

ÉVÉNEMENT HYBRIDE



Jeudi 18 décembre 2025
Fondation Biermans-Lapôtre ■ PARIS

www.masterclass-amylose.com

Futurs protocoles et essais cliniques en cours dans l'ATTR

Nicolas Piriou

CHU de Nantes – Centre de référence Cardiomyopathies



Nantes
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l'institut
du thorax
Centre de référence
Cardiomyopathies

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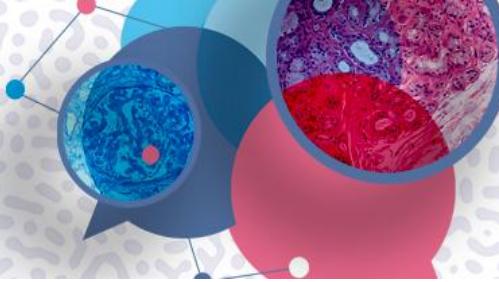


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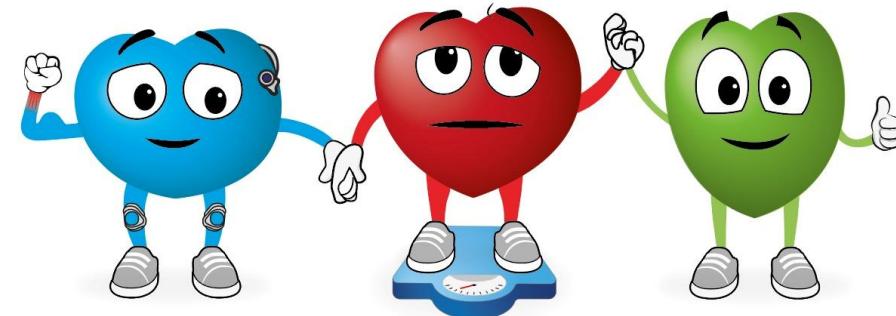


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Liens d'intérêts

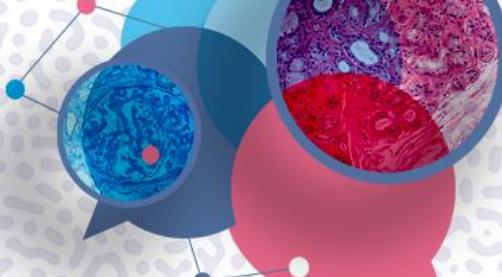
- Alnylam
- Pfizer
- Astra Zeneca
- Pfizer



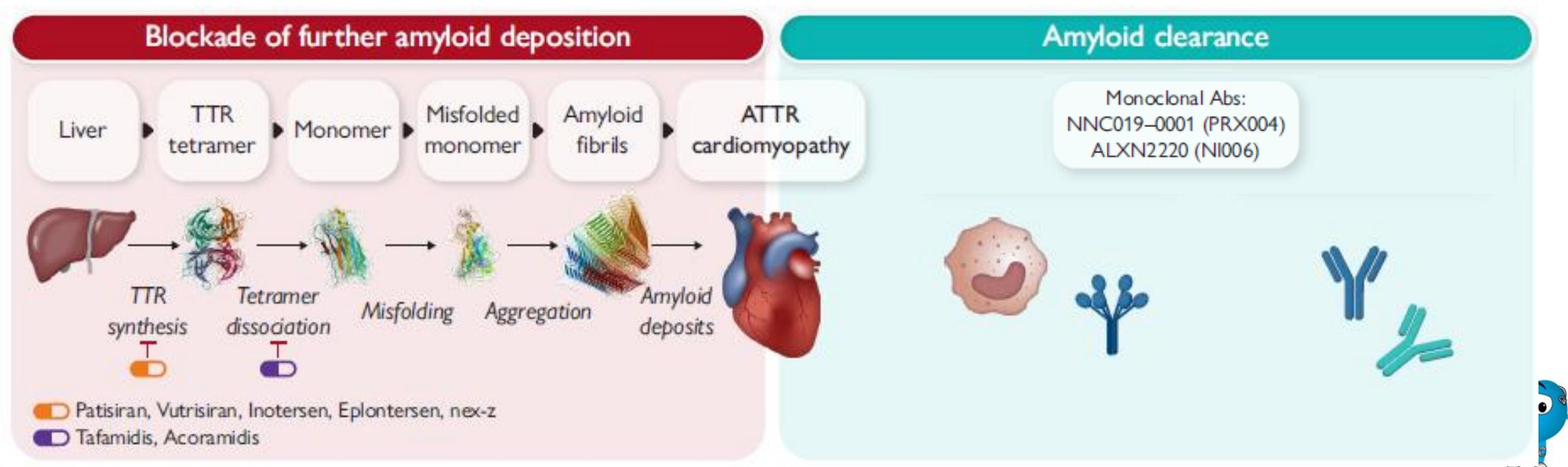
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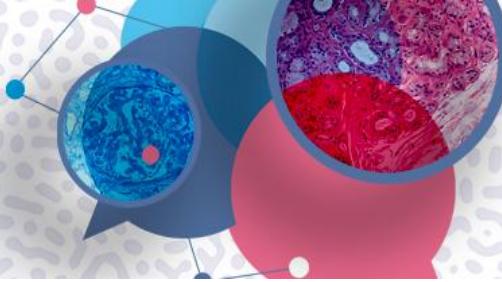
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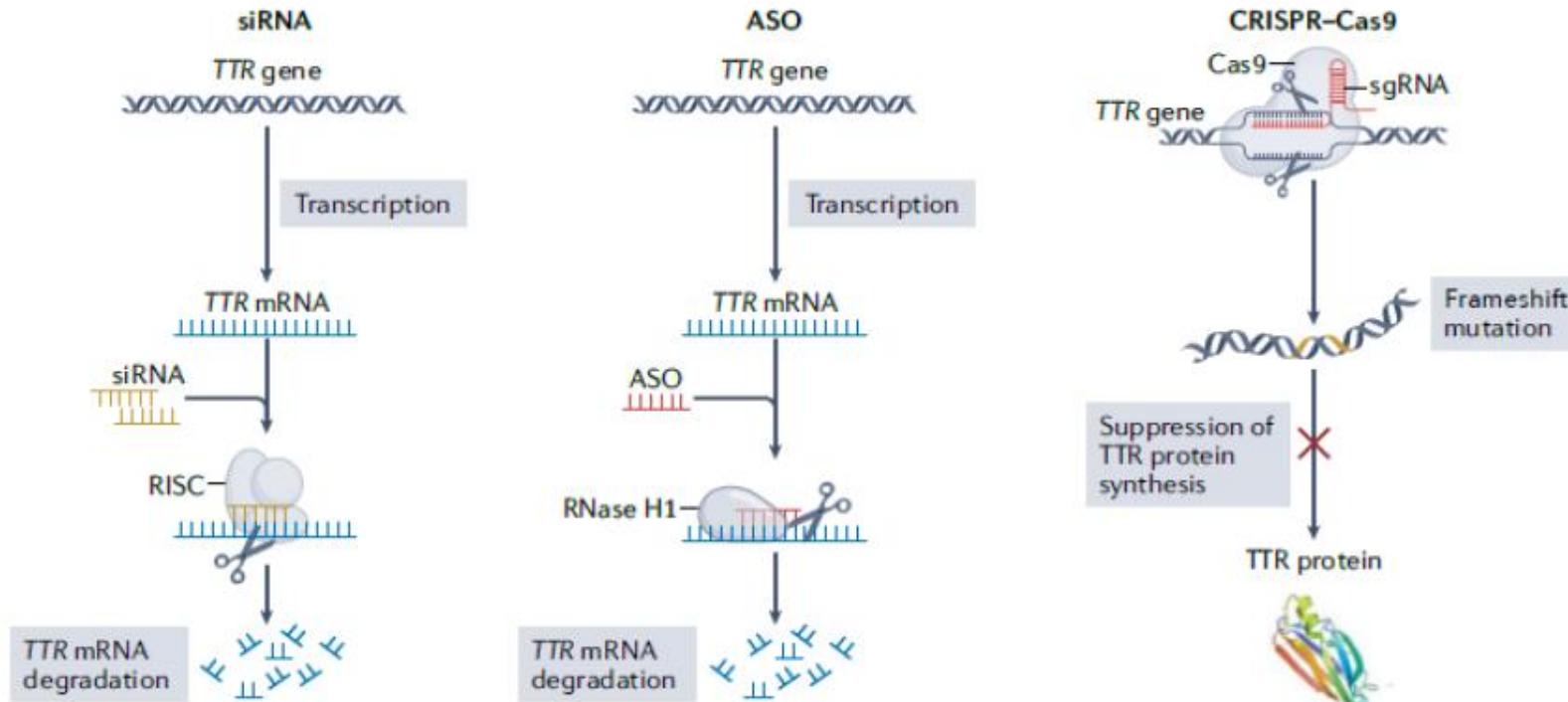
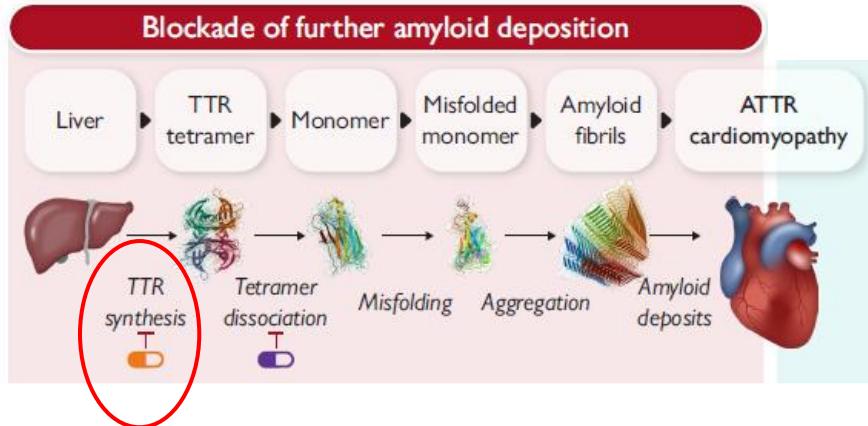


