4e CONGRÈS FRANCOPHONE MULTIDISCIPLINAIRE DE L'AMYLOSE

ÉVÉNEMENT HYBRIDE

Mercredi 17 décembre 2025
Fondation Biermans-Lapôtre ▪ PARIS
www.congres-amylose.com

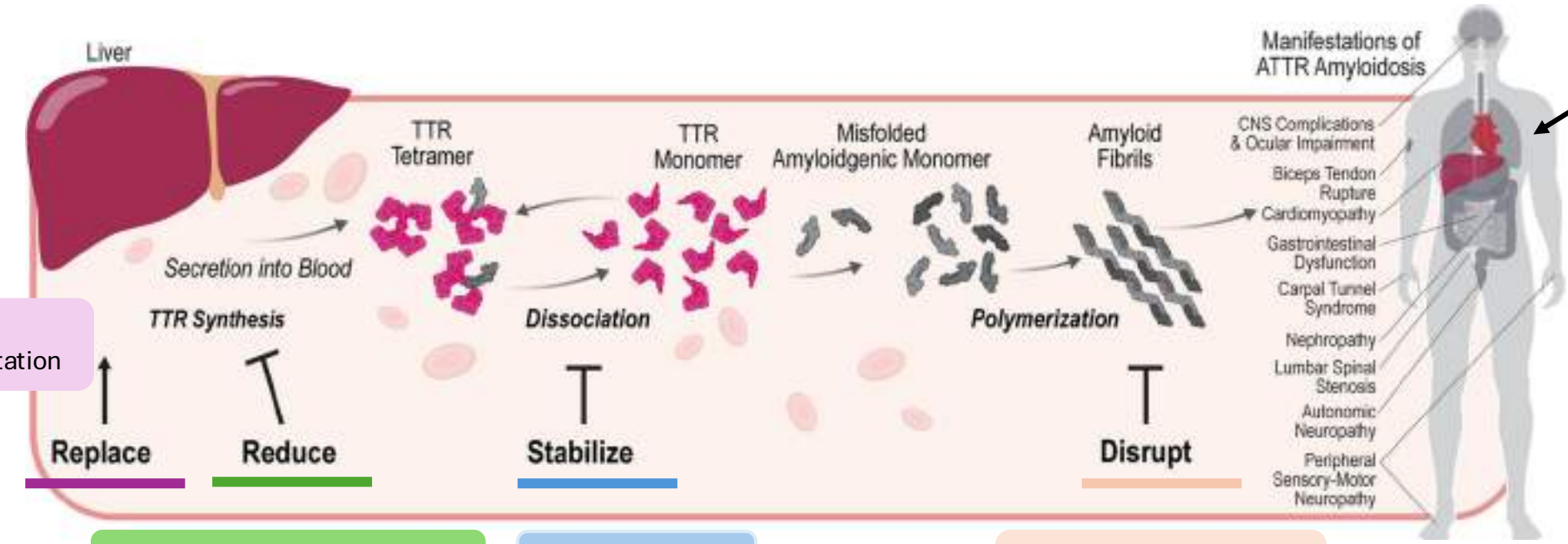
Les actualités thérapeutiques dans l'amylose cardiaque à TTR

Dr Bouchot Océane

CH Annecy

Liens d'intérêts

Pas de lien d'intérêts vis-à-vis de cette présentation.



Liver Transplantation

Heart Transplantation

Replace

Silencers

siRNA
Patisiran / Vutrisiran

Oligonucléotides antisens
Inotersen/Eplontersen

Gene editing (CRISPR-Cas9)
Nex z

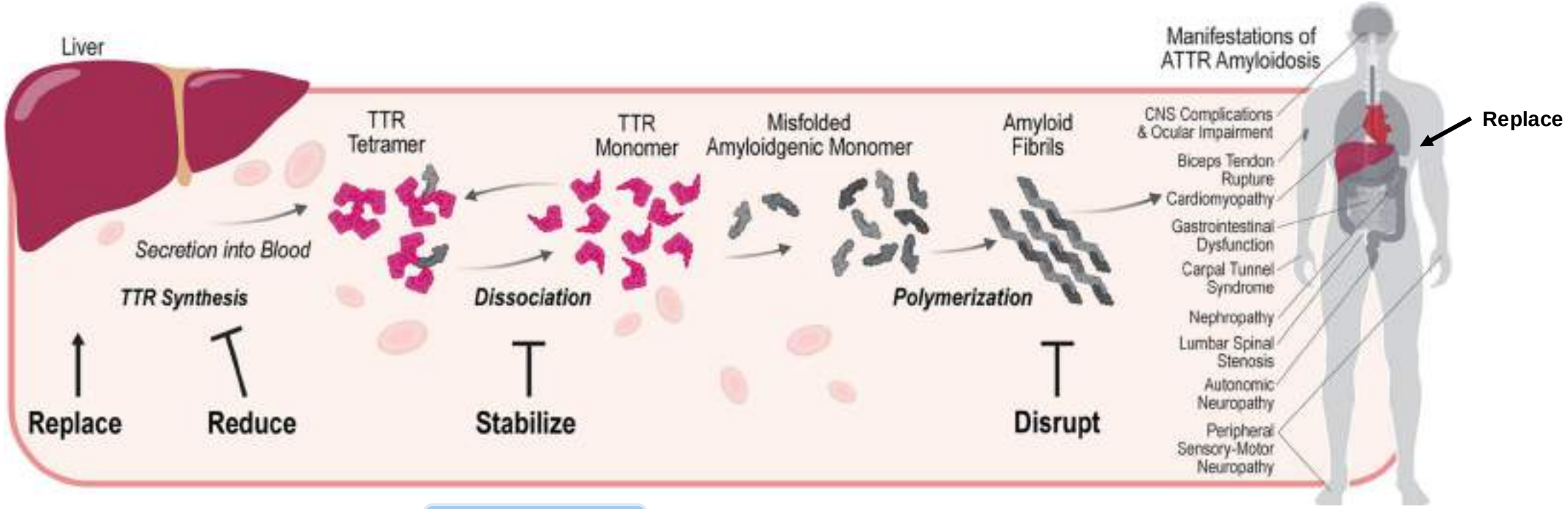
Stabilizers

Tafamidis
Acoramidis

↑ clairance

Anticorps monoclonaux
ALXN2220
NNC6019-0001
AT-02

Brannagan et al. J Peripher Nerv Syst. 2022

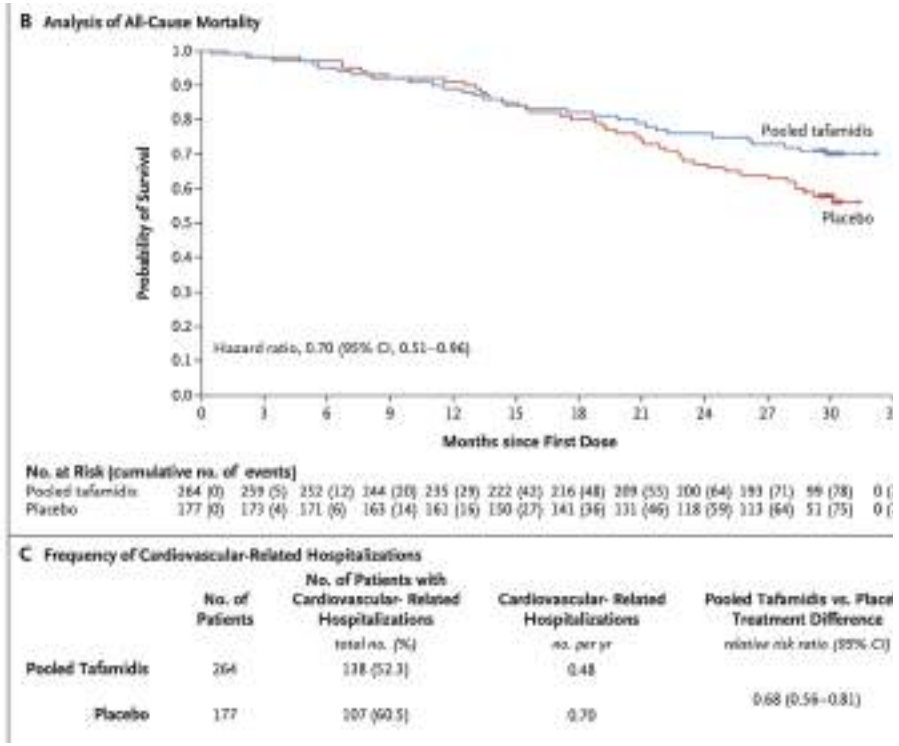


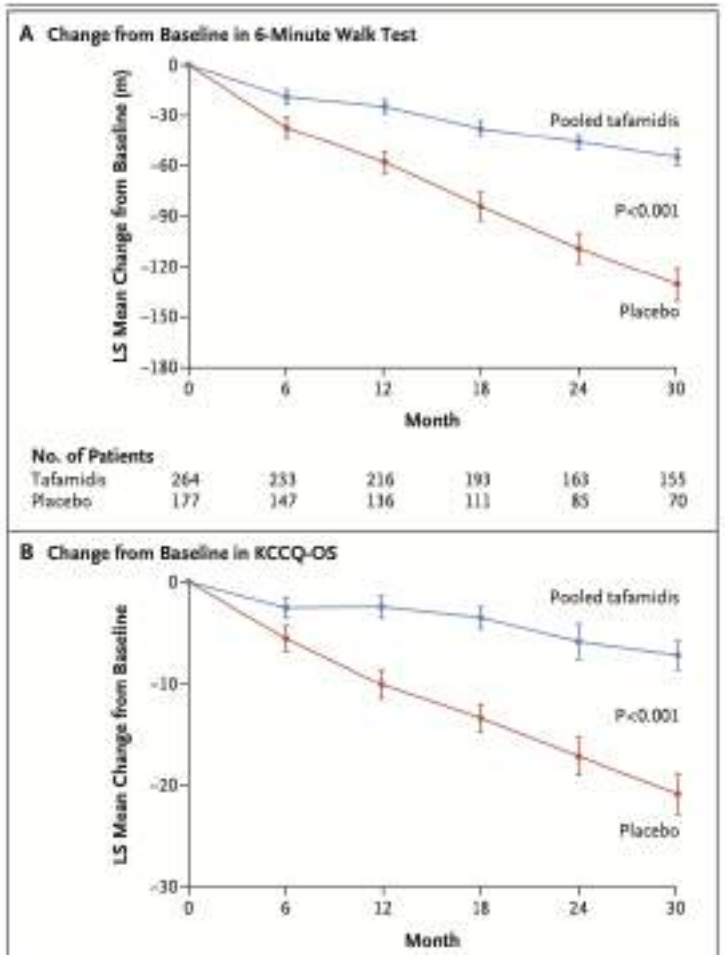
Stabilizers

Tafamidis
Acoramidis

Brannagan et al. J Peripher Nerv Syst. 2022

Tafamidis





Étude ATTR-ACT

Tafamidis vs placebo

441 pat
ATTR CM, 24% ATTRv
30 mois
Primary endpoint : décès toute cause suivie hospitalisations CV

Maurer et al. NEJM, 2018

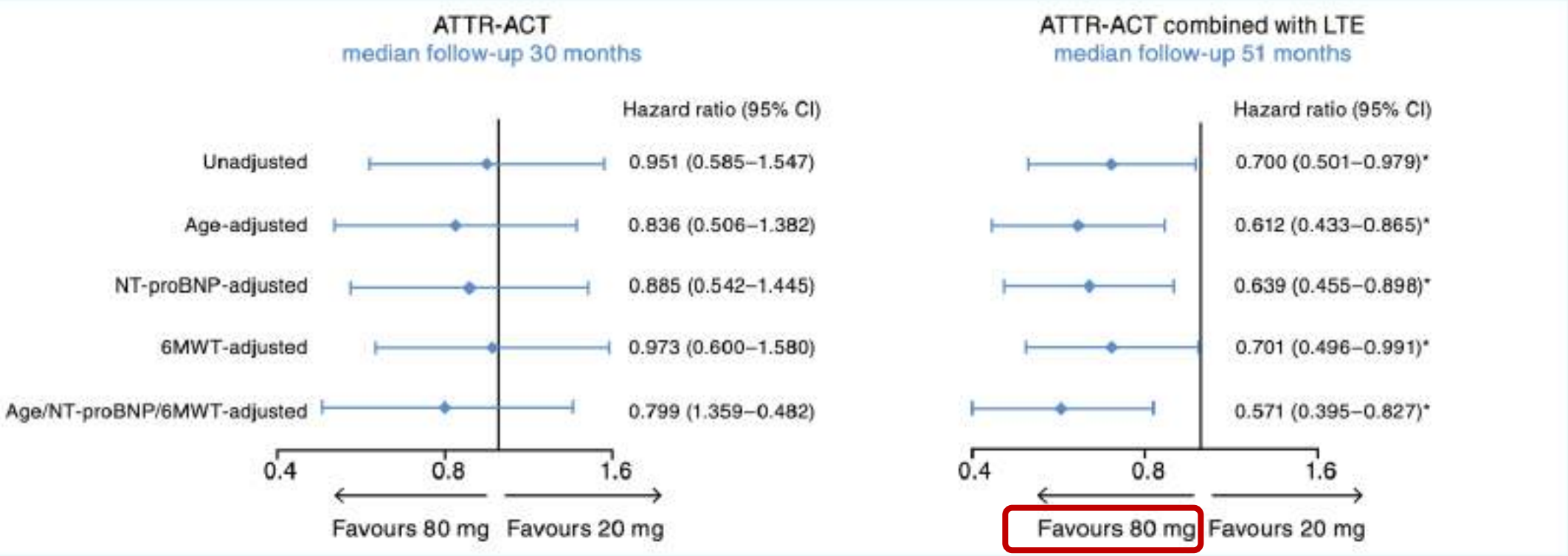


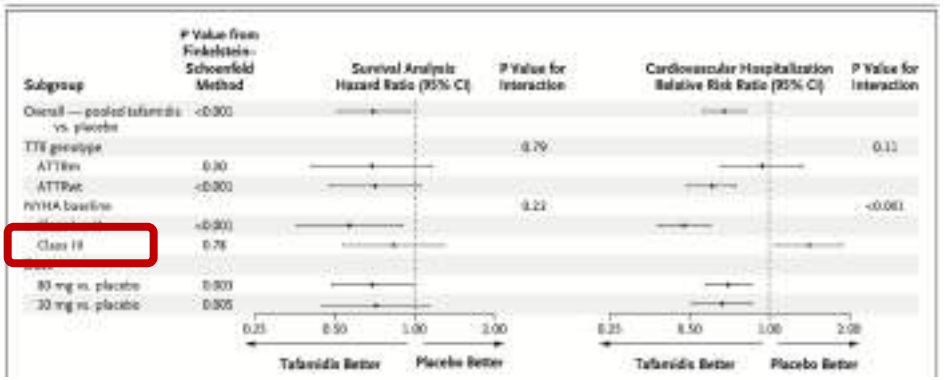
Figure 2 Forest plot of covariate-adjusted all-cause mortality in ATTR-ACT and ATTR-ACT combined with the long-term extension study

ATTR-ACT long-term extension study sur 51 mois

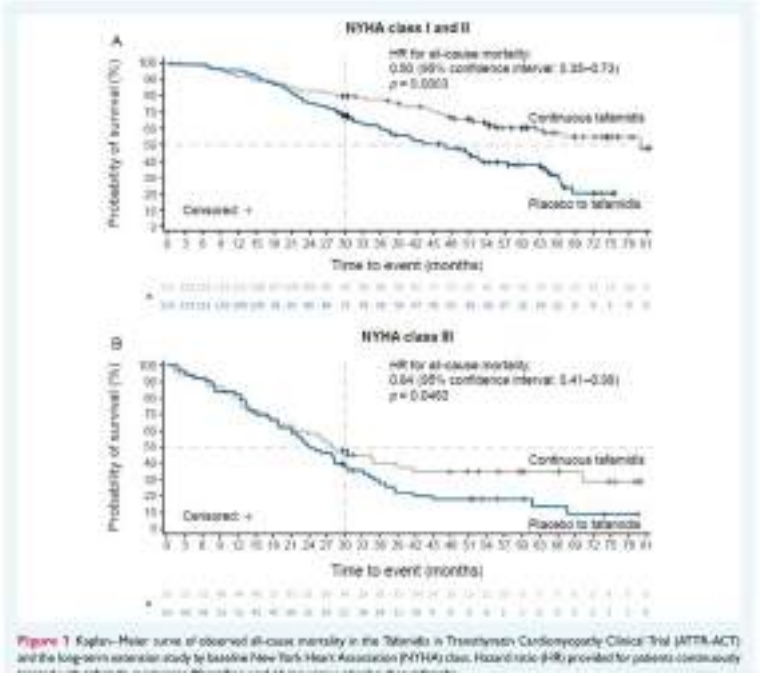
30% réduction relative du risque de décès pour 80 mg vs 20 mg

Damy et al. European Journal of Heart Failure. 2021

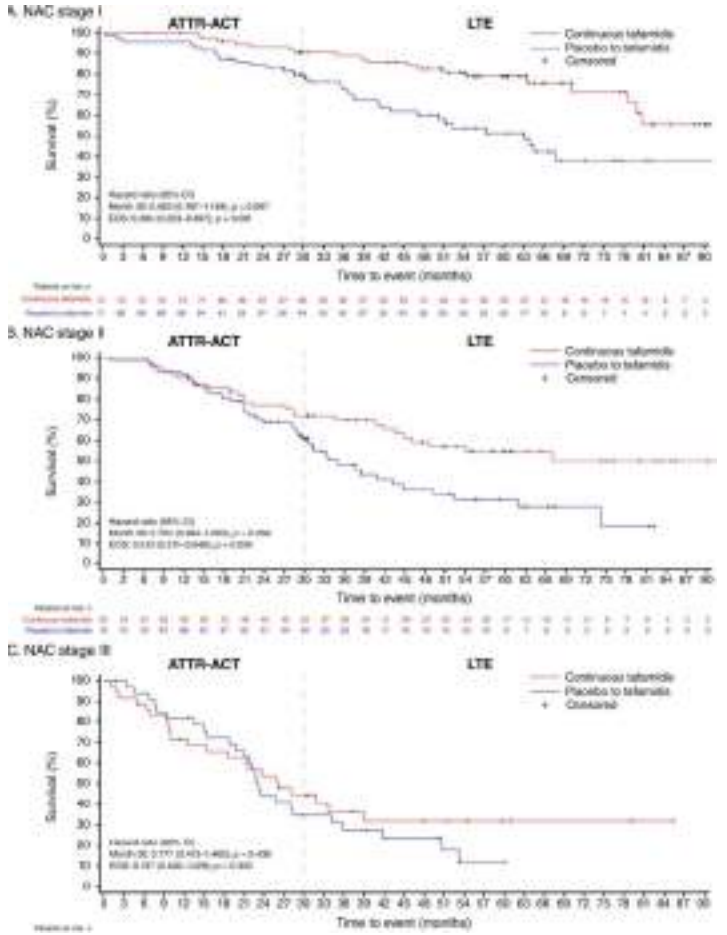
Tafamidis : dans les formes avançées?



