FAKULTNÍ NEMOCNICE® OLOMOUC

Lékařská fakulta
Univerzita Palackého v Olomouci

KOMPLEXNÍ KARDIOVASKULÁRNÍ CENTRUM
FAKULTNÍ NEMOCNICE OLOMOUC

Specifické terapeutické možnosti u ATTR-CM

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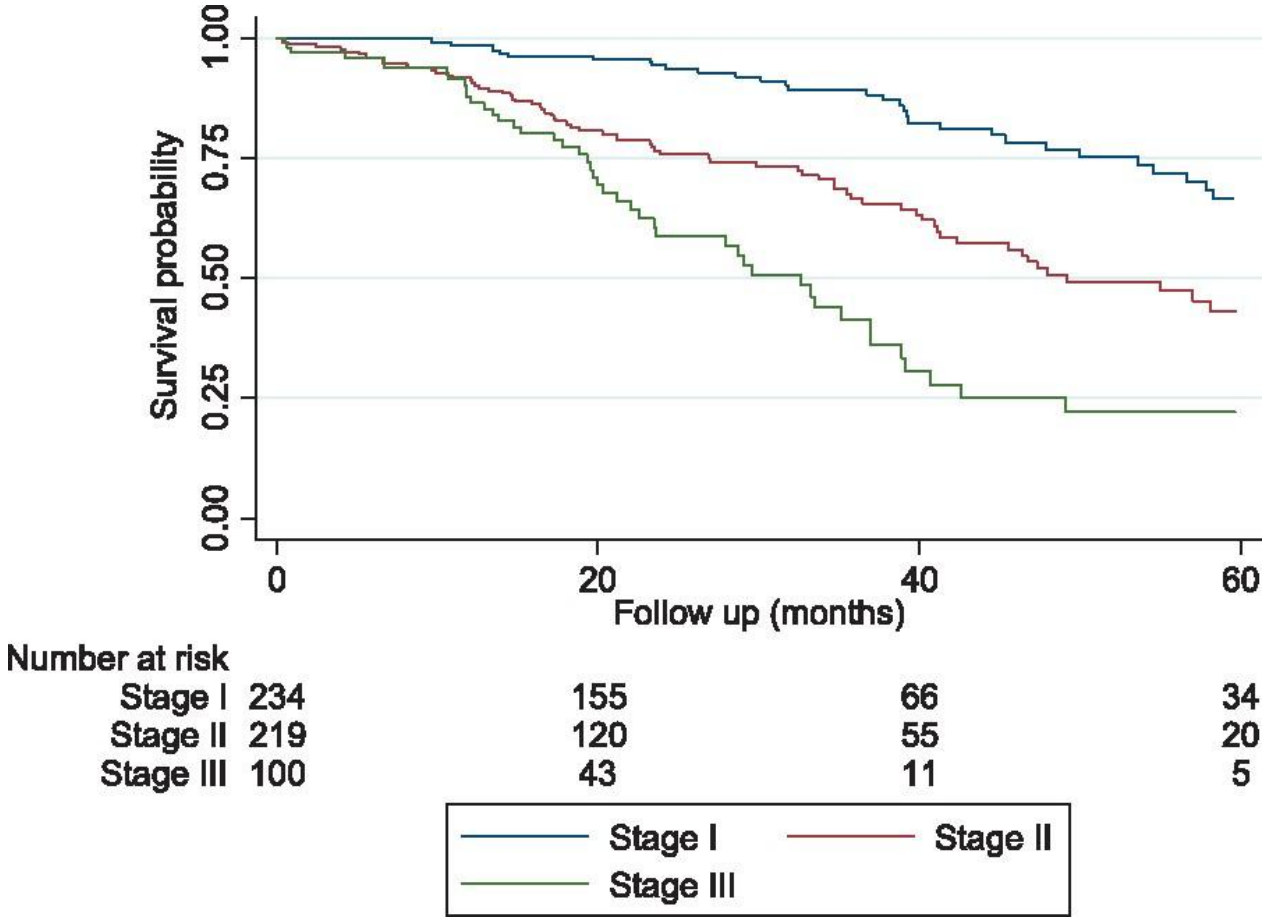
I. interní klinika – kardiologická
Fakultní nemocnice Olomouc

Prognóza ATTR-kardiomyopatie

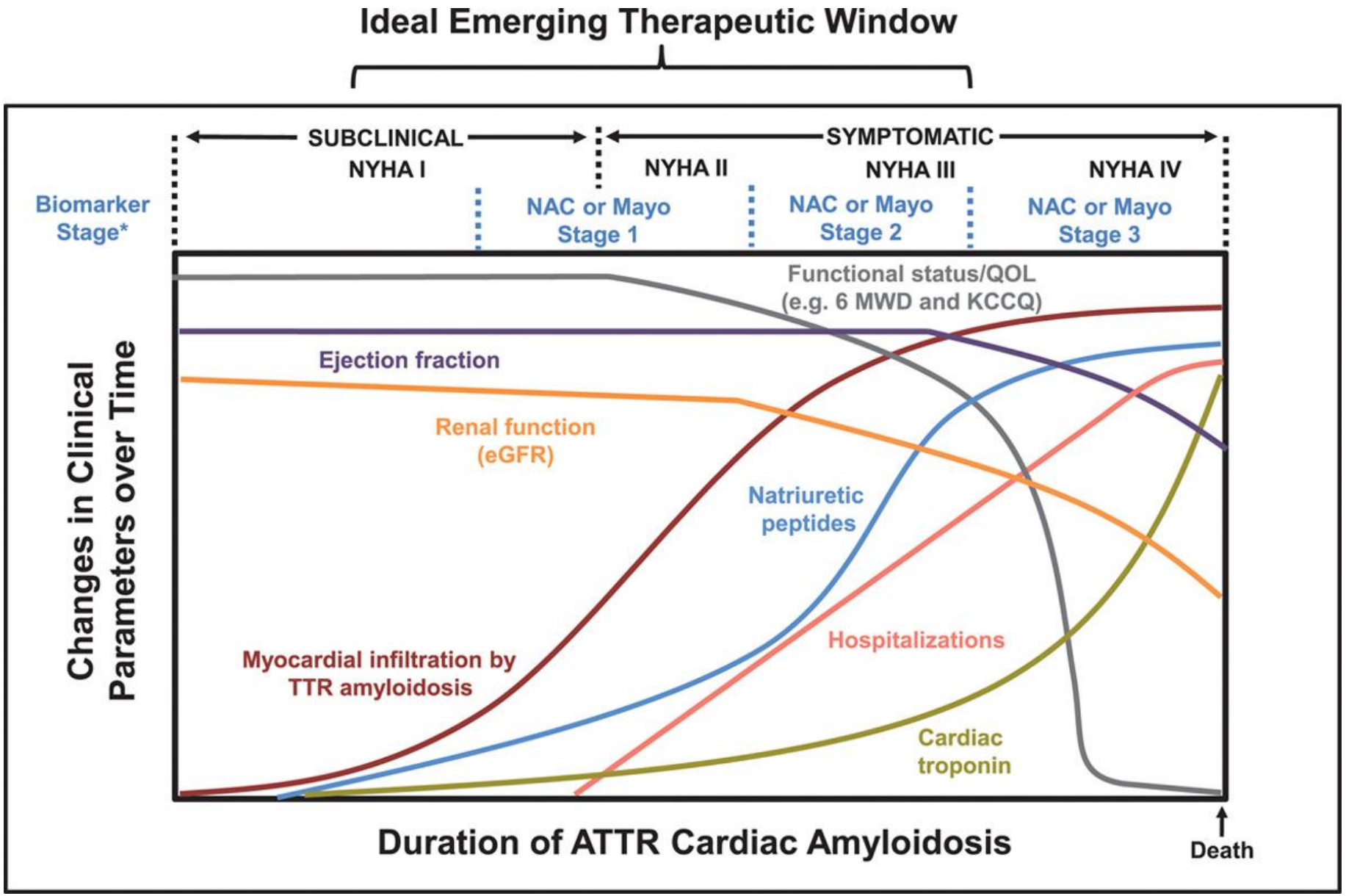


Medián přežití v jednotlivých stadiích ATTR-CM:

Stadium I	méně než 6 let
Stadium II	méně než 4 roky
Stadium III	2 roky

Včasné stanovení diagnózy významně ovlivňuje prognózu pacientů

Gonzalez-Lopez E, et al. Eur Heart J 2017;38:1895–1904



Circulation. 2019;140:27–30. DOI: 10.1161/CIRCULATIONAHA.119.041015

Léčba srdeční amyloidózy

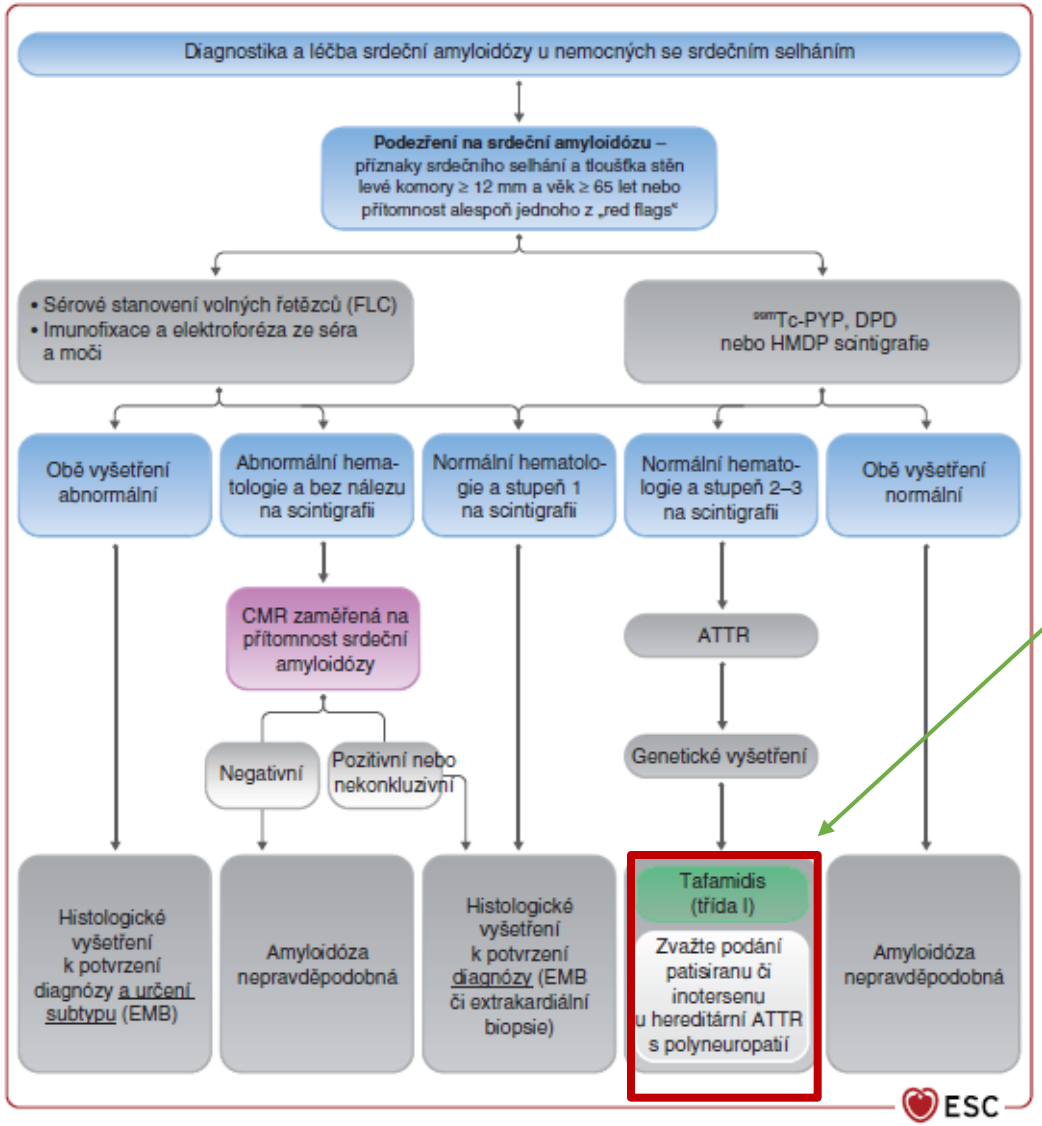
Podpůrná terapie

- Léčba srdečního selhání
- Léčba poruch rytmu
- Prevence kardioembolismu
- Léčba chlopenních vad

