7e MASTERCLASS AMYLOSES CARDIAQUES
ÉVÉNEMENT HYBRIDE
PRÉSENTIEL & DISTANCIEL
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Expérience française du Tafamidis et impact à long terme

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Clinical Epidemiology and Ageing

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Current therapeutic concepts in ATTR-CM[1-3]

Treatment of cardiac involvement

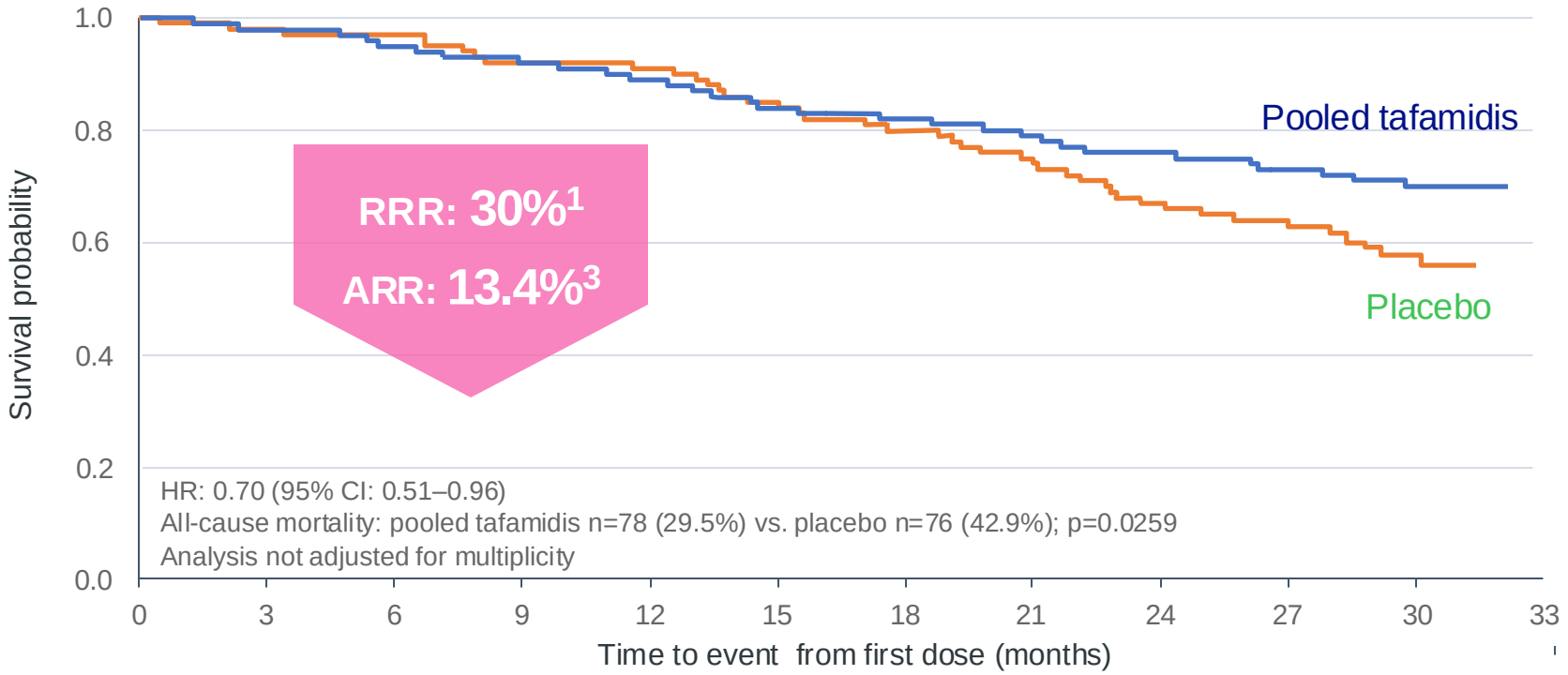
Image adapted from Ruberg FL, et al. *J Am Coll Cardiol* 2019;73:2872–91 and Emdin M, et al. *Eur Heart J* 2019;40:3699–706.

Tafamidis is the only licensed treatment in ATTR-CM that specifically targets TTR destabilisation —the cause of disease pathogenesis— and fortifies the TTR tetramer to preserve its natural function[3, 5–12]

ATTR-CM, transthyretin amyloid cardiomyopathy; TTR, transthyretin.

1. Ruberg FL, et al. *J Am Coll Cardiol* 2019;73:2872–91; 2 Emdin M, et al. *Eur Heart J* 2019;40:3699–706; 3. Bulawa CE, et al. *Proc Natl Acad Sci USA* 2012;109:9629–34; 4. Tess DA, Maurer TS, Li Z, et al. *Amyloid* 2023;30(2):208–19; 5. Coelho T, et al. *Neurology* 2012:79(8):785–92; 6. Johnson SM, et al. *J Mol Biol* 2012;421(2–3):185–203; 7. Donnelly JP, Hanna M. *Cleve Clin J Med* 2017;84(12 Suppl 3):12–26; 8. Sekijima Y. *J Neurol Neurosurg Psychiatry* 2015;86(9):1036–43; 9. Coelho T, et al. *Neurol Ther* 2016;5(1):1–25; 10. Adams D, et al. *Expert Opin Pharmacother* 2016;17(6):791–802; 11. Monteiro C, et al. *Amyloid* 2018;25(2):120–8; 12. Judge DP, et al. *J Am Coll Cardiol* 2019;74(3):285–95; 13. VYNDAQEL 61 mg (tafamidis) Summary of Product Characteristics.

Tafamidis reduced all cause-mortality by 30% in ATTR-CM over 30 months vs placebo



Number needed to treat[4]:

7.5

~8 patients would need to be treated to prevent one death within 30 month-study period

No. at risk (cumulative no. of events)[1]

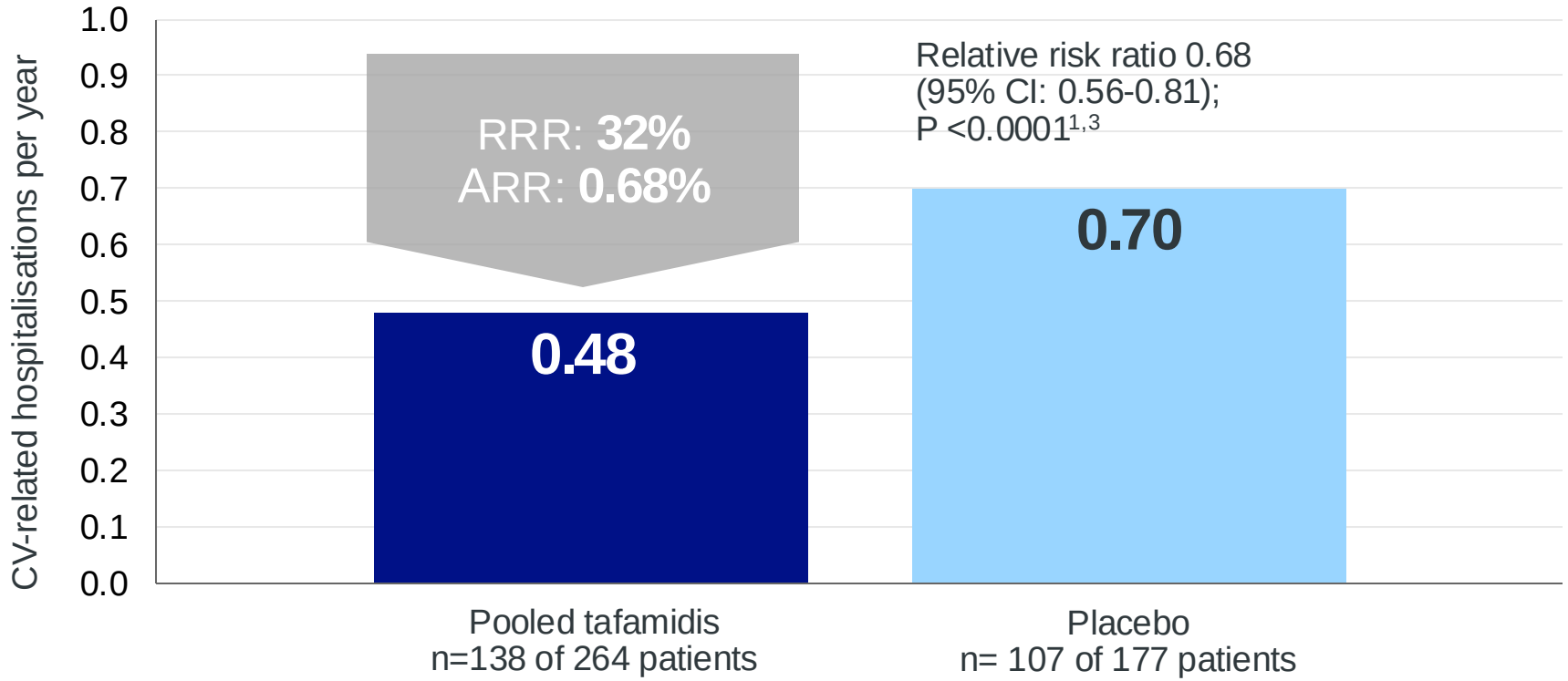
Figure adapted from Maurer MS, et al. *N Engl J Med* 2018;379:1007–16.