Maurer et al. NEJM, 2018

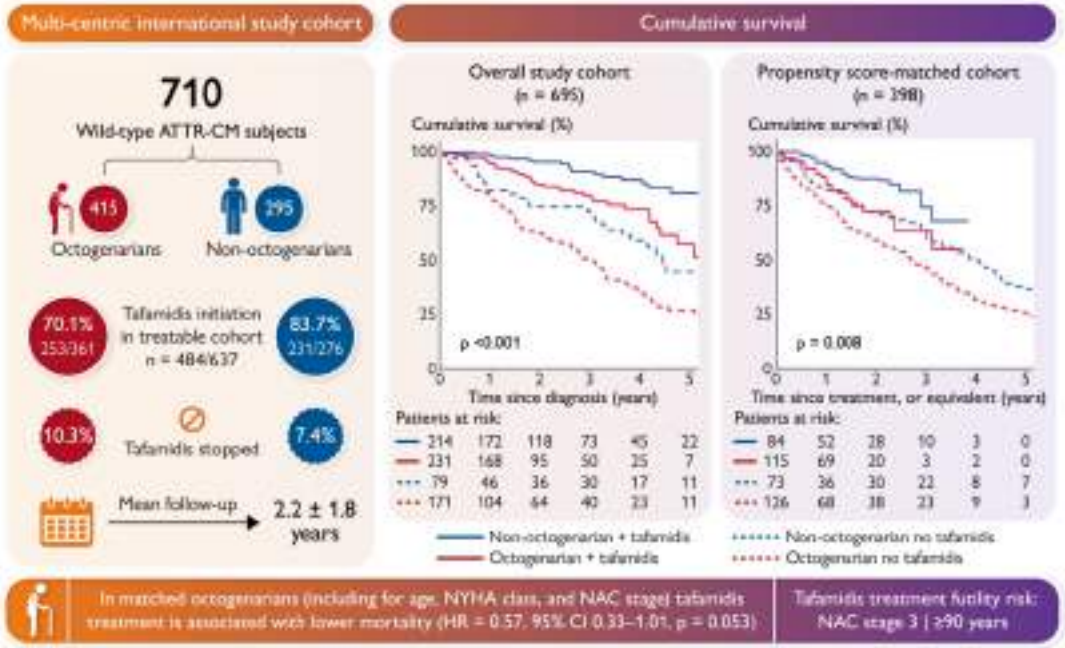


Eliott et al. European Journal of Heart Failure. 2023

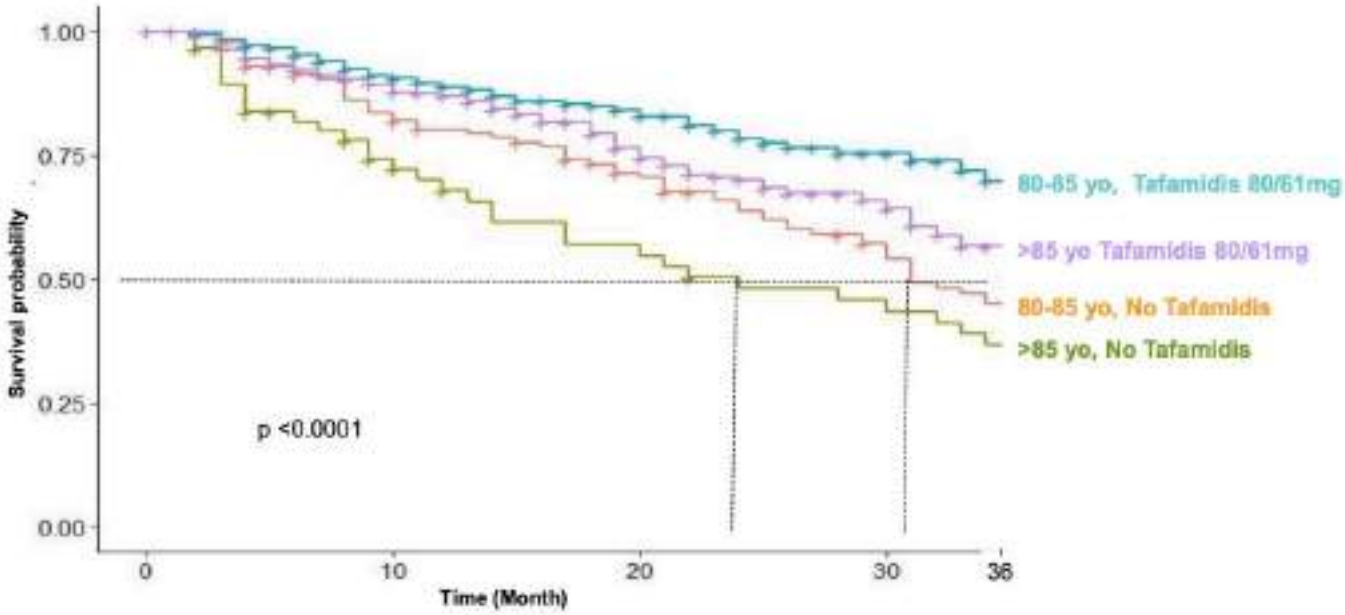


Damy et al. European Journal of Heart Failure. 2025

Tafamidis : chez l'octogénaire?

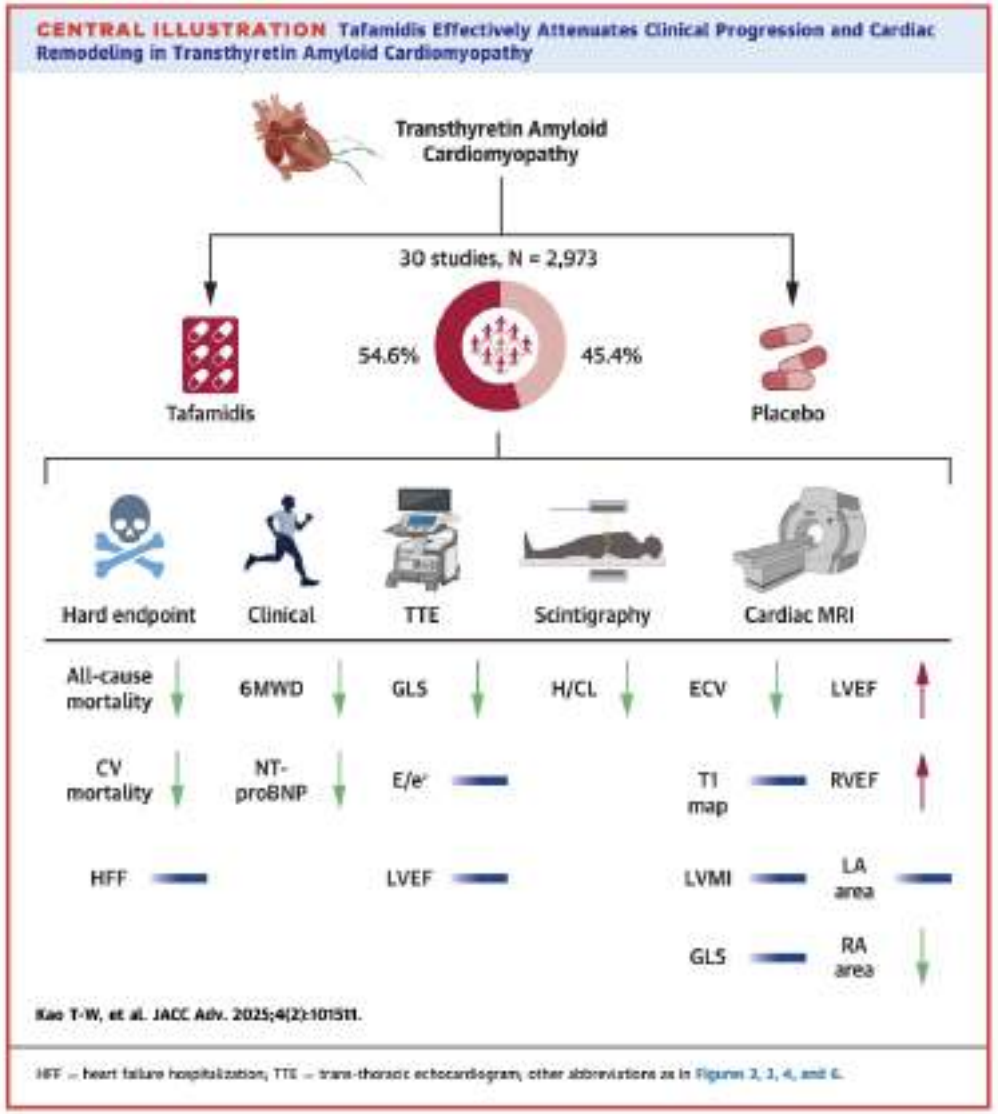


Debonnaire et al. European Heart Journal. 2025



Jobbé-Duval et al. International Journal of Cardiology. 2025

Tafamidis : données paracliniques?



Acoramidis

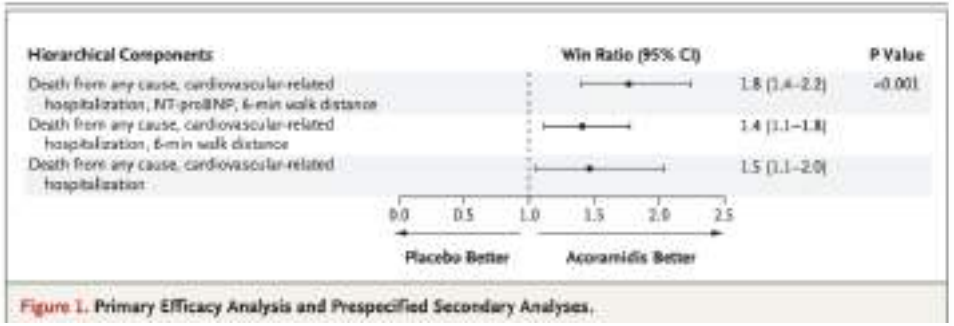


Figure 1. Primary Efficacy Analysis and Prespecified Secondary Analyses.

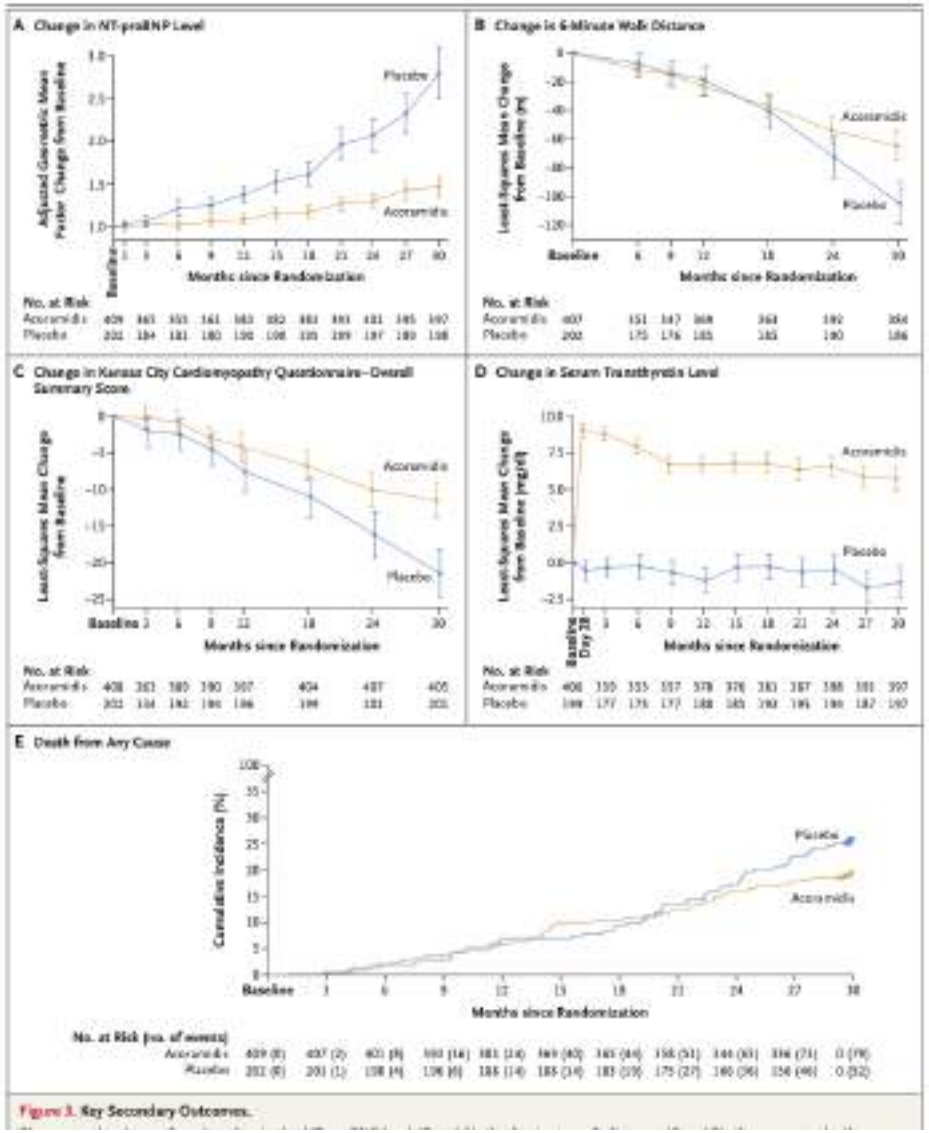


Figure 3. Key Secondary Outcomes.

ATTRibute-CM

Acoramidis vs placebo

632 pat

ATTR-CM

30 mois

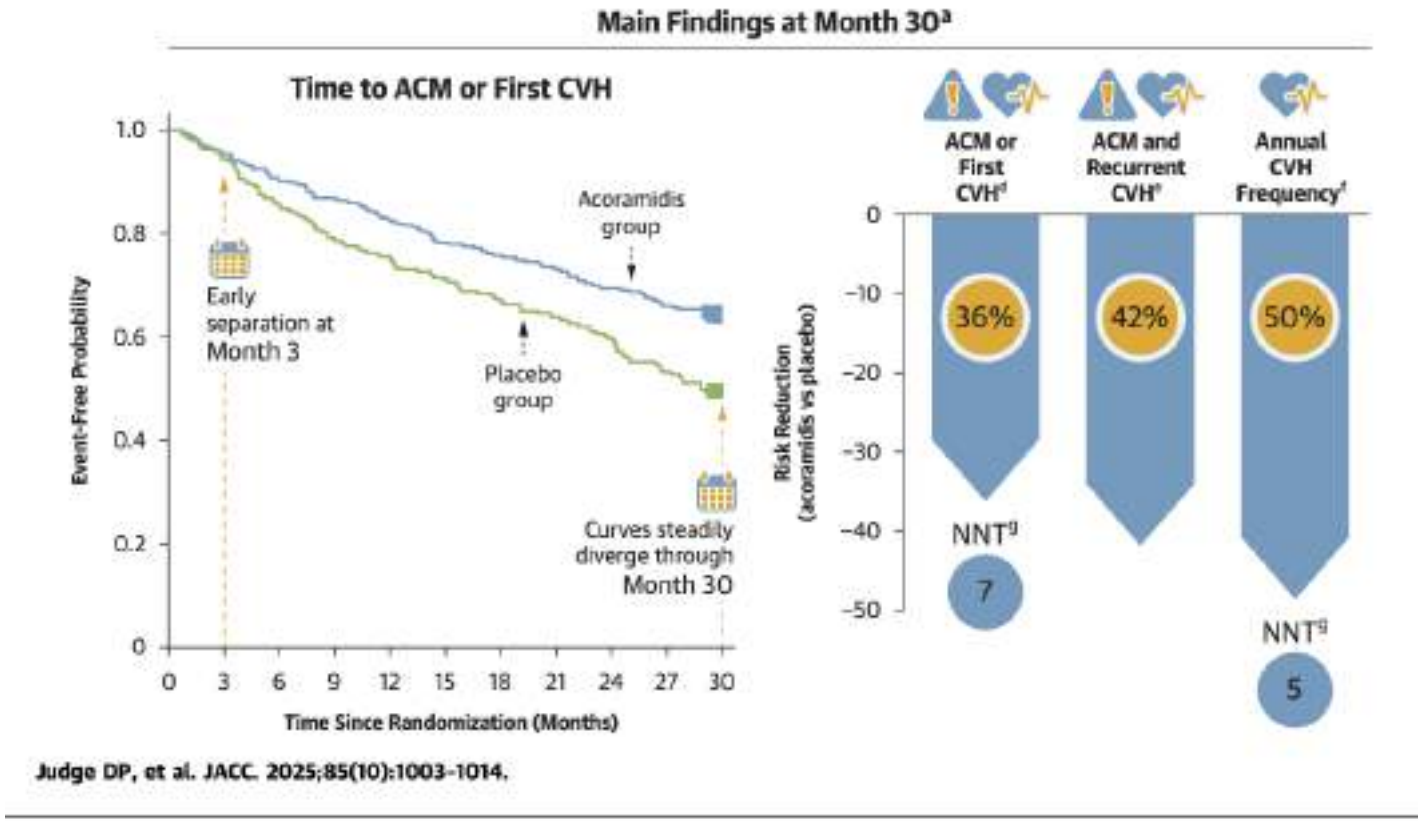
Primary endpoint composite : décès toute cause, hospitalisation CV, ↓ NTBNP, ↓ 6MWD

Tafamidis?