Specifická léčba

- AL amyloidóza – v režii hematologa
- TTR amyloidóza

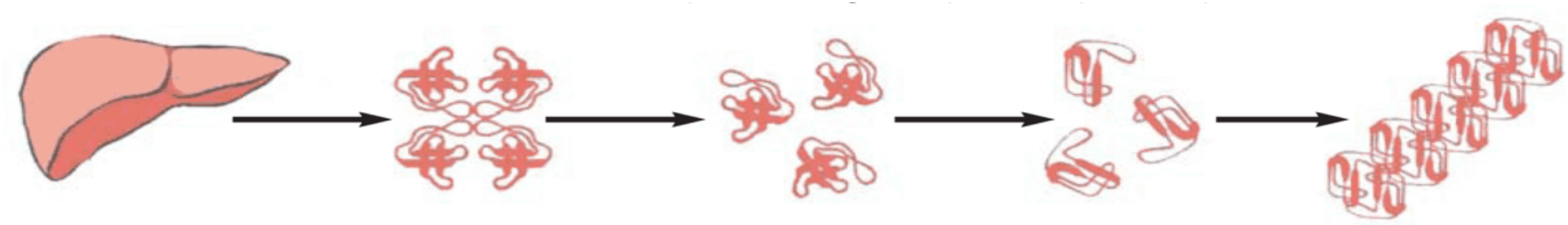
Management srdeční amyloidózy



Stabilizace tetramerů transthyretinu

Specifická terapie TTR-amylodózy

Produkce v játrech | **Tetramery transthyretinu** | **Oligomery a monomery** | **Amyloidní fibrily**



Inhibice exprese TTR genu:
Patisiran
Inotersen
Vutrisiran

Stabilizace tetramerů transthyretinu:
Tafamidis
Acoramidis
Diflunisal

Inhibice agregace a disrupce oligomerů:
Epigalokatechin-3-galát

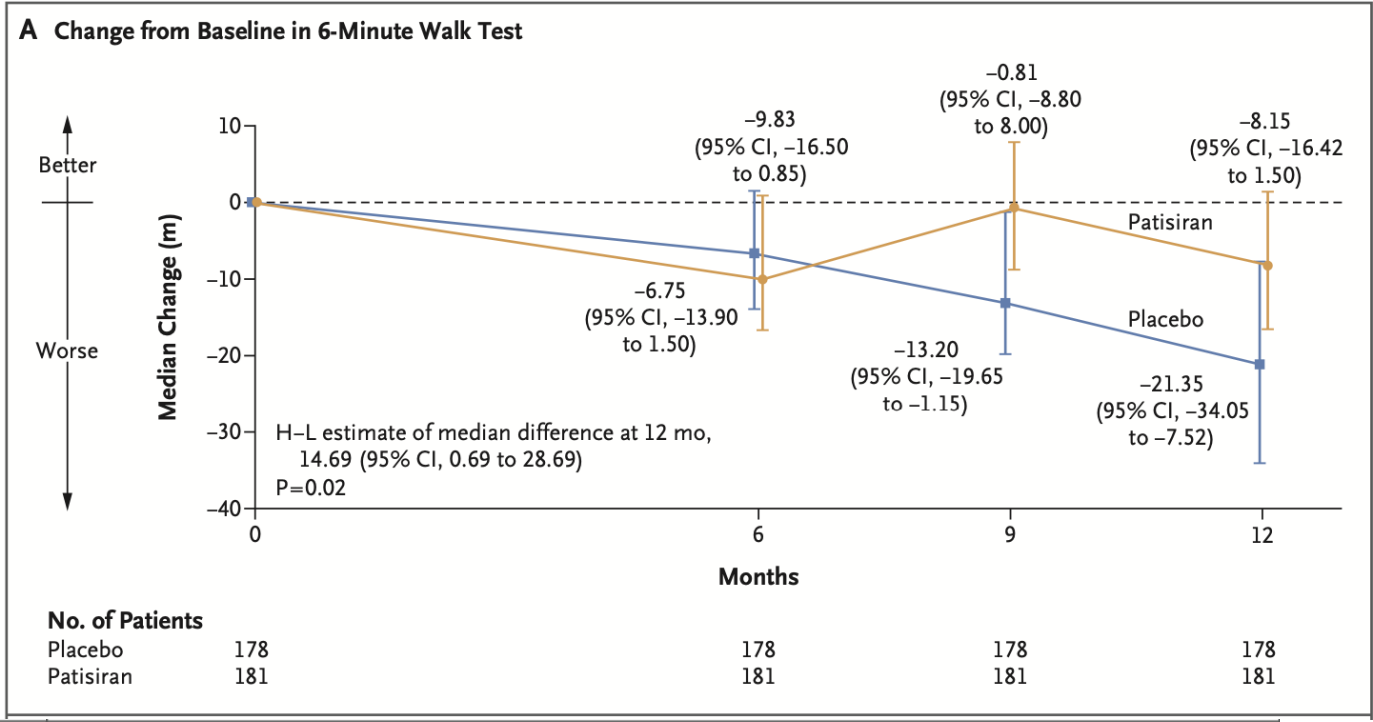
Degradace a reabsorpce fibril amyloidu:
TUDCA+doxycyklin
NI006

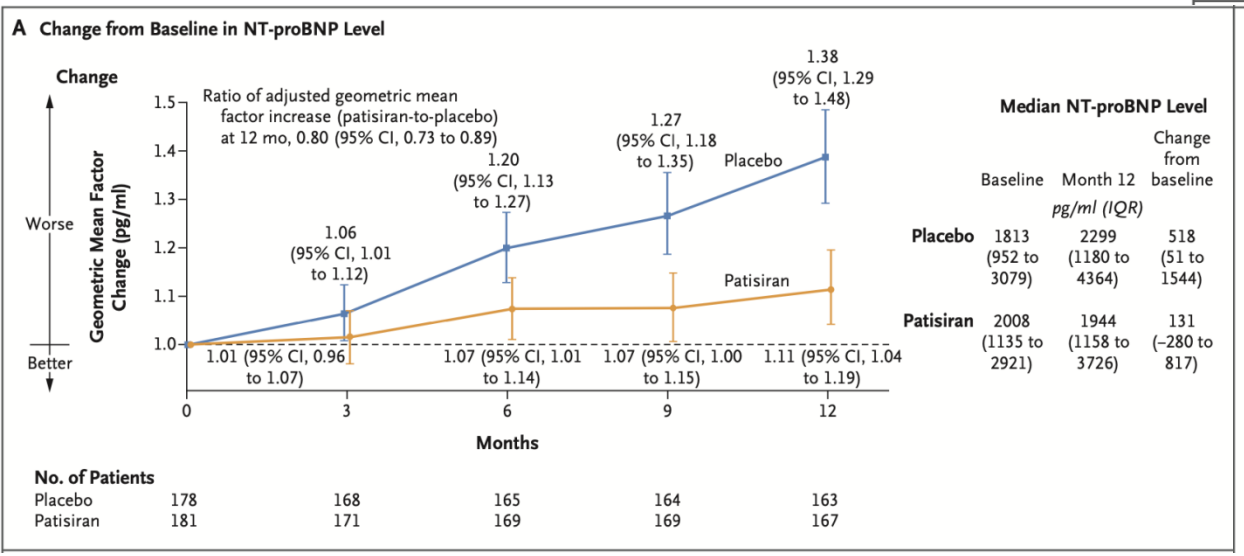
The NEW ENGLAND JOURNAL of MEDICINE

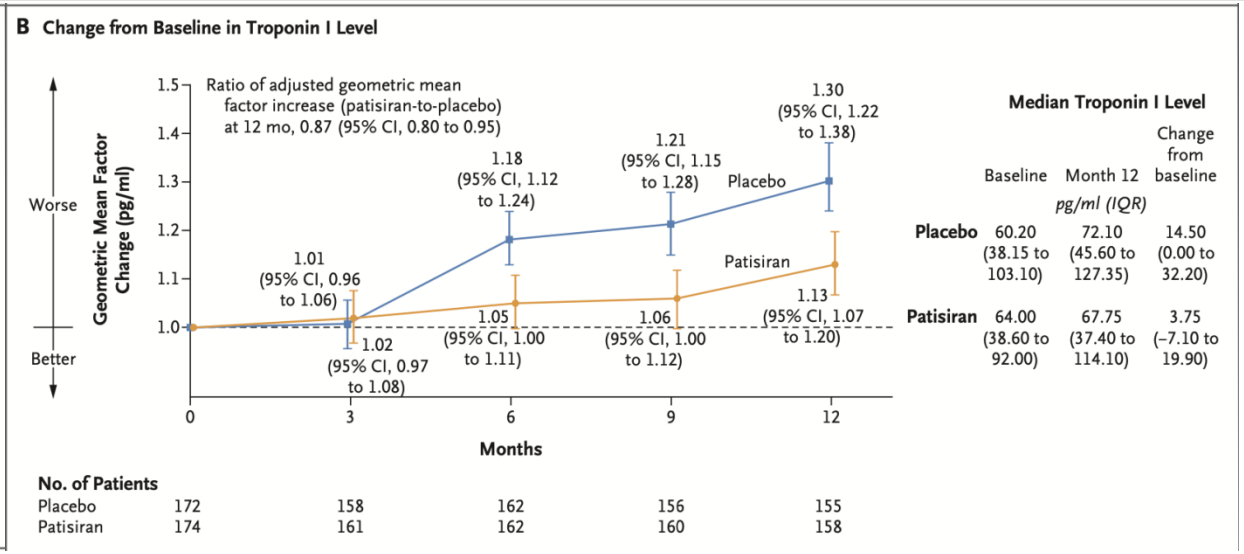
ESTABLISHED IN 1812 OCTOBER 26, 2023 VOL. 389 NO. 17

Patisiran Treatment in Patients with Transthyretin Cardiac Amyloidosis

M.S. Maurer, P. Kale, M. Fontana, J.L. Berk, M. Grogan, F. Gustafsson, R.R. Hung, R.L. Gottlieb, T. Damy, A. González-Duarte, N. Sarswat, Y. Sekijima, N. Tahara, M.S. Taylor, M. Kubanek, E. Donal, T. Palecek, K. Tsujita, W.H.W. Tang, W.-C. Yu, L. Obici, M. Simões, F. Fernandes, S.H. Poulsen, I. Diemberger, F. Perfetto, S.D. Solomon, M. Di Carli, P. Badri, M.T. White, J. Chen, E. Yureneva, M.T. Sweetser, P.Y. Jay, P.P. Garg, J. Vest, and J.D. Gillmore, for the APOLLO-B Trial Investigators*