Pooled tafamidis	264 (0)	259 (5)	252 (12)	244 (20)	235(29)	222 (42)	216 (48)	209 (55)	200 (64)	193 (71)	99 (78)	0 (78)
Placebo	177 (0)	173 (4)	171 (6)	163 (14)	161 (16)	150 (27)	141 (36)	131 (46)	118 (59)	113 (64)	51 (75)	0 (76)

Maurer M et al NEJM 2018

Tafamidis significantly reduced CV-related hospitalisations vs placebo over 30 months[1]

Individual component: CV-related hospitalisations frequency during 30 months[1]*



Number need to treat[2]:

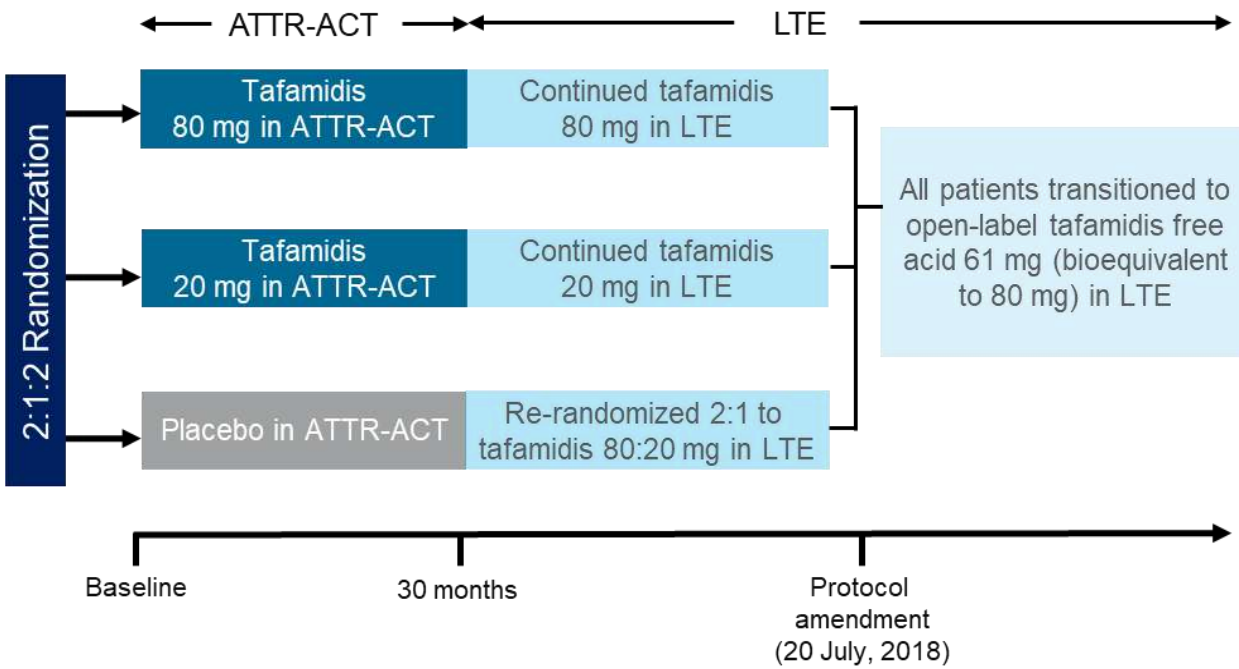
4

~4 patients would need to be treated to prevent 1 CV-related hospitalisation per year

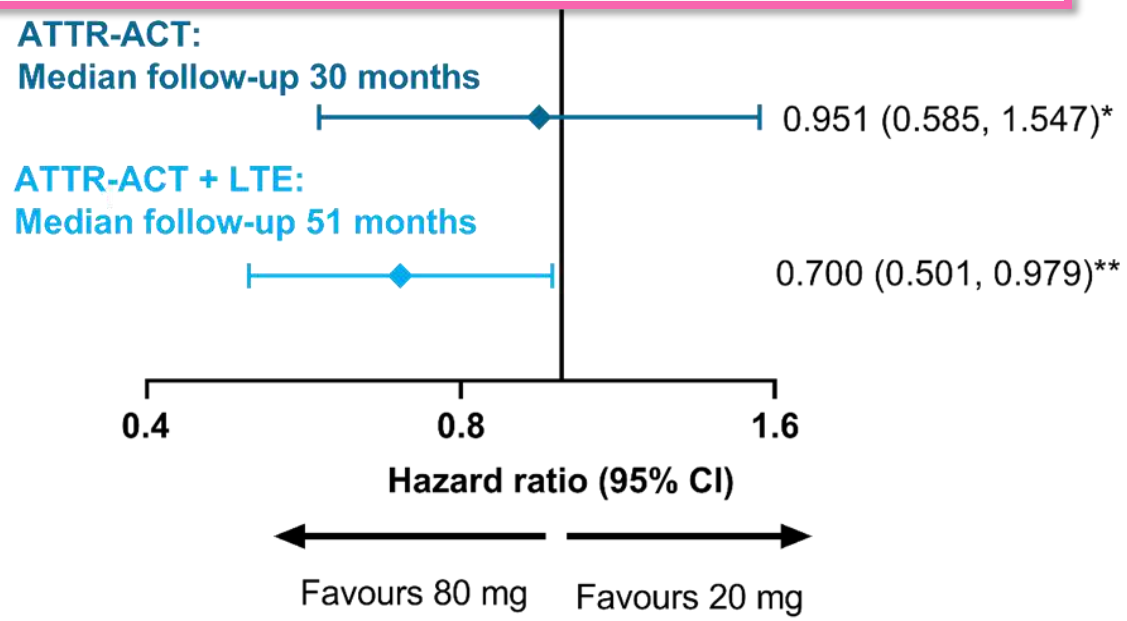
Maurer M et al NEJM 2018

Dose efficacy of Tafamidis in ATTR-CA

After 30 months treatment in ATTR-ACT, patients could continue in the long-term extension trial (LTE)



All-cause mortality was significantly reduced with tafamidis 80 mg / 61 mg compared with tafamidis 20 mg in ATTR-ACT combined with the LTE