Explorer de nouvelles voies thérapeutiques, de nouvelles molécules, de nouvelles stratégies



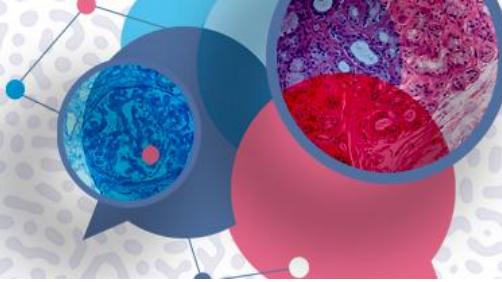


Essais en cours sur la voie du Silencage TTR

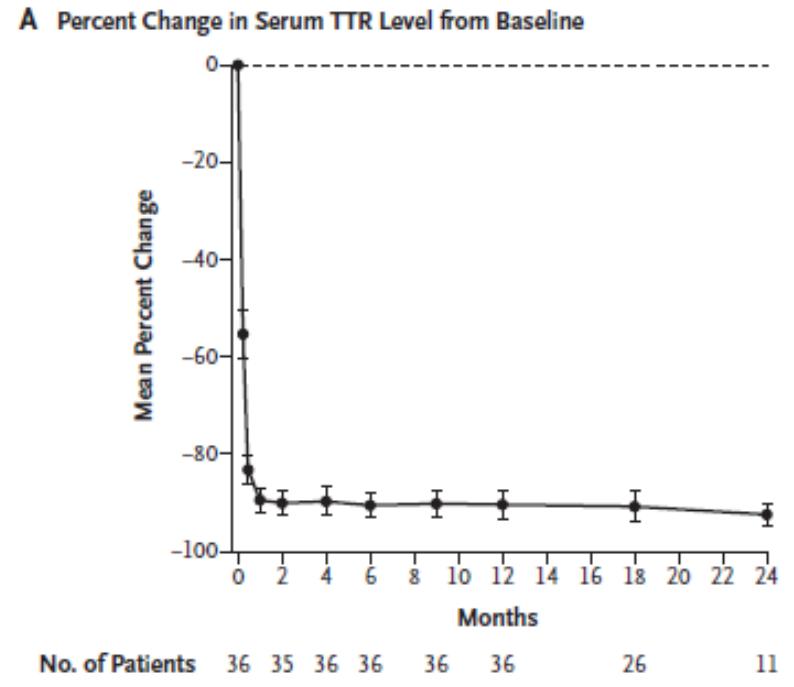
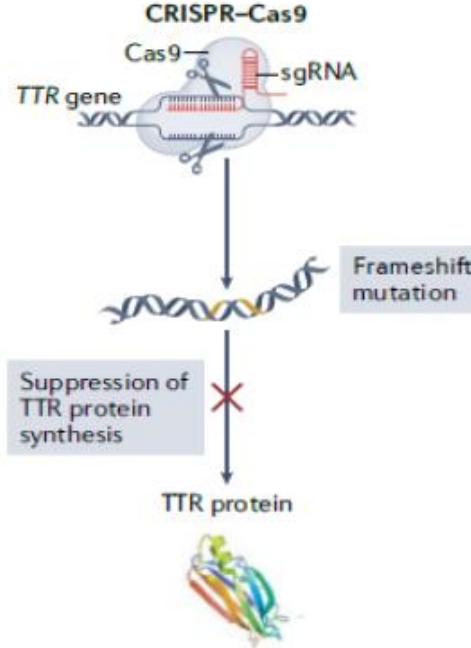