> 12 mois de ttt
14.9% acoramidis
22.8% placebo
Tps médian initiation 17.2m

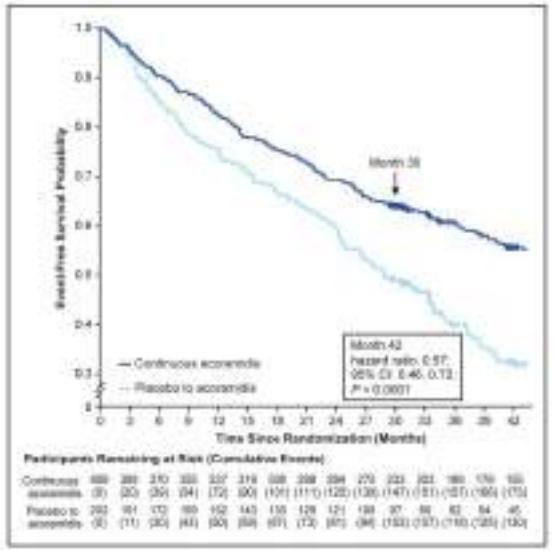
Gillmore et al. NEJM. 2024

Acoramidis

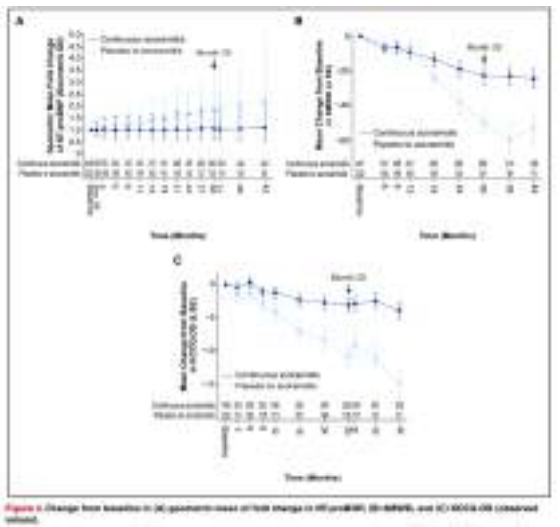


From ATTRIBUTE-CM with modified intention-to-treat population pat with DFG ≥30 mL/min/1.73 m^2

Judge et al. JACC. 2025



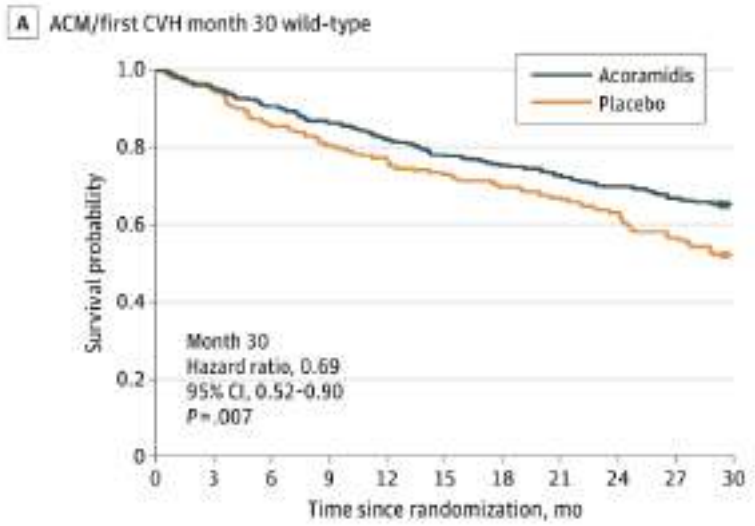
42 mois



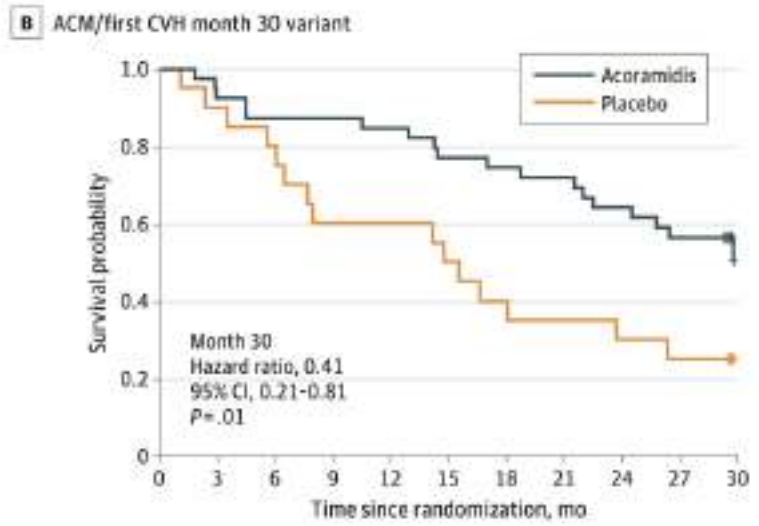
Judge et al. Circulation. 2025

Acoramidis : selon statut ATTR-CM?

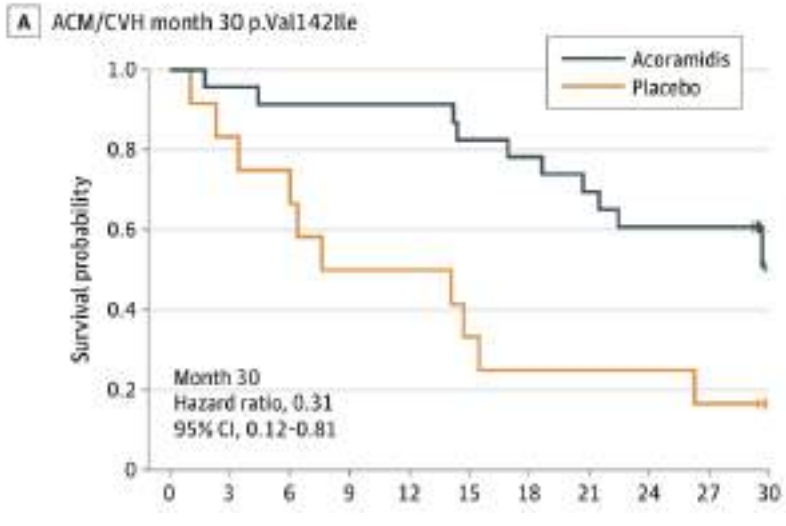
Figure 2. Kaplan-Meier Curves for Time to All-Cause Mortality (ACM) or First Cardiovascular Hospitalization (CVH) in the Wild-Type Transthyretin Amyloid Cardiomyopathy (ATTRwt-CM) and Variant Transthyretin Amyloid Cardiomyopathy (ATTRv-CM) Subgroups



↘ 31% RR



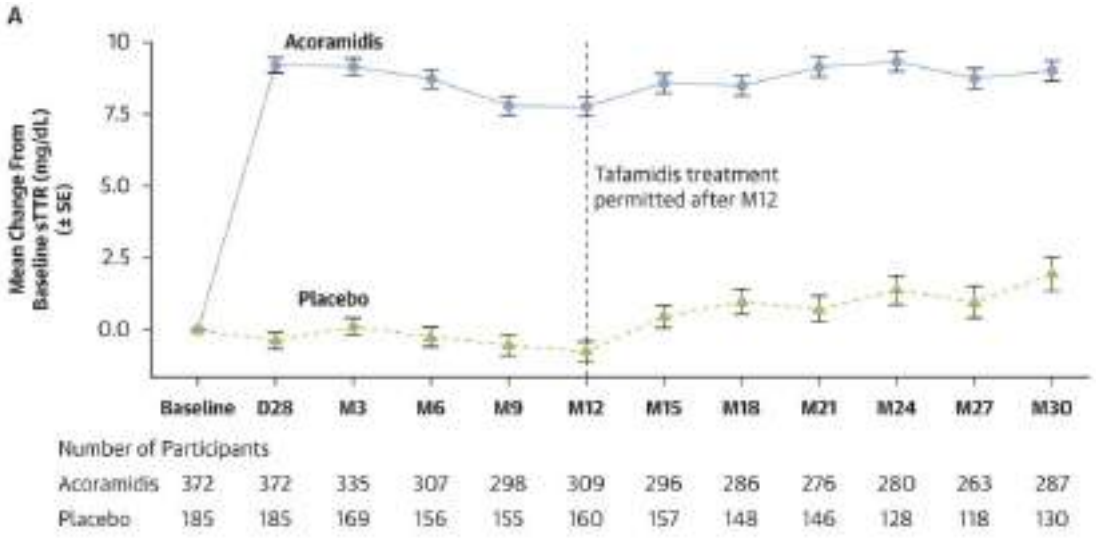
↘ 59% RR

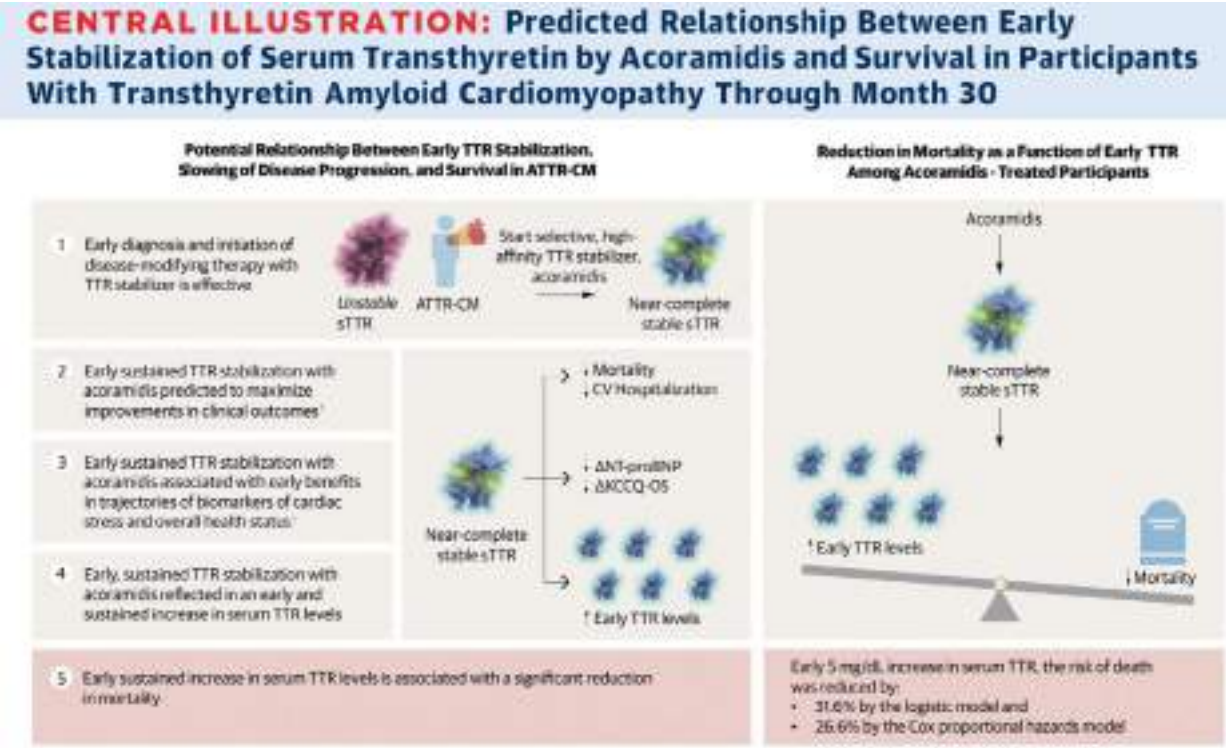


↘ 69% RR

Alexander et al. JAMA. 2025

Acoramidis : quid du taux de TTR circulant?





Différencier patients répondeurs des non répondeurs?

Maurer et al. JACC. 2025

Acoramidis : Chez des patients asymptomatiques ATTRv?

Recruiting

Acoramidis Transthyretin Amyloidosis Prevention Trial in the Young (ACT-EARLY) Study in Asymptomatic Carriers of a Pathogenic TTR Variant

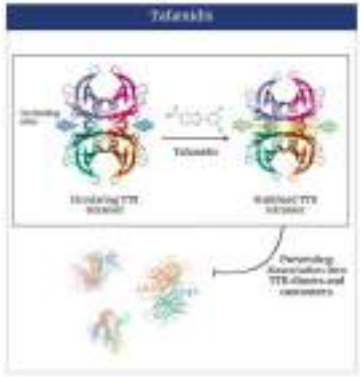
ClinicalTrials.gov ID NCT06563895

Sponsor Eidos Therapeutics, a BridgeBio company

Information provided by Eidos Therapeutics, a BridgeBio company (Responsible Party)

Last Update Posted 2025-11-04

Tafamidis



EMA PN 2011

RTU en France 2018

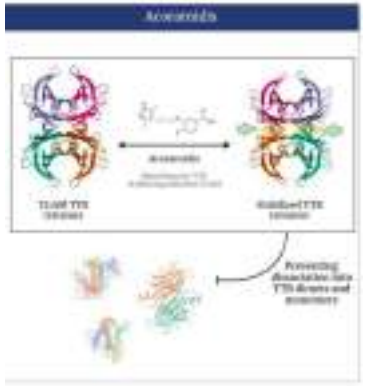
EMA et FDA 2019 ATTR-CM

2020 Avis HAS SMR et ASMR importants

Tafamidis 61 mg 1/j

= bioéquivalent tafamidis meglumine 80 mg (4 × 20 mg)