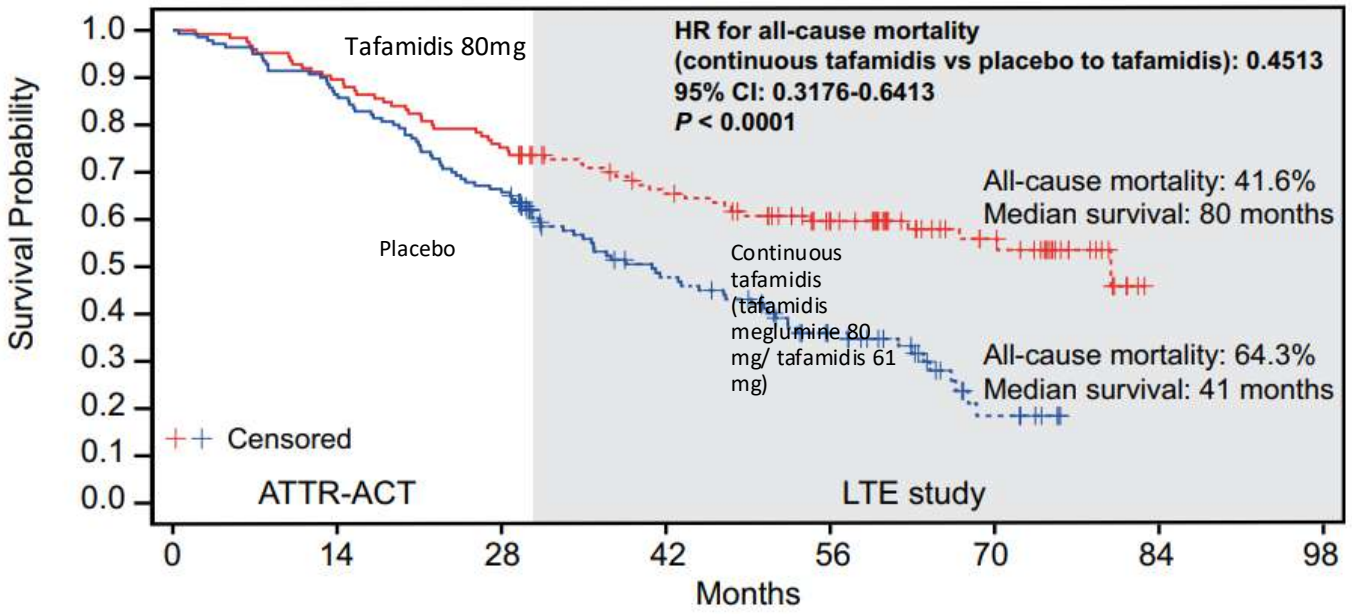
*P = 0.8404 **P = 0.0374

Damy et al, Eur J Heart Failure 2020

Post-hoc analysis of ATTR-ACT and LTE: All-cause mortality in patients <80 and ≥80 years of age treated with Tafamidis

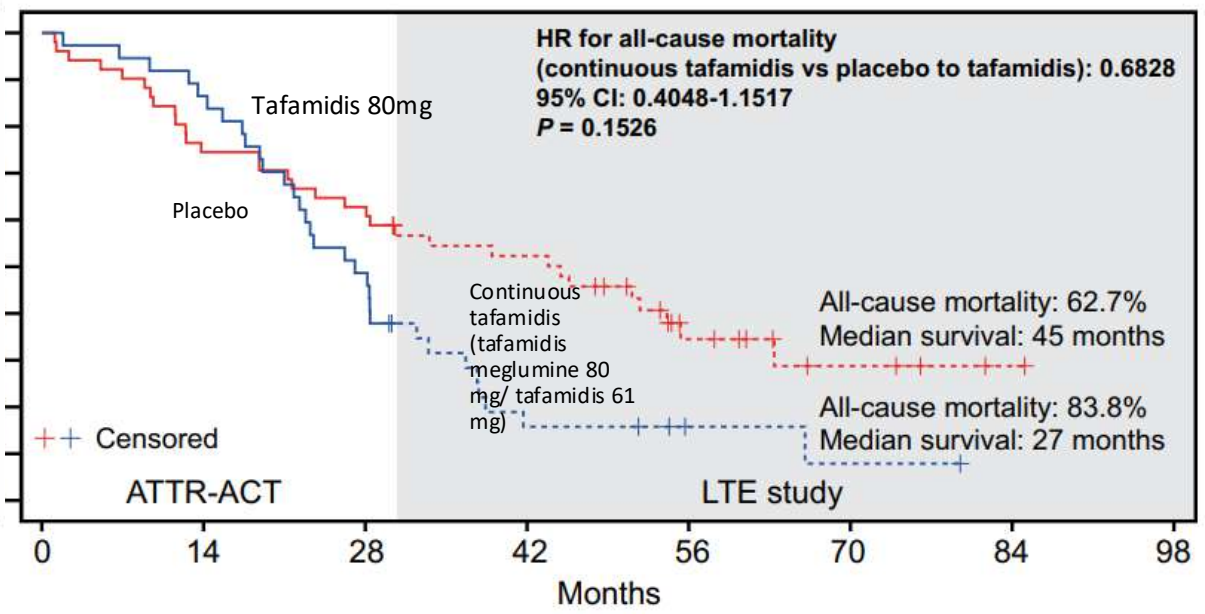
Patients aged <80 years

125 received tafamidis and 140 received placebo



Patients aged ≥80 years

51 received tafamidis and 37 received placebo

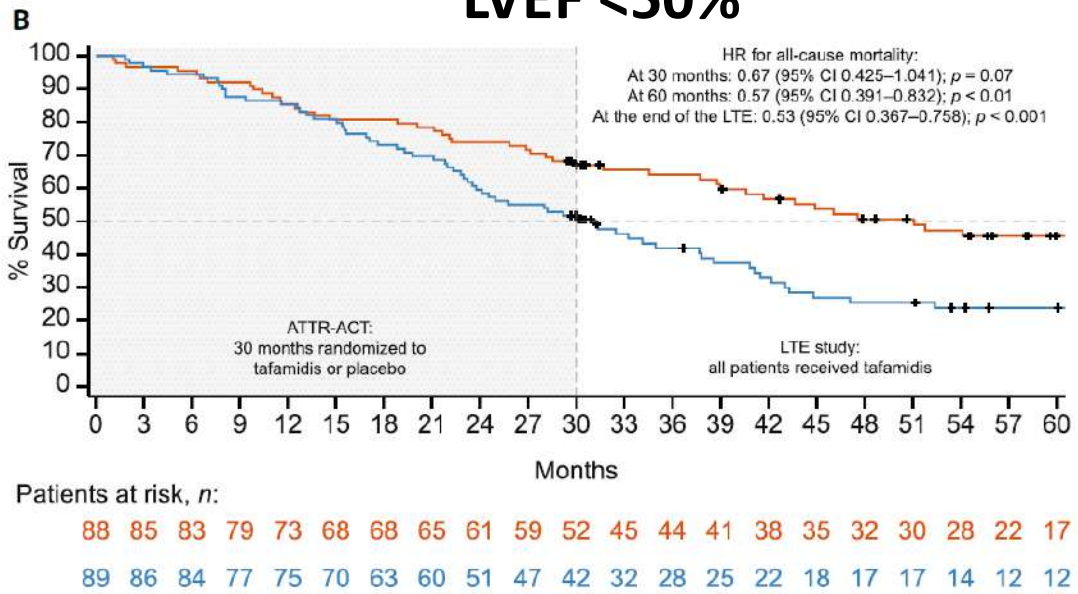


The use of continuous tafamidis in octogenarians resulted in longer median survival and lower mortality than those initially treated with placebo before transitioning to tafamidis free acid 61 mg