Nat Rev Cardiol. 2022 Oct;19(10):655-667

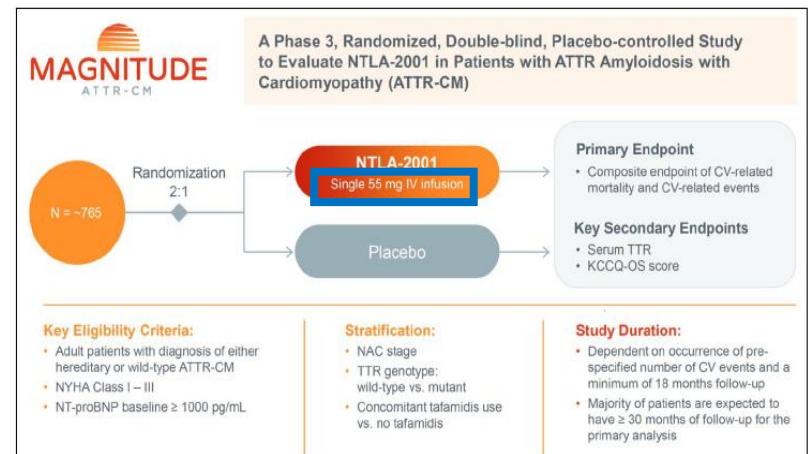
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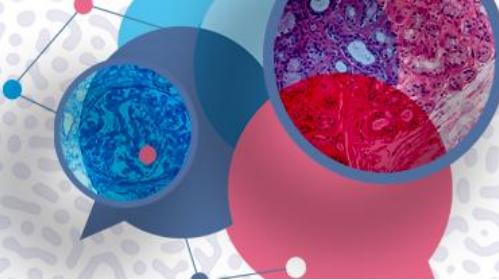
CRISPR-Cas 9 TTR gene editing (Nexiguran Ziclumeran)



Magnitude – Phase 3 Trial of CRISPR in ATTR-CA



34 patients : 2 avec élévation des transaminases reliée au traitement



Un nouveau siRNA : Nucresiran

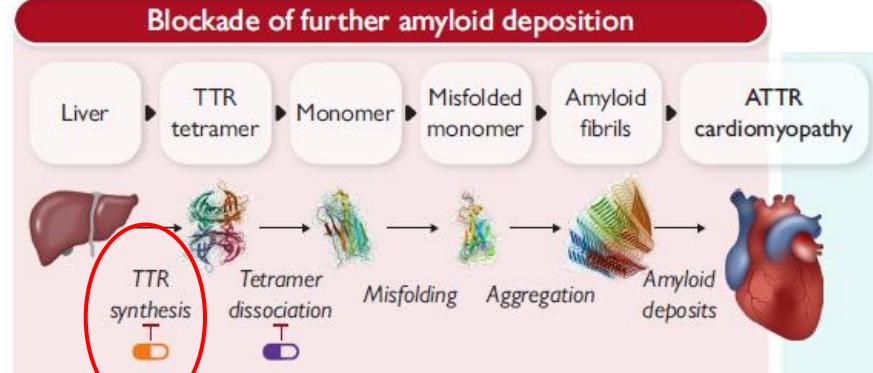
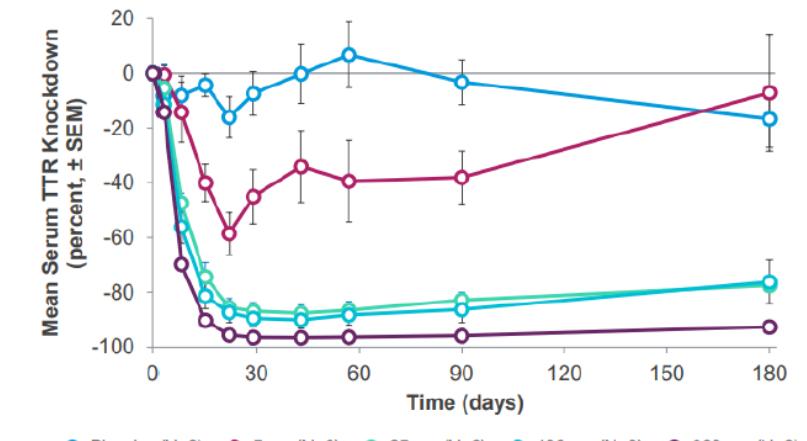
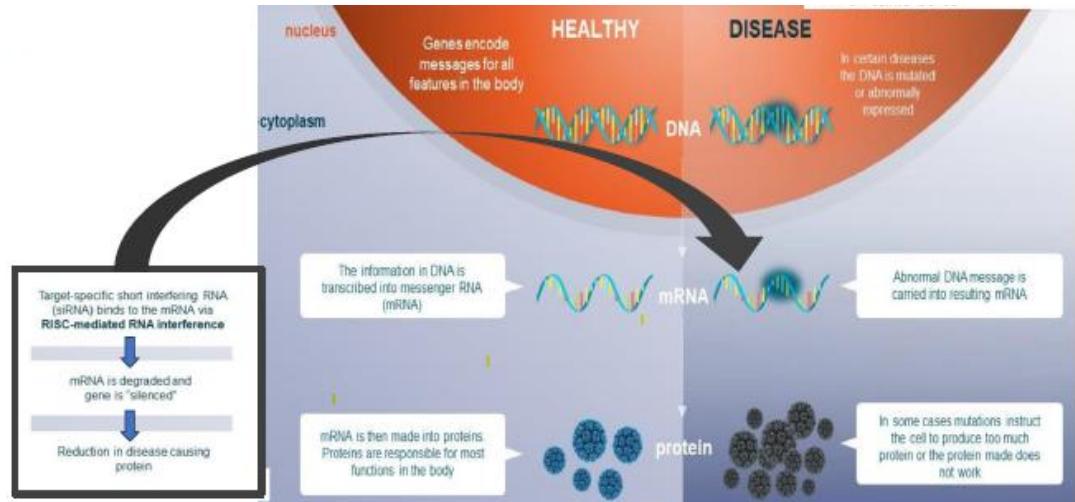
Nucresiran is a synthetic siRNA conjugated to GalNAc, which enables highly efficient delivery to the liver.

- GalNAc, a carbohydrate (sugar) molecule, is the ligand for the asialoglycoprotein receptor (ASGPR), which is highly and specifically expressed by hepatocytes.

Long-acting SC-administered GalNAc-conjugated siRNA targeting liver-expressed mRNA for TTR

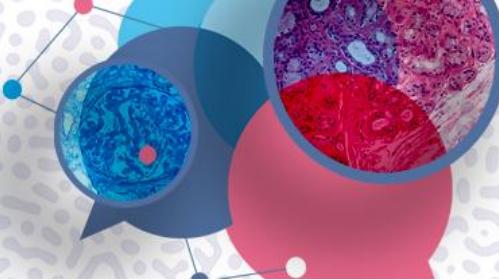


Phase 1 data supports best-in-class profile

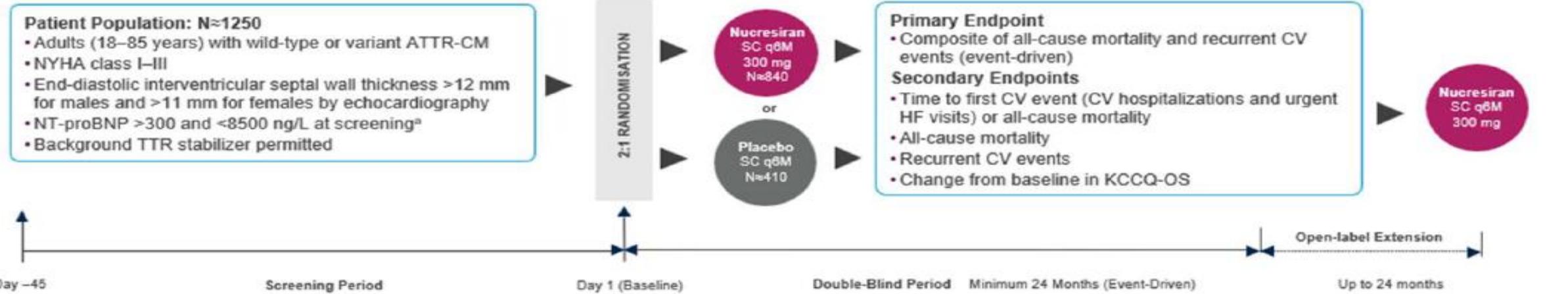


TRITON-CM
ATTR-CM CLINICAL STUDY

- Single 300 mg dose resulted in rapid, deep, and durable TTR reduction:
 - >90% at Day 15
 - 97% at Day 29
 - 93% at Day 180
- Safety profile:
 - All doses of nucresiran have been well tolerated; no adverse events considered related to study drug by investigator
- Frequency of administration:
 - Data support every 6 months subcutaneous dosing



