

SUPPLEMENTARY MATERIALS

Phenotypic Considerations for Tafamidis Use in a Real-World Cohort of Older Patients With Transthyretin Amyloid Cardiomyopathy

Carlo Fumagalli^{1,2}, Francesco Cappelli^{2,3}, Mathew S. Maurer⁴, Fabian aus dem Siepen⁵, Angela Dispenzieri⁶, Pablo Garcia-Pavia⁷, Mazen Hanna⁸, Martin Carlsson⁹, Thibaud Damy¹⁰

¹Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy

²Tuscan Regional Amyloidosis Centre, Careggi University Hospital, Florence, Italy

³Department of clinical and experimental medicine, University of Florence, Florence Italy

⁴Columbia University Irving Medical Center, New York, NY, USA

⁵Department of Cardiology, Angiology and Respiratory Medicine, University Hospital Heidelberg, Heidelberg, Germany

⁶Division of Hematology, Mayo Clinic, Rochester, MN, USA

⁷Hospital Universitario Puerta de Hierro de Majadahonda, IDIPHISA, CIBERCV, and Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain

⁸Amyloidosis Center, Department of Cardiovascular Medicine, Cleveland Clinic, Cleveland, OH, USA

⁹Pfizer Inc, New York, NY, USA

¹⁰National Referral Center for Cardiac Amyloidosis, Henri Mondor University Hospital, Créteil, France

Corresponding author: Dr. Carlo Fumagalli; Department of Advanced Medical and Surgical Sciences,
University of Campania "Luigi Vanvitelli", P.zza L. Miraglia, 2 80138, Naples, Italy
Email: carlo.fumagalli@unicampania.it

SUPPLEMENTARY RESULTS

Supplementary Analysis: Patients aged <80 and ≥80 years

Baseline Characteristics

Of the 1924 patients with transthyretin amyloid cardiomyopathy (ATTR-CM), 1188 and 736 were aged <80 and ≥80 years, respectively (**Supplementary Table S5**). Among patients aged <80 and ≥80 years, mean age at enrollment was 72.3 and 84.0 years, 90.2% and 86.7% were male, and 93.9% and 94.2% had a predominantly cardiac phenotype, respectively. A higher proportion of patients aged ≥80 versus <80 years had wild-type ATTR-CM (ATTRwt-CM; 94.6% vs 80.1%), New York Heart Association (NYHA) class III or IV heart failure (HF) symptoms (37.9% vs 25.8%), and National Amyloidosis (NAC) stage III ATTR-CM (31.3% vs 12.8%) (**Supplementary Table S5**). Patients aged ≥80 vs <80 years had a lower mean estimated glomerular filtration rate (eGFR; 46.6 vs 64.1 mL/min/1.73 m²) and lower mean modified body mass index (mBMI; 1072.6 vs 1134.3 kg·g/[m²·L]). Prior to tafamidis initiation, 74.1% and 70.2% of patients aged <80 and ≥80 years received concomitant HF medication, respectively; 34.1% and 36.3% received concomitant HF therapy on or after the first dose of tafamidis, respectively (**Supplementary Tables S1 and S2**).

All-Cause Mortality

In patients aged <80 and ≥80 years, mean follow-up was 1.6 and 1.4 years; median survival was not yet reached in patients <80 years and was 45.7 months in those ≥80 years, respectively (**Fig. 2B**). At the end of follow-up, all-cause mortality (ACM) occurred in 15.9% and 25.7% of patients aged <80 and ≥80 years (**Supplementary Table S6**). In adjusted analyses using Cox proportional hazards model, the risk of ACM was similar between age groups (Hazard ratio [HR] 0.84; 95% CI 0.70–1.00) (**Supplementary Table S6**). Moreover, among all patients, male participants had a 48% lower risk of ACM than female participants (HR 0.52; 95% CI 0.38–0.70; **Supplementary Table S3**). Kaplan–Meier survival estimates were significantly lower in patients aged ≥80 vs <80 years at months 30 (63.1% vs 77.0%) and 42 (53.0%

vs 70.9%) (**Fig. S4**). Using a delayed-entry model adjusted for time from diagnosis to enrollment, estimated survival rates were significantly reduced in patients aged ≥ 80 versus < 80 years at months 30 (69.0% vs 82.5%), 42 (59.0% vs 73.8%), and 60 (40.4% vs 59.8%) (**Supplementary Table S4**).

Survival Subgroup Analysis

Estimated overall survival rates at 30 and 42 months were lower in patients aged ≥ 80 vs < 80 years who were male, had ATTRwt-CM, and a predominantly cardiac phenotype (**Supplementary Figs. S5– S7**).

Among patients with baseline eGFR ≥ 45 ml/min/1.73 m², those aged ≥ 80 versus < 80 years had significantly reduced survival at 42 months (**Supplementary Fig. S8**). There were no significant differences in overall survival at 30 and 42 months between age groups in patients who were female, had ATTRv-CM, mixed phenotype, and baseline eGFR < 45 mL/min/1.73 m² and NYHA class III HF symptoms (**Supplementary Figs. S5–S9**). Survival rates were similar between age groups in patients with eGFR ≥ 45 ml/min/1.73 m² at 30 months (**Supplementary Fig. S8**) and NYHA class HF I/II symptoms at 42 months (**Supplementary Fig. S9**).

Hospitalizations

All-cause hospitalization occurred in 36.6% of patients aged < 80 years and in 40.2% of those aged ≥ 80 years whereas 23.0% and 23.4% had cardiovascular-related hospitalization (CVH); total annual rates for CVH were 0.59 and 0.69, respectively (**Supplementary Table S6**). Patients aged < 80 versus ≥ 80 years had a 21% lower risk of first CVH (HR 0.79; 95% CI 0.68–0.93), without significant differences in the risk for recurrent CVH (**Supplementary Table S6**).

Composite Outcome of ACM or CVH

The composite outcome of ACM or CVH occurred in 31.3% of patients aged < 80 years and 39.7% of patients aged ≥ 80 years (**Supplementary Table S6**). Patients aged < 80 versus ≥ 80 years had a 16% lower risk of ACM or first CVH (HR 0.84; 95% CI, 0.74–0.96). Risks for ACM or recurrent CVH were similar between age groups (**Supplementary Table S6**).

All-Cause Treatment-Emergent Adverse Events

In the early access cohort, treatment-emergent AEs occurred in 87.1% and 88.6% of patients aged <80, and ≥ 80 years, respectively (**Supplementary Table S7**). Serious and severe AEs were numerically more frequent in patients aged ≥ 80 years. Discontinuation of the study drug due to AEs was infrequent in patients aged <80 (0.4%) and ≥ 80 years (1.1%). In THAOS, treatment-emergent AEs occurred in 30.3% and 32.1% of patients aged <80 and ≥ 80 years, respectively. The proportion of patients with serious and severe AEs were comparable across age groups. Discontinuation of the study drug due to AEs was uncommon in patients <80 (3.4%) and ≥ 80 years (3.3%).