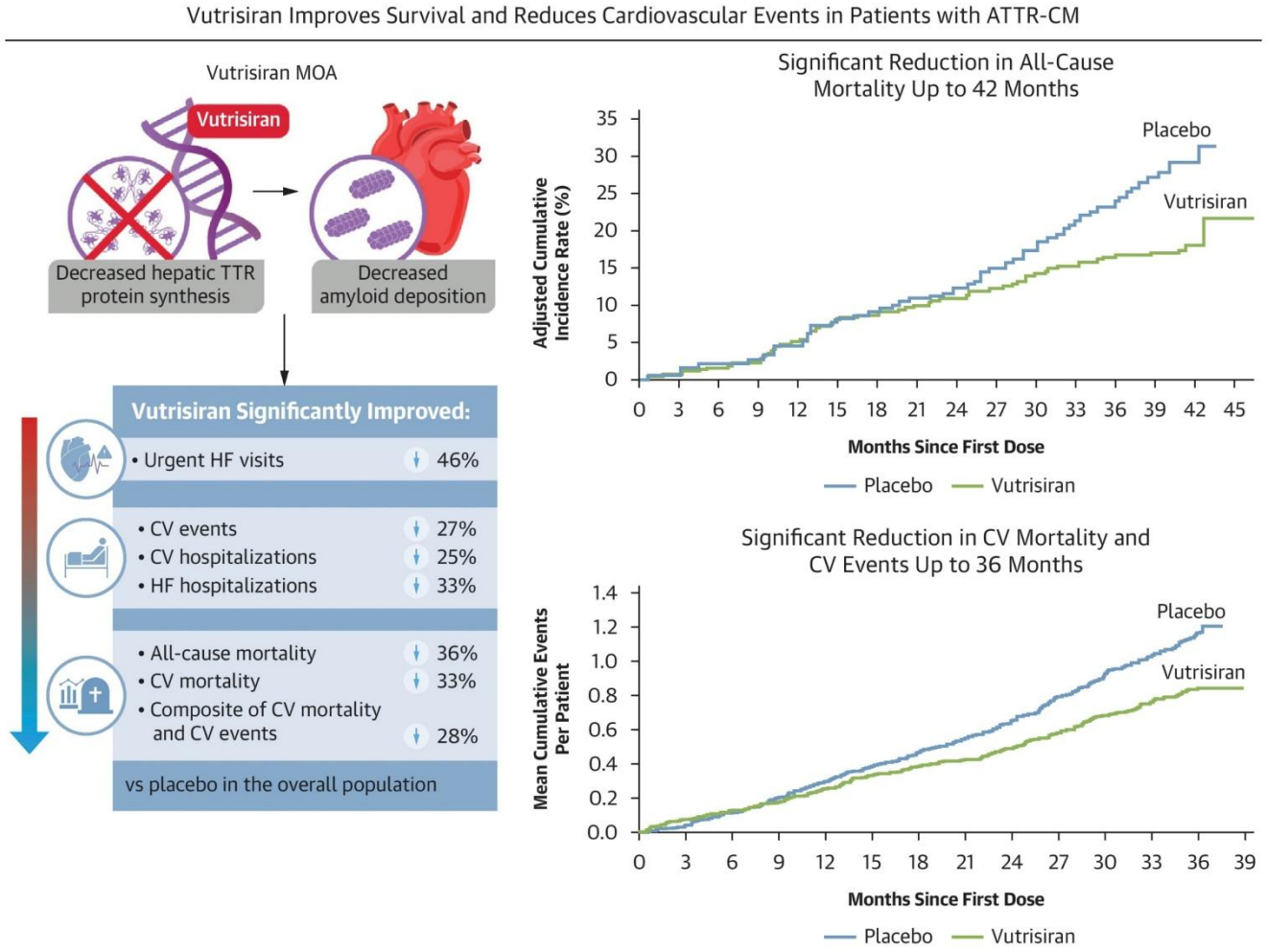






N Engl J Med 2023;389:1553-65.
DOI: 10.1056/NEJMoa2300757

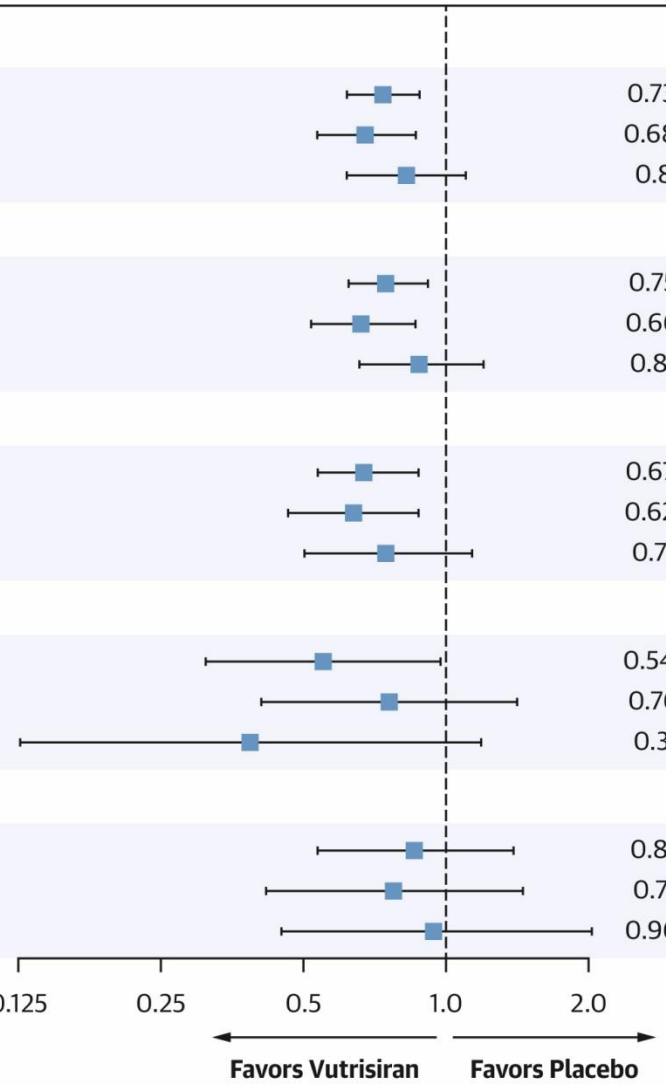
CENTRAL ILLUSTRATION: Vutrisiran Reduces the Risk of Mortality and Cardiovascular Events Among Patients With Transthyretin Amyloidosis With Cardiomyopathy



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

- Witteles, R, Garcia-Pavia, P, Damy, T. et al. Vutrisiran Improves Survival and Reduces Cardiovascular Events in ATTR Amyloid Cardiomyopathy: HELIOS-B. *JACC.* 2025 May, 85 (20) 1959–1970.https://doi.org/10.1016/j.jacc.2025.04.008

	Patients With ≥1 Event, n (%)		Total n Events		Adjusted Events per 100 Person-Years (SE)		RR (95% CI)	P Value
	Vutrisiran	Placebo	Vutrisiran	Placebo	Vutrisiran	Placebo		
CV Events								
Overall Population	112 (34.4)	133 (40.5)	200	263	21.09 (7.35)	28.76 (6.49)	0.73 (0.61-0.88)	<0.01
Monotherapy Population	66 (33.7)	87 (43.7)	119	165	20.67 (9.75)	30.58 (8.28)	0.68 (0.53-0.86)	<0.01
Baseline Tafamidis Subgroup	46 (35.4)	46 (35.7)	98	81	21.09 (11.27)	25.54 (10.64)	0.83 (0.61-1.11)	0.21
CV Hospitalizations								
Overall Population	105 (32.2)	120 (36.6)	174	224	18.76 (7.81)	25.05 (6.95)	0.75 (0.62-0.91)	<0.01
Monotherapy Population	61 (31.1)	79 (39.7)	97	139	33.95 (13.59)	51.16 (11.75)	0.66 (0.51-0.86)	<0.01
Baseline Tafamidis Subgroup	44 (33.8)	41 (31.8)	77	85	27.89 (15.43)	31.32 (14.67)	0.89 (0.65-1.21)	0.46
HF Hospitalizations								
Overall Population	64 (19.6)	82 (25.0)	98	143	9.41 (10.84)	14.11 (9.33)	0.67 (0.52-0.86)	<0.01
Monotherapy Population	41 (20.9)	51 (25.6)	60	91	20.77 (17.31)	33.45 (14.58)	0.62 (0.45-0.86)	<0.01
Baseline Tafamidis Subgroup	23 (17.7)	31 (24.0)	38	52	13.77 (20.99)	18.36 (18.97)	0.75 (0.49-1.14)	0.18
Urgent HF Visits								
Overall Population	17 (5.2)	22 (6.7)	22	34	2.01 (25.17)	3.70 (18.16)	0.54 (0.30-0.98)	0.04
Monotherapy Population	13 (6.6)	14 (7.0)	18	21	2.46 (47.90)	3.25 (45.31)	0.76 (0.40-1.42)	0.39
Baseline Tafamidis Subgroup	4 (3.1)	8 (6.2)	4	13	1.40 (60.52)	3.71 (42.58)	0.38 (0.12-1.19)	0.10
Arrhythmia Hospitalizations								
Overall Population	27 (8.3)	31 (9.5)	30	34	3.42 (18.46)	3.98 (17.35)	0.86 (0.53-1.41)	0.55
Monotherapy Population	17 (8.7)	20 (10.1)	17	21	3.80 (43.37)	4.91 (40.87)	0.77 (0.41-1.47)	0.43
Baseline Tafamidis Subgroup	10 (7.7)	11 (8.5)	13	13	4.52 (38.97)	4.72 (39.16)	0.96 (0.44-2.07)	0.91



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ESTABLISHED IN 1812 SEPTEMBER 13, 2018 VOL. 379 NO. 11

KOMPLEXNÍ KARDIOVASKULÁRNÍ CENTRUM
FAKULTNÍ NEMOCNICE OLOMOUC

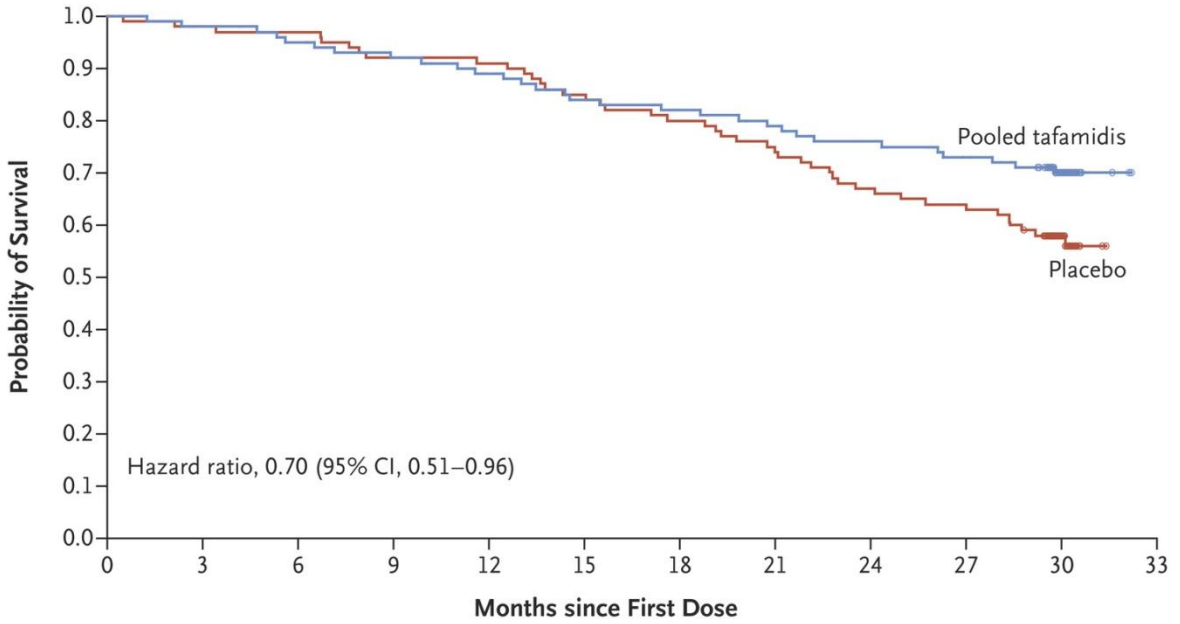
Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy

Mathew S. Maurer, M.D., Jeffrey H. Schwartz, Ph.D., Balarama Gundapaneni, M.S., Perry M. Elliott, M.D., Giampaolo Merlini, M.D., Ph.D., Marcia Waddington-Cruz, M.D., Arnt V. Kristen, M.D., Martha Grogan, M.D., Ronald Witteles, M.D., Thibaud Damy, M.D., Ph.D., Brian M. Drachman, M.D., Sanjiv J. Shah, M.D., Mazen Hanna, M.D., Daniel P. Judge, M.D., Alexandra I. Barsdorf, Ph.D., Peter Huber, R.Ph., Terrell A. Patterson, Ph.D., Steven Riley, Pharm.D., Ph.D., Jennifer Schumacher, Ph.D., Michelle Stewart, Ph.D., Marla B. Sultan, M.D., M.B.A., and Claudio Rapezzi, M.D., for the ATTR-ACT Study Investigators*

C Frequency of Cardiovascular-Related Hospitalizations

	No. of Patients	No. of Patients with Cardiovascular- Related Hospitalizations	Cardiovascular- Related Hospitalizations	Pooled Tafamidis vs. Placebo Treatment Difference
		total no. (%)	*no. per yr*	*relative risk ratio (95% CI)*
Pooled Tafamidis	264	138 (52.3)	0.48	
Placebo	177	107 (60.5)	0.70	0.68 (0.56–0.81)

B Analysis of All-Cause Mortality



No. at Risk (cumulative no. of events)

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)

30% redukce mortality
32% redukce KV hospitalizací

N Engl J Med 2018; 379:1007-1016

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

Brian Drachman[1], Thibaud Damy[2], Mazen Hanna[3], Ronnie Wang[4], Franca S. Angeli[5], and Pablo Garcia-Pavia[6,7,8]*

[1]University of Pennsylvania Health System, Philadelphia, PA, USA; [2]Referral Center for Cardiac Amyloidosis, CHU Henri Mondor, Créteil, France; [3]Department of Cardiovascular Medicine, Cleveland Clinic, Cleveland, OH, USA; [4]Pfizer Inc., Groton, CT, USA; [5]Pfizer Inc., New York, NY, USA; [6]Hospital Universitario Puerta de Hierro Majadahonda, IDIPHISA, CIBERCV, Madrid, Spain; [7]Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain; and [8]Universidad Francisco de Vitoria (UFV), Pozuelo de Alarcon, Spain

Received 26 January 2024; revised 1 May 2024; accepted 27 May 2024; online publish-ahead-of-print 26 June 2024

Table 2 Observed all-cause mortality by left ventricular ejection fraction at baseline

	LVEF <50%		LVEF ≥50%	
	Tafamidis 80/61 mg	Placebo/tafamidis	Tafamidis 80/61 mg	Placebo/tafamidis
n	88	89	85	86
All-cause mortality, *n* (%)	52 (59.1)	73 (82.0)	35 (41.2)	52 (60.5)
First event, *n* (%)				
All-cause death	45 (51.1)	69 (77.5)	33 (38.8)	50 (58.1)
Heart transplant	5 (5.7)	4 (4.5)	2 (2.4)	2 (2.3)
Implantation of a cardiac mechanical assist device	2 (2.3)	0	0	0

LVEF, left ventricular ejection fraction.
Heart transplant and implantation of a cardiac mechanical assist device were treated as death. Statistical analyses were conducted using the Kaplan–Meier method and are shown in *Figures 2* and *3*.

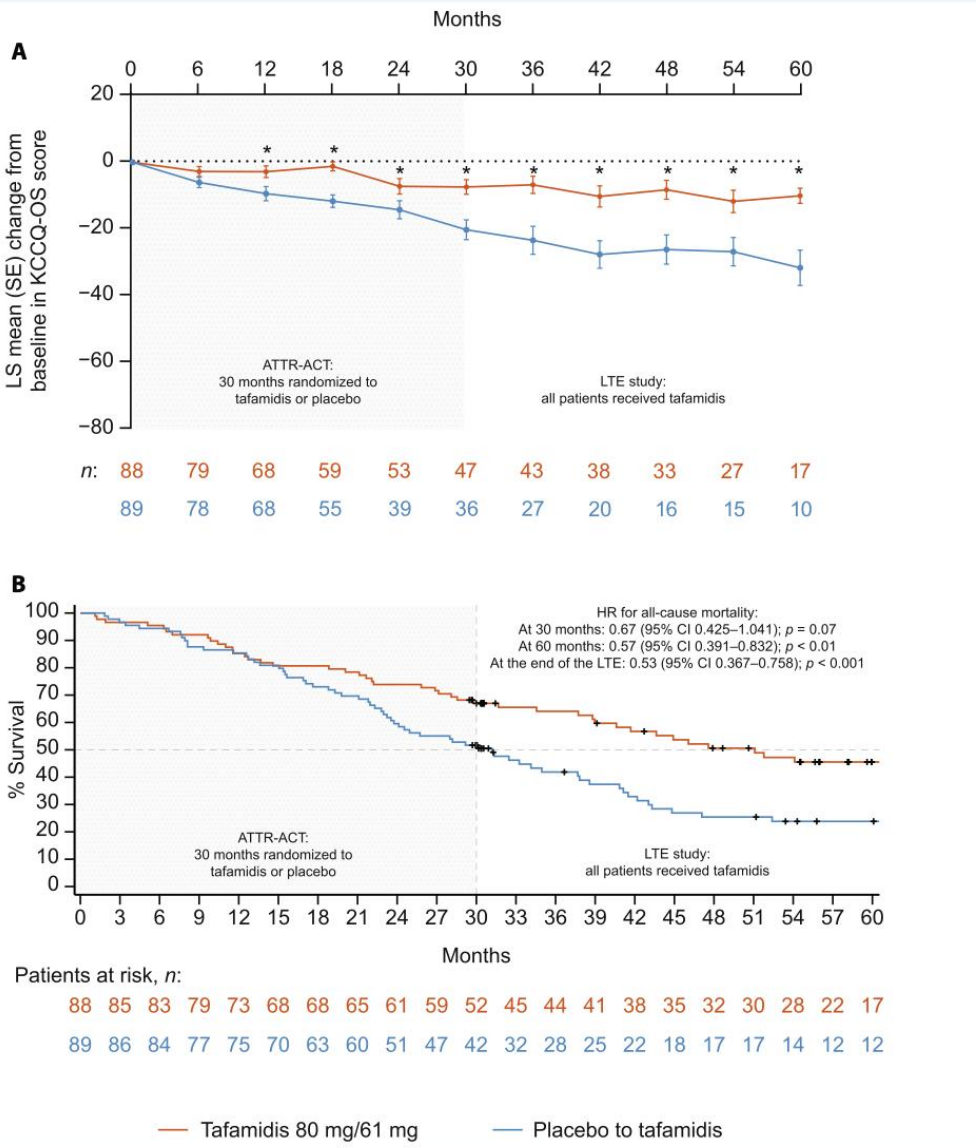
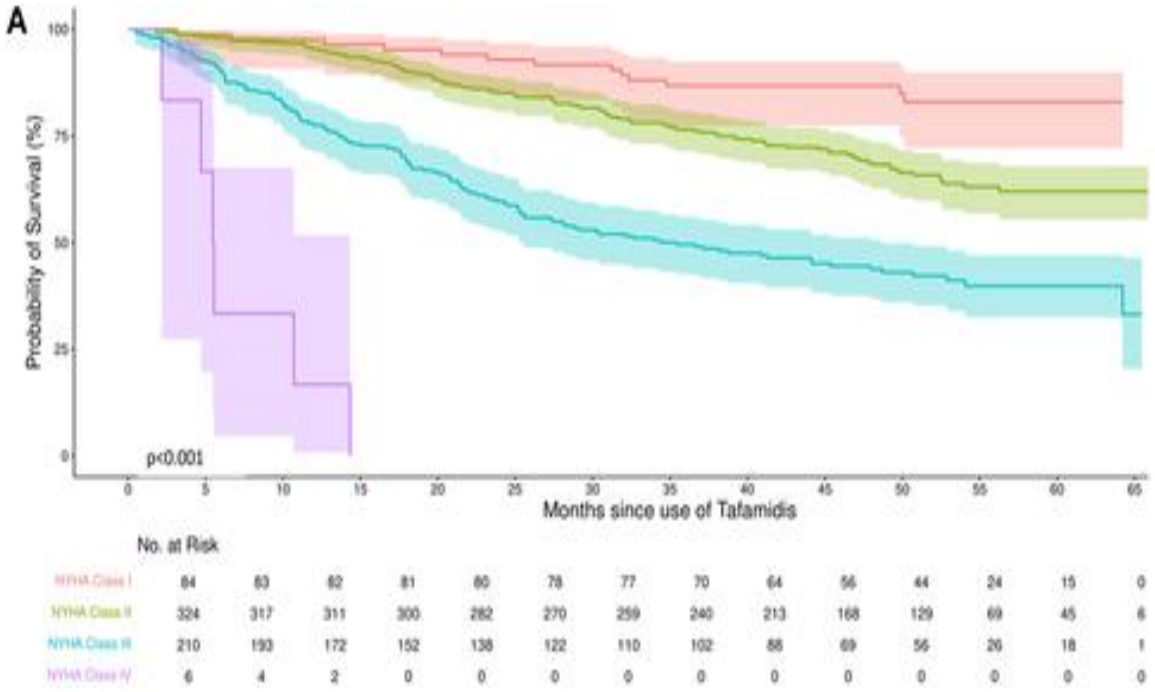
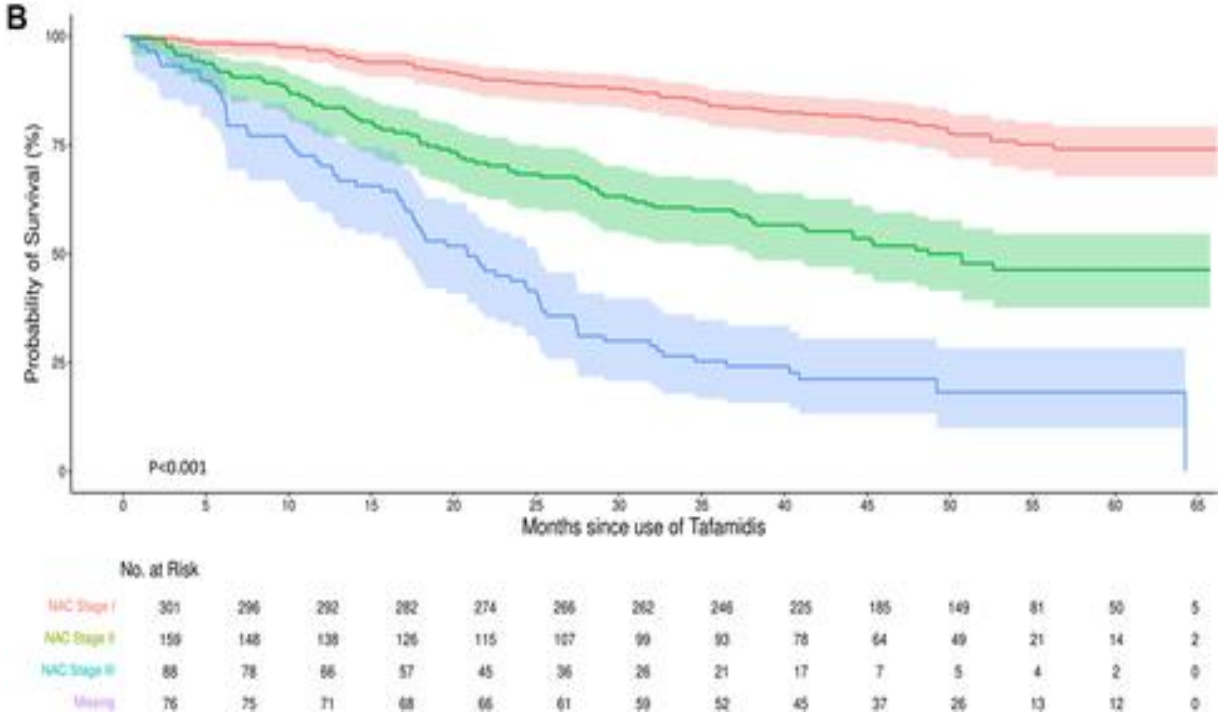


Figure 2 Health-related quality of life (*A*) and Kaplan–Meier plot of all-cause mortality (*B*) in patients with baseline left ventricular ejection fraction <50%. End of survival defined as death, heart transplant, or implantation of a cardiac mechanical assist device. ATTR-ACT, Tafamidis in Transthyretin Cardiomyopathy Clinical Trial; CI, confidence interval; HR, hazard ratio; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire overall summary; LS, least squares; LTE, long-term extension; SE, standard error. *$p < 0.05$; + = censored.