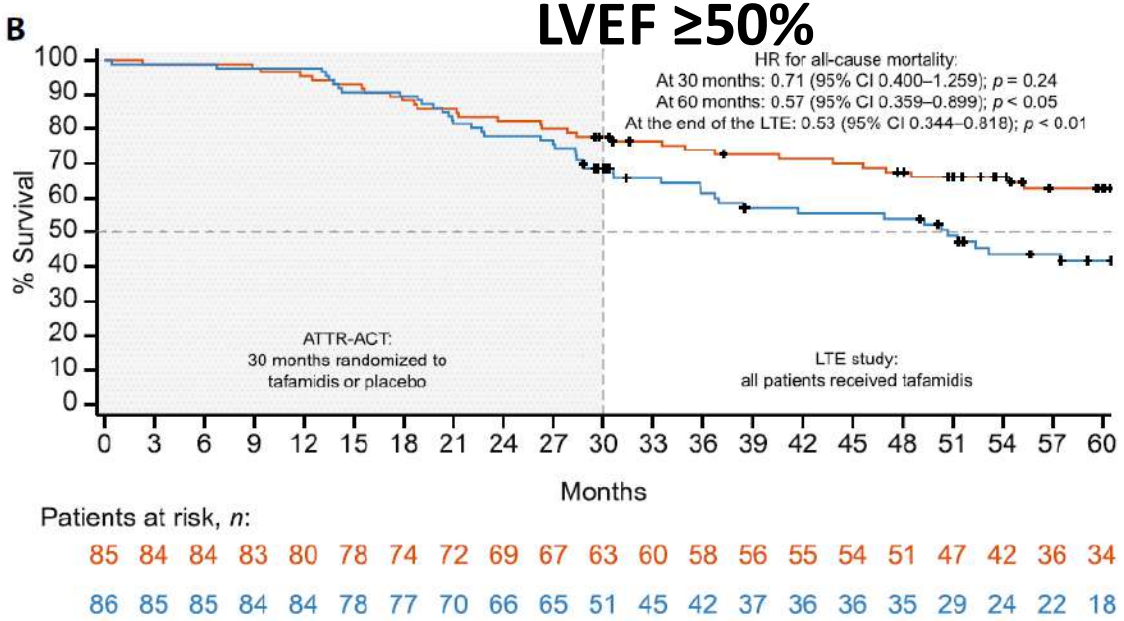
Garcia Pavia P et al, JACC HF 2023

Post-hoc analysis ATTR-ACT LTE study of the effect of Tafamidis on patients with mildly reduced/reduced or preserved ejection fraction

LVEF <50%



LVEF ≥50%



Figures reproduced from Drachman B, et al. *Eur J Heart Fail* 2024 doi: 10.1002/ejhf.3330.

These findings demonstrate the efficacy of tafamidis in patients with ATTR-CM irrespective of LVEF

+=censored. ATTR-ACT, Transthyretin Amyloidosis Cardiomyopathy Clinical Trial; ATTR-CM, transthyretin amyloid cardiomyopathy; LTE, long term extension; LVEF, left ventricular ejection fraction.

1. Drachman B, et al. *Eur J Heart Fail* 2024 doi: 10.1002/ejhf.3330; 2. VYNDAQEL 61 mg (tafamidis) Summary of Product Characteristics.

Tafamidis en France

INDICATION NEUROLOGIQUE

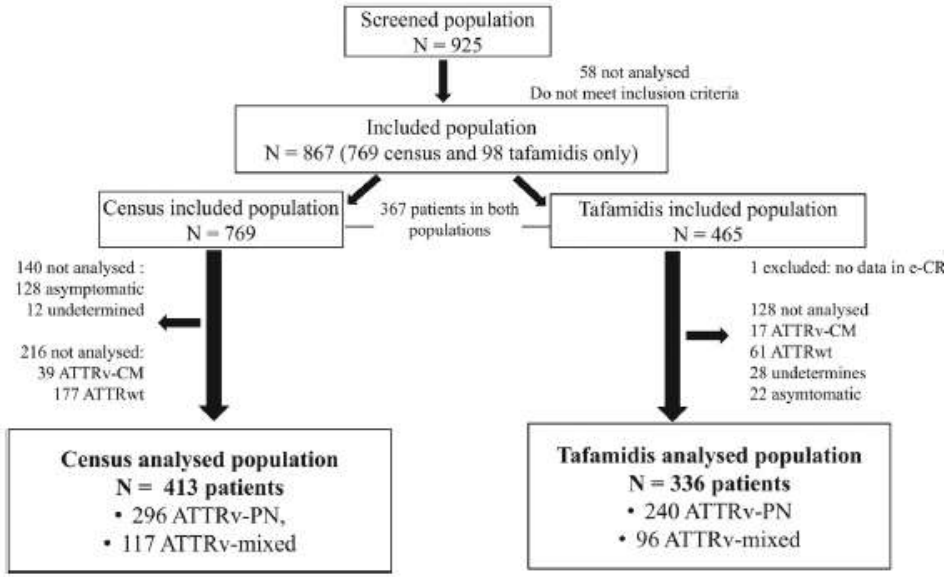
Tafamidis meglumine 20mg

INDICATION CARDIOLOGIQUE

2018 Nov	2021 Juin
“Accès Précoce” : “RTU”	**AMM**
Tafamidis meglumine 20mg **Tafamidis meglumine 80mg**	**Tafamidis Free Acid 61mg**

Transthyretin amyloid polyneuropathy in France: A cross-sectional study with 413 patients and real-world tafamidis meglumine use (2009–2019)

ATTRv- Neuro
Tafamidis 20mg



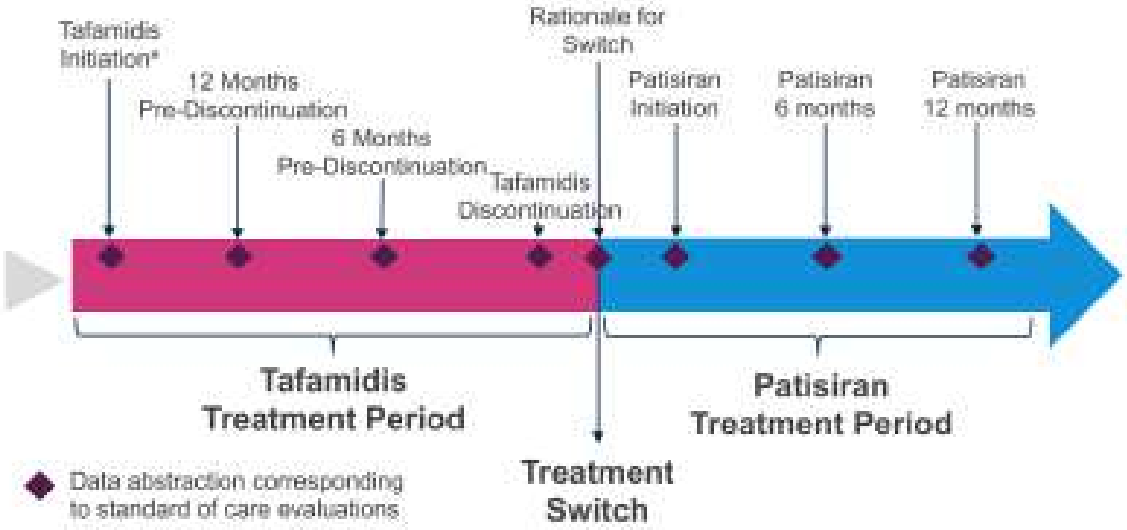
- Male (68.0%) with a mean age of 57.2+/-17.2 years
- First symptom(s-diagnosis was 3.4+/-4.3 years
- First symptoms:
  - Sensory complaints (85.9%)
  - Dysautonomia (38.5%)
  - Motor deficits (26.4%)
  - Carpal tunnel syndrome (31.5%)
  - Shortness of breath (13.3%)
  - Unexplained weight loss (16.0%)
- Tafamidis meglumine was initiated in 156/214 (72.9%)
- Median treatment duration was 6.00 years
- Tafamidis was well tolerated, with 20 adverse events likely related to study drug among the 336 patients

Adams D et al, Revue Neuro 2024

Effectiveness of patisiran after switching from tafamidis for the treatment of hereditary transthyretin-mediated amyloidosis with polyneuropathy

Key Selection Criteria

- Confirmed diagnosis of ATTRv amyloidosis with documented TTR variant
- Documented initiation and discontinuation of tafamidis for the treatment of ATTRv amyloidosis with polyneuropathy prior to initiation of patisiran
- Stage 1 or 2 polyneuropathy at the initiation of patisiran



Key Endpoints Assessed[b]

Clinical rationale for treatment switch:

- Disease progression due to new onset/worsening polyneuropathy or cardiomyopathy
- Other reasons