Table S1. Concomitant heart failure medications prior to the first dose of tafamidis

Indication category, <i>n</i> (%)	Main analysis			Supplementary analysis	
	<80 years (<i>n</i> = 1188)	80–85 years (<i>n</i> = 505)	>85 years (<i>n</i> = 231)	<80 years (<i>n</i> = 1188)	≥80 years (<i>n</i> = 736)
Any concomitant HF medication	910 (76.6)	387 (76.6)	144 (62.3)	880 (74.1)	517 (70.2)
Agents acting on the renin–angiotensin system	332 (27.9)	121 (24.0)	40 (17.3)	326 (27.4)	154 (20.9)
ACE inhibitors, combinations	5 (0.4)	1 (0.2)	1 (0.4)	5 (0.4)	2 (0.3)
ACE inhibitors, plain	160 (13.5)	56 (11.1)	17 (7.4)	155 (13.0)	70 (9.5)
Angiotensin II receptor blockers, combinations	40 (3.4)	13 (2.6)	4 (1.7)	40 (3.4)	17 (2.3)
Angiotensin II receptor blockers, plain	128 (10.8)	51 (10.1)	19 (8.2)	127 (10.7)	66 (9.0)
Other agents acting on the renin-angiotensin system	1 (0.1)	-	-	1 (0.1)	-
Beta-blocking agents	333 (28.0)	132 (26.1)	45 (19.5)	316 (26.6)	165 (22.4)
Beta-blocking agents	333 (28.0)	131 (25.9)	45 (19.5)	316 (26.6)	164 (22.3)
Beta-blocking agents and thiazides	-	1 (0.2)	-	-	1 (0.1)
Cardiovascular disease	811 (68.3)	359 (71.1)	135 (58.4)	760 (64.0)	474 (64.4)
ACE inhibitors	23 (1.9)	11 (2.2)	1 (0.4)	23 (1.9)	12 (1.6)
Aldosterone antagonists and other potassium-sparing agents	289 (24.3)	126 (25.0)	47 (20.3)	268 (22.6)	166 (22.6)
Angiotensin II receptor antagonists	25 (2.1)	13 (2.6)	5 (2.2)	25 (2.1)	18 (2.4)
Beta-blockers	58 (4.9)	26 (5.1)	7 (3.0)	58 (4.9)	33 (4.5)
Diuretics	77 (6.5)	27 (5.3)	14 (6.1)	77 (6.5)	41 (5.6)
Diuretics and potassium-sparing agents in combination	5 (0.4)	2 (0.4)	1 (0.4)	5 (0.4)	3 (0.4)
High-ceiling diuretics	653 (55.0)	288 (57.0)	113 (48.9)	573 (48.2)	354 (48.1)
Low-ceiling diuretics, excluding thiazides	40 (3.4)	31 (6.1)	9 (3.9)	38 (3.2)	39 (5.3)
Low-ceiling diuretics, thiazides	43 (3.6)	20 (4.0)	-	41 (3.5)	19 (2.6)
Other diuretics	12 (1.0)	1 (0.2)	-	12 (1.0)	1 (0.1)

ACE angiotensin-converting enzyme, *HF* heart failure

Table S2. Concomitant heart failure medications on or after the first dose of tafamidis

Indication category, <i>n</i> (%)	Main analysis			Supplementary analysis	
	<80 years (<i>n</i> = 1188)	80–85 years (<i>n</i> = 505)	>85 years (<i>n</i> = 231)	<80 years (<i>n</i> = 1188)	≥80 years (<i>n</i> = 736)
Any concomitant HF medication	596 (50.2)	247 (48.9)	109 (47.2)	405 (34.1)	267 (36.3)
Agents acting on the renin–angiotensin system	124 (10.4)	49 (9.7)	24 (10.4)	85 (7.2)	49 (6.7)
ACE inhibitors, combinations	4 (0.3)	1 (0.2)	1 (0.4)	3 (0.3)	2 (0.3)
ACE inhibitors, plain	57 (4.8)	24 (4.8)	11 (4.8)	35 (2.9)	24 (3.3)
Angiotensin II receptor blockers, combinations	33 (2.8)	6 (1.2)	4 (1.7)	25 (2.1)	9 (1.2)
Angiotensin II receptor blockers, plain	49 (4.1)	22 (4.4)	9 (3.9)	37 (3.1)	18 (2.4)
Other agents acting on the renin-angiotensin system	-	-	-	-	-
Beta-blocking agents	177 (14.9)	70 (13.9)	19 (8.2)	104 (8.8)	55 (7.5)
Beta-blocking agents	177 (14.9)	69 (13.7)	19 (8.2)	104 (8.8)	54 (7.3)
Beta-blocking agents and thiazides	-	1 (0.2)	-	-	1 (0.1)
Cardiovascular disease	508 (42.8)	225 (44.6)	101 (43.7)	317 (26.7)	223 (30.3)
ACE inhibitors	3 (0.3)	1 (0.2)	-	3 (0.3)	1 (0.1)
Aldosterone antagonists and other potassium-sparing agents	165 (13.9)	73 (14.5)	35 (15.2)	120 (10.1)	76 (10.3)
Angiotensin II receptor antagonists	4 (0.3)	-	-	4 (0.3)	-
Beta-blockers	11 (0.9)	-	2 (0.9)	11 (0.9)	2 (0.3)
Diuretics	18 (1.5)	4 (0.8)	2 (0.9)	18 (1.5)	6 (0.8)
Diuretics and potassium-sparing agents in combination	2 (0.2)	-	-	2 (0.2)	-
High-ceiling diuretics	447 (37.6)	205 (40.6)	92 (39.8)	192 (16.2)	147 (20.0)
Low-ceiling diuretics, excluding thiazides	61 (5.1)	27 (5.3)	10 (4.3)	57 (4.8)	29 (3.9)
Low-ceiling diuretics, thiazides	46 (3.9)	18 (3.6)	10 (4.3)	43 (3.6)	24 (3.3)
Other diuretics	1 (0.1)	2 (0.4)	1 (0.4)	1 (0.1)	3 (0.4)

ACE angiotensin-converting enzyme, *HF* heart failure

Table S3. Effect of male vs female sex on clinical outcomes

Outcomes	Main analysis			Supplementary analysis	
	<80 years	80–85 years	≥85 years	<80 years	≥80 years
	(n = 1188)	(n = 505)	(n = 231)	(n = 1188)	(n = 736)
ACM					
HR (95% CI), male vs female		0.49 (0.33, 0.72)		0.52 (0.38, 0.70)	
First CVH					
HR (95% CI), male vs female		0.89 (0.65, 1.23)		0.97 (0.78, 1.20)	
Recurrent CVH					
Risk Ratio (95% CI), male vs female		1.25 (0.96, 1.64)		1.29 (1.07, 1.56)	
ACM or first CVH					
HR (95% CI), male vs female		0.86 (0.66, 1.14)		0.93 (0.76, 1.12)	
ACM or recurrent CVH					
HR (95% CI), male vs female		0.70 (0.52, 0.93)		0.73 (0.96, 1.92)	
Risk ratio (95% CI), male vs female		1.33 (1.04, 1.69)		1.35 (1.15, 1.58)	

ACM all-cause mortality, *CI* confidence interval, *CVH* cardiovascular-related hospitalization, *HR* hazard ratio.

