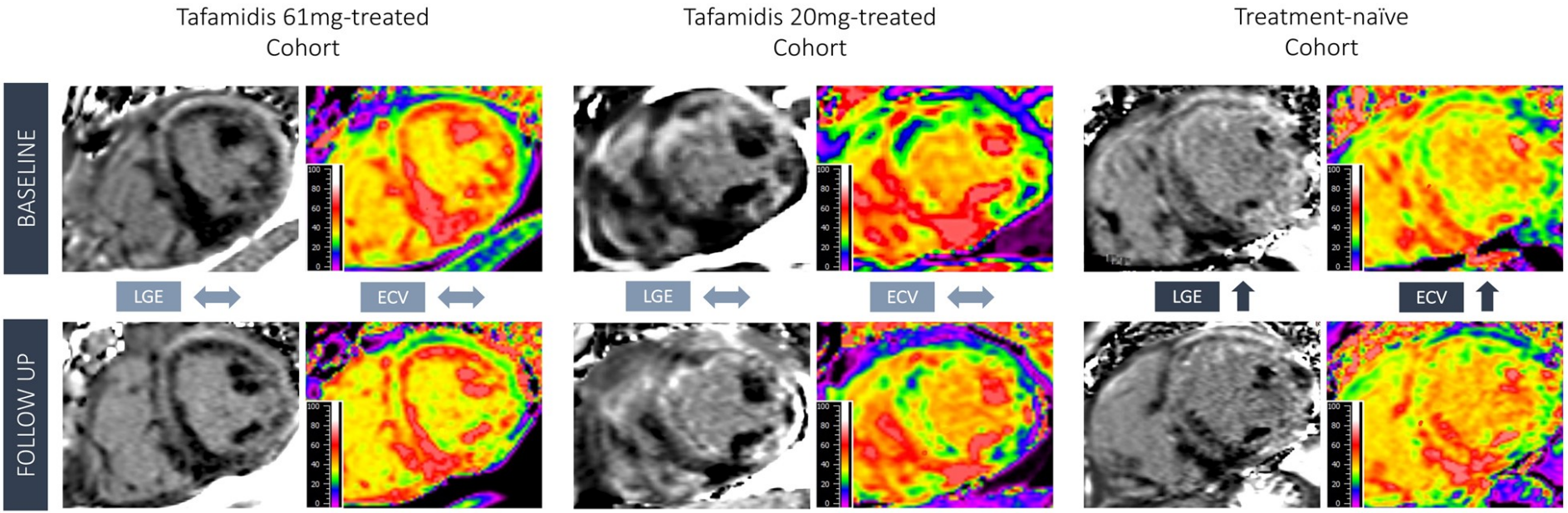


García-Pavía et al J A C C : H E A R T F A I L U R E 2 0 2 5 Monitoring Progression in ATTR-CM