TRITON-CM Study Design



Other Key Inclusion Criteria

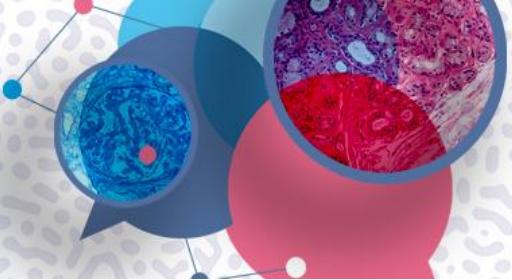
- Medical history of HF with ≥1 prior hospitalization for HF OR clinical evidence^b of HF that requires treatment with a diuretic
- Demonstration of ATTR cardiomyopathy by one of the following:
 - Documented TTR amyloid deposits in cardiac tissue regardless of MGUS status
 - In the absence of MGUS, ^{99m}Tc scintigraphy with Grade 2 or 3 cardiac uptake
 - In the presence of MGUS, documentation of TTR protein in noncardiac tissue AND Grade 2 or 3 cardiac uptake on ^{99m}Tc scintigraphy

Key Exclusion Criteria

- NYHA class IV HF; or NYHA class III heart failure AND ATTR Amyloidosis Disease Stage 3^c
- Polyneuropathy Disability Score ≥IIIa at screening visit^d
- Estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m²
- Non-TTR cardiomyopathy, hypertensive cardiomyopathy, cardiomyopathy due to valvular heart disease, or cardiomyopathy due to ischemic heart disease
- Received prior TTR-lowering therapy OR plan for or anticipate beginning treatment during screening or the first 24 months following randomization

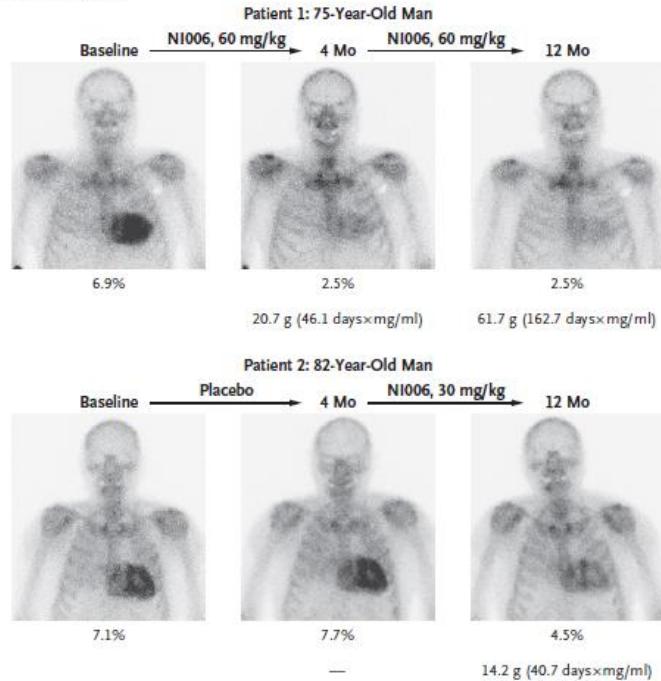
^aNT-proBNP >600 pg/mL and <8500 pg/mL for patients with atrial fibrillation. ^bManifested by signs and symptoms of volume overload or elevated intracardiac pressures.

^cDefined as NT-proBNP >3000 ng/L and eGFR <45 mL/min.¹³ ^dRequires cane or stick to walk or is wheelchair-bound due to polyneuropathy.

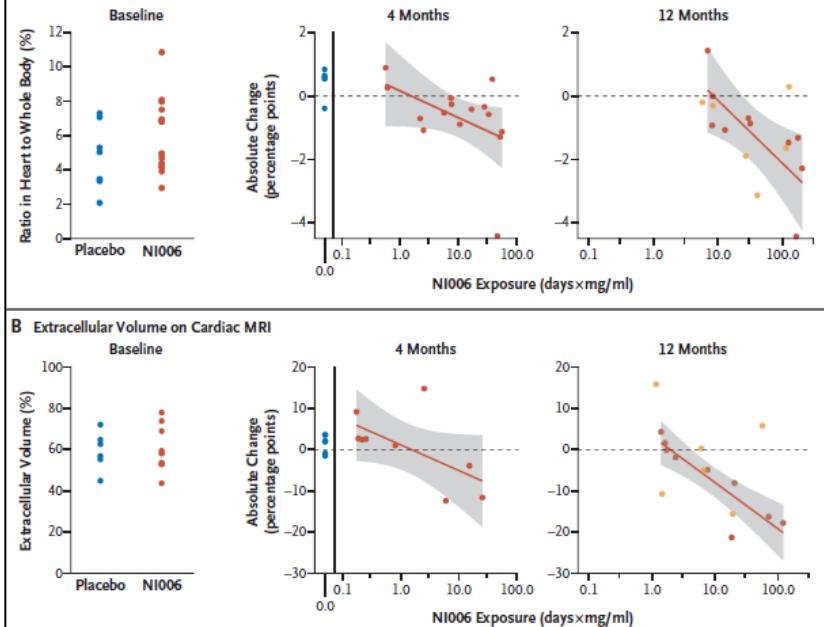


La voie des dépléteurs

Cardiac Tracer Uptake on Scintigraphy



A Cardiac Tracer Uptake on Scintigraphy



B Extracellular Volume on Cardiac MRI

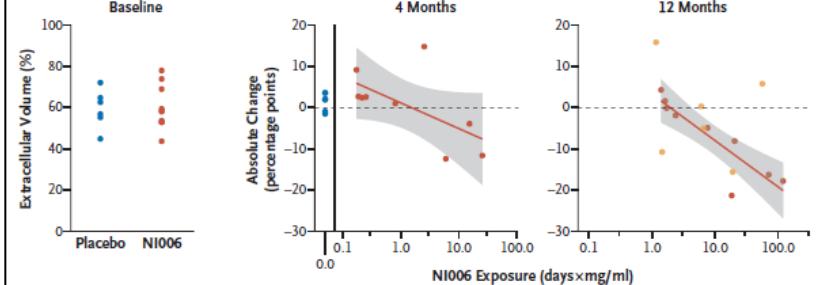


Figure 1. Cardiac Tracer Uptake on Scintigraphy and Extracellular Volume on Cardiac MRI.