Table S4. Delayed-entry model: overall survival estimates

Treatment period	Main analysis			Supplementary analysis	
	<80 years	80–85 years	>85 years	<80 years	≥80 years
	(<i>n</i> = 1114)	(<i>n</i> = 485)	(<i>n</i> = 208)	(<i>n</i> = 1114)	(<i>n</i> = 693)
% Survival (95% CI), months					
30 months	82.5 (79.1, 86.0)	73.2 (67.7, 79.1)	59.4 (50.5, 69.8)	82.5 (79.1, 86.0)	69.0 (64.2, 74.1)
42 months	73.8 (69.9, 77.9)	63.7 (57.7, 70.5)	48.0 (38.9, 59.4)	73.8 (69.9, 77.9)	59.0 (53.8, 64.8)
60 months	59.8 (54.4, 65.8)	45.0 (37.8, 53.7)	30.7 (21.4, 44.0)	59.8 (54.4, 65.8)	40.4 (34.3, 47.5)
<i>CI</i> confidence interval					

Table S5. Supplementary analysis: baseline demographics and clinical characteristics of patients treated with tafamidis

Characteristic	<80 years (<i>n</i> = 1188)	≥80 years (<i>n</i> = 736)	<i>p</i> value
Age at enrollment, years			
Mean (SD)	72.3 (6.12)	84.0 (3.29)	<0.001
Sex, <i>n</i> (%)			0.016
Male	1072 (90.2)	638 (86.7)	
Female	116 (9.8)	98 (13.3)	
Race, <i>n</i> (%)	<i>n</i> = 1163	<i>n</i> = 696	<0.001
White	961 (80.9)	631 (85.7)	
Black or African American	131 (11.0)	40 (5.4)	
Asian	58 (4.9)	16 (2.2)	
Latino American	1 (0.1)	1 (0.1)	
American Hispanic	1 (0.1)	0	
Other	11 (0.9)	8 (1.1)	
Age at diagnosis, years	<i>n</i> = 1114	<i>n</i> = 693	
Mean (SD)	71.7 (6.13)	83.1 (3.51)	<0.001
Time from diagnosis to enrollment, years	<i>n</i> = 1114	<i>n</i> = 693	
Mean (SD)	1.1 (1.32)	1.1 (1.32)	0.921
Follow up time, years			
Mean (SD)	1.6 (1.17)	1.4 (1.09)	<0.001
Median (10th, 90th percentile)	1.3 (0.4, 3.5)	1.0 (0.3, 3.2)	
TTR genotype, <i>n</i> (%)			<0.001
Wild-type	952 (80.1)	696 (94.6)	
Variant	236 (19.9)	40 (5.4)	
Phenotype, <i>n</i> (%)			0.787
Cardiac	1115 (93.9)	693 (94.2)	
Mixed	73 (6.1)	43 (5.8)	
NYHA class, <i>n</i> (%)	<i>n</i> = 1155	<i>n</i> = 700	<0.001
I	210 (18.2)	68 (9.7)	
II	647 (56.0)	367 (52.4)	
III	288 (24.9)	254 (36.3)	
IV	10 (0.9)	11 (1.6)	
mBMI	<i>n</i> = 1012	<i>n</i> = 582	
Mean (SD)	1134.3 (206.27)	1072.6 (182.35)	<0.001

NT pro-BNP, pg/mL	<i>n</i> = 294	<i>n</i> = 192	
Mean (SD)	8933.2 (22,541.98)	8265.0 (14,544.67)	0.691
eGFR, mL/min/1.73 m ²	<i>n</i> = 1119	<i>n</i> = 691	
Mean (SD)	64.1 (24.11)	46.6 (16.08)	<0.001
NAC stage, <i>n</i> (%)	<i>n</i> = 289	<i>n</i> = 192	<0.001
I	129 (44.6)	51 (26.6)	
II	123 (42.6)	81 (42.2)	
III	37 (12.8)	60 (31.3)	

Baseline refers to at enrollment or the start of tafamidis treatment for patients treated with tafamidis.

eGFR estimated glomerular filtration rate, *mBMI* modified body mass index, *NAC* National Amyloidosis Center, *NT-proBNP* N-terminal pro-B-type natriuretic peptide, *NYHA* New York Heart Association; SD, standard deviation; TTR, transthyretin

Table S6. Supplementary analysis: clinical outcomes of all-cause mortality and hospitalizations

Outcomes	<80 years (<i>n</i> = 1188)	≥80 years (<i>n</i> = 736)
ACM, <i>n</i> (%)	189 (15.9)	189 (25.7)
HR (95% CI) ^a		
<80 vs ≥80 years	0.84 (0.70, 1.00)	
First CVH, <i>n</i> (%)	273 (23.0)	172 (23.4)
HR (95% CI) ^a		
<80 vs ≥80 years	0.79 (0.68, 0.93)	
Recurrent CVH, <i>n</i> (%)	273 (23.0)	172 (23.4)
Risk Ratio (95% CI) ^b		
<80 vs ≥80 years	1.00 (0.87, 1.15)	
ACM or first CVH, <i>n</i> (%)	372 (31.3)	292 (39.7)
HR (95% CI) ^a		
<80 vs ≥80 years	0.84 (0.74, 0.96)	
ACM or recurrent CVH, <i>n</i> (%)	372 (31.3)	292 (39.7)
HR (95% CI) ^c		
<80 vs ≥80 years	1.03 (0.81, 1.31)	
Risk ratio (95% CI) ^b		
<80 vs ≥80 years	0.99 (0.89, 1.11)	
All-cause hospitalizations, <i>n</i> (%)	435 (36.6)	296 (40.2)
CVH, <i>n</i> (%)	273 (23.0)	172 (23.4)
Duration of hospitalization, median (range), days	5.00 (0.0, 161.0)	6.00 (0.0, 77.0)
Total annual rate among all patients ^d	0.59	0.69

^a Analyzed using a stratified Cox proportional regression model with age (<80, ≥80 years), phenotype (cardiac vs mixed), *TTR* genotype (variant vs wild-type), baseline NYHA class (I/II vs III), baseline eGFR, and gender (male vs female) as covariates. Patients with NYHA class IV symptoms were excluded from the analysis.