Acoramidis

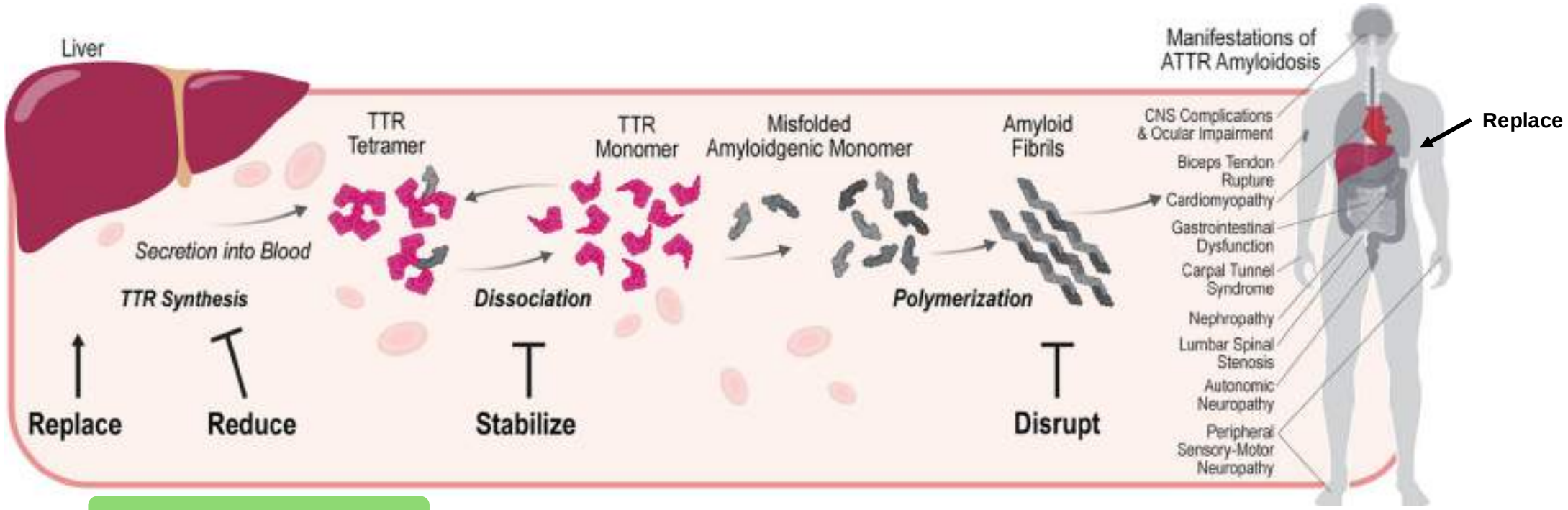


FDA 2024 et EMA 2025

Avis HAS SMR/ASMR 1/12/2025

Acoramidis 712 mg x2/j

= acoramidis hydrochloride 800x2/j



Silencers

siRNA
Patisiran / Vutrisiran

Oligonucléotides antisens
Inotersen/Eplontersen

Gene editing (CRISPR-Cas9)
Nex z

Brannagan et al. J Peripher Nerv Syst. 2022

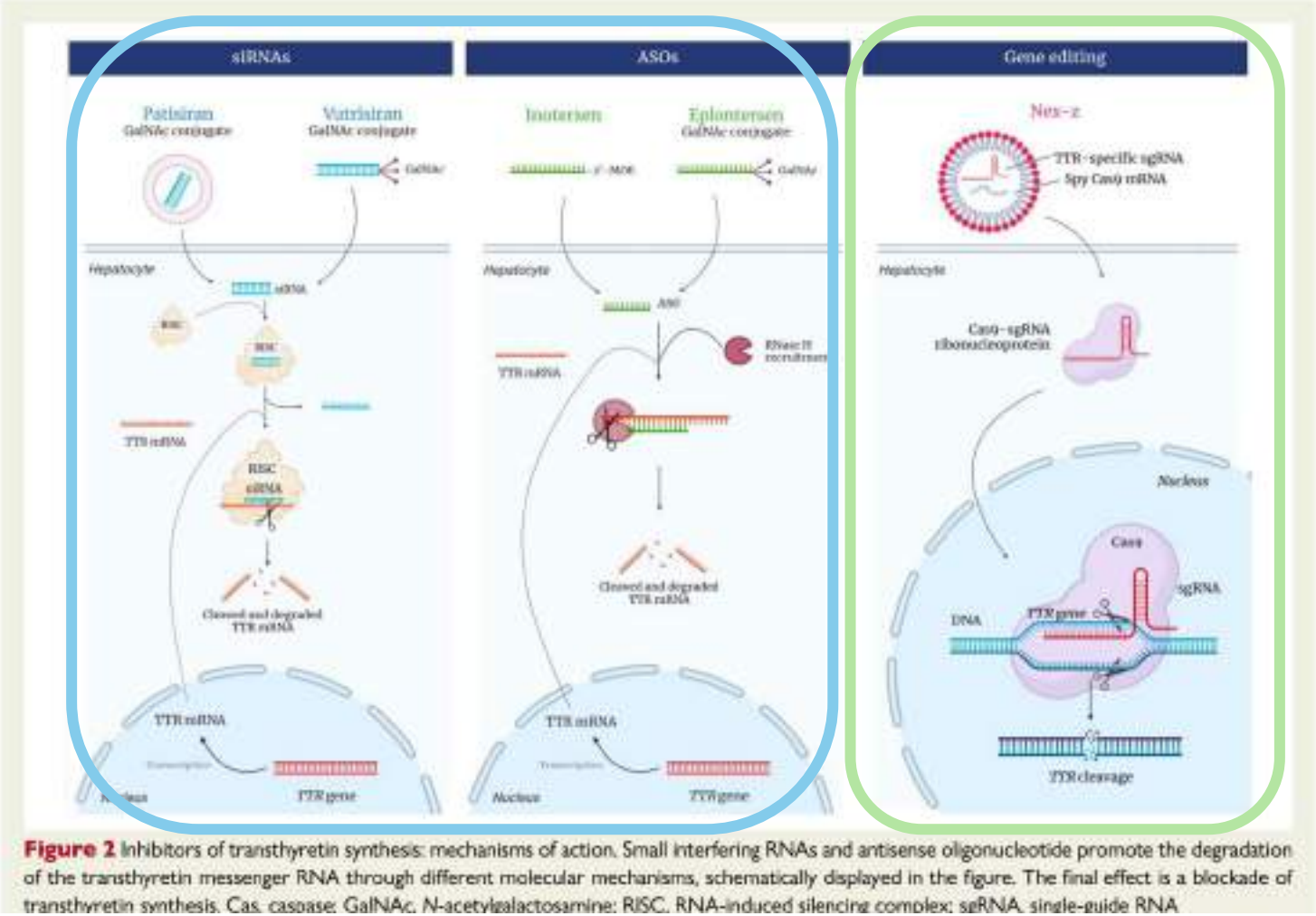


Figure 2 Inhibitors of transthyretin synthesis: mechanisms of action. Small interfering RNAs and antisense oligonucleotide promote the degradation of the transthyretin messenger RNA through different molecular mechanisms, schematically displayed in the figure. The final effect is a blockade of transthyretin synthesis. Cas, caspase; GalNAc, *N*-acetylgalactosamine; RISC, RNA-induced silencing complex; sgRNA, single-guide RNA

RNA therapies (si RNA or ASO)

Alter gene expression = degradation of TTR RNAm in hepatocytes

Transient effects

Gene therapies (CRISPR-Cas9)

Altering host DNA directly through gene addition, editing or silencing.

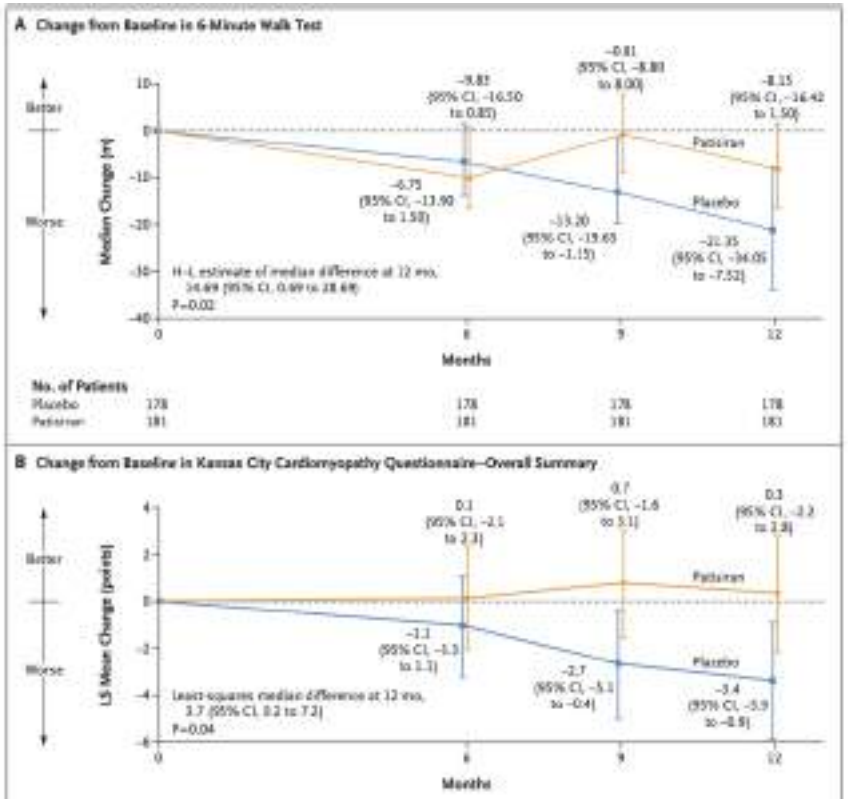
Permanent effects

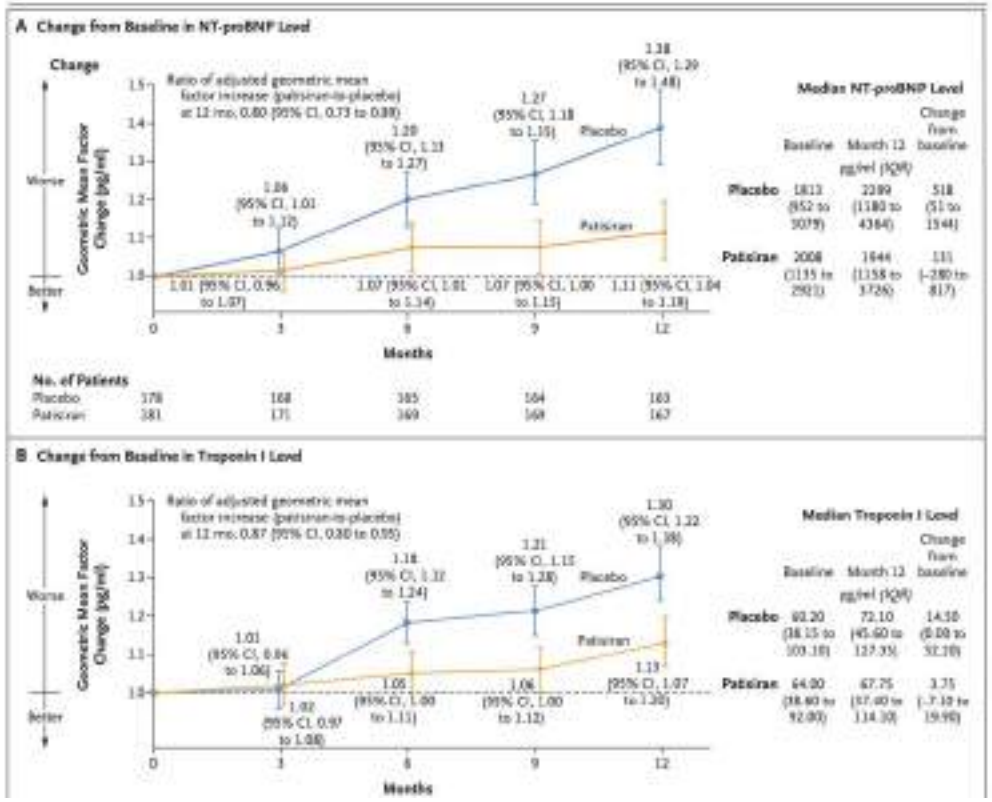
↓ Production protéine TTR

Fontana et al. EHJ. 2025
Jordan AJ, et al. Heart. 2025

Vit A suppl for any therapy that reduces circ TTR prod

siRNA
Patisiran





APOLLO B
Patisiran vs placebo

360 pat
ATTR CM, 20% ATTRv
12 mois
Randomisation tafamidis
25% sous tafamidis

Endpoint : 6 MWT
Secondary endpoint KCCMQ OS

NS sur morbimortalité CV

Maurer et al. NEJM. 2023

05/2024 : Cadre de Prescription Compassionnelle pour le Patisiran

Cardiomyopathie
ATTRwt ou ATTRv

+

Intolérant au Tafamidis
ou
Non réponse Tafamidis à 1 an

+

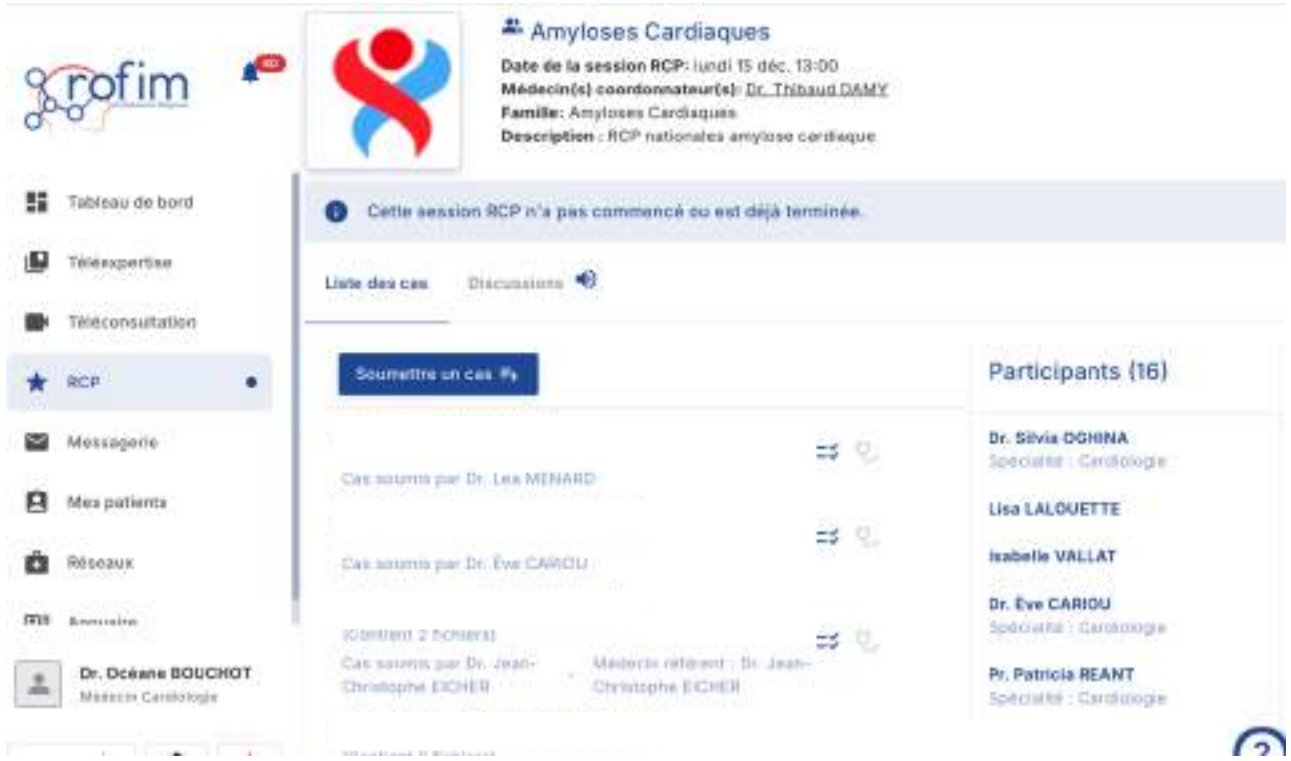
Edv >1 an

EVALUATION DE LA PROGRESSION SOUS TAFAMIDIS 61mg selon le consensus de l'ESC ATTR-CM de 2021

1 paramètre minimum doit être coché dans 2 des domaines suivants : clinique ou biologique ou imagerie ou initiation/majoration des diurétiques

Clinique	Biologique	Imagerie
☐ Nouvelle Hospitalisation pour IC en l'absence de facteurs déclenchants modifiables (inobservance, régime hyposodé, inobservance du traitement diurétique, fibrillation atriale paroxystique, infection)	☐ Augmentation de NT-proBNP (30% ou 300pg/mL)	☐ Augmentation de l'épaisseur myocardique (2mm)
☐ Augmentation de Classe NYHA	☐ Augmentation de Troponine (30%)	☐ Augmentation du grade de fonction diastolique
☐ Dégradation de Qualité de vie (déclin de 5-10 pts KCCQ ou 10% EQ-5D)	☐ Augmentation du Score NAC	☐ Changement de la fonction systolique (≥5% déclin de la FEVG, ≥5mL de déclin du VES, ≥1% augmentation du SLG)
☐ Déclin du TDM6 (30-40m)		☐ Apparition ou aggravation de troubles conductifs

☐ **L'initiation d'emblée ou la majoration de la dose de diurétique de l'anse d'au moins 40 mg (équivalent furosémide) au cours des 12 mois précédents peut aussi être considérée comme un critère de progression.**



24 patients en France

siRNA
Vutrisiran

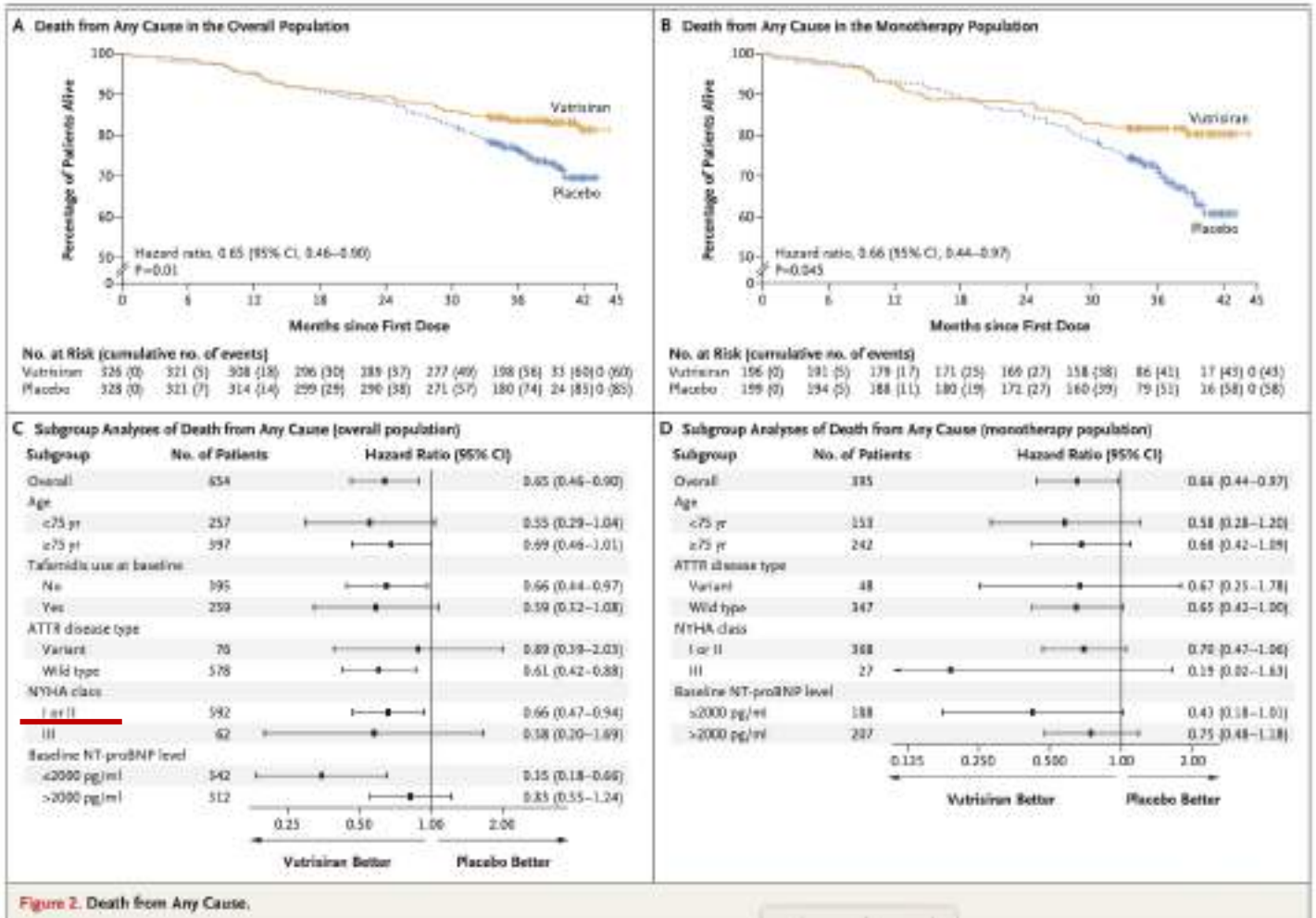


Figure 2. Death from Any Cause.