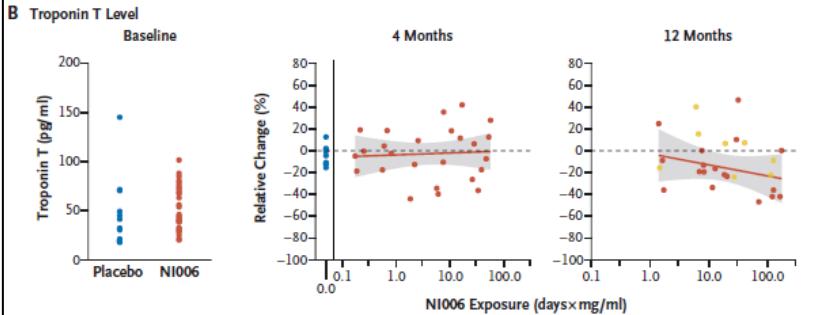
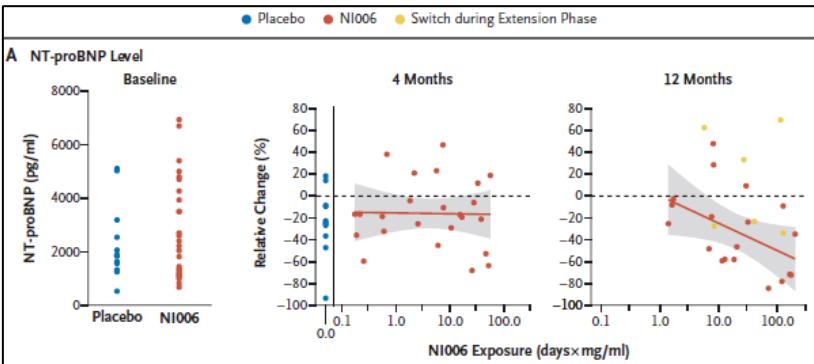
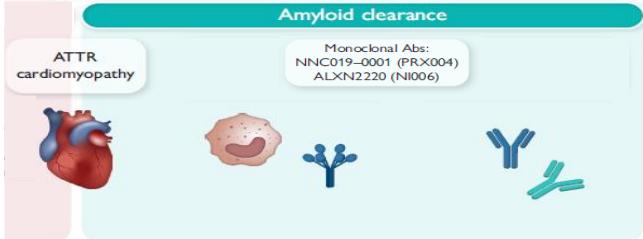
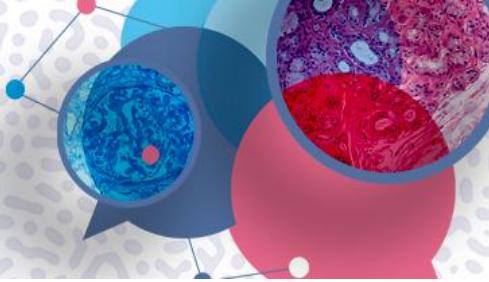
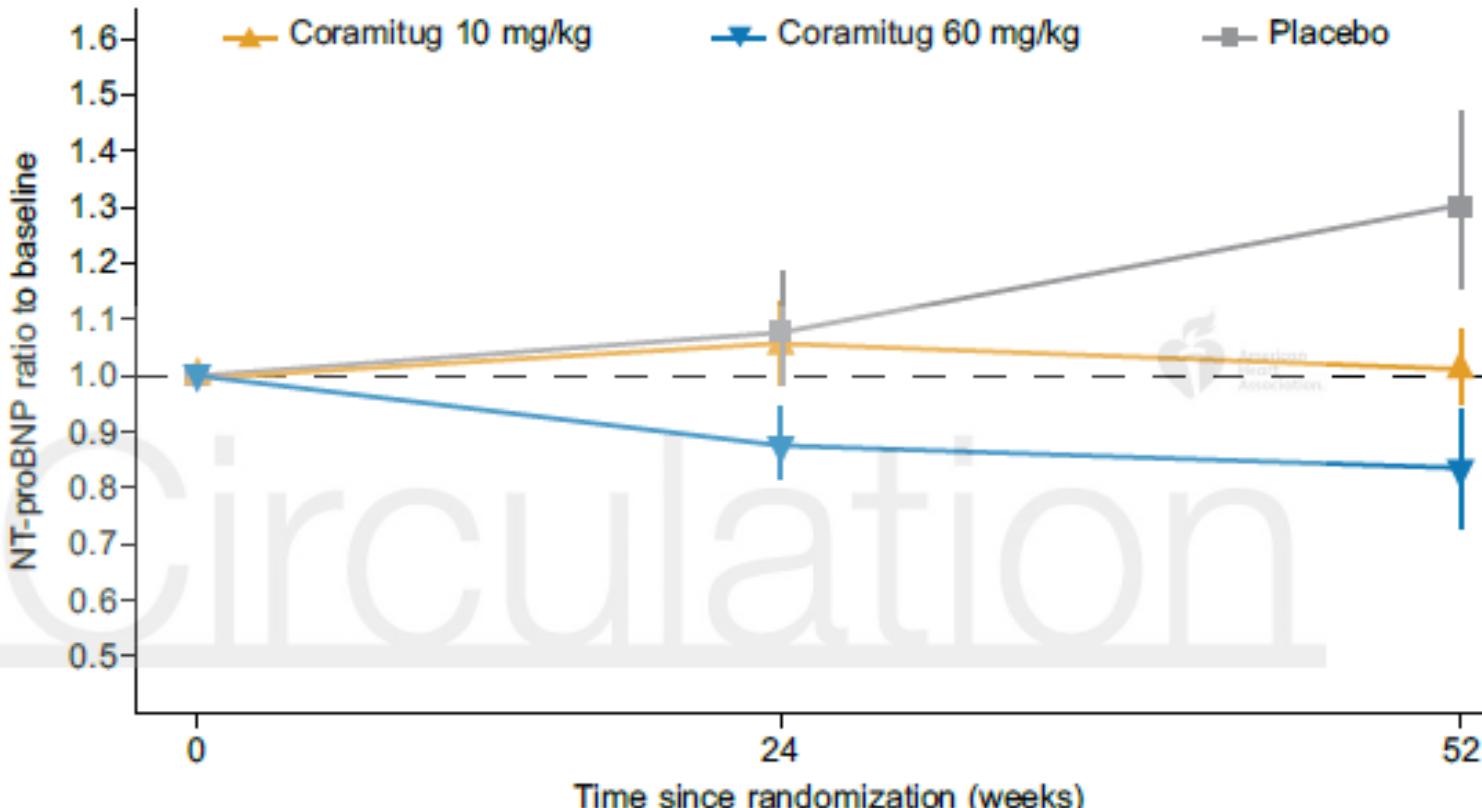


Figure 3. Cardiac Biomarker Levels.