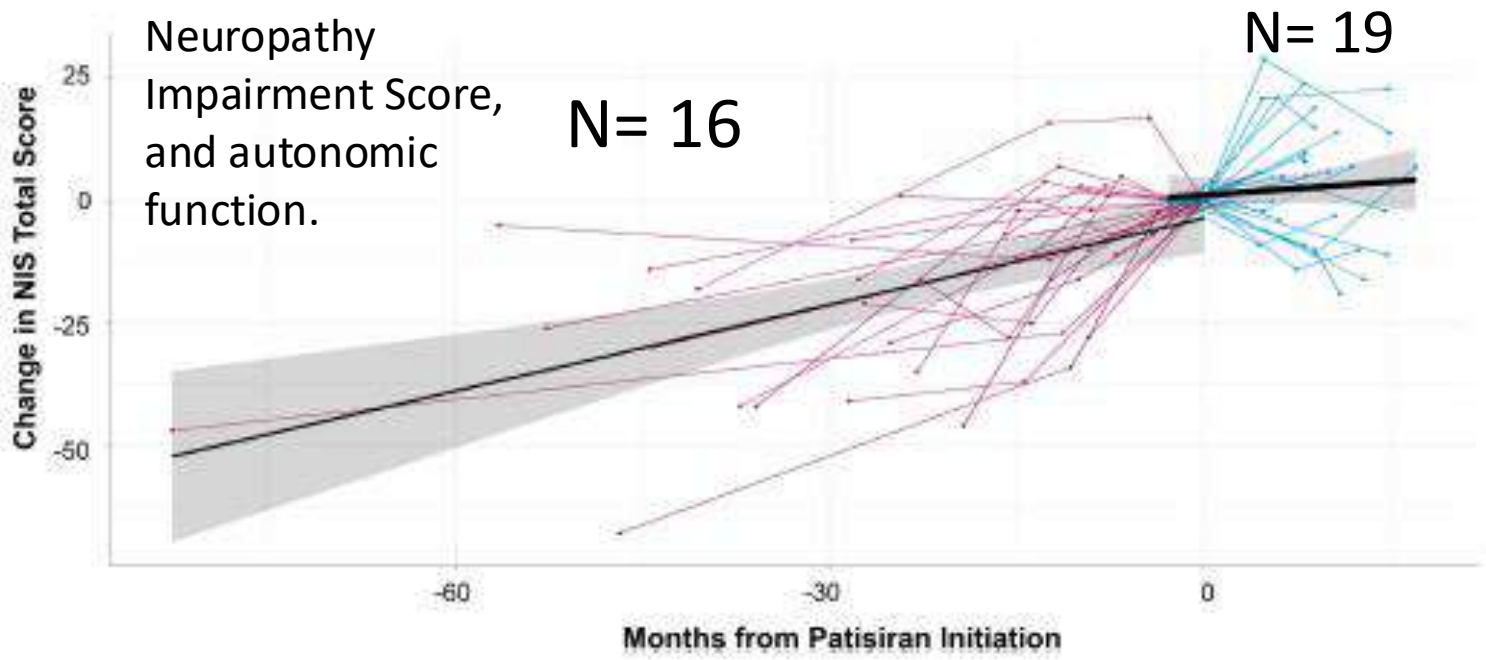
Select effectiveness measurements during tafamidis and patisiran treatment periods:

- PND score
- Walking difficulties
- NIS

Labeyrie C et al, European Journal of Neurology 2024

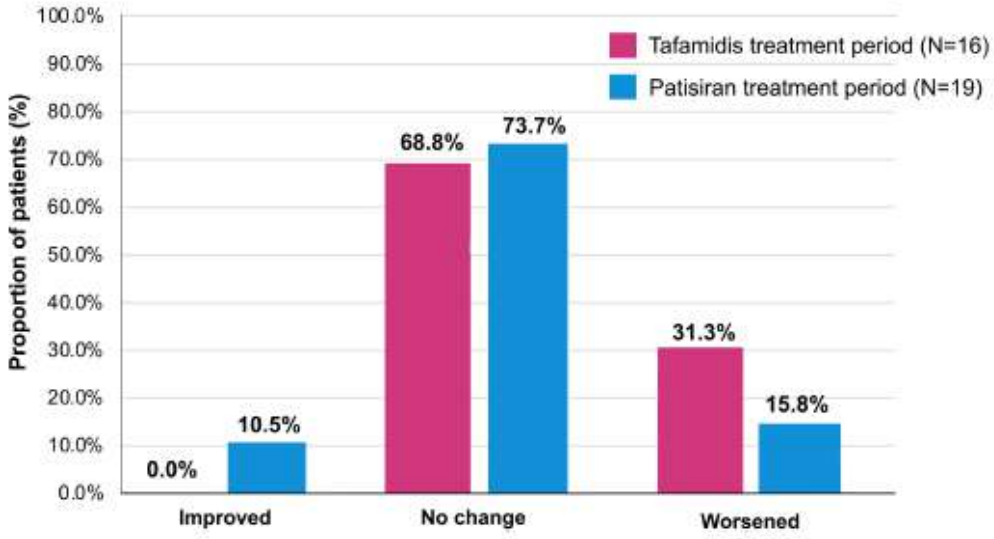
Effectiveness of patisiran after switching from tafamidis for the treatment of hereditary transthyretin-mediated amyloidosis with polyneuropathy

Neuropathy Impairment Score, and autonomic function.



mNIS

Change in PND score during the tafamidis and patisiran treatment periods.



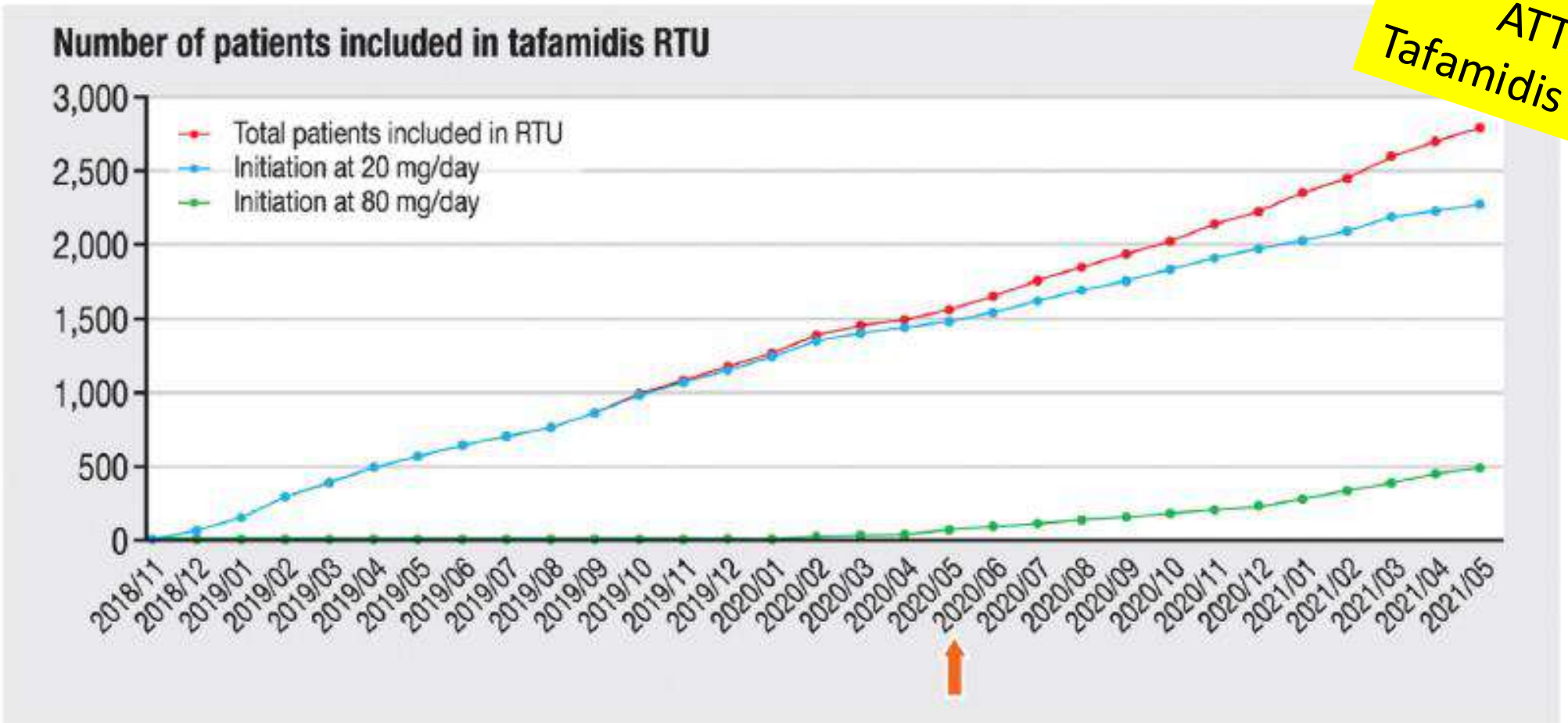
PND

- Trouble sensoriel, Marche OK
- Marche altérée sans canne
- Marche altérée avec une canne
- Marche altérée avec 2 cannes ou béquilles