^b Analyzed using the negative binomial regression model with genotype, NYHA class of genotype, and study, with an offset term based on the logarithm of the follow-up duration in years.

^c Analyzed using a Lin-Wei-Yang-Ying model.

^d Calculated as the total CVH across all patients divided by total years of study participation across all patients.

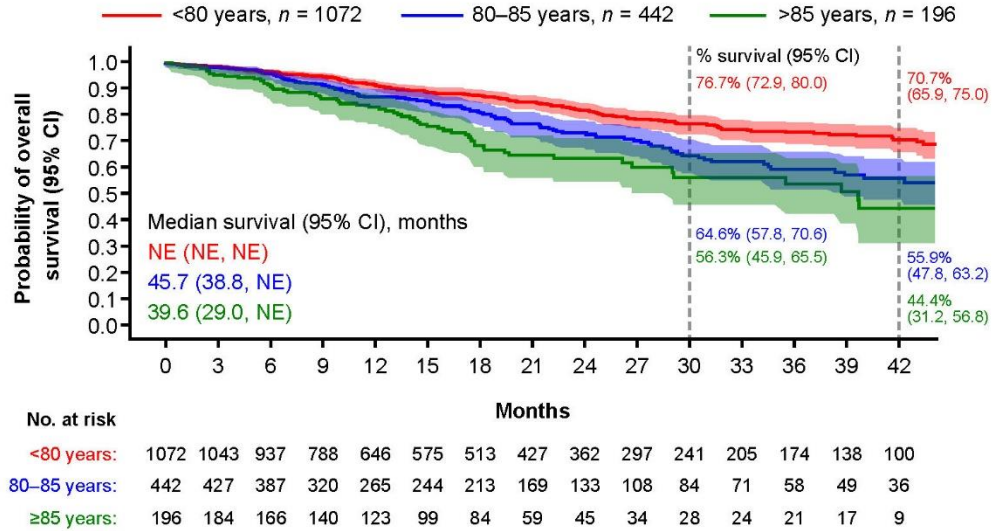
ACM all-cause mortality, *CI* confidence interval, *CVH* cardiovascular-related hospitalization, *HR* hazard ratio

Table S7. Supplementary analysis: all-cause, treatment-emergent adverse events in patients treated with tafamidis

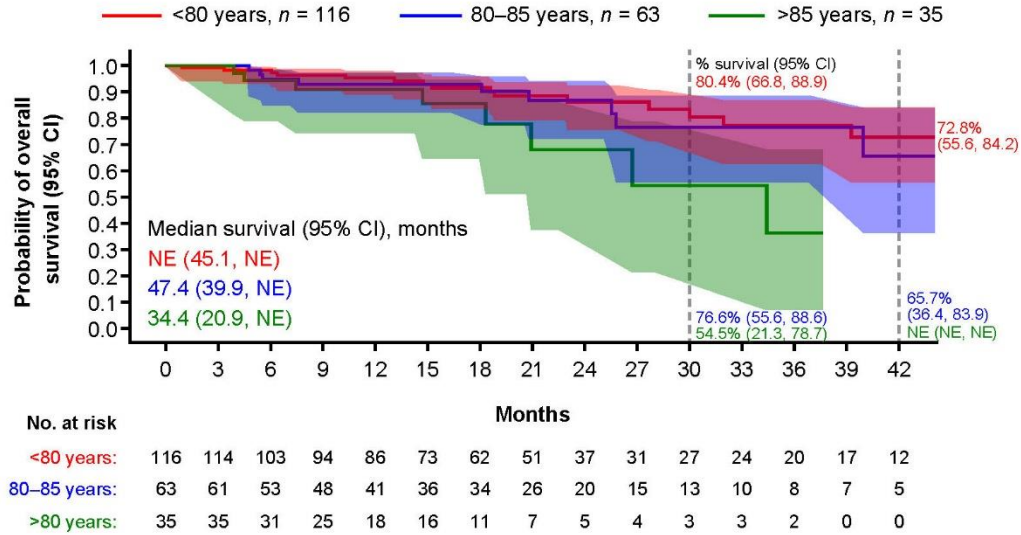
	Early access cohort B		THAOS	
	<80 years <i>n</i> = 924	≥80 years <i>n</i> = 552	<80 years <i>n</i> = 264	≥80 years <i>n</i> = 184
All-causality AEs, <i>n</i>	1127	876	217	151
Patients with AEs	805 (87.1)	489 (88.6)	80 (30.3)	59 (32.1)
Patients with serious AEs	436 (47.2)	300 (54.3)	61 (23.1)	45 (24.5)
Patients with severe AEs	316 (34.2)	240 (43.5)	50 (18.9)	41 (22.3)
Patients discontinued treatment due to AEs	4 (0.4) ^a	6 (1.1) ^a	9 (3.4) ^b	6 (3.3) ^b
Patients with dose reduced due to AEs	6 (0.6)	2 (0.4)	0	0
Patients temporarily discontinued study due to AEs	43 (4.7)	39 (7.1)	-	-
Patients discontinued study due to AEs	50 (5.4)	47 (8.5)	-	-
Patients with medication error events	0	0	65 (24.6)	43 (23.4)
Values are <i>n</i> (%) unless otherwise indicated.				
^a Treatment was withdrawn but patient continued in the study.				
^b For THAOS, this includes all patients for whom study drug was withdrawn (temporarily, permanently, or delayed) due to AEs and continued in the study.				
<i>AE</i> adverse event, <i>THAOS</i> Transthyretin Amyloidosis Outcomes Survey				

Fig. S1. Main analysis: Kaplan–Meier curve of overall survival by age group (<80, 80–85, and >85 years) in (a) male and (b) female patients with ATTR-CM treated with tafamidis