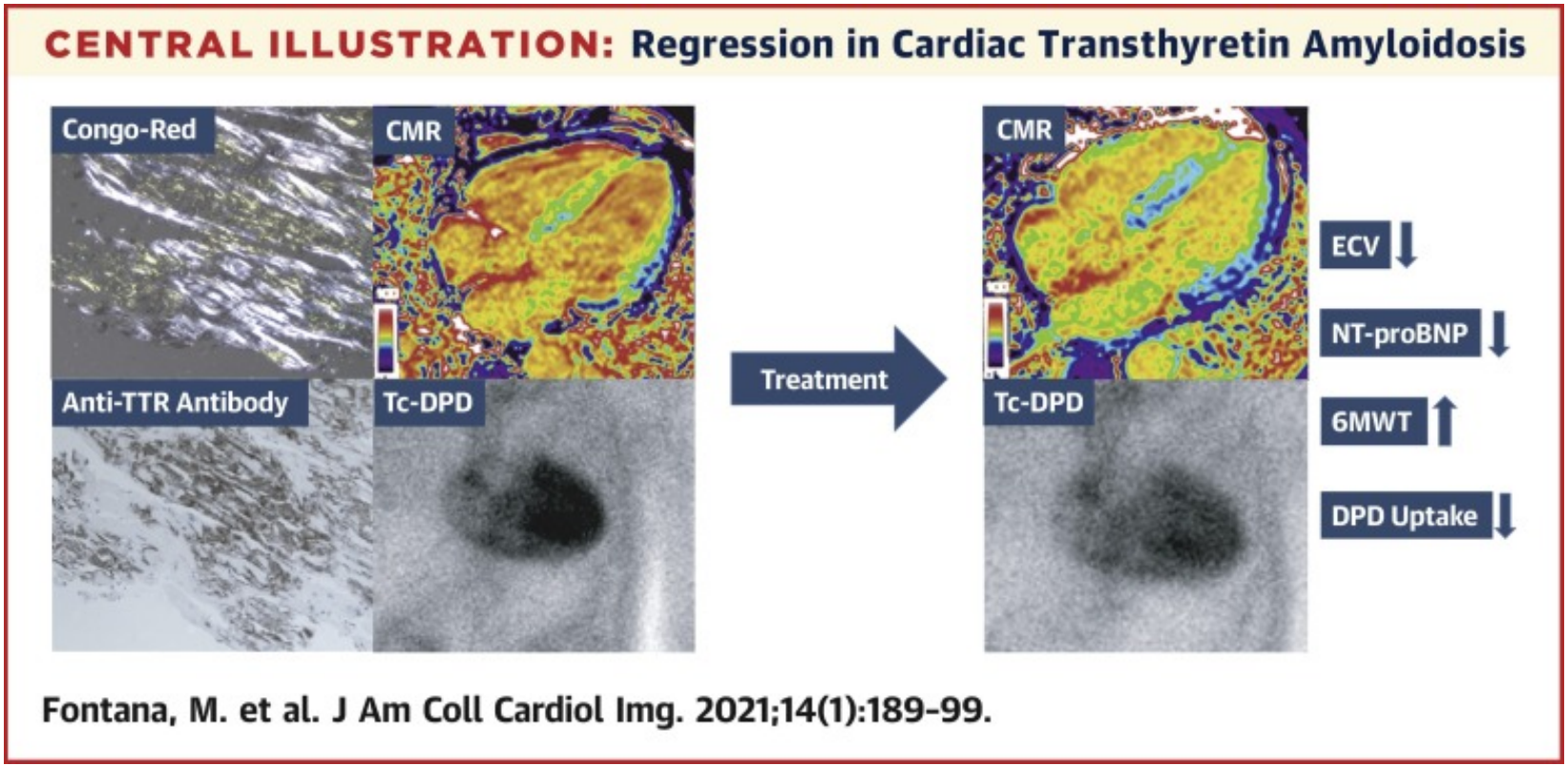
Tafamidis treatment delays structural and functional changes of the left ventricle in patients with transthyretin amyloid cardiomyopathy

René Rettl [1], Christopher Mann[1], Franz Duca[1], Theresa-Marie Dachs [1], Christina Binder[1], Luciana Camuz Ligios [1], Lore Schrutka [1], Daniel Dalos[1], Matthias Koschutnik [1], Carolina Donà [1], Andreas Kammerlander [1], Dietrich Beitzke [2], Christian Loewe [2], Silvia Charwat-Resl [3], Christian Hengstenberg [1], Johannes Kastner[1], Roza Badr Eslam[1]*, and Diana Bonderman [1,3]*

EACVI
European Association of Cardiovascular Imaging
European Society of Cardiology