HELIOS-B

vutrisiran vs placebo

655 pat

36 mois

ATTR CM, 11% ATTRv

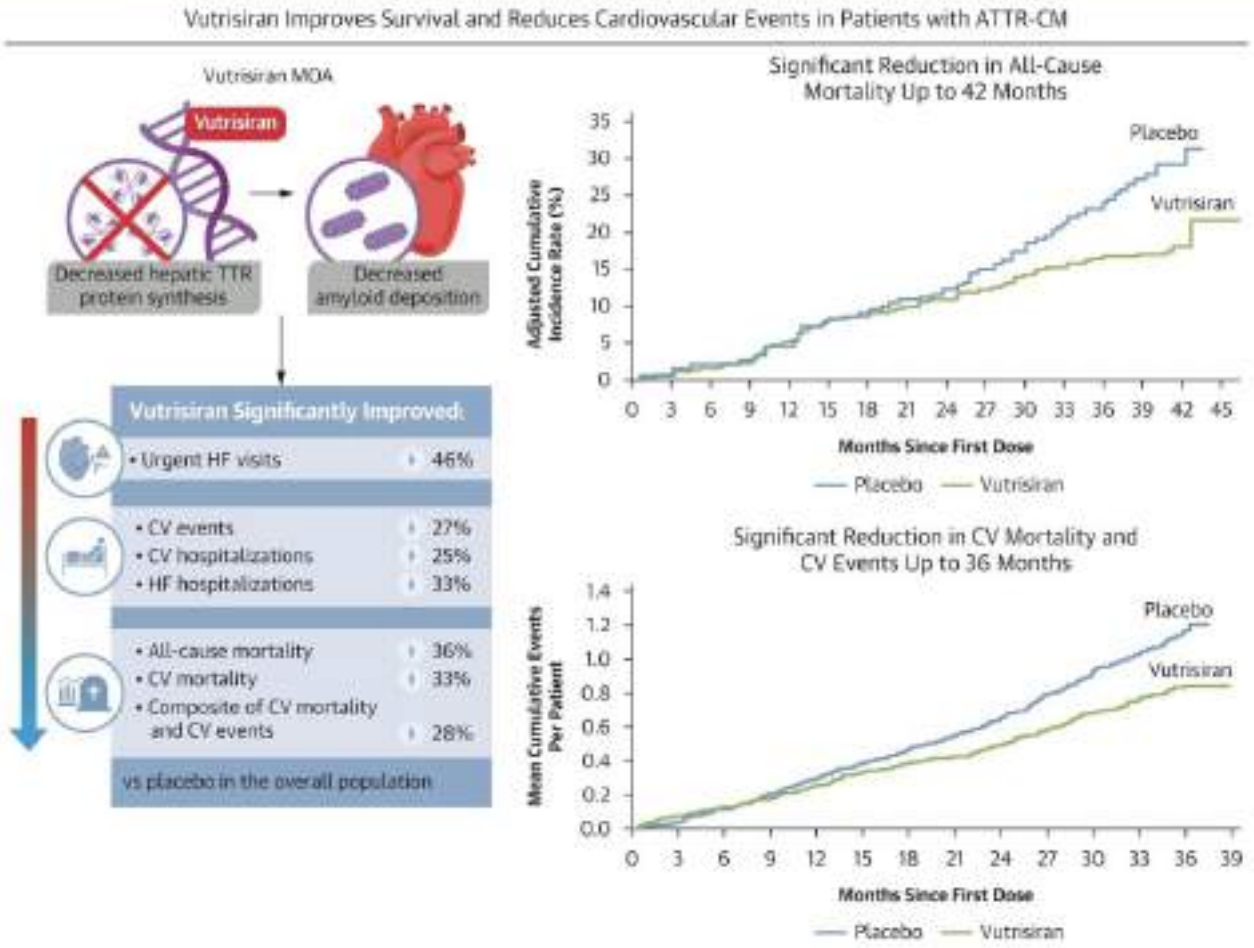
40% sous tafamidis gpe Vutrisiran

Primary end point : composite décès toute cause et evts CV

Secondary end points : death from any cause, 6 MWT, KCCQ-OS scores

Fontana et al. NEJM. 2024

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



open-label extension study from HELIOS-B on 42 months

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

Patisiran

First generation siRNA
300 mg/kg/3S en IV

FDA et AMM 2018 ATTRv PN
CPC 2024 FR ATTR CM

Vutrisiran

Second generation siRNA
25 mg /3M en SC

FDA 2022 ATTRv PN
FDA et EMA 2025 ATTR CM
Refus accès précoce FR
Fixation ASMR en attente HAS

NCT07052903 Recruiting

TRITON-CM: A Study to Evaluate **Nucresiran** in Patients With Transthyretin **Amyloidosis** With Cardiomyopathy

Conditions

Transthyretin **Amyloidosis** With Cardiomyopathy

Locations

- Washington D.C., District of Columbia, United States
- Brandon, Florida, United States
- Gainesville, Georgia, United States
- Tucker, Georgia, United States

Show all 36 locations

Etude de phase I : Murad A., American Heart Association. Scientific Sessions 2024, unpublished data

Oligonucléotides antisens
Inotersen

Table 2. Summary of Adverse Events.*

Event	Placebo (N=60)	Inotersen (N=112)
	no. of patients (%)	
Any adverse event	60 (100)	111 (99)
Event related to trial regimen†	23 (38)	87 (78)
Any serious adverse event	13 (22)	36 (32)
Event related to trial regimen†	1 (2)	8 (7)
Glomerulonephritis	0	3 (3)‡
Thrombocytopenia	0	2 (2)
Deep-vein thrombosis	1 (2)	1 (<1)
Intracranial hemorrhage	0	1 (<1)§
Tubulointerstitial nephritis	0	1 (<1)¶
Pulmonary embolism	0	1 (<1)
Embolic stroke	0	1 (<1)
Myelopathy	0	1 (<1)
Death	0	5 (4)

NEURO-TTR

inotersen SC 1/S vs placebo

ATTRh avec PN

63% ATTR CM

172 pat

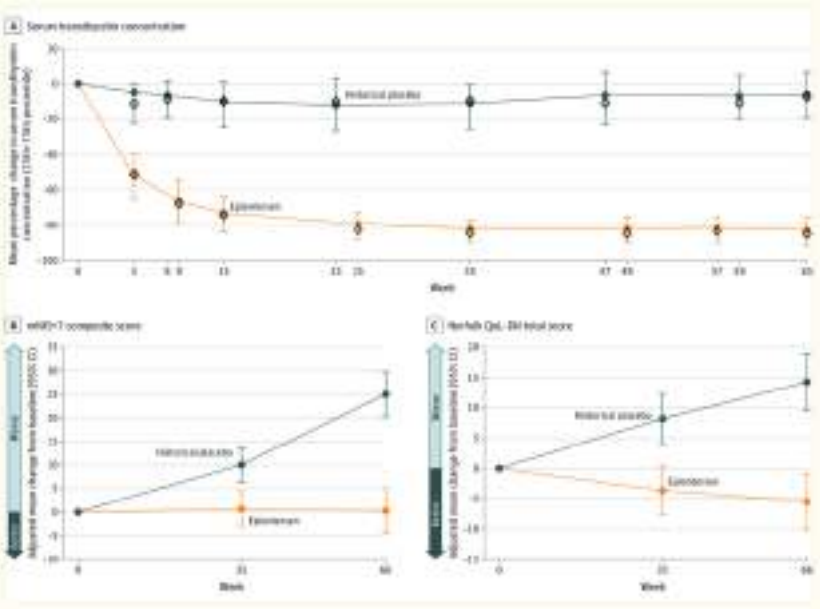
15 mois

Bénéfice sur QdV et neuropathie

Attention données de Safety

Benson et al. NEJM. 2018

Oligonucléotides antisens
Eplontersen



Active, not recruiting

CARDIO-TTRansform: A Study to Evaluate the Efficacy and Safety of Eplontersen (Formerly Known as ION-682884, IONIS-TTR-LRx and AKCEA-TTR-LRx) in Participants With Transthyretin-Mediated Amyloid Cardiomyopathy (ATTR CM)

ClinicalTrials.gov ID NCT04136171

Sponsor Ionis Pharmaceuticals, Inc.

Information provided by Ionis Pharmaceuticals, Inc. (Responsible Party)

Last Update Posted 2025-08-08

A débuté en 2020

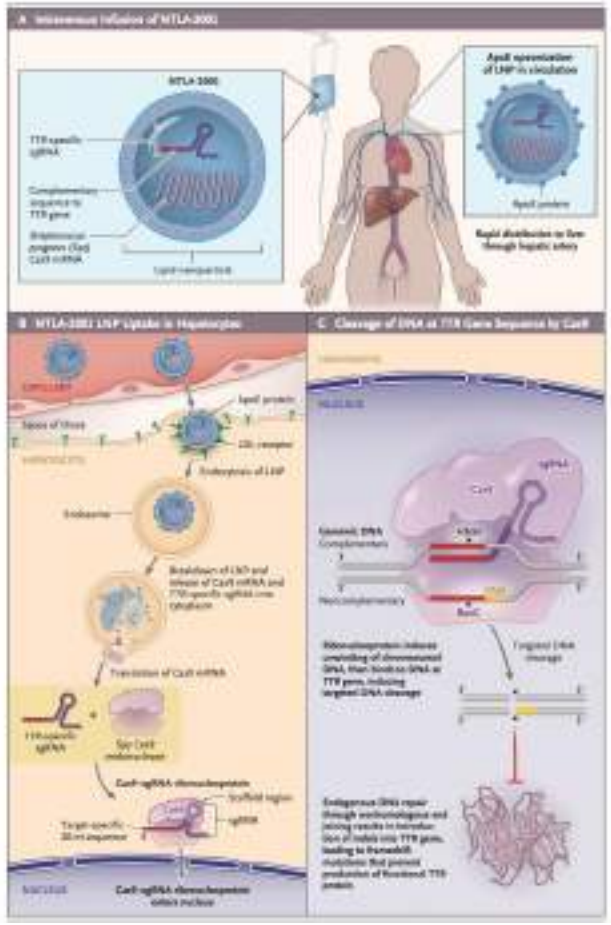
>1400 pat
ATTR CM wt et h
Eplontersen vs placebo
140 sem
SC 1/M
70% stabilizers estimated
composite endpoint : décès CV et recurrent CV evts

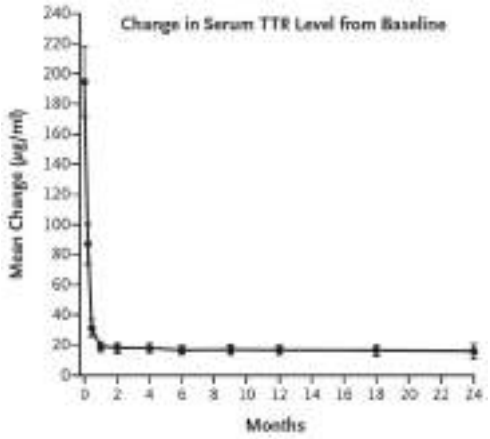
Etude NEURO-TTRansform
ATTRv polyneuropathies
34% cardiomyopathies et 69% sous tafamidis ou diflunisal groupe eplontersen

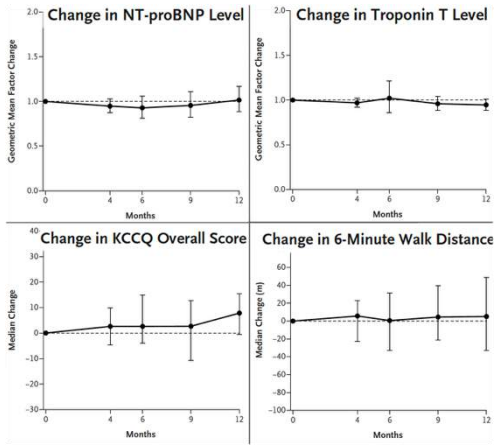
Coelho et al. JAMA. 2023

Données attendues également Scinti et MRI
Résultats pour ESC 2026

Gene editing (CRISPR-Cas9)
NTLA-2001 or nexiguran ziclumeran or nex z







Active, not recruiting

MAGNITUDE: A Phase 3 Study of NTLA-2001 in Participants With Transthyretin Amyloidosis With Cardiomyopathy (ATTR-CM)

ClinicalTrials.gov ID NCT06128629

Sponsor Intellia Therapeutics

Information provided by Intellia Therapeutics (Responsible Party)

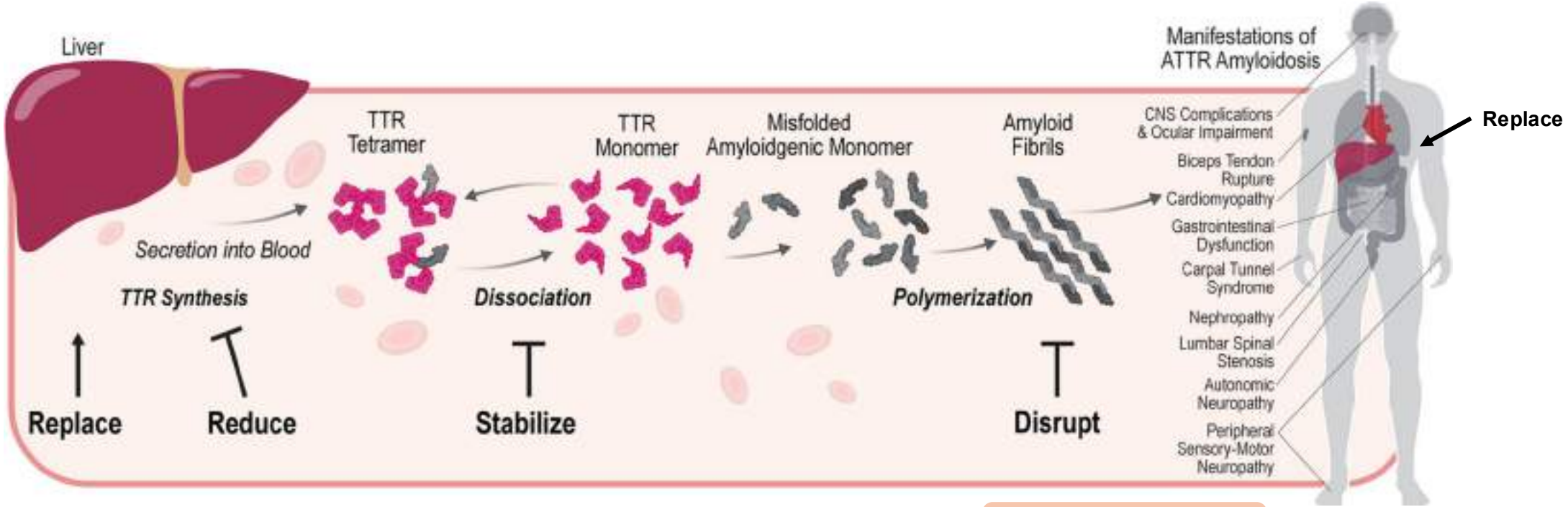
Last Update Posted 2025-12-02

interrompue

Estimated 1200 pat
composite outcome : CV mortality and CV events

6 puis 36 patients
2 études de phase I
Une injection IV de Nex z
ATTR avec polyneuropathy et CM
Knockout mutation

Gillmore et al. NEJM. 2021
Fontana et al. NEJM. 2024



↑ clairance

Anticorps monoclonaux
ALXN2220
NNC019-0001
AT-02

Fontana et al. NEJM. 2023
Brannagan et al. J Peripher Nerv Syst. 2022

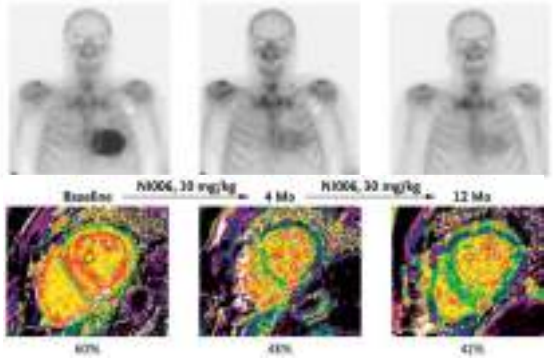
Anticorps monoclonaux
NI006 = ALXN2220

recombinant human IgG1 monoclonale Ac anti monomère TTR et fibrille amyloide
Stimule phagocytose par macrophages des fibrilles amyloides

Etude de phase I
ALXN2220 vs placebo

ATTR CM avec IC
40 pat
Inj IV / 4S
90% sous Tafamidis

↘ fixation scintigraphie et ECV à M12, NTBNP, troponin T
↑ KCCQ-OS scores
Safety : mild cytokine release syndrome
or transient musculoskeletal symptoms



Garcia Pavia et al. NEJM. 2023

Active, not recruiting

Study of ALXN2220 Versus Placebo in Adults With ATTR-CM (DepleTTR-CM)

ClinicalTrials.gov ID NCT06183931

Sponsor Alexion Pharmaceuticals, Inc.