a) Male



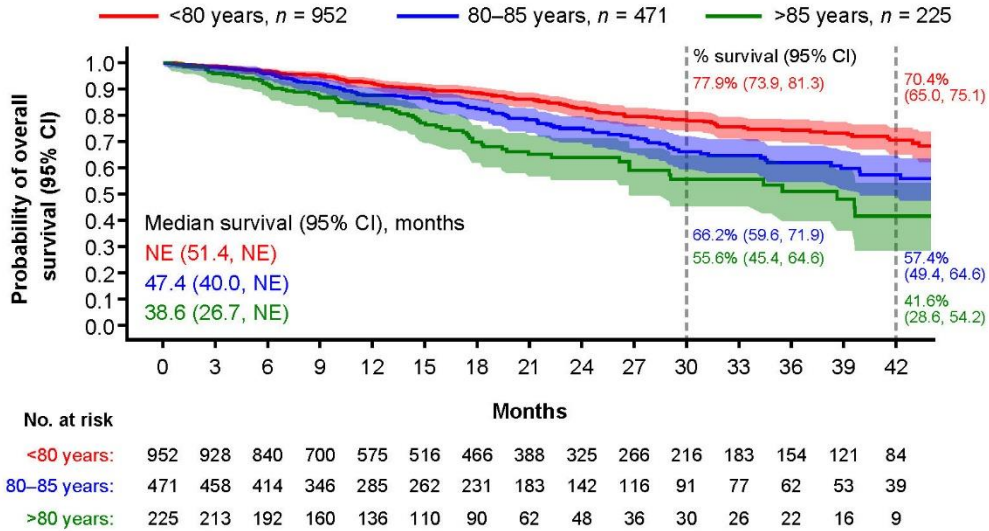
b) Female



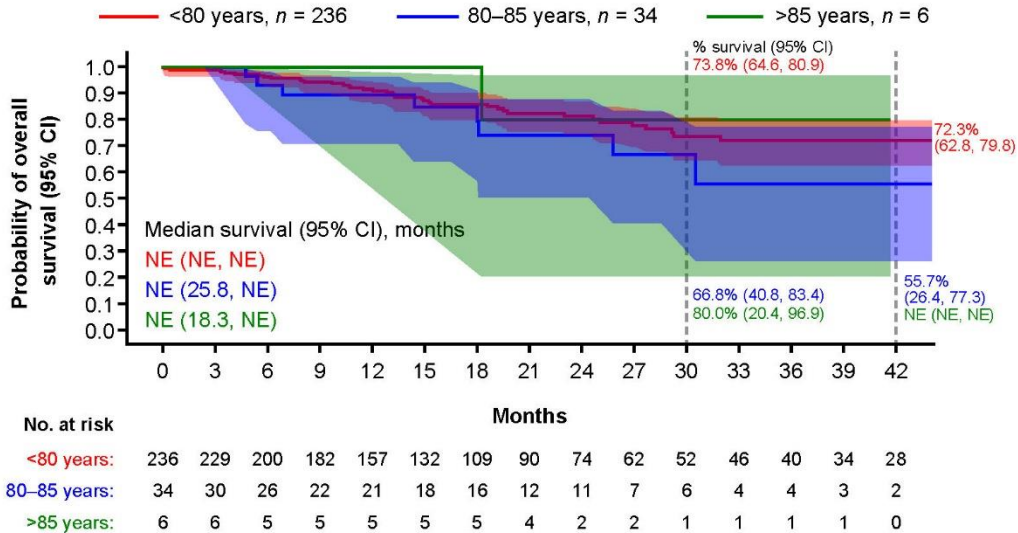
ATTR-CM transthyretin amyloid cardiomyopathy; CI confidence interval; NE non-estimable.

Fig. S2. Main analysis: Kaplan–Meier curve of overall survival by age group (<80, 80–85, and >85 years) in patients with (a) ATTRwt-CM and (b) ATTRv-CM treated with tafamidis

a) ATTRwt-CM



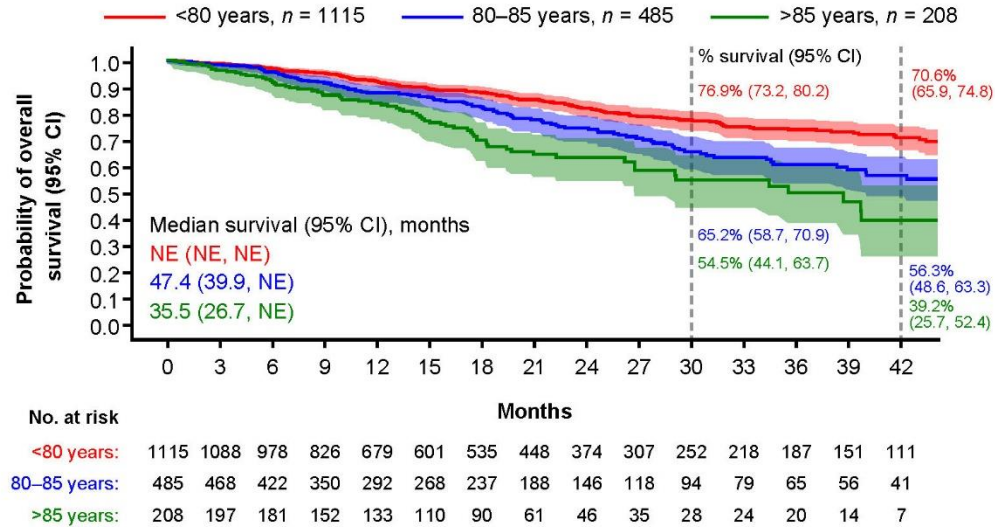
b) ATTRv-CM



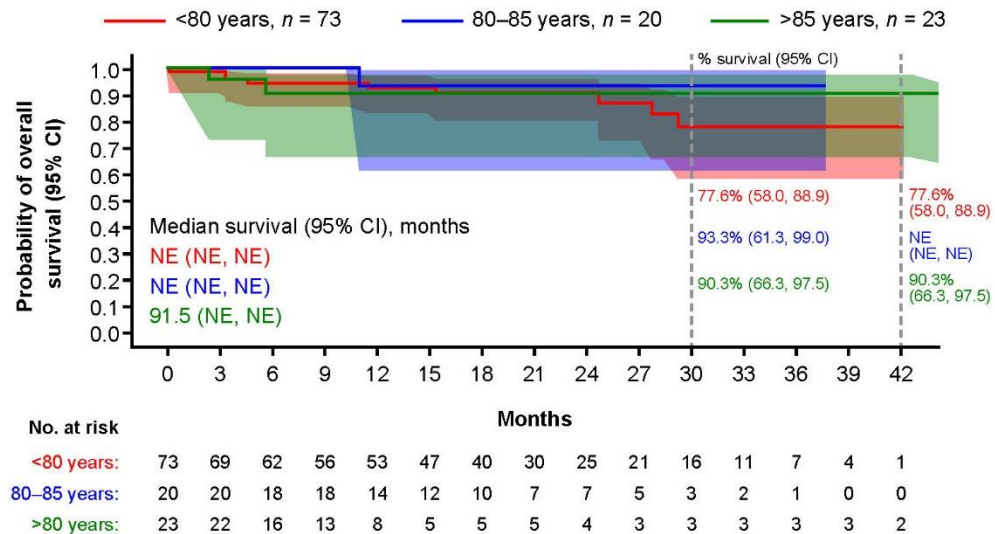
ATTR-CM variant transthyretin amyloid cardiomyopathy; ATTRwt-CM wild-type transthyretin amyloid cardiomyopathy; CI confidence interval; NE non-estimable.