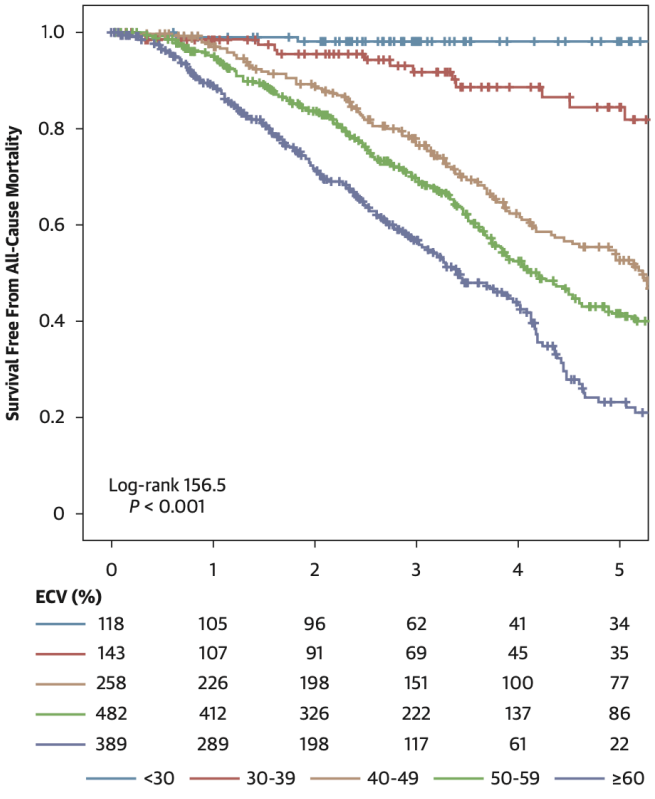


Reduction in CMR Derived Extracellular Volume With Patisiran Indicates Cardiac Amyloid Regression



JACC VOL. 87,

FIGURE 5 ECV Categories and Survival: Kaplan-Meier Analysis



Myocardial Amyloid Burden in Transthyretin Amyloidosis

Awais Sheikh, MBChB,[a,*] Anouk Achten, MD,[b,*] Alberto Aimo, MD, PhD,[c,d] Yousuf Razvi, MBChB, BSc,[a]

ECV independently predicted mortality (HR: 1.22 per 10% increase; $P < 0.001$) after multivariable analysist.

ECV retained prognostic value across hs-troponin and N-terminal pro-B-type natriuretic peptide (NT-proBNP) strata, Perugini grades 1 to 3, and left ventricular mass index (LVMI) tertiles, with steeper gradients in low-biomarker/low-LVMI strata.

↑ ECV is associated with worse survival
HR 1.22 per 10% increase (95% CI 1.10-1.34, P = 0.001)

STUDY DESIGN AND POPULATION

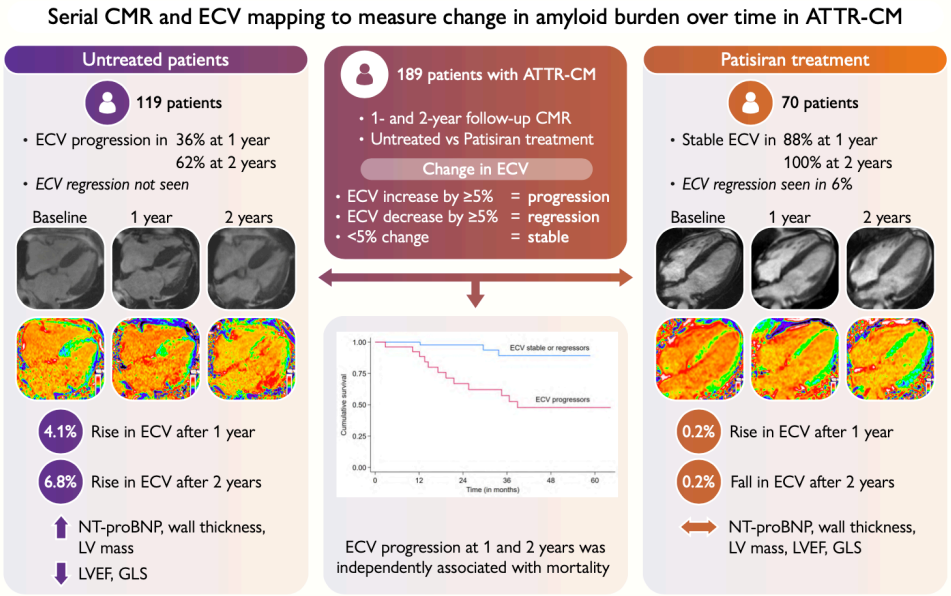
- Prospective cohort study
- UK National Amyloidosis Centre
- 2011–2024
- 1,541 individuals across the ATTR spectrum
- 8% asymptomatic TTR variant carriers
- 3% with extra-cardiac ATTR
- 5% with early-stage ATTR-CM
- 85% with overt ATTR-CM

Primary Endpoint
All-cause mortality over a median follow-up of 2.8 years

ESC European Society of Cardiology
European Heart Journal (2025) **46**, 5049–5058
https://doi.org/10.1093/eurheartj/ehaf412