Information provided by Alexion Pharmaceuticals, Inc. (Responsible Party)

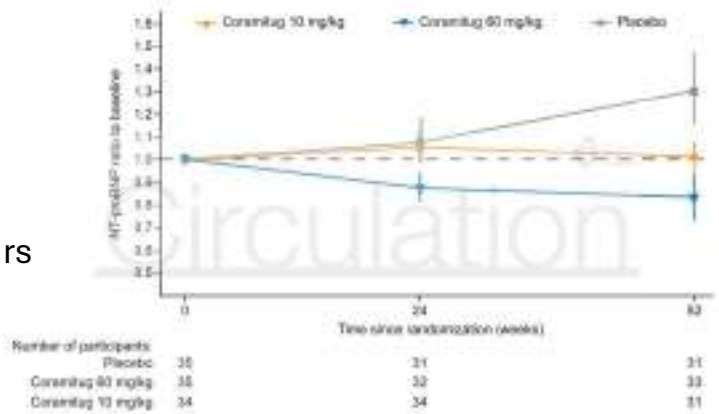
Last Update Posted 2025-11-17

Enrollement actual 1159 pat

Anticorps monoclonaux
NNC6019-0001 = PRX004 = coramitug

Coramitug vs placebo
Etude phase II

104 pat
ATTR-CM
Inj IV / 4S pdt 52S puis 12S FU
84% sous tafamidis et 7% silencers
primary endpoints :
↘ NT-proBNP
NS 6MWT



Recruiting

CLEOPATTRA: A Research Study to Look at the Effects of Treatment With a Medicine Called Coramitug (NNC6019-0001) in People With Heart Failure Due to Transthyretin Amyloid (ATTR) Amyloidosis (CLEOPATTRA)

ClinicalTrials.gov ID NCT07207811
Sponsor Novo Nordisk A/S
Information provided by Novo Nordisk A/S (Responsible Party)
Last Update Posted 2025-10-16

Fontana et al. Circulation. 2025

Anticorps monoclonaux

AT-02

Recruiting

Study of AT-02 in Healthy Volunteers and Subjects With Systemic Amyloidosis (AT02-001)

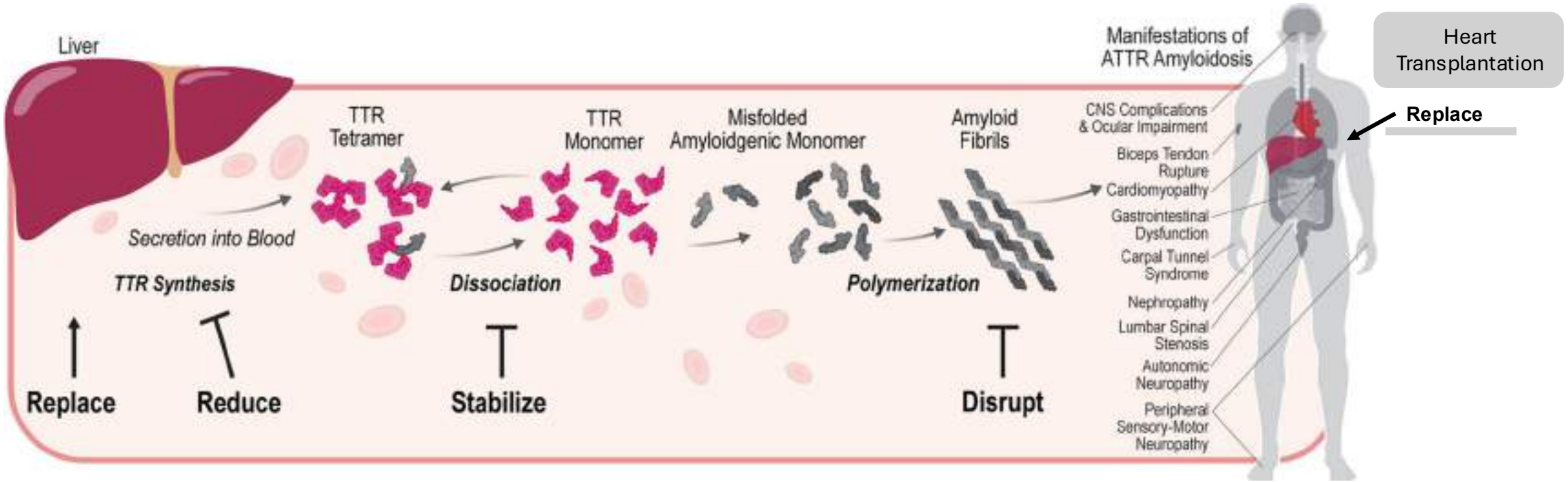
ClinicalTrials.gov ID NCT05521022

Sponsor Attralus, Inc.

Information provided by Attralus, Inc. (Responsible Party)

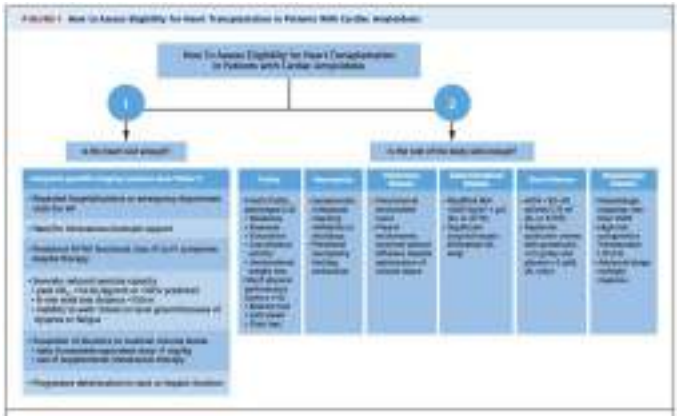
Last Update Posted 2024-04-03

Etude phase I

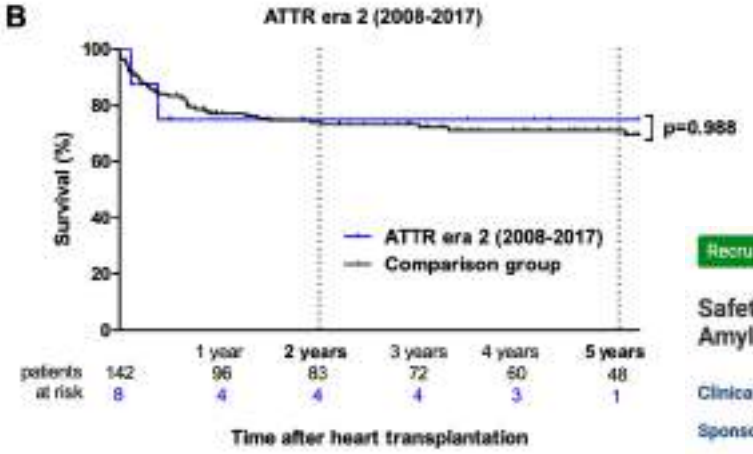


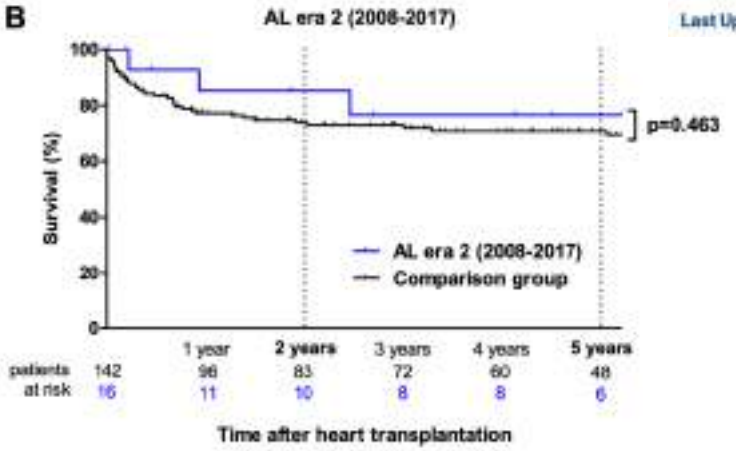
Brannagan et al. J Peripher Nerv Syst. 2022

Heart Transplantation



which required inpatient management. There were no higher grades of rejection. There was no evidence of recurrent amyloidosis in the graft on any biopsies.





Recruiting

Safety, Efficacy, and Pharmacokinetics of Tafamidis in Patients With Transthyretin-mediated Amyloidosis Post Orthotopic Heart Transplantation

ClinicalTrials.gov ID NCT05489523

Sponsor University of Texas Southwestern Medical Center

Information provided by Justin Grodin, University of Texas Southwestern Medical Center (Responsible Party)

Last Update Posted 2025-09-05

Ambardekar et al. JACC Heart Failure. 2023
Lakhdar et al. Heart Failure Reviews. 2022
Rosenbaum et al. Transplantation. 2018
Kristen et al. Journal of Heart and Lung transplantation. 2017

Accélération de l'innovation thérapeutique

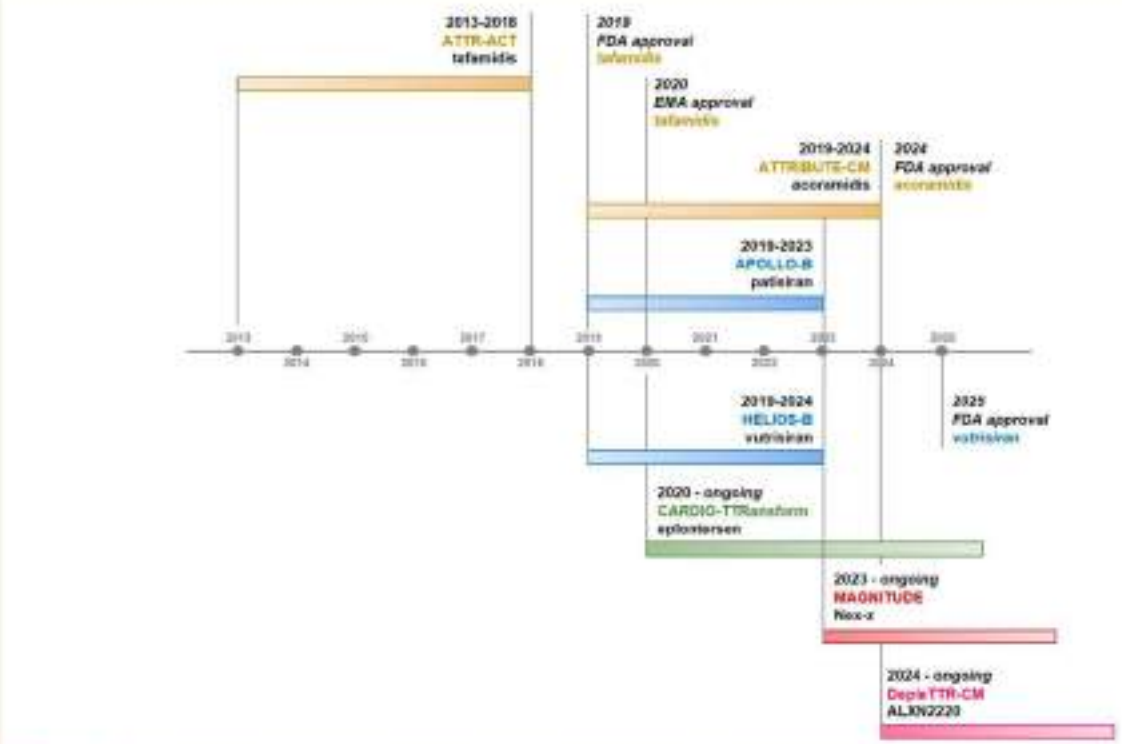


Figure 4 Evolving landscape of treatment for transthyretin amyloid cardiomyopathy. Completed and ongoing Phase 3 trials are reported together with the years of approval by the Food and Drug Administration or European Medicines Agency

Table 1 Approved or investigational therapies for transthyretin amyloidosis

	ATTRv-PN: clinical use	ATTR-CM			
		Phase 1	Phase 2	Phase 3	Clinical use
Inhibitors of ATTR accumulation					
TTR stabilizers					
Tafamidis	Approved			Completed	Approved (FDA, EMA)
Acoramidis				Completed	Approved (FDA, EMA)
Blockers of TTR synthesis					
Patisiran	Approved			Completed	Not approved
Vutrisiran	Approved			Completed	Approved (FDA)
Nucresiran		Completed			
Inotersen	Approved				
Eplontersen	Approved			Ongoing	
Nexagenin zidurnersen		Ongoing		Ongoing	
Promotors of ATTR amyloid degradation					
Monoclonal antibodies					
PRX004			Ongoing		
ALXN2220 (NI006)				Ongoing	

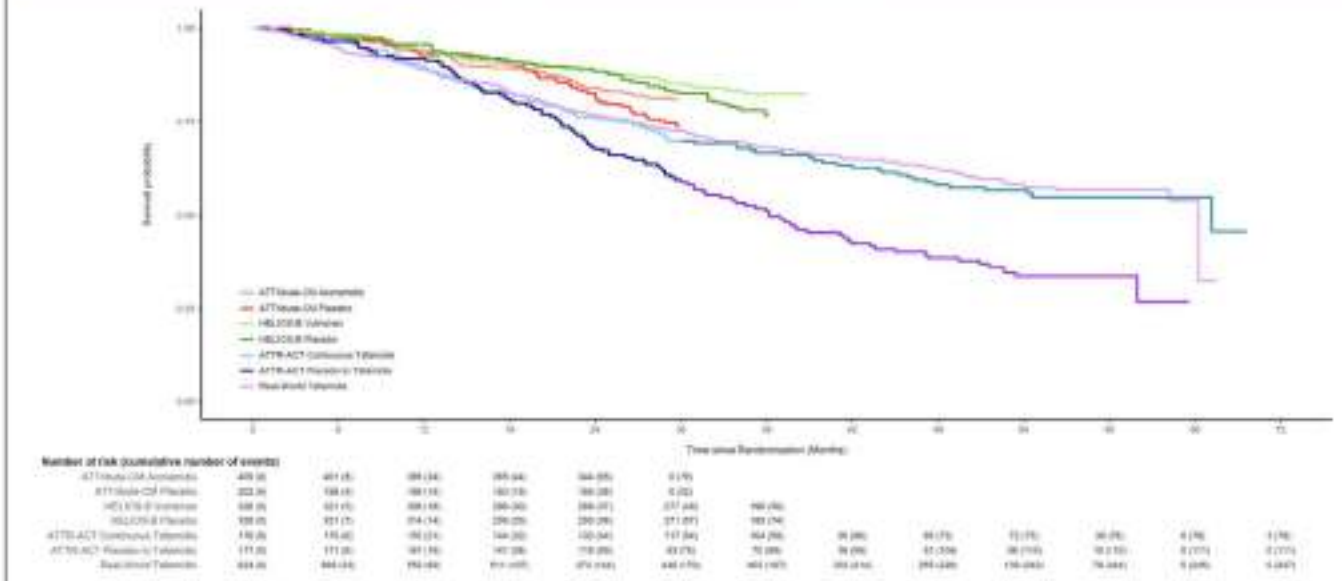
CM, cardiomyopathy; EMA, European Medicines Agency; FDA, Food and Drug Administration; PN, polyneuropathy

Fontana et al. European Heart Journal. 2025

TABLE 1 Comparison of Therapies for ATTR-CM

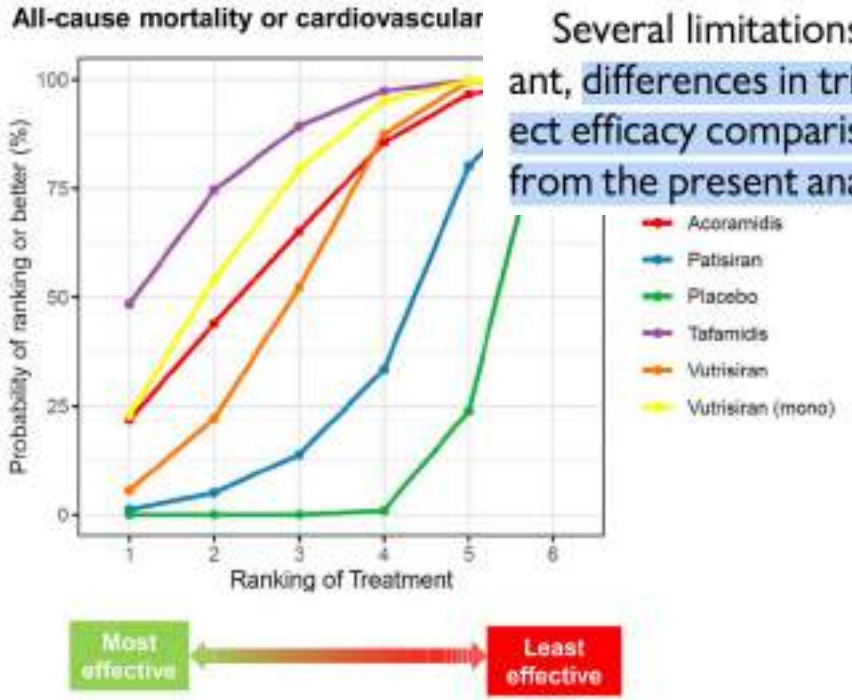
	Tafamidis	Acoramidis	Vutrisiran
Mechanism of action	TTR stabilizer	TTR stabilizer	siRNA; gene silencer
Primary trial	ATTR-ACT (n = 441)	ATTRibute-CM (n = 632)	HELIOS-B (n = 655)
Year conducted	2013-2018	2019-2023	2019-2024
Age of participants, y	75	72	77
ATTRwt/ATTRv	335 (76)/106 (24)	574 (91)/58 (9)	578 (88)/77 (12)
Placebo mortality at 30 mo, %	43	26	18
Placebo CV event rate per year	0.70	0.45	0.288
NYHA functional class			
I	37 (8)	68 (11)	84 (13)
II	263 (60)	455 (72)	508 (78)
III	141 (32)	109 (17)	62 (9)
NT-proBNP, pg/mL, median	3,078	2,134	1,911
Mortality	0.70 (0.51-0.96)*	0.77 (0.54-1.10)*	0.69 (0.49-0.98)*
CV events	0.68 (0.56-0.81)	0.50 (0.36-0.70)	0.68 (0.53-0.86)
Least square mean difference in 6MWD at 30 mo	75.7 (57.6-93.8)	39.6 (21.1-58.2)	26.5 (13.4-39.6)
Least square mean difference in KCCQ-OSS at 30 mo	13.65 (9.48-17.83)	9.94 (5.97-13.91)	5.8 (2.4-9.2)
Binding site	T4 binding sites	T4 binding sites	N/A
Brand name	Vyndaqel or Vyndamax	ATTRuby	Amvuttra
Dose	80 mg or 61 mg	712 mg orally twice daily	25 mg subcutaneously every 3 mo
TTR stabilization			N/A
TTR occupancy with FPE assay, %	~65	96.6 ± 2.1	
Tetramer dissociation assay, %	>96 at 28 μm	>96 at 11 μm	
Increase in serum TTR, %	33	39	N/A
Knockdown in serum TTR, %	N/A	N/A	81
Cost†	$267,908	$225,108	$477,404

FIGURE 4 Nonstatistical Comparison of All-Cause Mortality in the Current Cohort and Contemporary ATTR-CM Clinical Trials



Griffin et al. JACC. 2025
Masri A, et al. JACC CardioOncol. 2025

Drug-to-drug indirect comparisons



Several limitations must be acknowledged. First, and more important, differences in trial design and in study populations complicate direct efficacy comparisons, and any definite conclusion cannot be drawn from the present analyses. For example, a longer follow-up may reveal