Fig. S3. Main analysis: Kaplan–Meier curve of overall survival by age group (<80, 80–85, and >85 years) in patients with ATTR-CM with (a) predominantly cardiac and (b) mixed phenotype treated with tafamidis

a) Predominantly cardiac phenotype

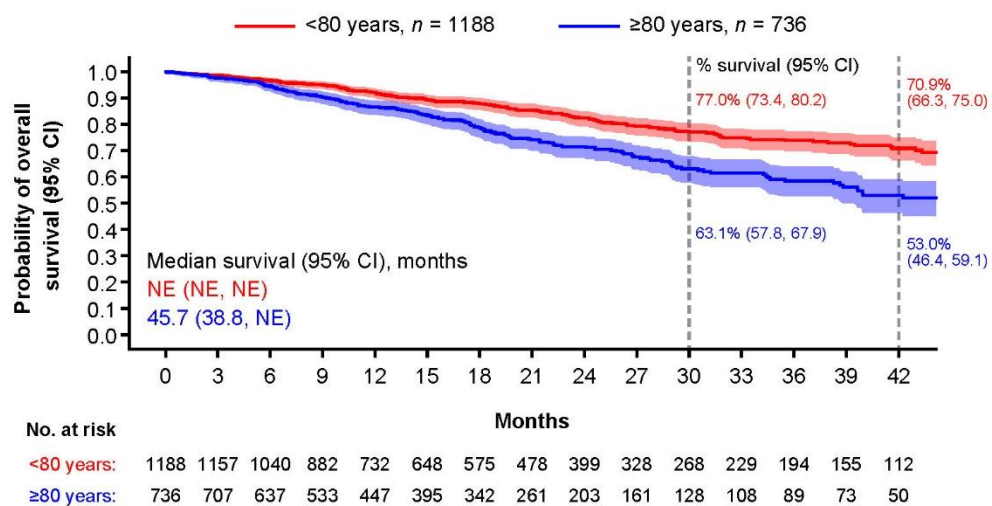


b) Mixed phenotype



ATTR-CM transthyretin amyloid cardiomyopathy; CI confidence interval; NE non-estimable.

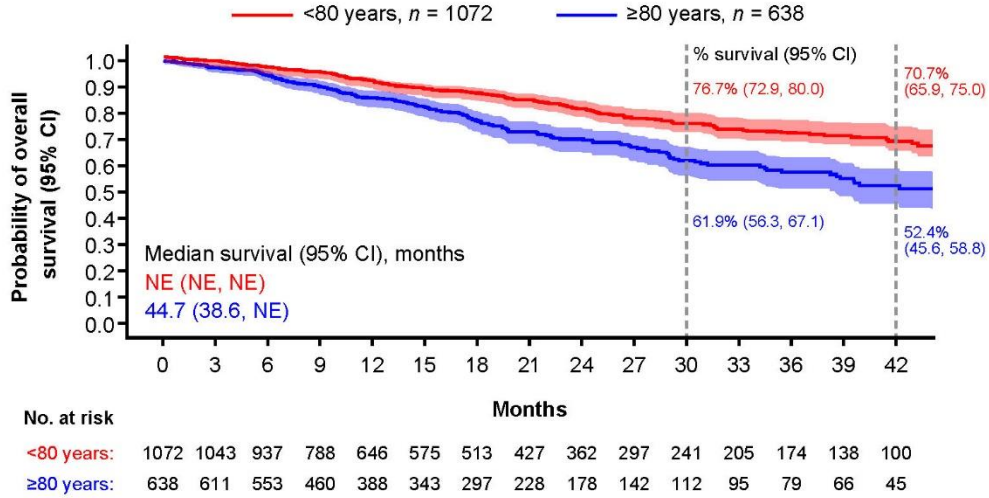
Fig. S4. Supplementary analysis: Kaplan–Meier curve of overall survival in patients treated with tafamidis stratified by age group (<80 vs ≥80 years)



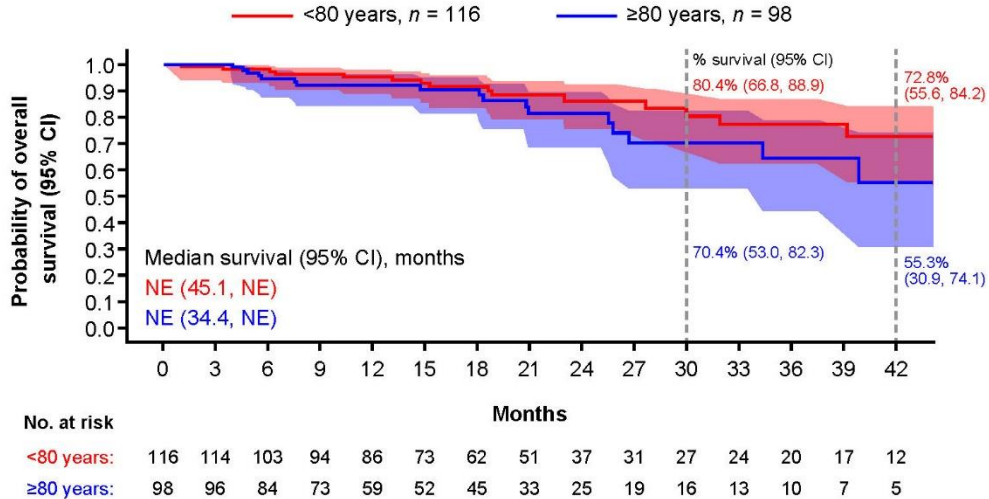
CI confidence interval; NE non-estimable.

Fig. S5. Supplementary analysis: Kaplan–Meier curve of overall survival by age group (≥ 80 and <80 years) in (a) male and (b) female patients with ATTR-CM treated with tafamidis