Transthyretin amyloid cardiomyopathy: natural history and treatment response assessed by cardiovascular magnetic resonance

Rishi K. Patel [1], Adam Ioannou [1], Awais Sheikh[1], Yousuf Razvi [1],



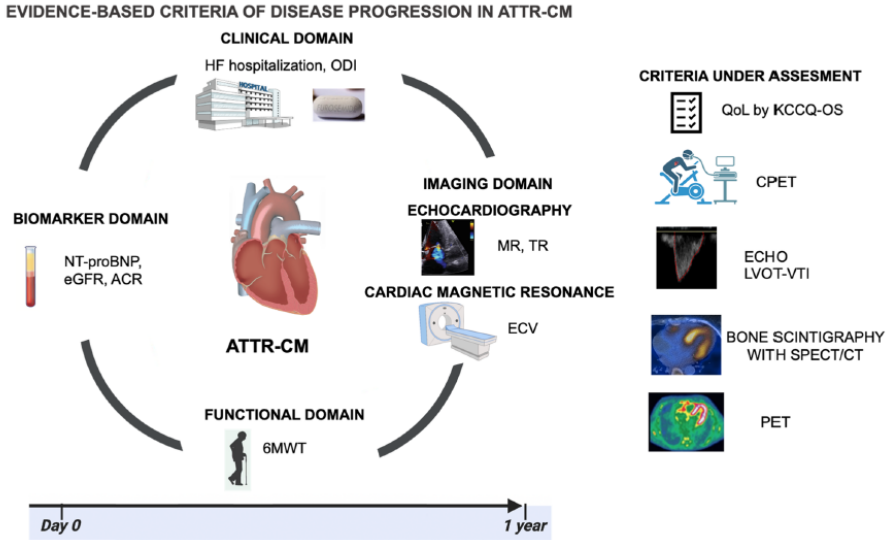
In untreated patients, 36% progressed at 1 year which significantly increased to 62% at 2 years. Mean increase in ECV of 4.1% (after 1 year) and 6.8% (after 2 years).

In Patisiran group, stable ECV was observed in 88% of patients (after 1 year) and 100% of patients (after 2 years).

ECV progression after 1 year was independently associated with mortality after adjusting for known predictors (hazard ratio 2.021; 95% confidence

Genotype, n (%)

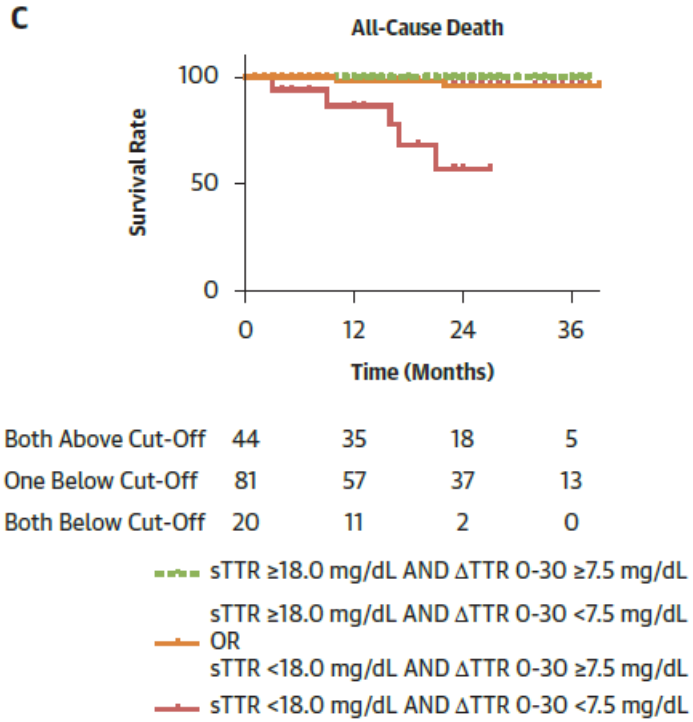
- **Wild type** 100 (52.9%)
- **V122I** 20 (10.6%)
- **T60A** 28 (14.8%)
- **Other** 41 (21.7%)