A Multicenter Study of Contemporary Long-Term Tafamidis Outcomes in Transthyretin Amyloid Cardiomyopathy

Ahmad Masri, MD, MS,[a] Priyanka Bhattacharya, MD,[b] Brent Medoff, MD,[c] Ain U. Ejaz, MD,[d] Miriam R. Elman, MS, MPH,[a] Pranav Chandrashekar, MD,[a] Lauren Ives, MPH,[e] Alfonsina Miralxal Santos, MD,[b] Sergio L. Teruya, MD,[b] Yuanzi Zhao, MD, PhD,[a] Shuaiqi Huang, PhD,[f] Xiaofeng Wang, PhD,[f] Brett W. Sperry, MD,[d] Mathew S. Maurer, MD,[b] Prem Soman, MD, PhD,[c] Mazen Hanna, MD[e]





- *Ahmad Masri et al. J Am Coll Cardiol CardioOnc 2025; 7:282-293.*

A Multicenter Study of Contemporary Long-Term Tafamidis Outcomes in Transthyretin Amyloid Cardiomyopathy

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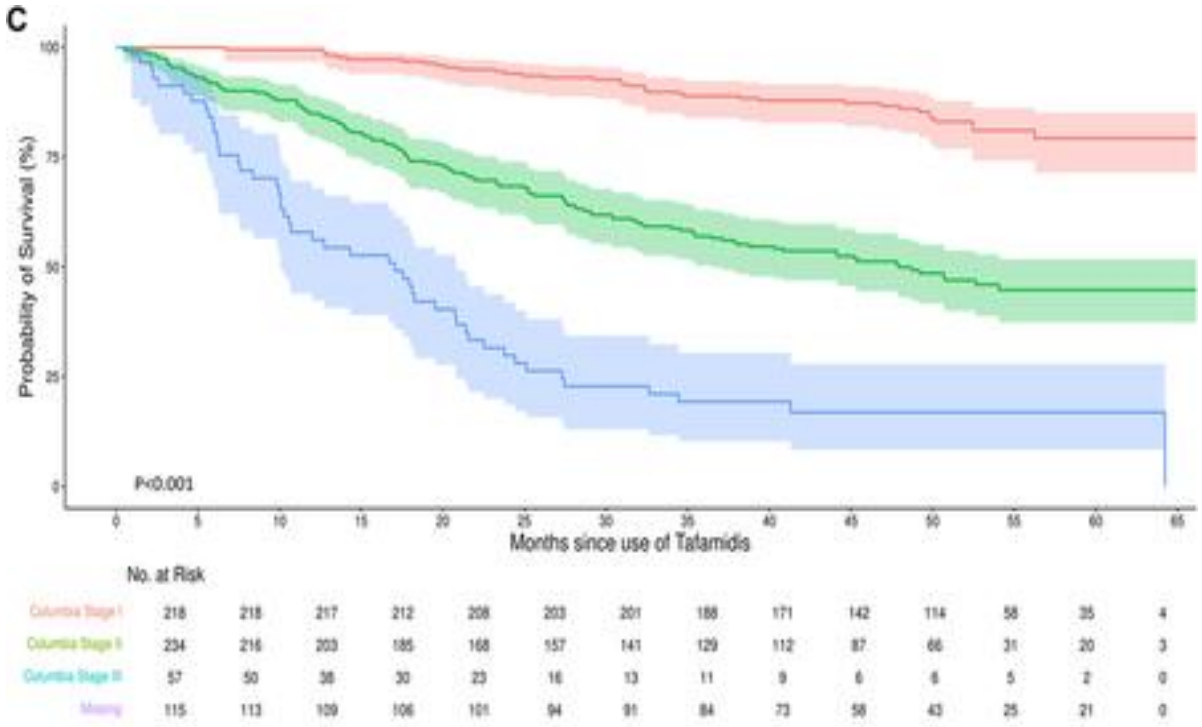
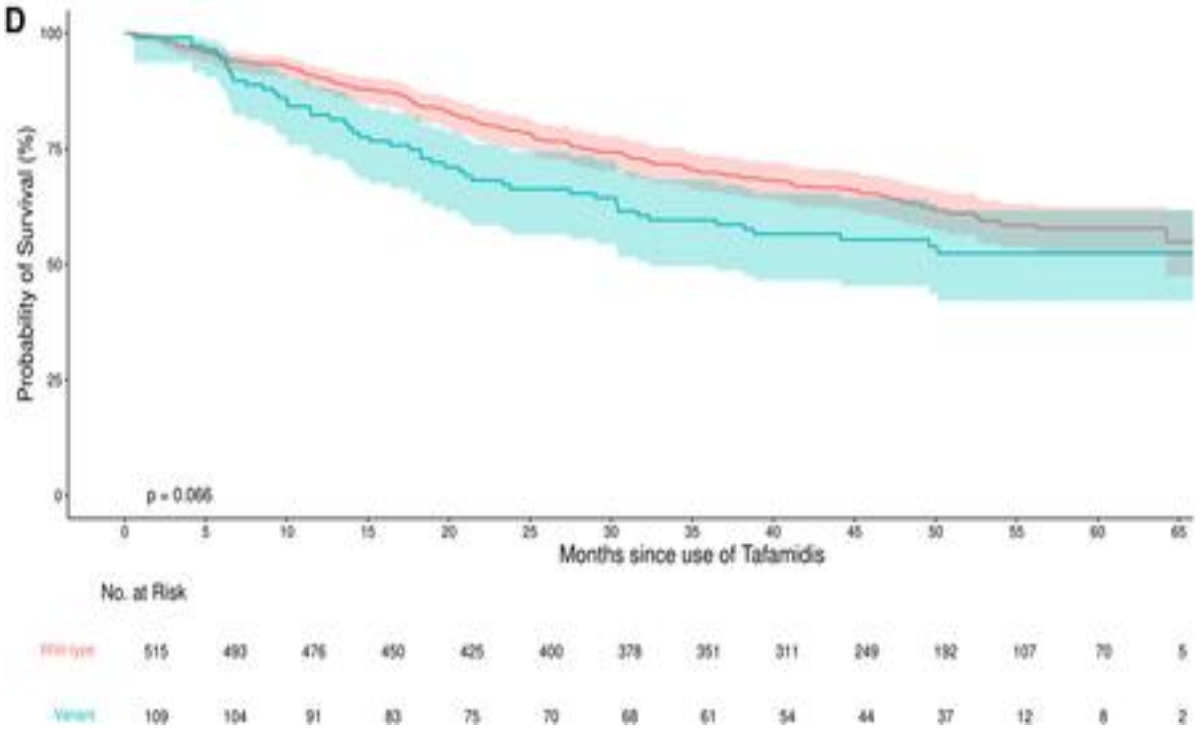


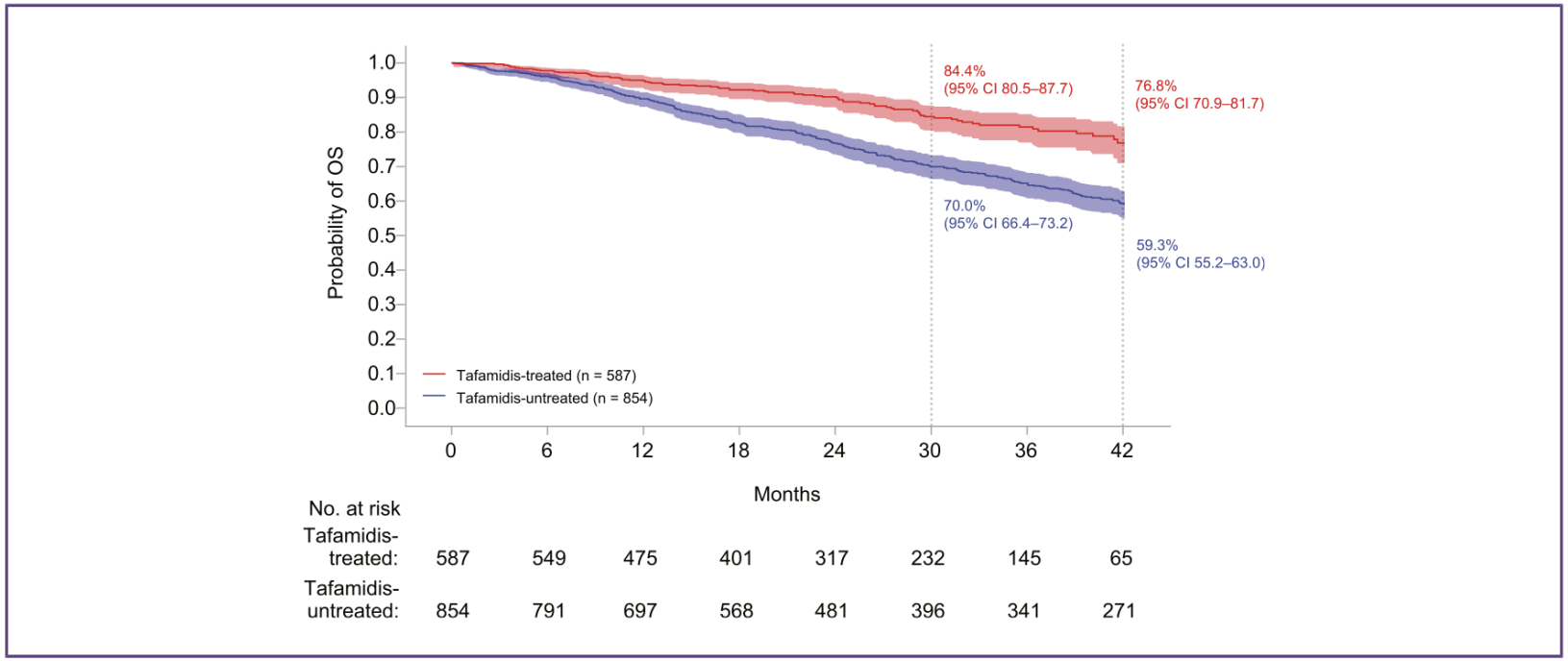


- *Ahmad Masri et al. J Am Coll Cardiol CardioOnc 2025; 7:282-293.*

Survival in a Real-World Cohort of Patients With Transthyretin Amyloid Cardiomyopathy Treated With Tafamidis: An Analysis From the Transthyretin Amyloidosis Outcomes Survey (THAOS)

PABLO GARCIA-PAVIA, MD, PhD[1,2,3] ARNT V. KRISTEN, MD[4] BRIAN DRACHMAN, MD[5] MARTIN CARLSSON, MS[6] LESLIE AMASS, PhD[6] FRANCA STEDILE ANGELI, MD, PhD[6] and MATHEW S. MAURER, MD[7], on behalf of the THAOS investigators[a]

Madrid, and Pozuelo de Alarcon, Spain; Heidelberg, Germany; and Philadelphia, and New York, USA