a) Male



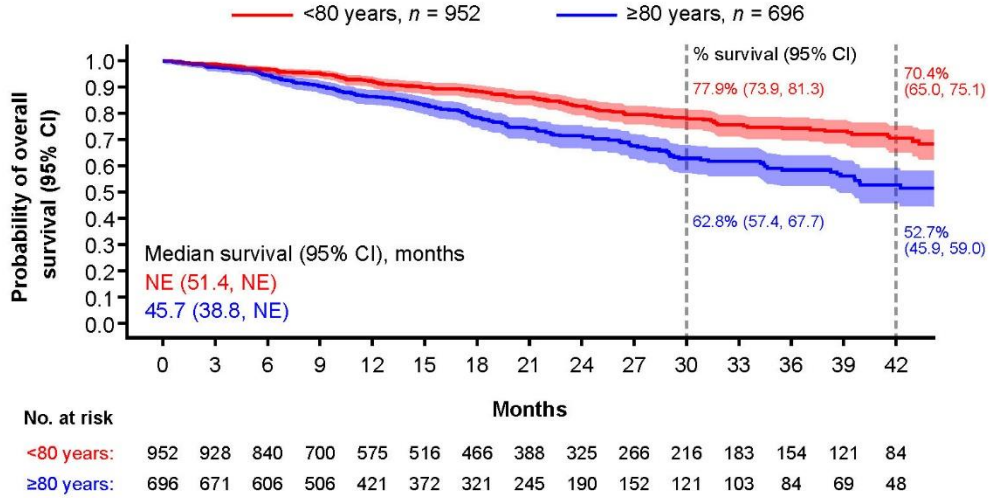
b) Female



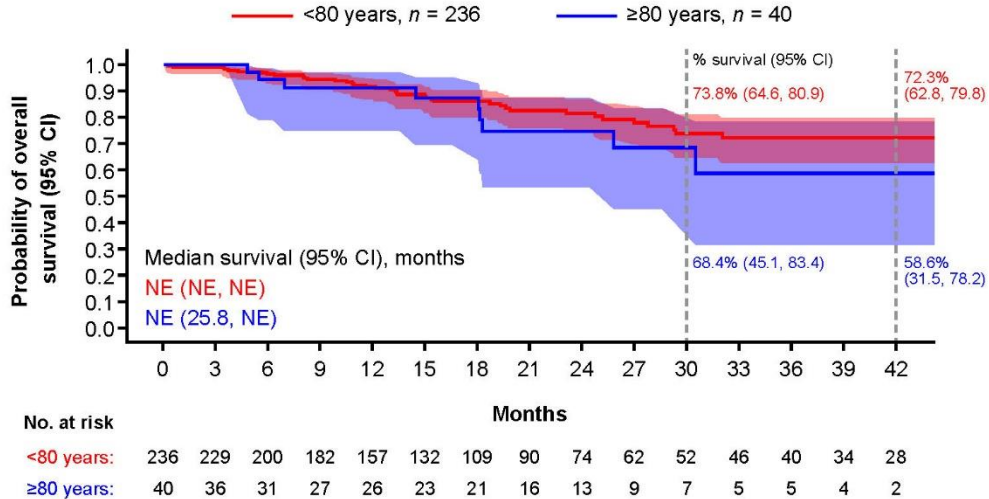
ATTR-CM transthyretin amyloid cardiomyopathy; CI confidence interval; NE non-estimable.

Fig. S6. Supplementary analysis: Kaplan–Meier curve of overall survival by age group (≥ 80 and <80 years) in patients with (a) ATTRwt-CM and (b) ATTRv-CM treated with tafamidis

a) ATTRwt-CM



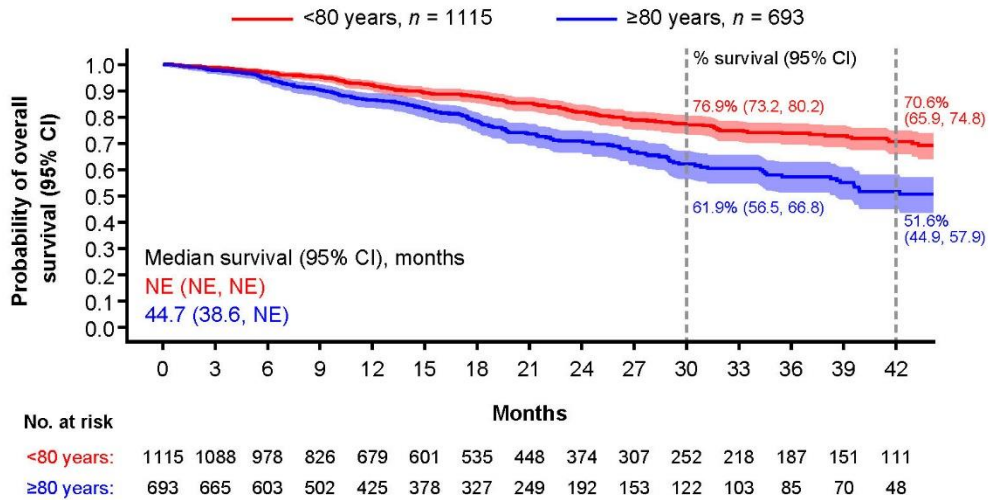
b) ATTRv-CM



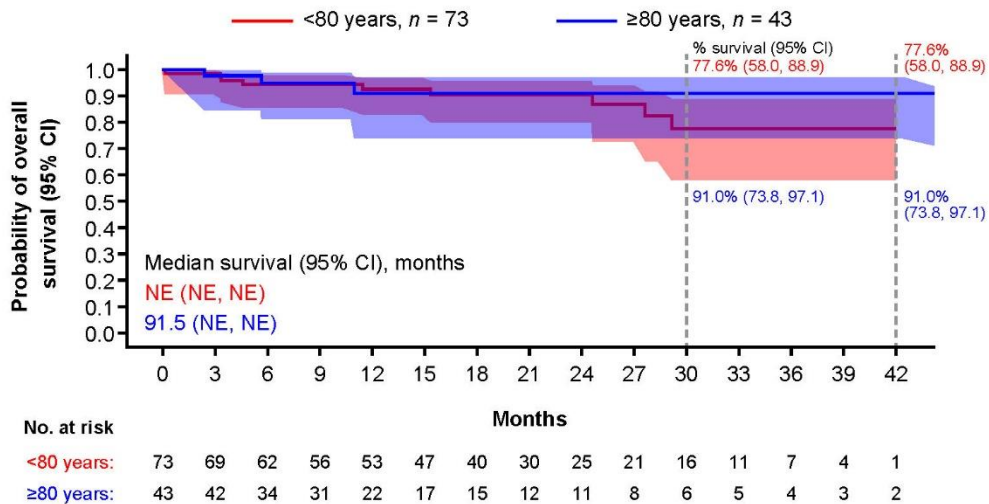
ATTRv-CM variant transthyretin amyloid cardiomyopathy; ATTRwt-CM wild-type transthyretin amyloid cardiomyopathy; CI confidence interval; NE non-estimable.