Labeyrie C et al, European Journal of Neurology 2024

Clinical outcomes for 2788 patients with transthyretin amyloidosis: Tafamidis meglumine early access program in France☆

Données de la RTU
ATTR-CM
Tafamidis 20 /80mg



Lairez O et al, ACVD 2024

Clinical outcomes for 2788 patients with transthyretin amyloidosis: Tafamidis meglumine early access program in France☆

Données de la RTU
ATTR-CM
Tafamidis 20 /80mg

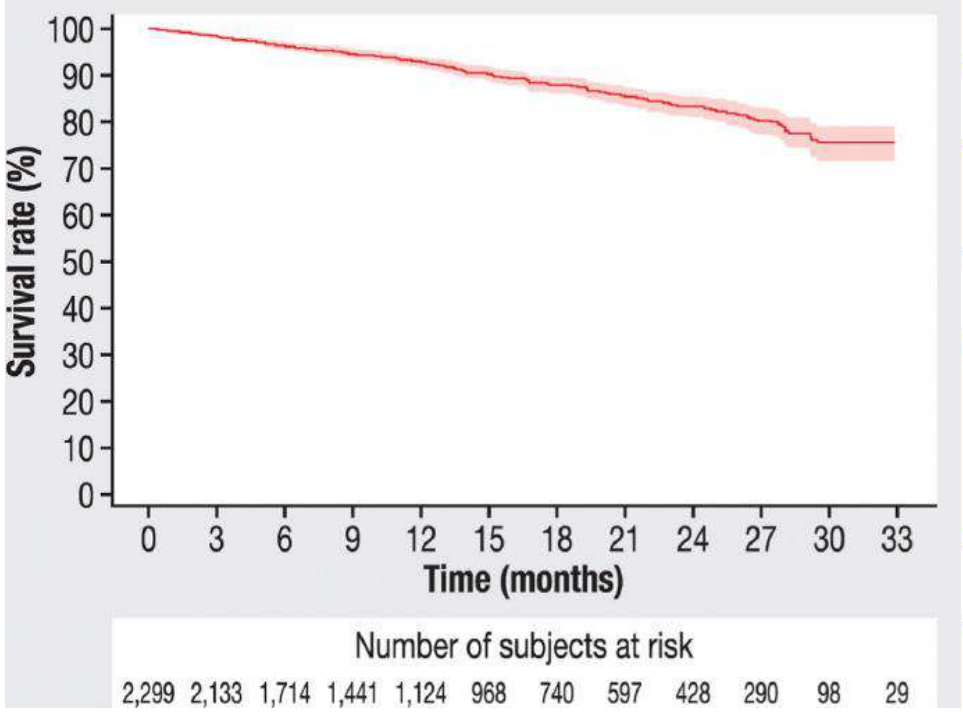
Données de la fiche d'initiation de la RTU

	Total (*n* = 2788)	ATTRwt (*n* = 995)	ATTRv (*n* = 213)	Ongoing/missing (*n* = 918)	Not done (*n* = 662)
Age at tafamidis initiation (years)					
Mean ± SD	80.4 ± 7.2	80.0 ± 6.7	73.7 ± 8.3	81.0 ± 6.7	82.1 ± 6.9
Median (IQR)	82.0 (76.0–85.0)	81.0 (76.0–85.0)	74.0 (70.0–80.0)	82.0 (77.0–86.0)	83.0 (79.0–87.0)
Age group at tafamidis initiation					
< 50 years	6 (0.2)	0 (0.0)	4 (1.9)	0 (0.0)	2 (0.3)
50–59 years	16 (0.6)	3 (0.3)	7 (3.3)	3 (0.3)	3 (0.5)
60–69 years	185 (6.6)	68 (6.8)	41 (19.2)	48 (5.2)	28 (4.2)
70–79 years	891 (32.0)	357 (35.9)	105 (49.3)	289 (31.5)	140 (21.2)
80–84 years	831 (29.8)	290 (29.1)	50 (23.5)	272 (29.7)	219 (33.1)
85–89 years	669 (24.0)	226 (22.7)	3 (1.4)	234 (25.5)	206 (31.2)
≥ 90 years	188 (6.7)	51 (5.1)	3 (1.4)	71 (7.7)	63 (9.5)
Missing	2	0	0	1	1
Sex					
Male	2276 (81.6)	843 (84.7)	152 (71.4)	744 (81.0)	537 (81.1)
Female	512 (18.4)	152 (15.3)	61 (28.6)	174 (19.0)	125 (18.9)

Lairez O et al, ACVD 2024

Clinical outcomes for 2788 patients with transthyretin amyloidosis: Tafamidis meglumine early access program in France☆

Données de la RTU ATTR-CM Tafamidis 20 /80mg

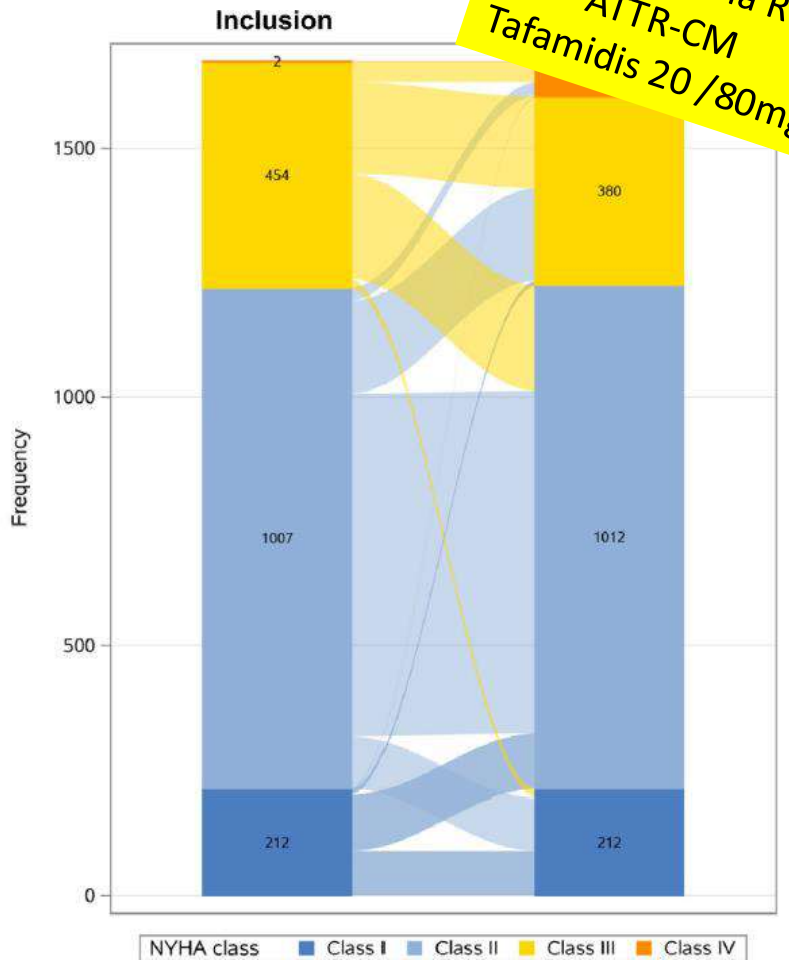


2788 ATTR-CM patients taking tafamidis 20mg or 80 mg in the French early access program.

Real-world patient pathway, disease severity, and progression data.