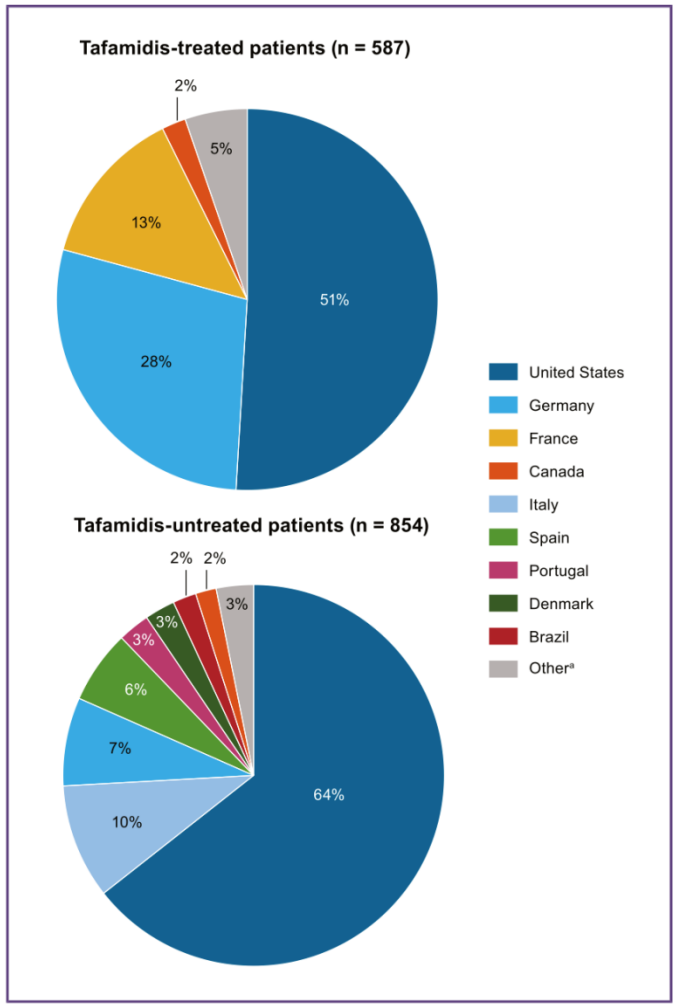


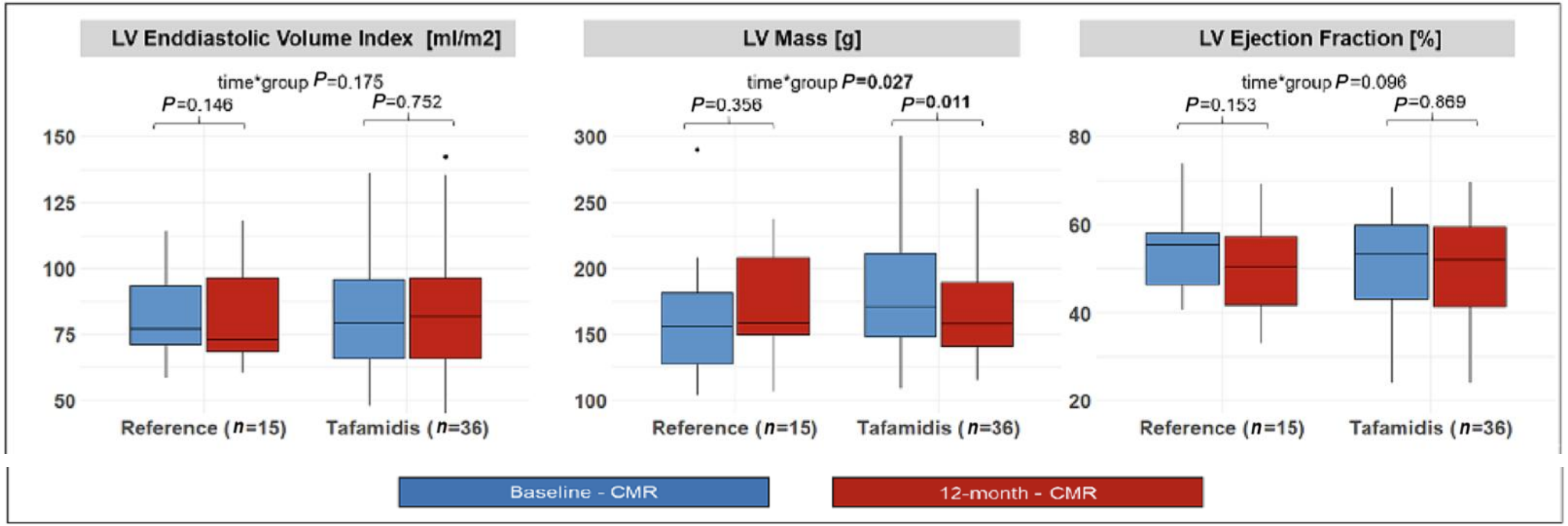
Fig. 1. Country of enrollment for tafamidis-treated and tafamidis-untreated patients. [a]Includes countries with fewer than 10 enrolled patients.

• *https://doi.org/10.1016/j.cardfail.2024.06.003.*

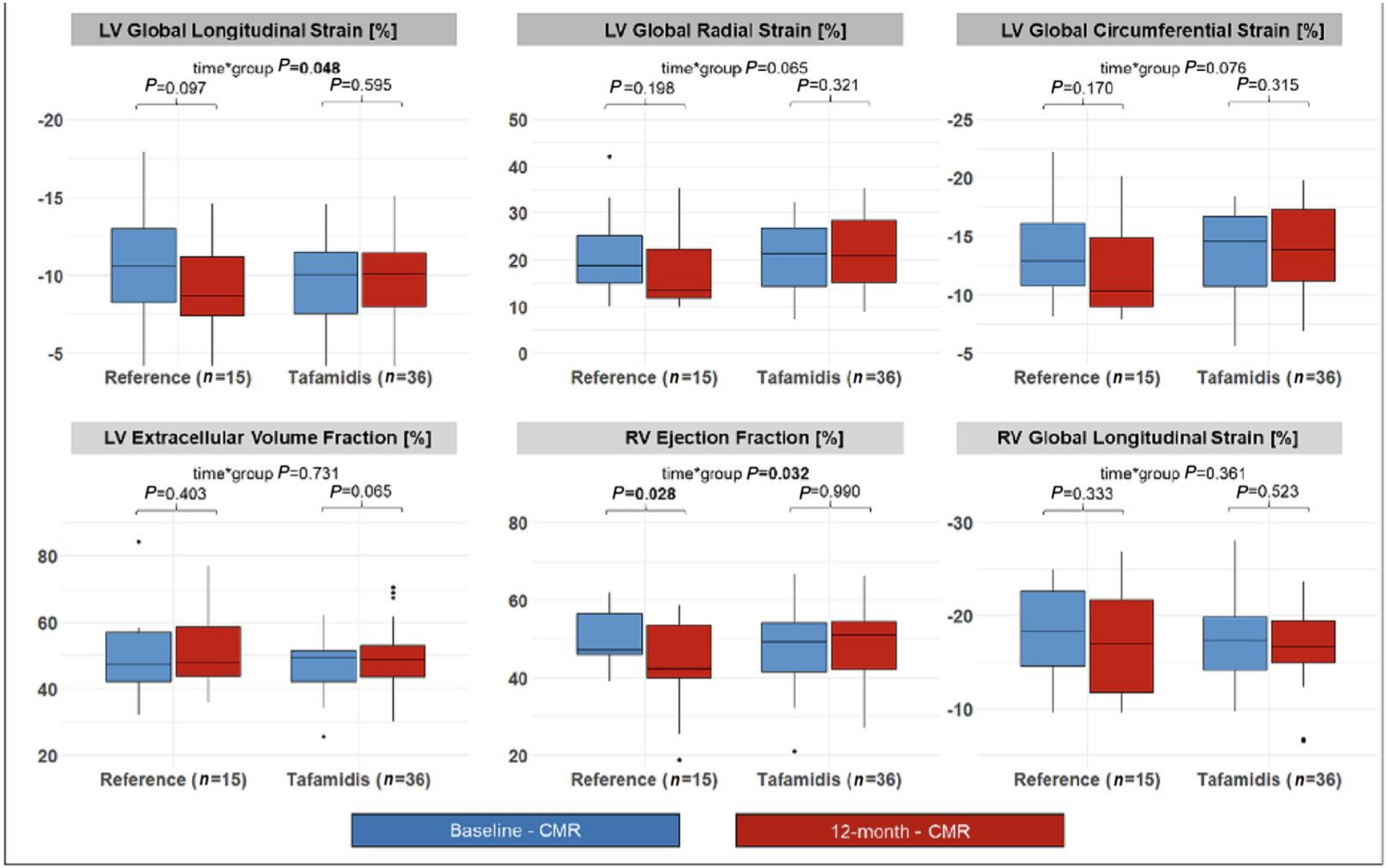
Impact of tafamidis on myocardial function and CMR tissue characteristics in transthyretin amyloid cardiomyopathy

Stephan Dobner, Benedikt Bernhard, Lorenz Ninck, Monika Wieser, Adam Bakula, Andreas Wahl, Valentin Köchli, Giancarlo Spano, Martina Boscolo Berto, Elena Elchinova, Yasaman Safarkhanlo, Stefan Stortecky, Jonathan Schütze, Isaac Shiri, Lukas Hunziker and Christoph Gräni*

Department of Cardiology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland



- DOI: 10.1002/ehf2.14815



- DOI: 10.1002/ehf2.14815

Tafamidis - úhrada

Léčivý přípravek Vyndaqel je hrazen k léčbě transthyretinové amyloidózy divokého typu zahájené u dospělých pacientů s kardiomyopatií (ATTR-CM) s funkční třídou NYHA I až II.

Léčba předmětným přípravkem je přerušena v případě, že je u pacienta zjištěn některý z dále uvedených klinických stavů:

a) Setrvalé zhoršení do funkční třídy NYHA IV

b) Pokles GRF < 25 ml/min/1,73m2

c) Progredující těžká hepatopatie

d) Neovlivnitelná těžká malnutrice

e) Závažné nežádoucí účinky spojené s léčbou léčivým přípravkem Vyndaqel

f) Jiné závažné onemocnění s životní prognózou do 12 měsíců

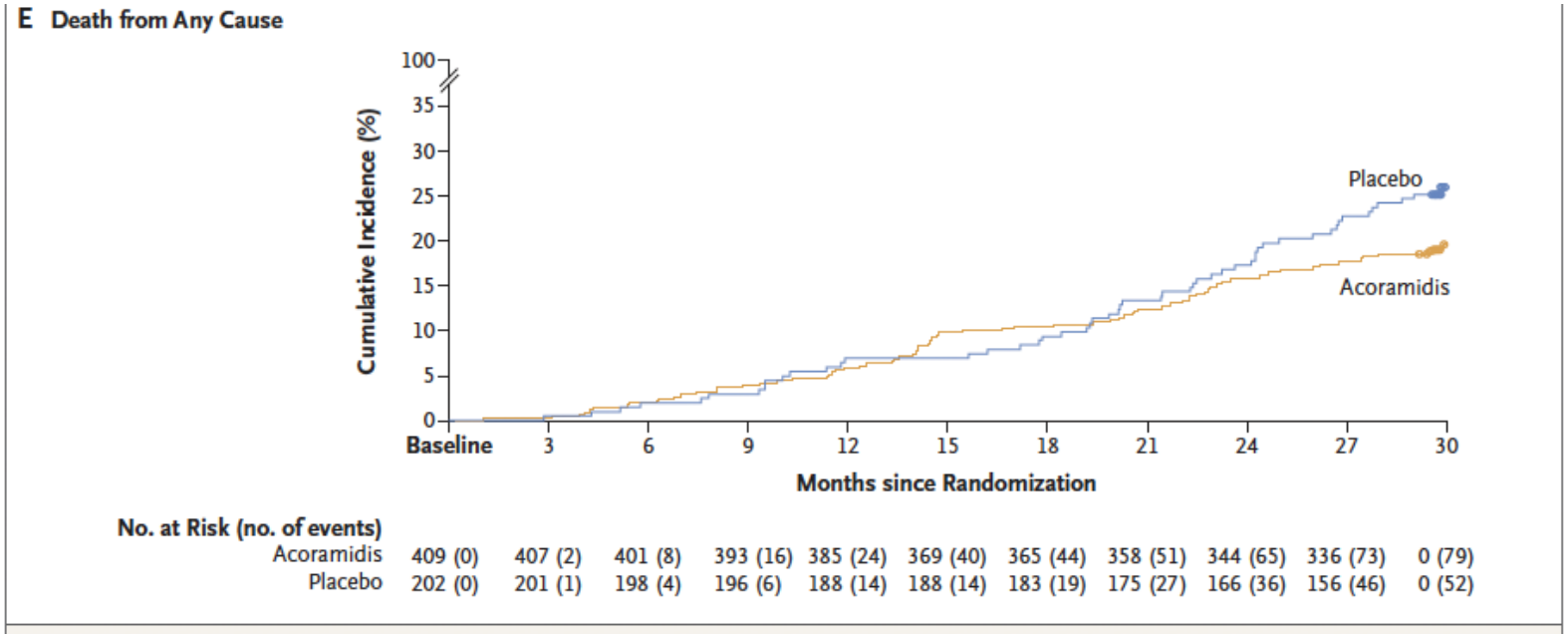
g) Rozvoj těžké demence či jiného devastujícího neurologického onemocnění