Fig. S7. Supplementary analysis: Kaplan–Meier curve of overall survival by age group (≥ 80 and <80 years) in tafamidis-treated patients with (a) predominantly cardiac and (b) mixed phenotype treated with tafamidis

a) Predominantly cardiac phenotype



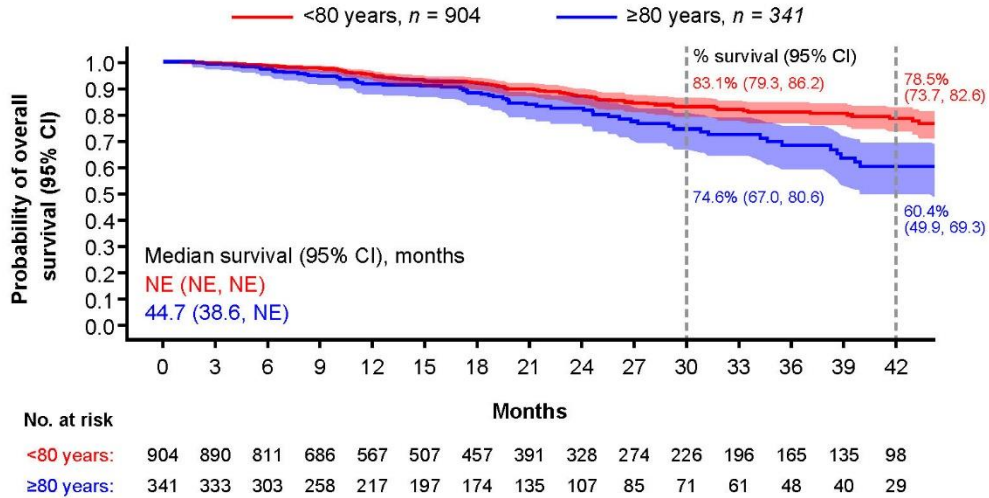
b) Mixed phenotype



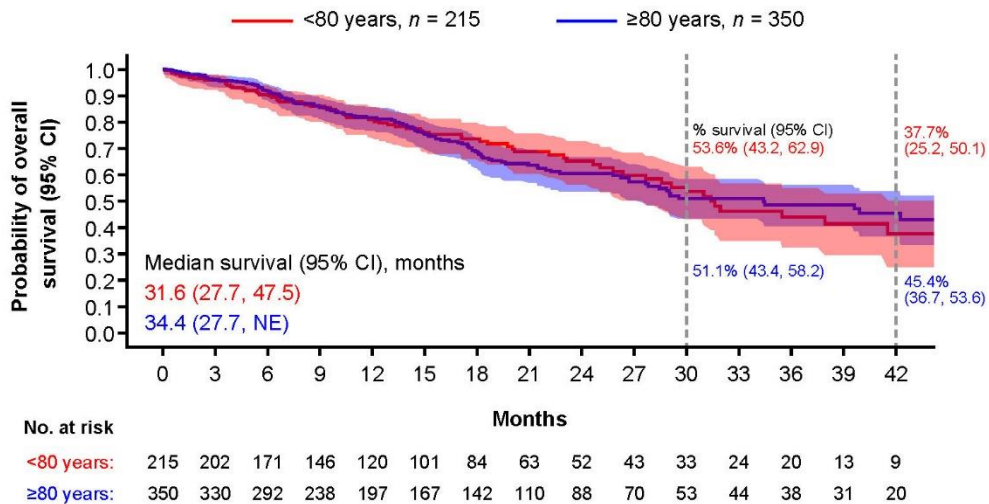
ATTR-CM transthyretin amyloid cardiomyopathy; CI confidence interval; NE non-estimable.

Fig. S8. Supplementary analysis: Kaplan–Meier curve of overall survival by age group (≥ 80 and < 80 years) in patients with ATTR-CM with (a) eGFR ≥ 45 and (b) < 45 mL/min/1.73 m² treated with tafamidis

a) eGFR ≥ 45 mL/min/1.73 m²



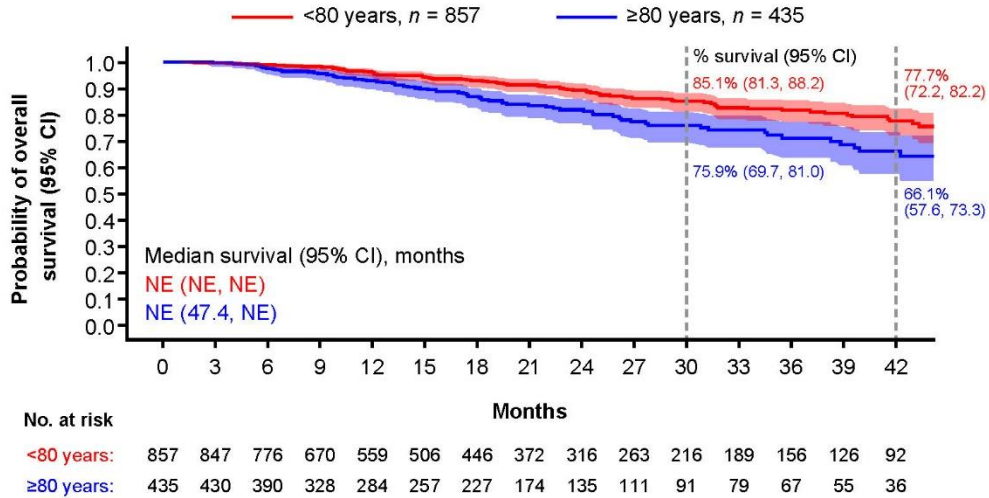
b) eGFR < 45 mL/min/1.73 m²



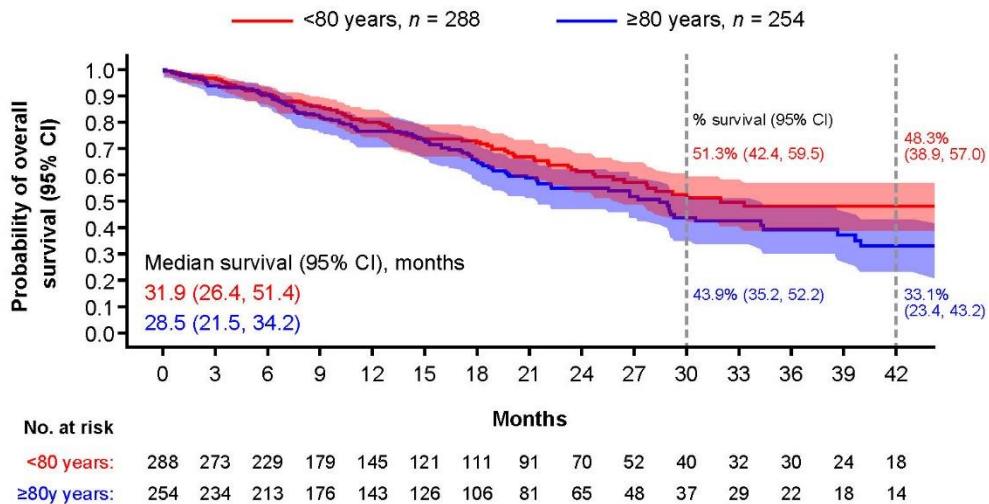
ATTR-CM transthyretin amyloid cardiomyopathy; CI confidence interval; eGFR estimated glomerular filtration rate; NE non-estimable.

Fig. S9. Supplementary analysis: Kaplan–Meier curve of overall survival by age group (≥ 80 and <80 years) in patients with ATTR-CM with NYHA functional class (a) I/II and (b) III heart failure symptoms treated with tafamidis

a) NYHA class I/II



b) NYHA class III



ATTR-CM transthyretin amyloid cardiomyopathy; CI confidence interval; NE non-estimable; NYHA New York Heart Association.