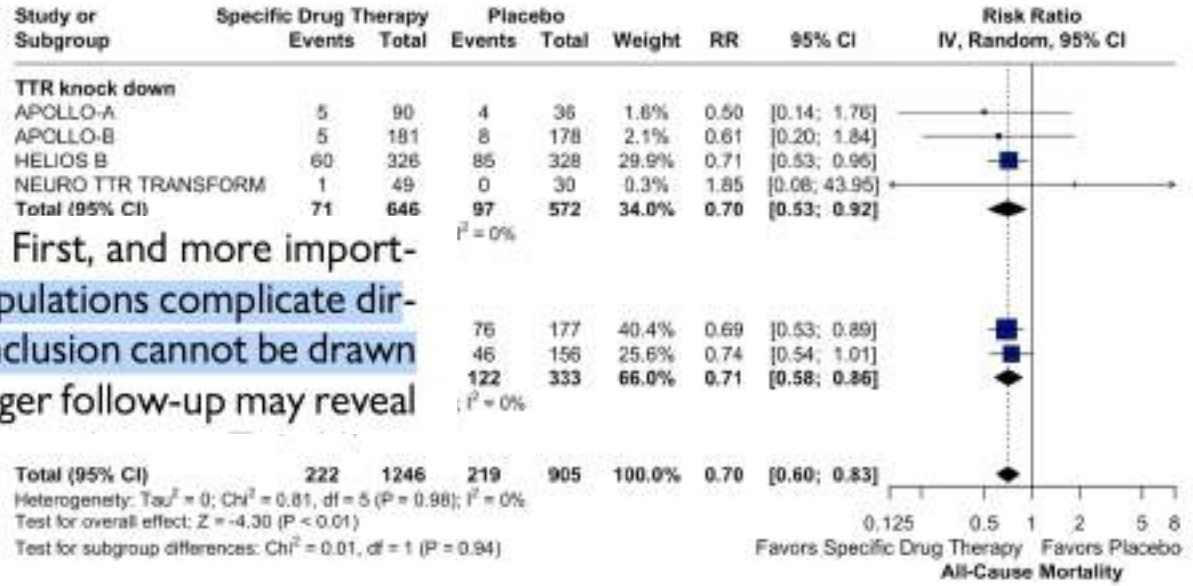
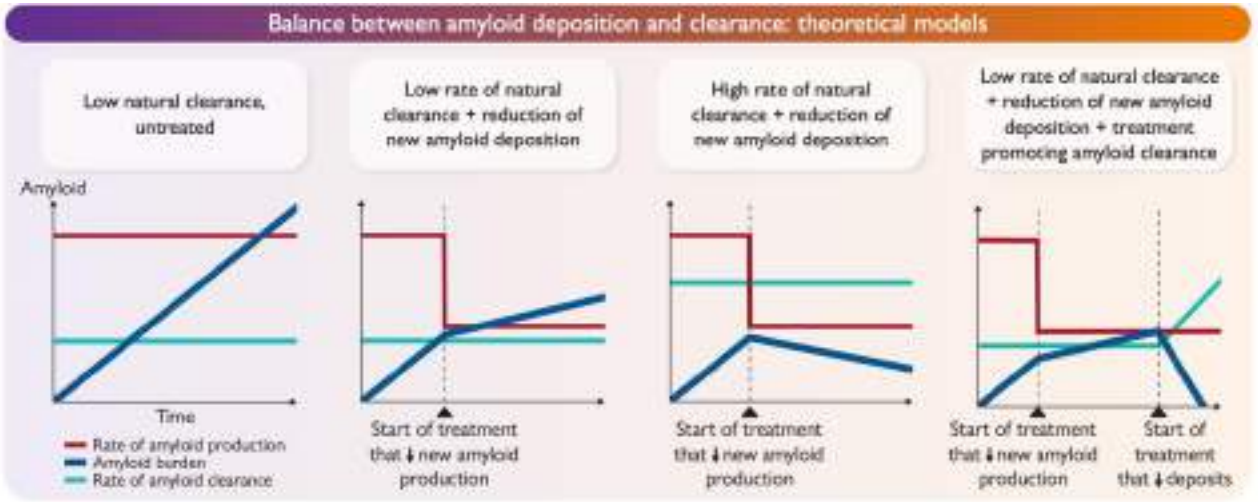


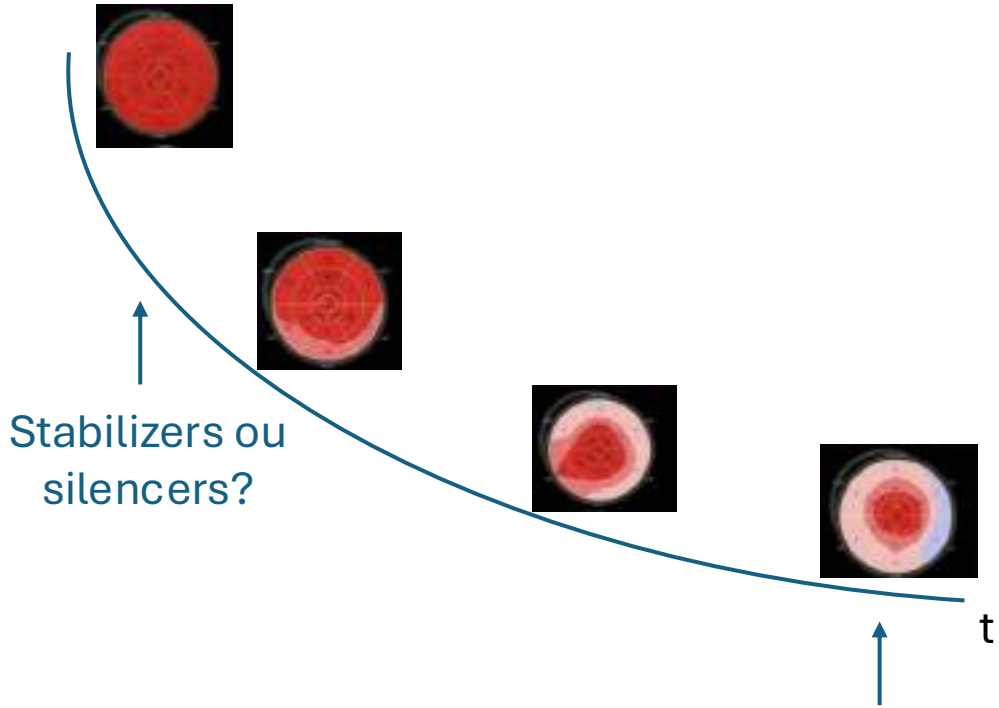
Fig. 5 Forest Plot for Subgroup analysis of All Cause Mortality. TTR knock-down therapies and TTR stabilizers showed an equally effective reduction in all-cause mortality compared to placebo. Abbreviations: CI Confidence Interval; RR: Risk Ratio; TTR Transthyretin

2713 patients

Prata et al. BMC Cardiovasc Disord. 2025

Aimo et al. European Heart Journal Open. 2025





Fontana et al. EHJ. 2025

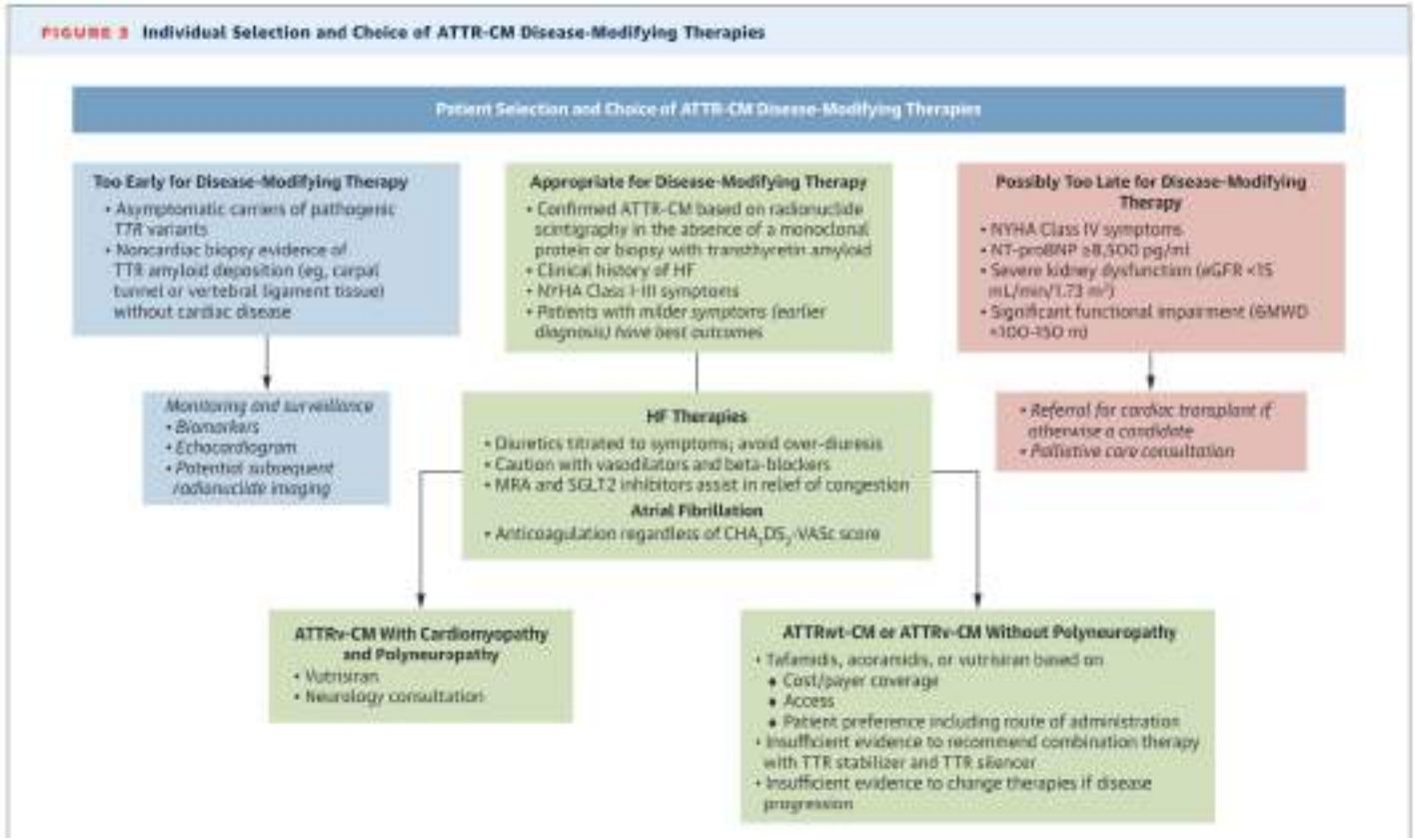
Questions en suspens

TABLE 3 Unanswered Therapeutic Questions and Future Directions

Therapeutic Area	Question(s)	Potential Approaches to Address Emerging Questions
Initial therapy	Stabilizer or silencer? Which stabilizer? Which silencer?	Comparative effectiveness research using national data repositories of real-world data. Single- or multicenter collaborative research studies using existing registries. Endpoints could include progression of disease and financial toxicity as well as mortality and cardiovascular events.
Combining therapies	Which combination? Initially or in series?	Determine efficacy of combination therapy compared with monotherapy. Compare combination therapy at diagnosis versus sequential initiation (eg, with disease progression). Switch studies evaluating disease progression in those who switch vs continue initial therapy. Cross-over studies comparing single and combination therapy.
De-prescribing	Could de-prescribing reduce costs without adversely effecting efficacy?	Trials of de-prescribing one TTR therapy while maintaining another on both short- and long-term outcomes. Cost effective analyses.
Prevention of disease	Can we prevent the development of ATTR-CM?	Randomized trials of stabilizers in carriers of TTR variants near predicted age of disease onset (NCT06563895). Randomized trials of DMTs in older adults at risk of developing TTR amyloid cardiomyopathy (TTR amyloid in carpal tunnel or in other orthopedic or noncardiac tissue).
Long-term data	Safety of therapy? Emerging phenotypes?	Use FDA Adverse Event Reporting System, Sentinel Initiative, sponsors of pharmacovigilance safety databases, Vigibase, European Health Data and Evidence Network to evaluate for any long-term safety issues. Studies focused on clinical manifestations in "protected" areas (ocular, CNS) in those on DMT. Novel delivery mechanisms to target ocular and CNS production of TTR.

Griffin et al. JACC HF. 2025

Consensus d'expert?



ATTR CM en France?

Tafamidis depuis 2018
Patisiran : CPC depuis 2024

Acoramidis Avis HAS SMR/ASMR 1/12/2025
Vutrisiran : Avis HAS SMR/ASMR en attente

Kittleson et al. JACC. 2025

Non-amyloid specific treatment for TTR cardiac amyloidosis: a clinical consensus statement of the ESC Heart Failure Association

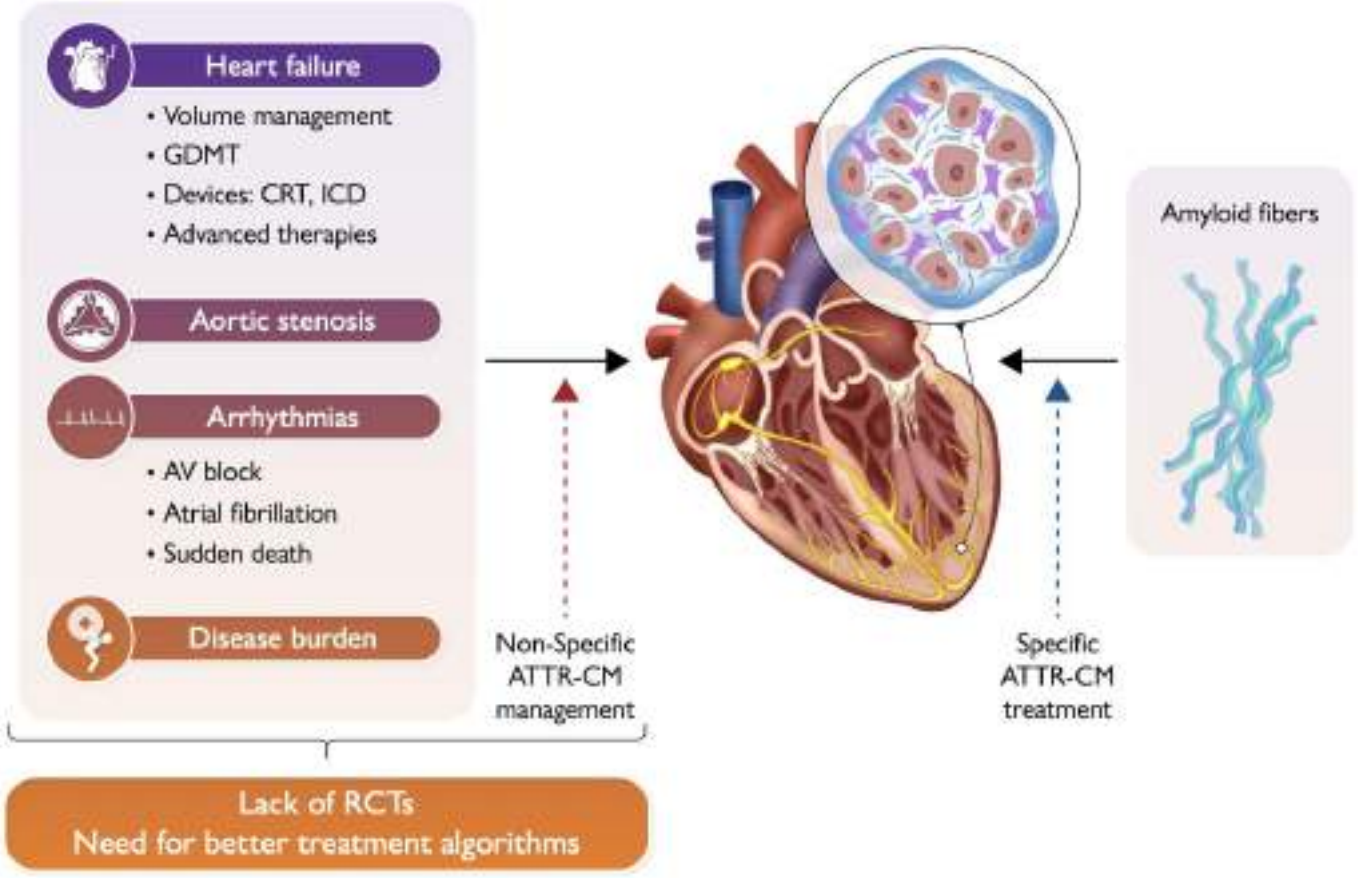


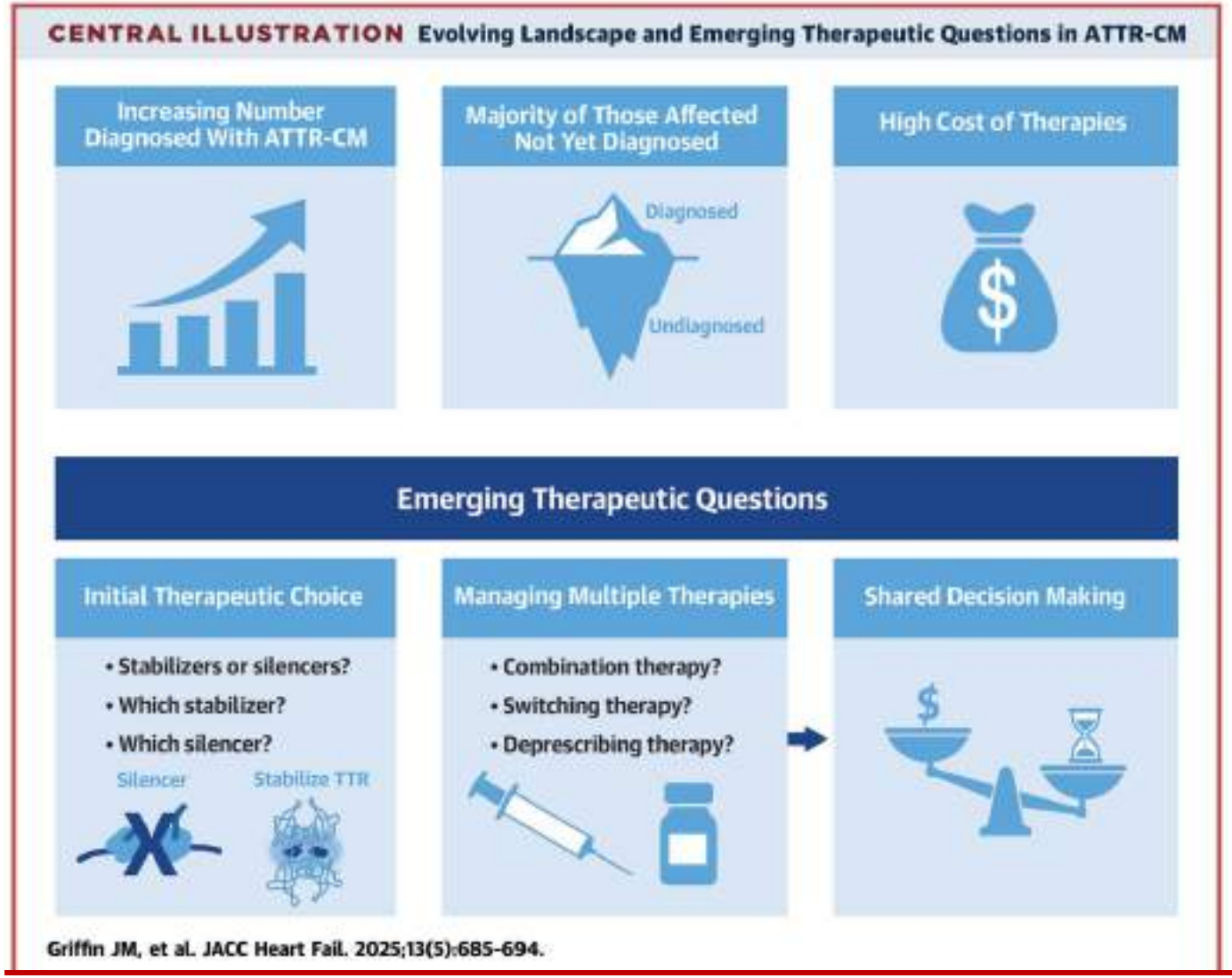
Table of advice HF medications

Advice	Evidence	Strength
Advice TO DO		
Treatment with MRAs and SGLT2i regardless of LVEF	OBS	
May Be Appropriate TO DO		
Treatment with low-dose beta-blockers for patients with LVEF <40%	OBS	
Advice NOT TO DO		
Treatment with ACEi/ARBs/ ARNI, unless the patient is hypertensive	OBS	