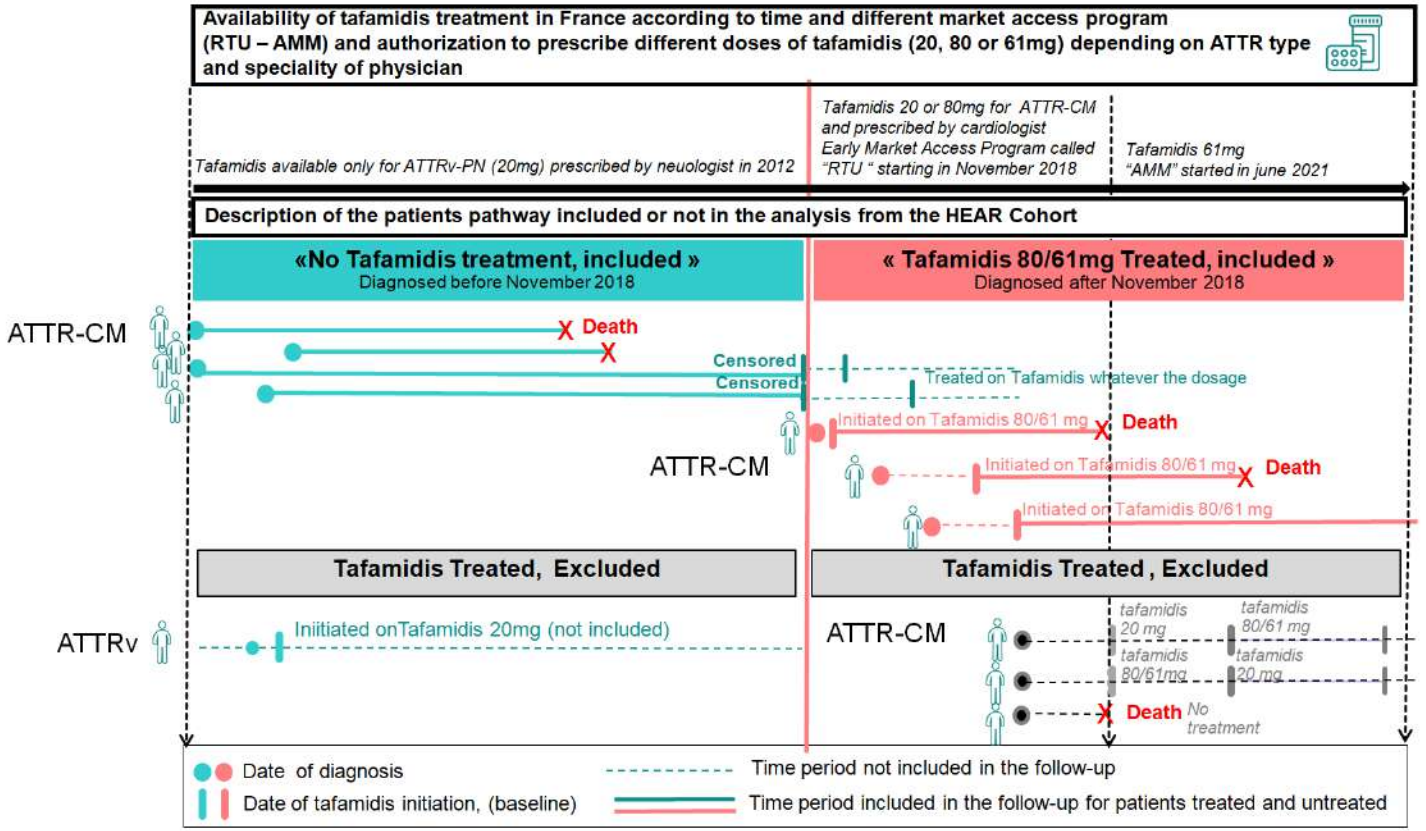
NYHA class improved or remained stable for 1299 (77.6%), and 376 (22.4%) worsened between inclusion and last follow-up.

In this population with a median age of 82 years old, 88% of patients were still alive at 18 months.



Impact of Tafamidis on survival of elderly patients in real-world setting - Healthcare European Amyloidosis Registry

Figure 1 : Description of the availability of tafamidis treatment in France according to time and different market access program (RTU – AMM) and authorization to prescribe different doses of tafamidis (20, 80 or 61mg) depending on ATTR type and speciality of physician and description of patients' pathways included or not in the study



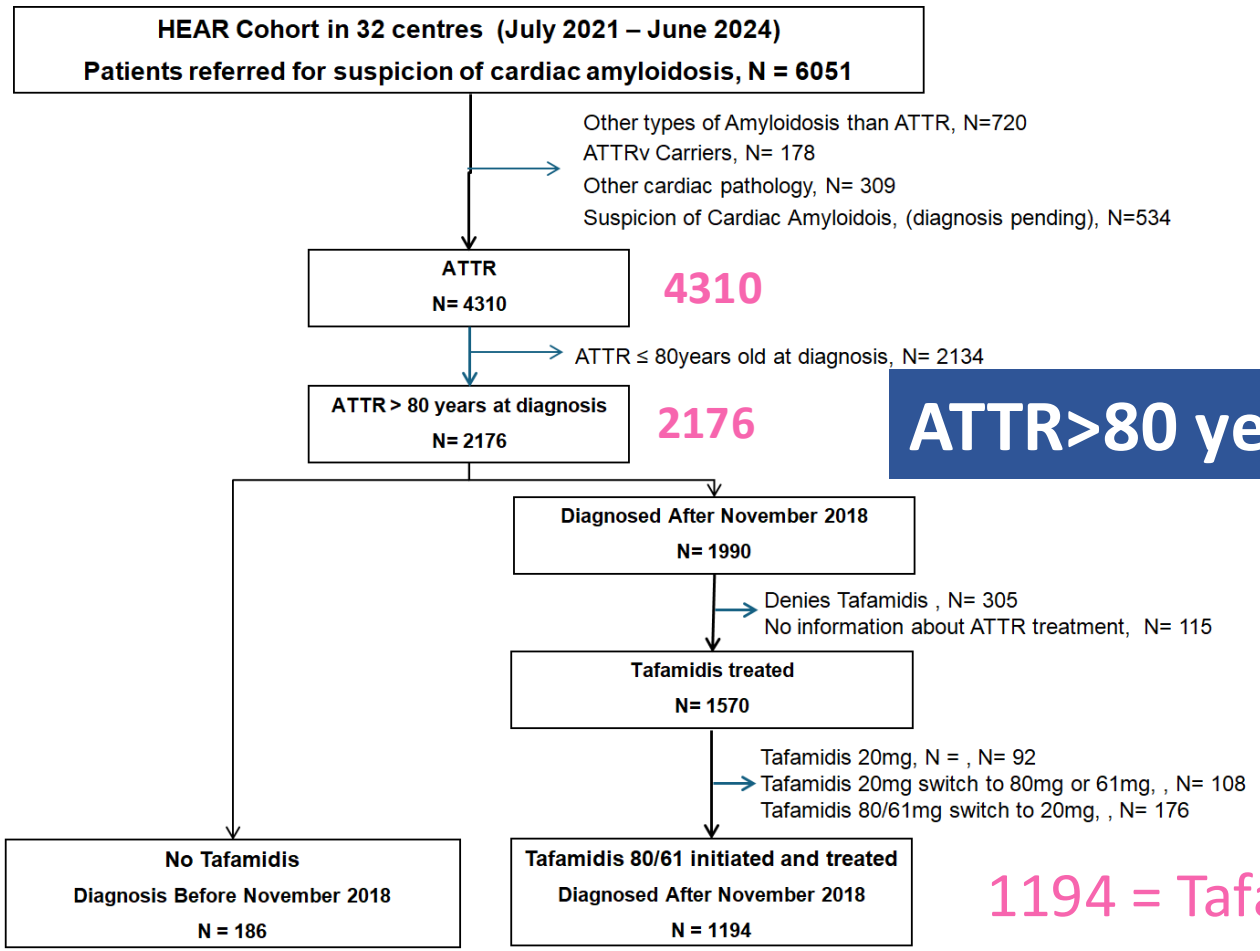
HEART's

HEAR Registry, database JUNE 2021-JUNE 2024

Jobbe-Duval A et al, in preparation

Impact of Tafamidis on survival of elderly patients in real-world setting – Healthcare European Amyloidosis Registry