The NEW ENGLAND JOURNAL of MEDICINE

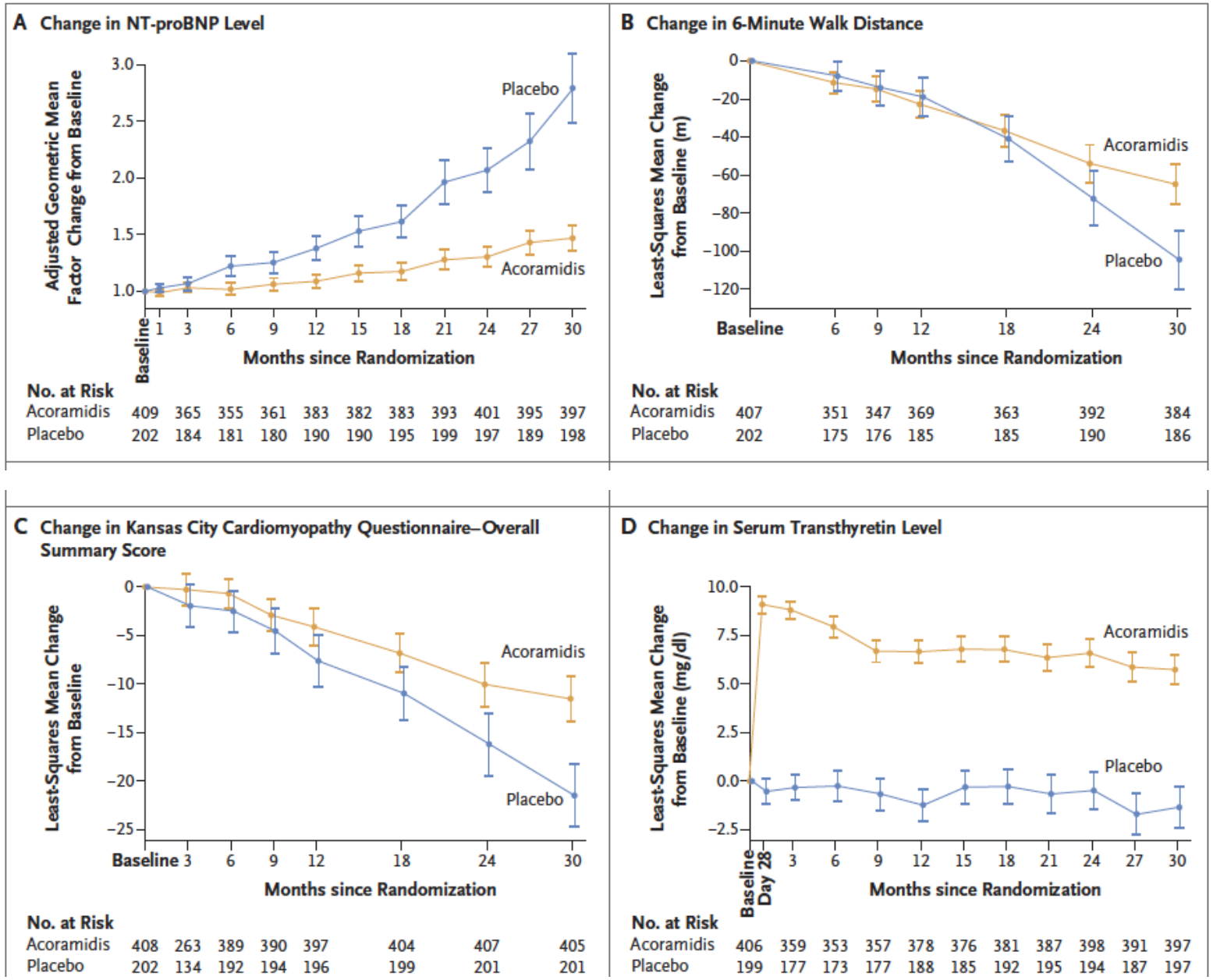
ORIGINAL ARTICLE

Efficacy and Safety of Acoramidis in Transthyretin Amyloid Cardiomyopathy

J.D. Gillmore, D.P. Judge, F. Cappelli, M. Fontana, P. Garcia-Pavia, S. Gibbs, M. Grogan, M. Hanna, J. Hoffman, A. Masri, M.S. Maurer, J. Nativi-Nicolau, L. Obici, S.H. Poulsen, F. Rockhold, K.B. Shah, P. Soman, J. Garg, K. Chiswell, H. Xu, X. Cao, T. Lystig, U. Sinha, and J.C. Fox, for the ATTRibute-CM Investigators*