P.Garcia-Pavia et al. NEJM 2023



Coramitug : données de phase 2



Pas de différence d'effet sur le 6MWT
vs placebo



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M.Fontana et al. Circulation 2025

8^e MASTERCLASS AMYLOSES CARDIAQUES

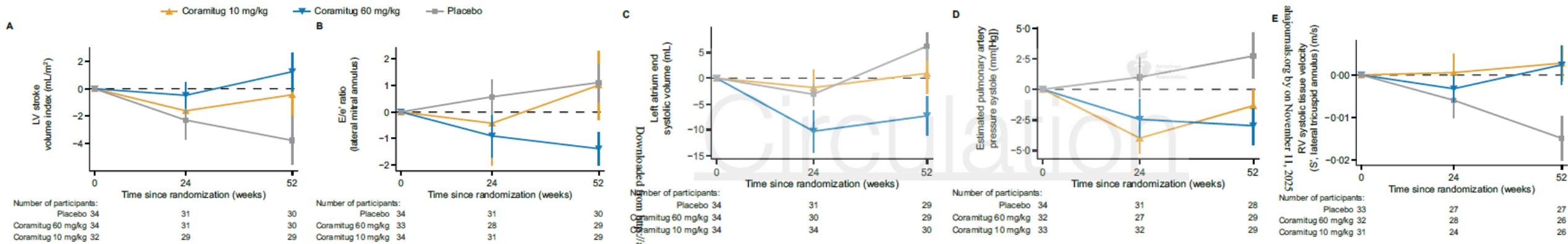


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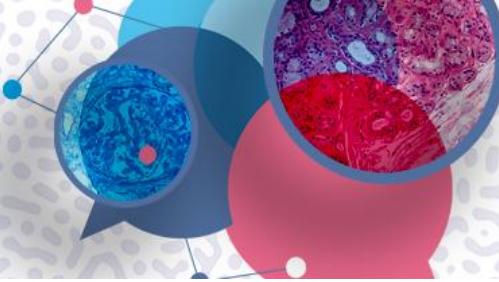


M.Fontana et al. Circulation 2025



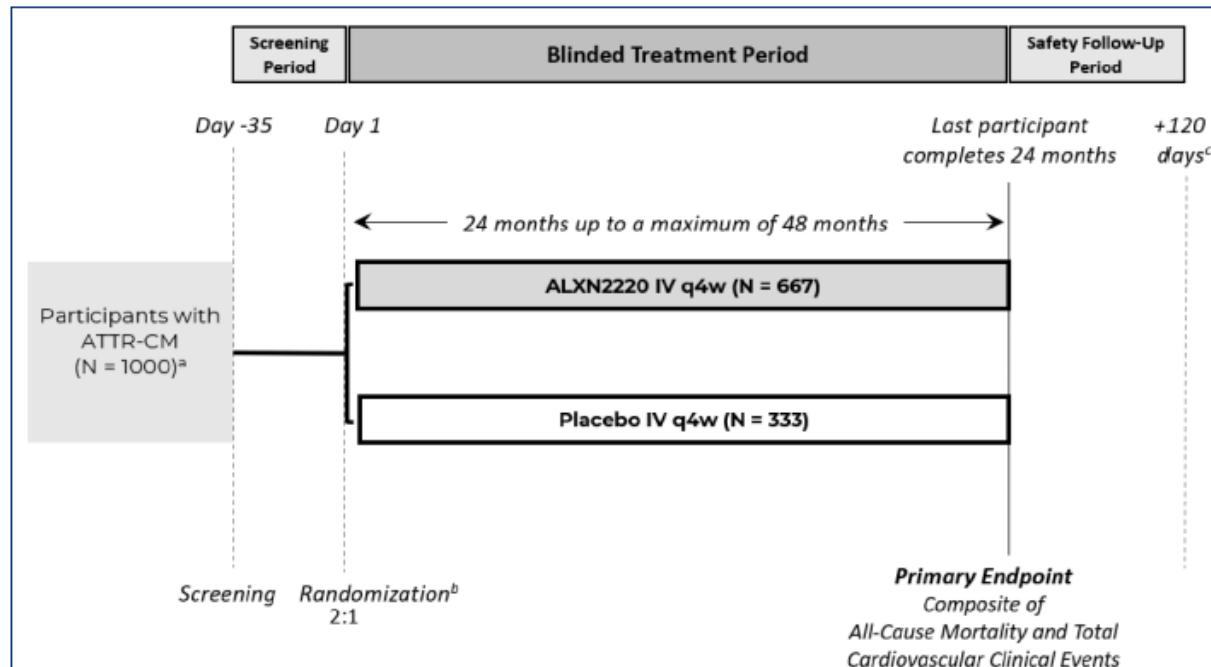
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 cardiogen
filière nationale de santé
maladies cardiaques héréditaires ou rares



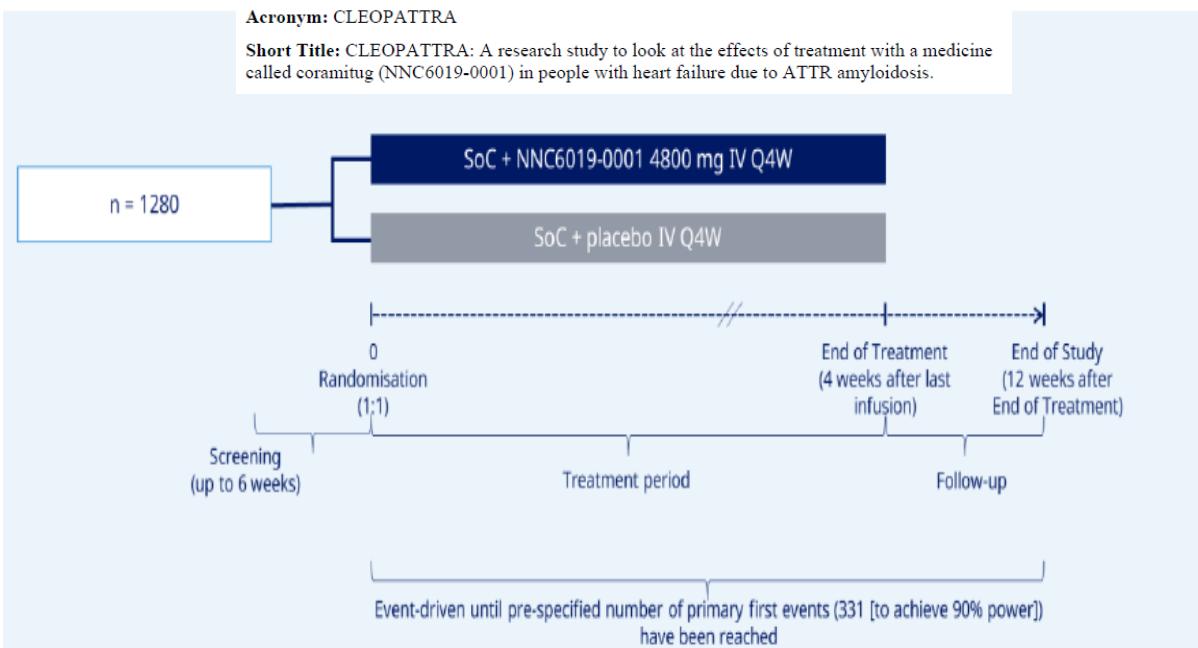
Les dépléteurs en Phase 3

DepleTTR-CM
Study



Acronym: CLEOPATTRA

Short Title: 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 ATTR amyloidosis.