Figure 2 : Flow chart



HEART's

186 = No Tafa

1194 = Tafa 80mg/61mg

HEAR Registry, database JUNE 2021-JUNE 2024

Jobbe-Duval A et al, in preparation

Impact of Tafamidis on survival of elderly patients in real-world setting Healthcare European Amyloidosis Registry

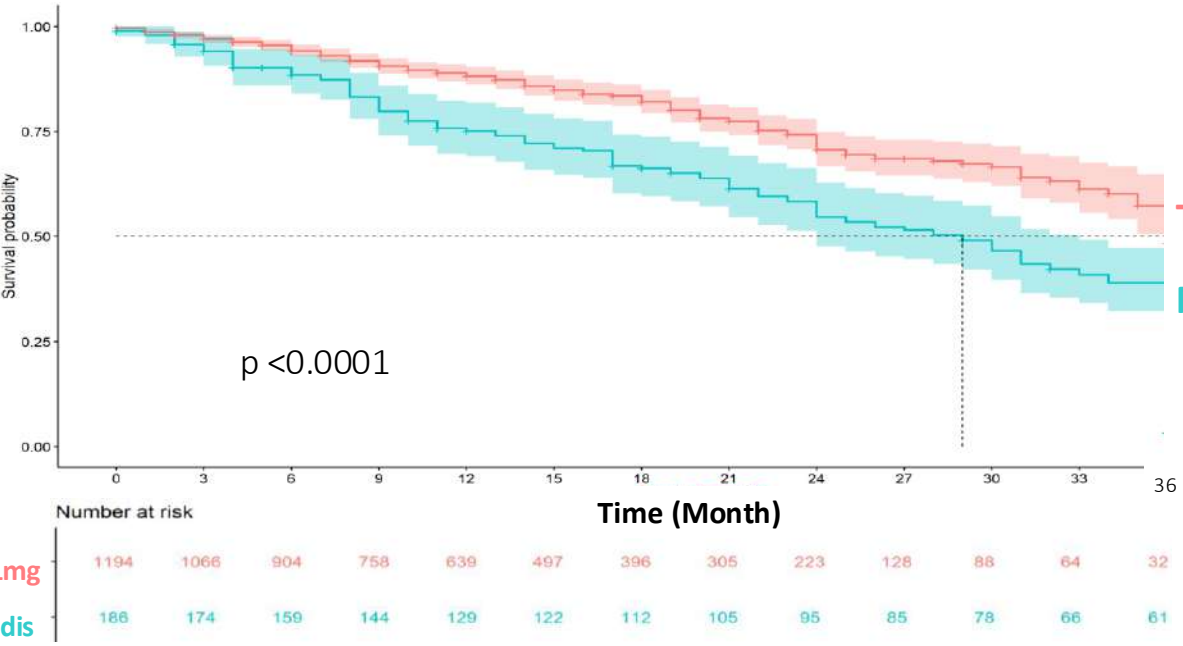
Table 1. Baseline characteristics of the study population according to treatment status

Variables	Overall	No Tafamidis	Tafamidis 80/61mg	*P value*
N (%)	1380	186 (13)	1194 (87)	
Demographic data				
Age, years	85 [83 - 88]	83 [82 - 85]	86 [84 - 88]	<0.001
Time to diagnosis from 1st CV symptom, months	13.0 [3.0 - 64.0]	14.5 [4.0 - 65.0]	13.0 [3.0 - 52.0]	0.362
Men, n(%)	1075 (77.9)	140 (75.2)	934 (78.2)	0.384
BMI, kg/m2	24.8 [22.8 - 27.1]	24.6 [23.1 - 27.1]	24.8 [22.8 - 27.1]	0.611
Diagnosis				
ATTRwt, n(%)	957 (69.4)	114 (61.1)	841 (70.4)	0.017
ATTRv, n(%)	75 (5.5)	32 (17.2)	47 (3.9)	<0.001
ATTR not genotyped, n(%)	180 (13.0)	39(21.0)	143 (12.0)	0.001
ATTR undergoing genetic testing, n(%)	166 (12.1)	1 (0.7)	163 (13.7)	<0.001
HR, bpm	75.0 [66.0 - 86.0]	75.0 [65.5 - 87.0]	77.0 [69.0 - 85.0]	0.200
SBP, mmHg	134.0 [121.0 - 146.0]	128.0 [117.0-143.0]	134.0 [121.5 - 146.0]	<0.001
DBP, mmHg	73.0 [66.0 - 81.0]	74.0 [66.5 - 80.5]	73.0 [66.0 - 81.0]	0.008
Biomarkers				
NT-proBNP, ng/L	2492.5 [1264.0 - 4741.5]	4854.0 [2049.5 - 8903.0]	2330.0 [1202.5 - 4483.0]	<0.001
hs-TnT, ng/L	56.0 [41.8 - 80.0]	74.0 [55.0 - 108.0]	55.0 [40.5 - 77.0]	<0.001
Creatinin, µmol/L	106.0 [87.8 - 131.3]	117.0 [89.0 - 140.0]	106.0 [86.5 - 130.0]	0.130
eGFR, ml/min/1,73m2	44.2 [34.2 - 54.2]	41.7 [35.85 - 49.2]	45.1 [34.1 - 54.5]	0.042
PAL, UI/L	91.0 [69.0 - 115.0]	107.0 [80.5 -133.5]	88.0 [68.5 -114.0]	<0.001
Hemoglobin, g/dl	13.1 [12.2 - 14.2]	13.0 [11.8 - 14.0]	13.2 [12,.3 - 14.2]	0.049
Echocardiographic features				
IVS, mm	16.2 [14.3 - 18.7]	18.0 [15.0 - 20.0]	16.0 [14.1 - 18.0]	<0.001
LVEDD, mm	43.5 [39.0 - 48.0]	44.0 [40.0 - 49.0]	43.0 [39.0 - 48.0]	0.469
LVEF, %	54.4 [46.4 - 61.0]	48.0 [39.0 - 56.0]	55.0 [48.0 - 62.0]	<0.001
GLS, %	11.7 [9.0 - 14.0]	9.7 [7.6 - 11.7]	12.0 [9.4 - 14.4]	<0.001
PAPs, mmHg	29.7 [21.2 - 36.0]	32.1 [27.0 - 37.9]	29.2 [21.2 - 36.0]	0.047

HEART's

HEAR Registry, database JUNE 2021-JUNE 2024

Impact of Tafamidis on survival of elderly patients in real-world setting Healthcare European Amyloidosis Registry



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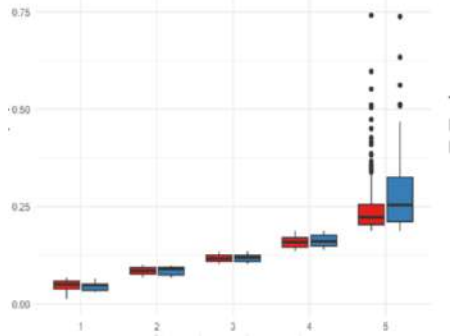
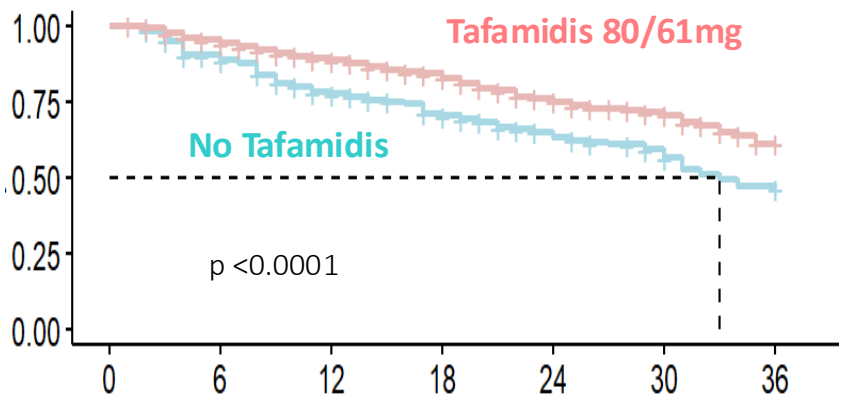
Score de Propension





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Merci aux collaborateurs du RÉSEAU AMYLOSE !

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