Table 2 Unanswered questions

- How to better tune diuretics and beta-blockers dose?
- Is there a role for sacubitril/valsartan in ATTR-CM?
- Should be atrial standstill an 'off label' anticoagulation indication in ATTR-CM?
- Is there a role for loop recorders in ATTR-CM monitoring?
- How to define the optimal heart rate for pacing in these patients?
- Which is the role of cardiac rehabilitation and exercise in ATTR-CM?
- How to manage end-stage HF and palliative care from a cardiac point of view?
- Which are the recommendations for caregivers?
- How do we prognosticate for patients in the era of evolving targeted TTR therapies?
- How to quantify extra-cardiac amyloidosis and its clinical burden?

Garcia Pavia et al. European Heart Journal. 2025
Cabrera-Romero et al. Amyloid. 2024
Kang et al. International Journal of Cardiology. 2024
Ioannou A et al. Eur Heart J. 2023



En conclusion

Beaucoup de molécules
Mécanismes différents
Pas de comparaison directe
Pour quelle temporalité?

Beaucoup de questions
Vivement 2026

Griffin et al. JACC. 2025
Fontana et al. EHJ. 2025
Vergaro et al. Heart 2025

Merci

Platinium sponsor

BAYER

Premium sponsors

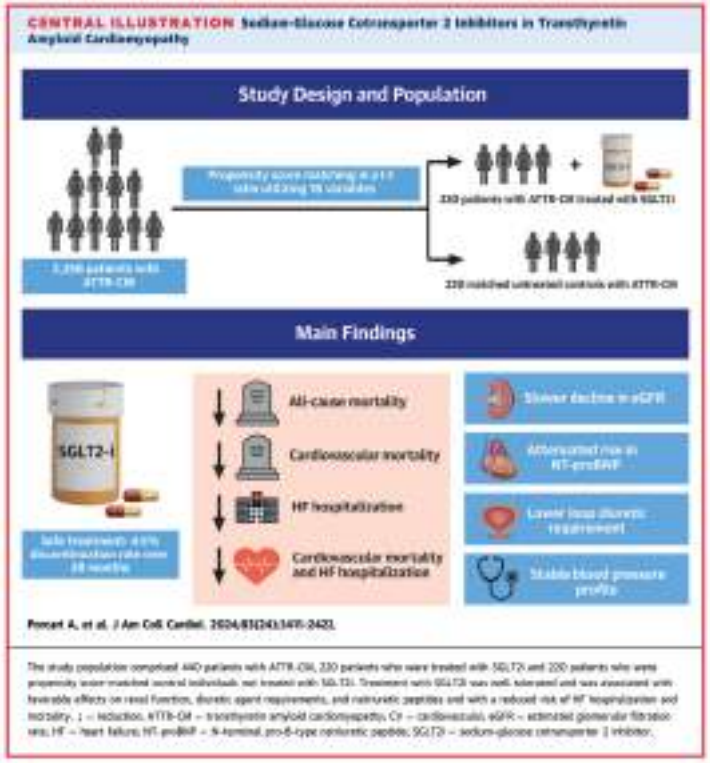
Alnylam AstraZeneca Pfizer

Silver sponsors

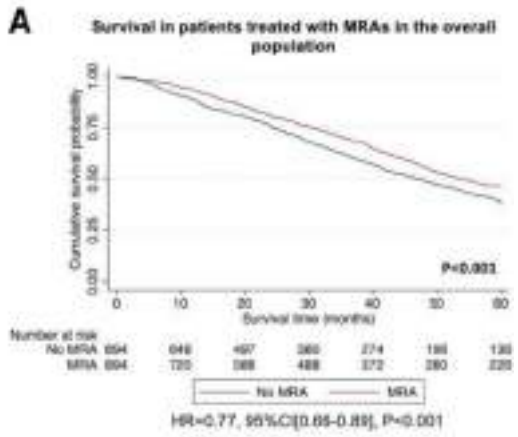
Binding Site impetomedical

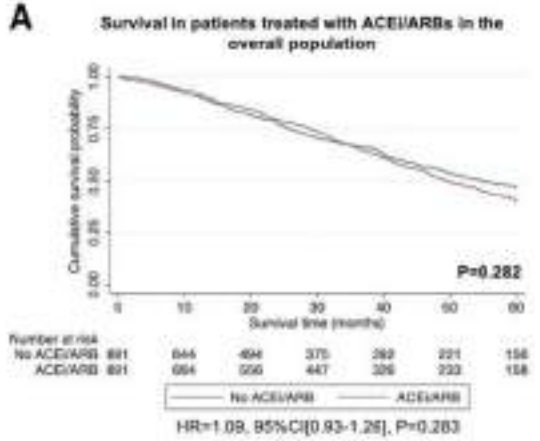
www.congres-amylose.com

Iglt2? MRA? BB? ACEI/ARBs?

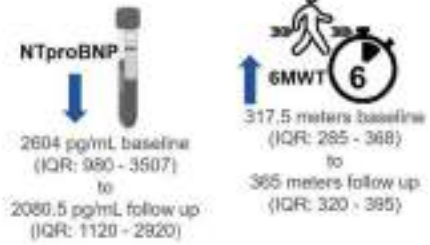


Porcari et al. JACC. 2024



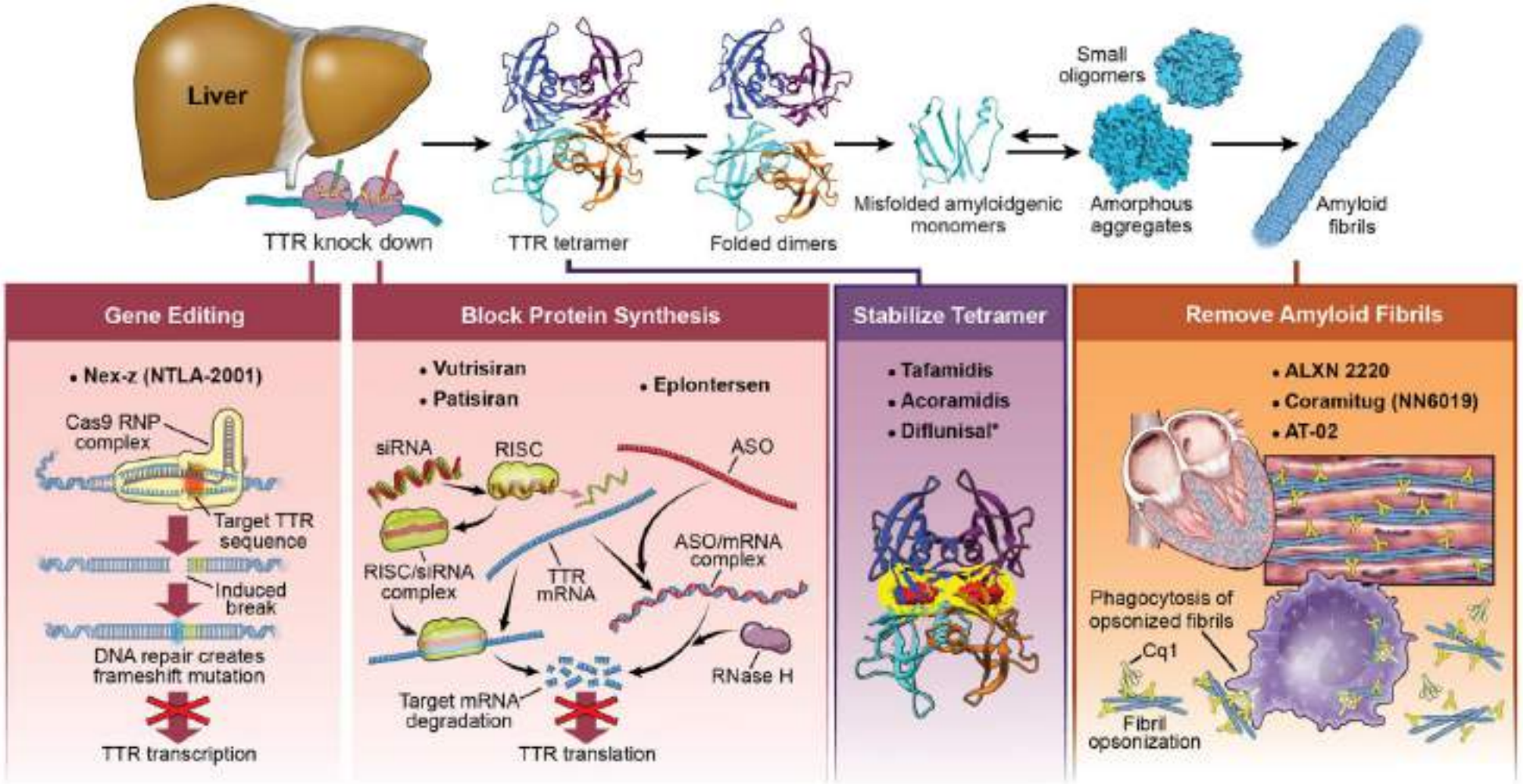


ATTR CM
rétrospective
2371 pat



Ioannou A et al. Eur Heart J. 2023
Cabrera-Romero et al. Amyloid. 2024
Kang et al. International Journal of Cardiology. 2024

FIGURE 1 Pathogenesis of Transthyretin Cardiac Amyloidosis and Disease-Modifying Therapies



Griffin et al. JACC. 2025
Fontana et al. EHJ. 2025
Vergaro et al. Heart 2025

Table 2 Summary of clinical and pharmacological properties of ATTR amyloidosis treatments approved by the FDA and European Medicines Agency

	Dosage and administration	Dose adjustments	Food interactions	Drug-drug interactions	Lab test anomalies	Contraindications	Pregnancy	Side effects
Tafamidis	80 mg orally once a day (Tafamidis meglumine) 61 mg orally once a day (Tafamidis)	Not required, limited data in severe hepatic and kidney dysfunction	None	In vitro breast cancer resistance protein inhibition; potential interactions with substrates (eg, methotrexate, rosuvastatin and imatinib)	Possible decrease in T4 levels without affecting free T4 or thyroid-stimulating hormone	Hypersensitivity to the active ingredient or any of the excipients	Effective contraception is required during treatment and for 1 month after discontinuation.	Very common: urinary tract infections, vaginal infections, diarrhoea and upper abdominal pain
Acoramidis**	712 mg orally two times a day	Not required	None	Avoid concomitant use with uridine 5'-diphospho-glucuronosyltransferase inducers and strong CYP3A inducers. Consider more frequent monitoring when co-administered with sensitive CYP2C9 substrates.	Possible increase in serum creatinine generally occurs within 4 weeks of starting therapy and stabilises	None	Insufficient data	Diarrhoea and upper abdominal pain
Patisiran	0.3 mg/kg intravenous every 3 weeks if weight <100 kg (maximum dose 30 mg) *premedication required*	Not required. It has not been studied in severe hepatic and kidney dysfunction	None	None	Decrease in serum vitamin A levels	None	No available data	Upper respiratory tract infections and infusion-related reactions
Vutrisiran	25 mg SC once every 3 months	Not required. It has not been studied in moderate/severe hepatic and severe kidney dysfunction	None	None	Decrease in serum vitamin A levels	None	No available data	Pain in extremity, arthralgia and dyspnoea
Inotersen	284 mg SC once weekly	Not required. It has not been studied in moderate/severe hepatic and severe kidney dysfunction	None	Because of the risk of thrombocytopenia and renal toxicity, caution should be used when using antiplatelet/anticoagulants and nephrotoxic drugs, respectively	Possible decrease in platelet count and increase in creatinine, aspartate transaminase and alanine transaminase	► Platelet count $<100\times10^9$/L ► Urine protein-to-creatinine ratio ≥1000 mg/g ► History of acute glomerulonephritis caused by inotersen ► Hypersensitivity to inotersen	No available data	Warnings: thrombocytopenia, glomerulonephritis, renal toxicity, stroke and cervicocephalic arterial dissection, liver injury, inflammatory and immune effects
Eplontersen	45 mg SC once monthly	Not required. It has not been studied in moderate/severe hepatic and severe kidney dysfunction	None		Decrease in serum vitamin A levels	None	No available data	Vomiting and injection site reactions

*Approved only by the FDA (November 2024) for the treatment of ATTR cardiomyopathy.
ATTR, amyloid transthyretin; CYP, cytochrome P450; FDA, Food and Drug Administration; SC, subcutaneous; T4, thyroxine.;

Liver Transplantation

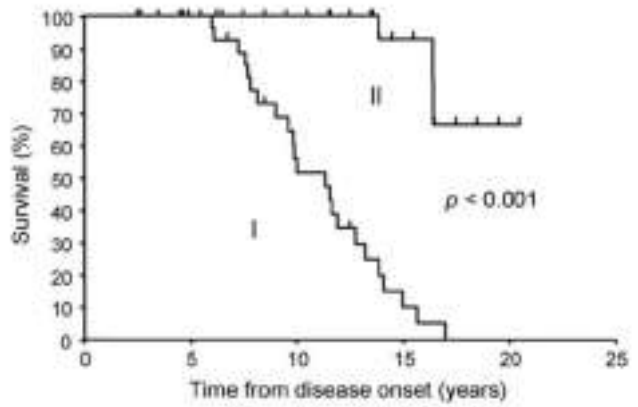
Author	N	Age (years)	Follow Up (months)	Time of symptoms after LT, years	Treatment	Study Type	Main Findings
Gond et al. 2021	1	67	12	22	Patisiran	Case Report	Improvement in fatigue and dyspnea; well tolerated.
Kon et al. 2015	1	31	12	NA	Tafamidis (pre & post OLT)	Case Report	Improvement in GI, urinary and autonomic symptoms; no improvement in muscle strength or BNP.
Romero-Imbroda et al. 2017	1	57	18	5	Tafamidis	Case Report	Minimal neurological deterioration over 18 months; well tolerated.
Schmidt et al. 2022	23	58 (43–75) Median (range)	12	9,4 (5,1) Mean (SD)	Patisiran	Prospective, Open-label	91 % reduction in TTR, improved NIS, QOL, and COMPASS-31; common AEs: diarrhea, infusion reactions.
Moshe-Lilie et al. 2020	9	61 median	12 (median)	7,5 (median)	Inotersen	Multicenter Retrospective	Stable/improved NIS; 5 patients discontinued due to thrombocytopenia or liver rejection.
Okumura et al. 2024	3	48 median	12	20	Tafamidis	Retrospective Case Series	Improved dyspnea, BNP, and troponin; no major adverse events.
Bulinski et al. 2022	1	44	18	5	Tafamidis → Patisiran	Case Report	No response to Tafamidis; improved NIS after 18 months of Patisiran despite cardiac progression.

TABLE 1. Factors to Consider for the Selection of OLT Candidates

Age < 50 years
Duration of symptoms < 7 years
Low polyneuropathy disability score
Modified body mass index ≥ 600 kg/m^2·g/L
No severe autonomic dysfunction
Absence of amyloid cardiomyopathy
No significant renal dysfunction

37 pat val met30

Figure 2 Kaplan-Meier survival estimates for all patients



I indicates the curve for the nontransplant group; II indicates the curve for the transplant group.

Wilczek et al. Amyloid. 2011
Adams et al. Nat Rev Neurol 2019
Yamashita et al. Neurology. 2012
Carvalho et al. Liver Transplantation. 2015
Ericzon et al. Transplantation. 2015
Santo et al. Transplantation Reviews. 2025