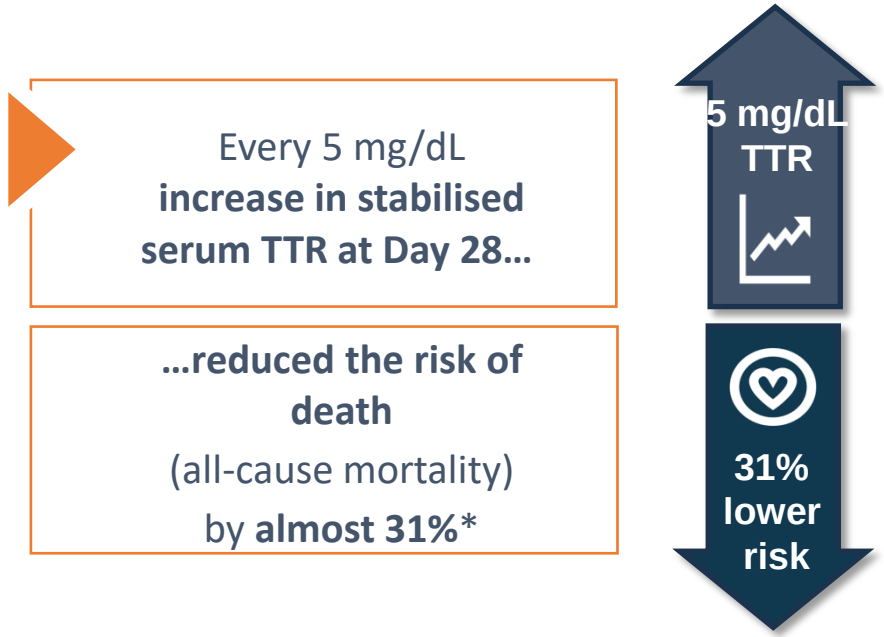
- *N Engl J Med 2024;390:132-42.*



- *N Engl J Med 2024;390:132-42.*

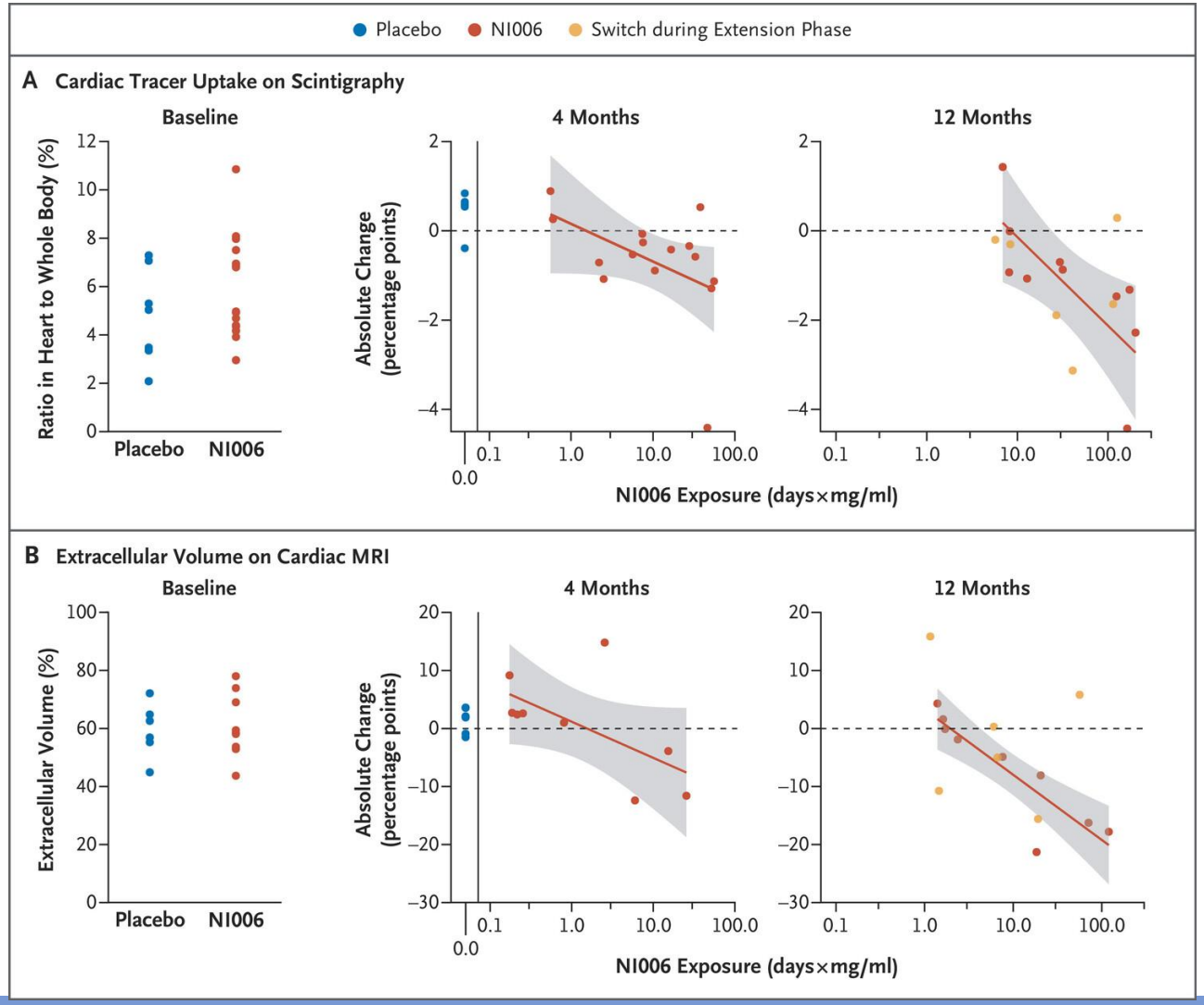
Sérová koncentrace transthyretinu

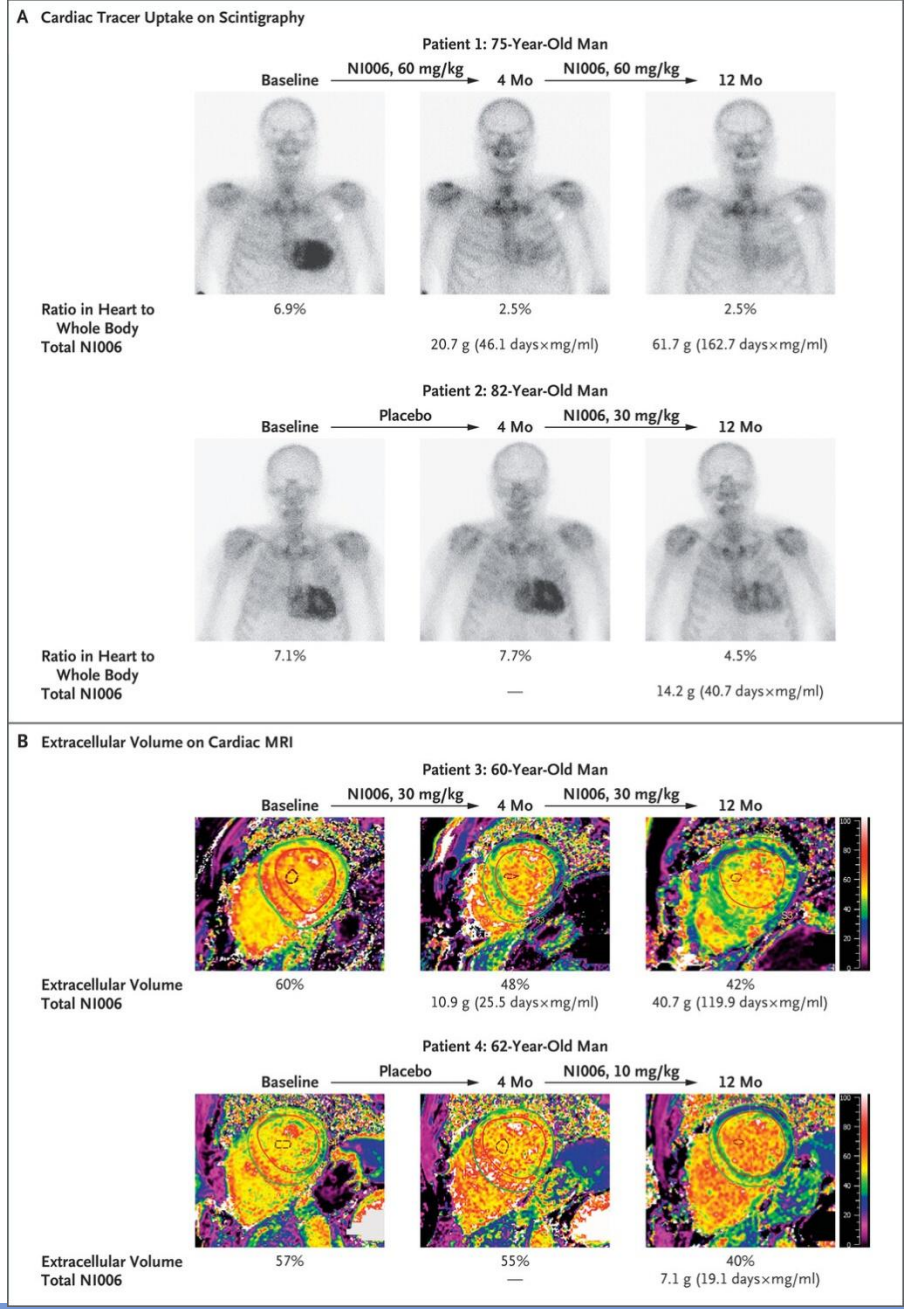
- Stabilizace tetramerů transthyretinu zvyšuje jeho sérové hodnoty – což koreluje s klinickým benefitem pacientů
- ATTRibute-CM – sérové hodnoty TTR nezávislým prediktorem přežití



- Maurer M, et al. *Presented at: International Symposium on Amyloidosis 2024; 26–30 May 2024; Rochester, MN.* Poster #2024-ISA-B-295

NI006 - *rekombinantní lidská anti-TTR protilátka*





- N Engl J Med 2023;389:239-250
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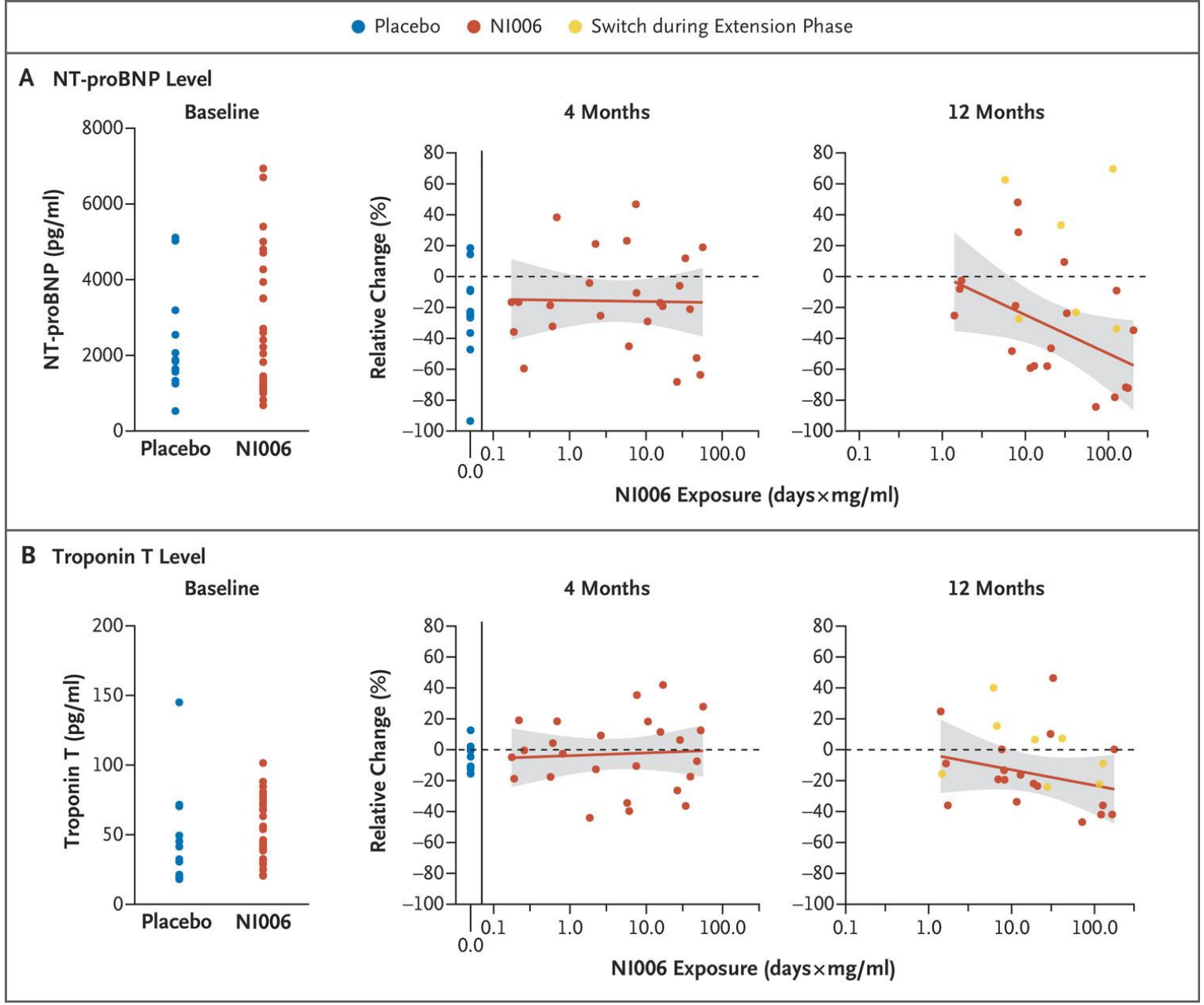

- N Engl J Med 2023;389:239-250
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Jak jsme se posunuli v managementu ATTR-CM?

Pro prognózu pacientů je důležitá včasná diagnostika a včasná indikace specifické terapie

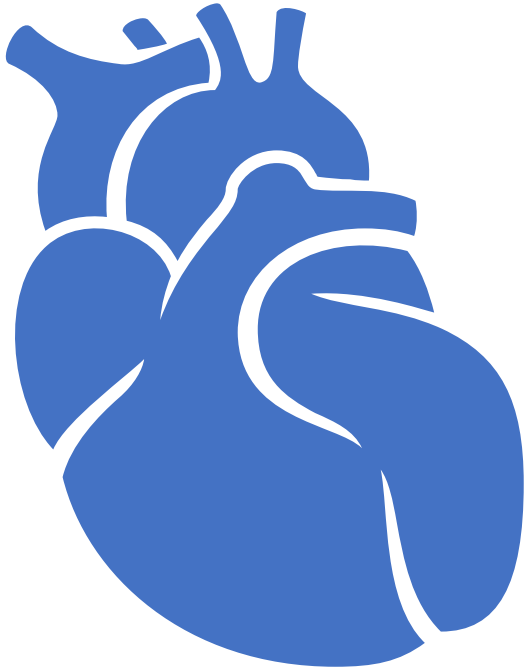
V léčbě ATTR-CM je u pacientů NYHA I-II indikována specifická terapie tafamidisem - hrazen od 1.6.2023 jako centrová léčba

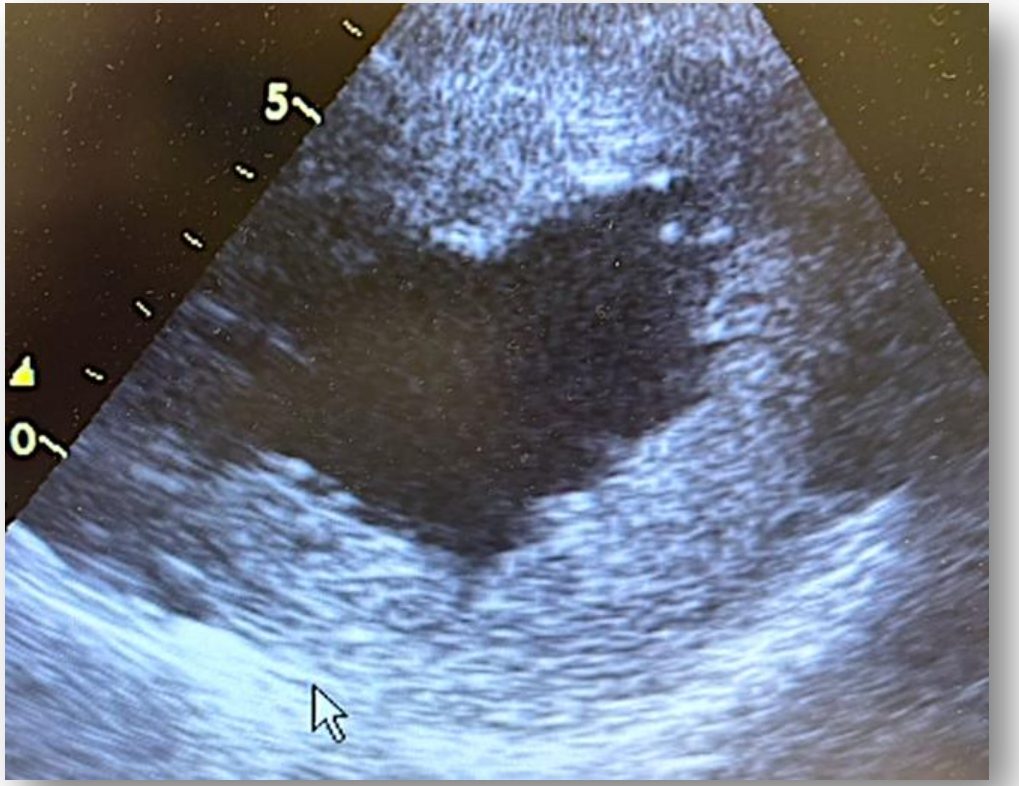
(II. Interní klinika VFN Praha, IKEM, I. interní klinika kardioangiologická FNUSA Brno,

I. interní klinika-kardiologická FN Olomouc, nově FN Ostrava).

Změna schématu specifické terapie ATTR s příchodem nových molekul.

Vypracování algoritmu pro sledování progrese onemocnění a efektivity specifické terapie.





Děkuji za pozornost.