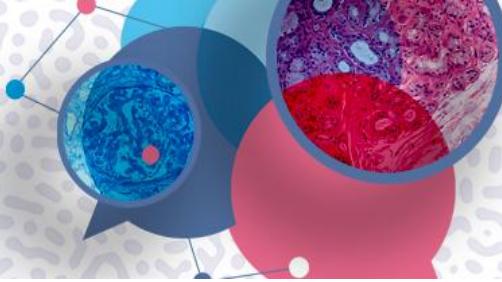


Primary objective

Objective	Endpoint
To assess the efficacy of ALXN2220 in the treatment of adult participants with ATTR-CM by evaluating the difference between the ALXN2220 and placebo groups as assessed by the composite endpoint of all-cause mortality (ACM), and the total cardiovascular (CV) clinical events.	Composite of all-cause mortality, and total CV clinical events during the blinded treatment period. (Anderson-Gill model with robust variance)

Objectives

Primary	Title	Time frame
To demonstrate superiority of NNC6019-0001 versus placebo, both added to SoC ^a , in reducing the CV death & morbidity in participants with ATTRwt-CM or ATTRv-CM	The composite outcome of: <ul style="list-style-type: none"> • CV death^b • Recurrent CV events (CV hospitalisation^{b,c} and urgent HF visits^b) 	From baseline (week 0) up to EOS ^d



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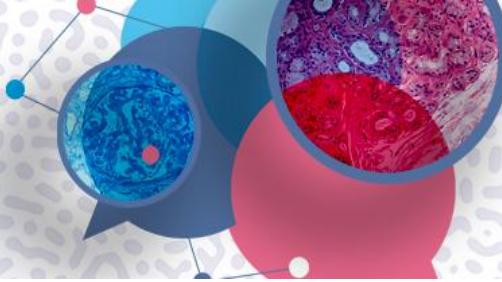
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Les essais de stratégie thérapeutique



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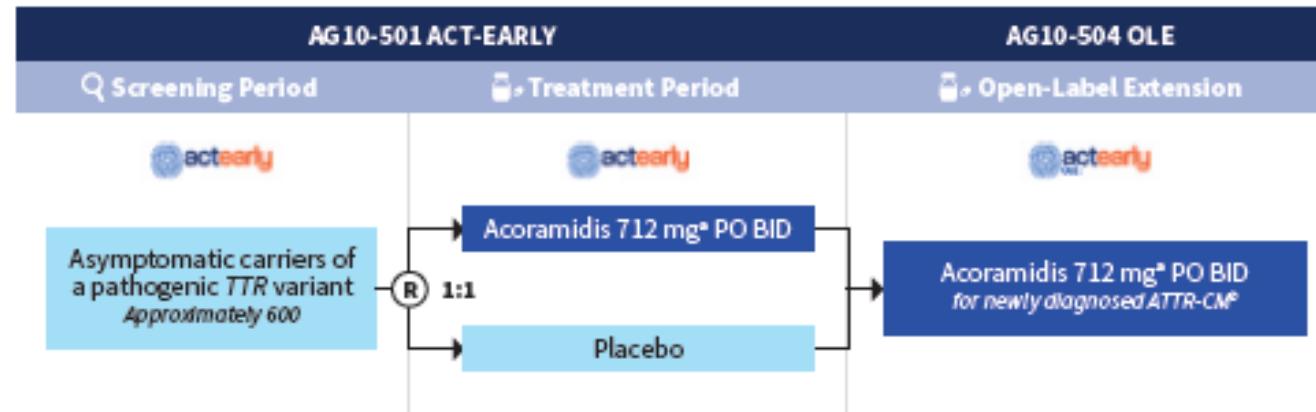
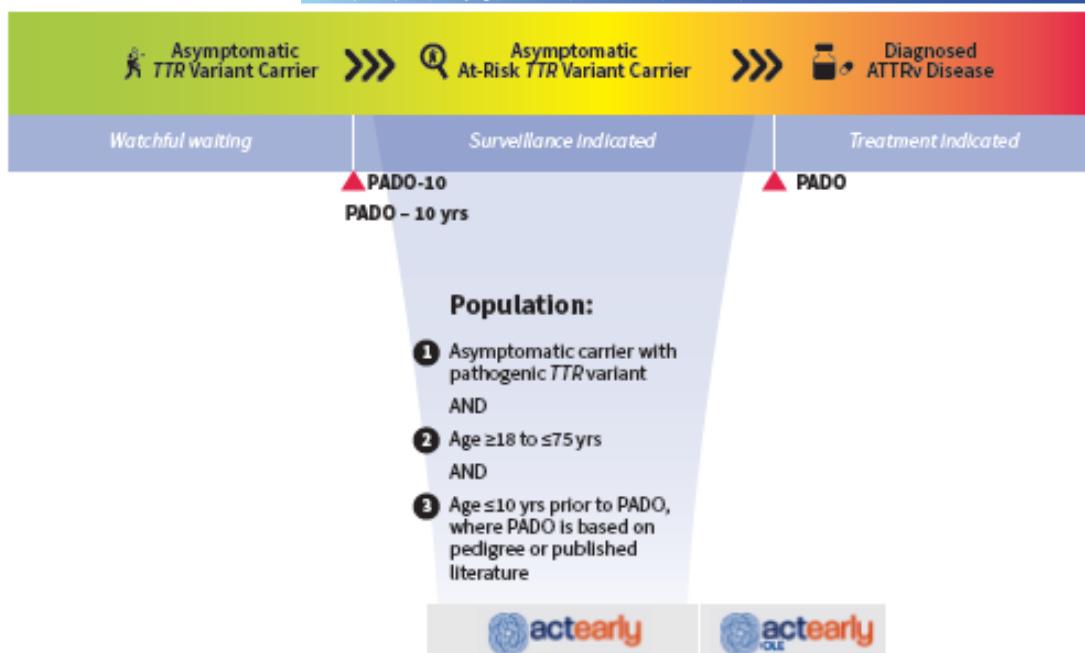


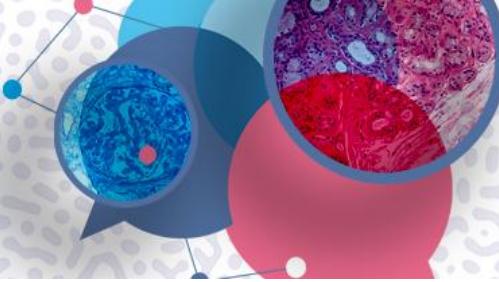


Traitements PRÉ-SYMPOMATIQUE des apparentés porteurs du variant génétique pathogène