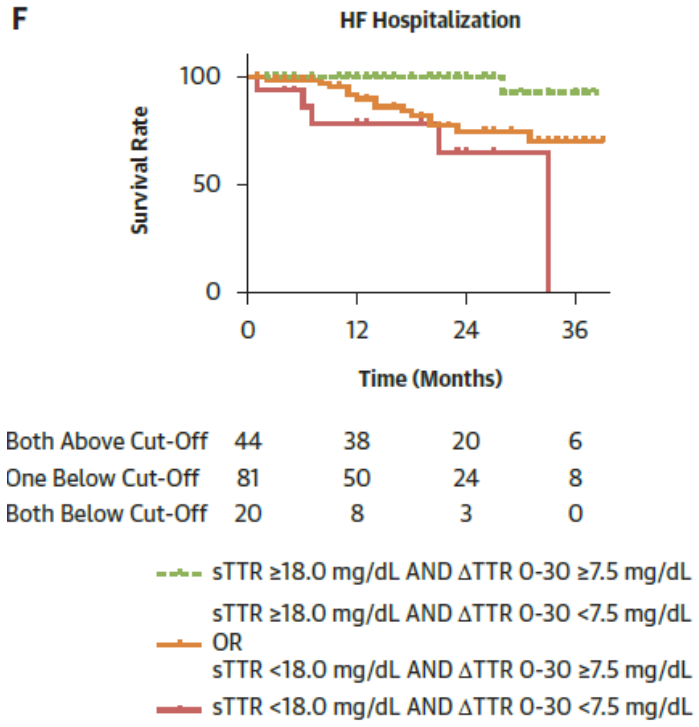


Markers Clinical domain	Definition of progression	HR for death (95 %CI)	Sample size (n)	Follow up assessment
QoL by KCCQ-OS	Decrease >5 points	2.5 (1.12–5.60) *	205	12 mo
6MWT distance	Decrease >35 m (absolute reduction)	1.80 (1.51–2.15)	2141	12 mo
	Decrease >5 % (relative reduction)	1.89 (1.59–2.24)		
CPET	Decrease in peak VO_2 >1.5 ml/kg/min	1.59 (1.15–2.20)	365	12 mo
	Increase in VE/VCO_2 > 5	1.56 (1.12–2.28)		
ODI	Any initiation or increment in the LD dose	1.79 (1.58–2.04)	2275	12 mo
Biomarker domain				
NT-proBNP progression	Increase of >700 ng/L and >30 %	1.81 (1.59–2.05)	2275	12 mo
Troponin T	Increase of >10 ng/L and >20 %	1.84 (1.44–2.34)	2275	12 mo
Decline in eGFR	Decrease of >20 %	1.71 (1.43–2.04)	2001	12 mo
Urinary ACR	Increase of ≥30 %	1.84 (1.06–3.19)	1181	12 mo
Cardiac imaging domain				
LVOT-VTI (AI-derived on echocardiogram)	Decrease of ≥5 %	1.44 (1.17–1.76)	752	12 mo
Mitral regurgitation (on echocardiogram)	Worsening by ≥1 grade	1.43 (1.14–1.80)	877	12 mo
Tricuspid regurgitation (on echocardiogram)	Worsening by ≥1 grade	1.38 (1.10–1.75)		12 mo
Myocardial ECV (on CMR)	Increase ≥5 %	2.02 (1.08–3.78)	189	12 mo

Porcari et al, European Journal of Internal Medicine 2026

Serum Transthyretin Before and After Starting Tafamidis as Outcome Predictors in ATTR Cardiomyopathy





Vincenzo Castiglione et al, JACC 2026; Vergaro et al, Clin Chem Lab Med 2026; aop

Conclusions …

- Multiple assessment tools are required for appropriate monitoring of ATTR-CA disease progression.

- This approach is based on clinical, biomarker, and functional parameters that may not fully capture the underlying mechanisms driving disease progression, nor accurately reflect biological pathways that can be targeted by therapeutic interventions.

- Definite response criteria await validation to drive therapeutic decisions.

and Questions…

- Do all the "progression criteria" have the same importance?
- Is there still a role for echocardiography and EKG in monitoring pts?
- Other imaging technics (MRI and Bone-scintigraphy) may provide insight into treatment response?
- Disease progression is not linear so do we need to assess more frequently in advanced patients?
- How a NON-cardiac progression influence our therapeutic decision-making?
- When and how should we change treatment?
- How long a therapy should be administered before considering a change?