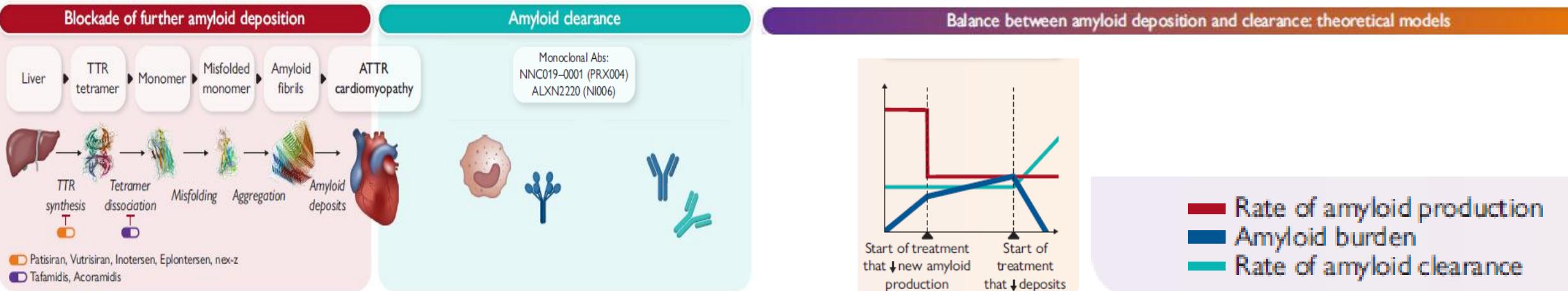
Rationale and Design of ACT-EARLY, the Acoramidis Transthyretin Amyloidosis Prevention Trial

Pablo Garcia-Pavia¹, Julian D. Gillmore², David Adams³, Isabel Conceicao⁴, Teresa Coelho⁵, Daniel P. Judge⁶, Mathew S. Maurer⁷, Frederick L. Ruberg⁸, Scott Solomon⁹, Ahmad Masri¹⁰, Thibaud Damy¹¹, Marianna Fontana¹², Mary M. Reilly¹³, Nitasha Sarswat¹⁴, Peter van der Meer¹⁵, Mazen Hanna¹⁶, Morie Gertz¹⁷, Xiaofan (Martha) Cao¹⁸, Ted Lystig¹⁹, Uma Sinha²⁰, Adam Castaño²¹, Leonid Katz²², Jonathan C. Fox²³





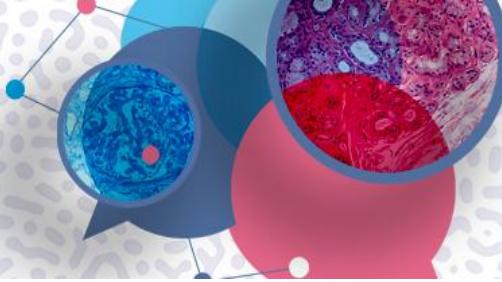
L'arrivée des essais de COMBINAISONS thérapeutiques



Adapted from M.Fontana et al. Eur Heart J 2025

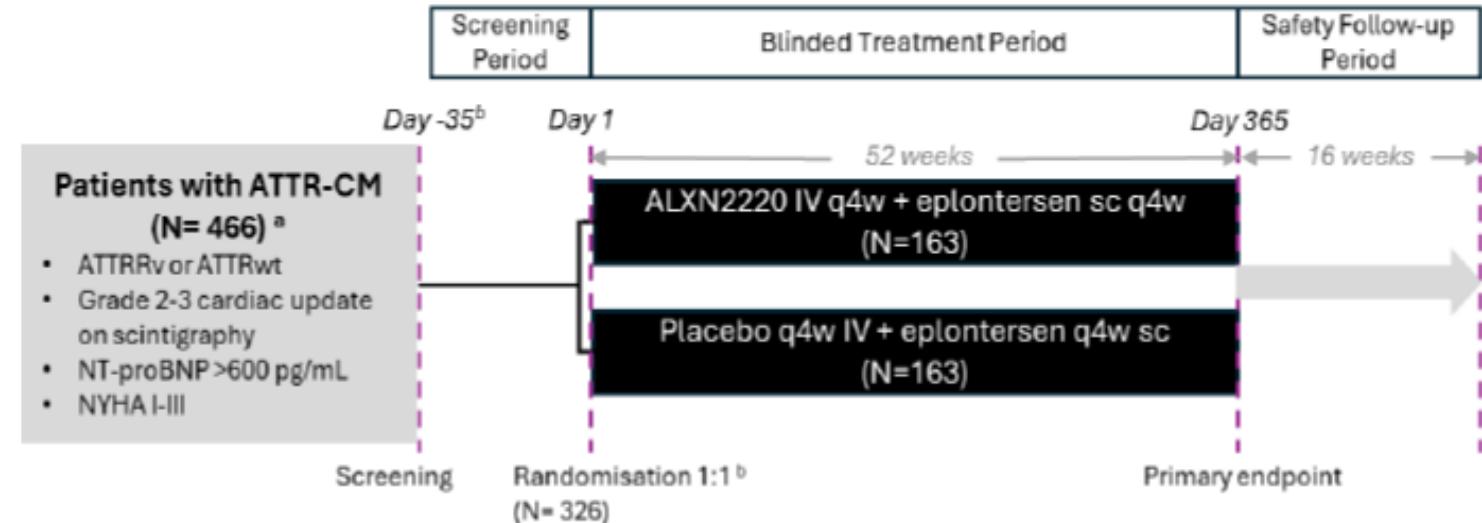


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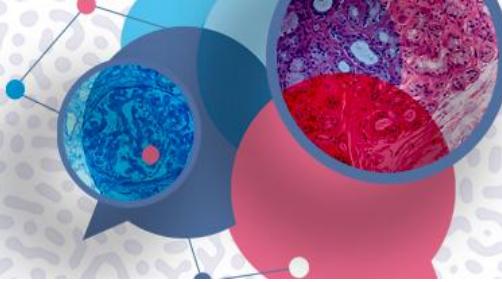


A Phase 2b, Randomized, Double-blind, Active-controlled, Multicenter Study to Evaluate the Efficacy and Safety of Eplontersen and ALXN2220 Compared to Eplontersen and Placebo in Adult Participants with Transthyretin-Mediated Amyloid Cardiomyopathy (ATTR-CM)

Brief Title: Efficacy and Safety of Eplontersen and ALXN2220 for the Treatment of ATTR-CM



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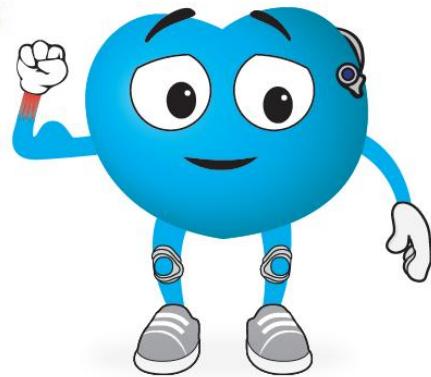


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Les atteintes rhumatisantes
(synoviales) de l'amylose
surviennent plusieurs années avant
l'insuffisance cardiaque (EPOF)

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- Surdité
- Essoufflement
- Canal carpien
- Prise de poids
- Doigt à ressaut
- Œdèmes
- Rupture du tendon du long biceps
- Fatigue
- Canal lombaire étroit
- Prothèse de hanche/genou



Et si c'était une
Amylose
Cardiaque à
transthyrétine ?

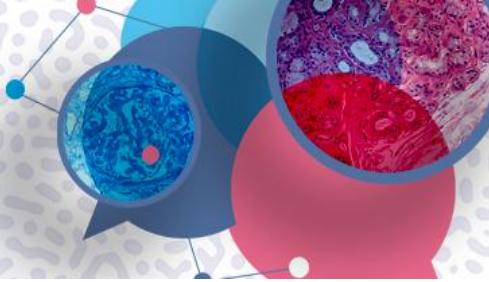


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