1er CONGRÈS FRANCOPHONE MULTIDISCIPLINAIRE DE L'AMYLOSE
2012-2022: retour sur 10 années d'innovations
Vendredi 17 juin 2022
Espace Saint-Martin ■ PARIS
www.congres-amylose.com

Amyloses cardiaques TTR sauvages et héréditaires : traitements

Dr Pauline Fournier

Hôpitaux de Toulouse

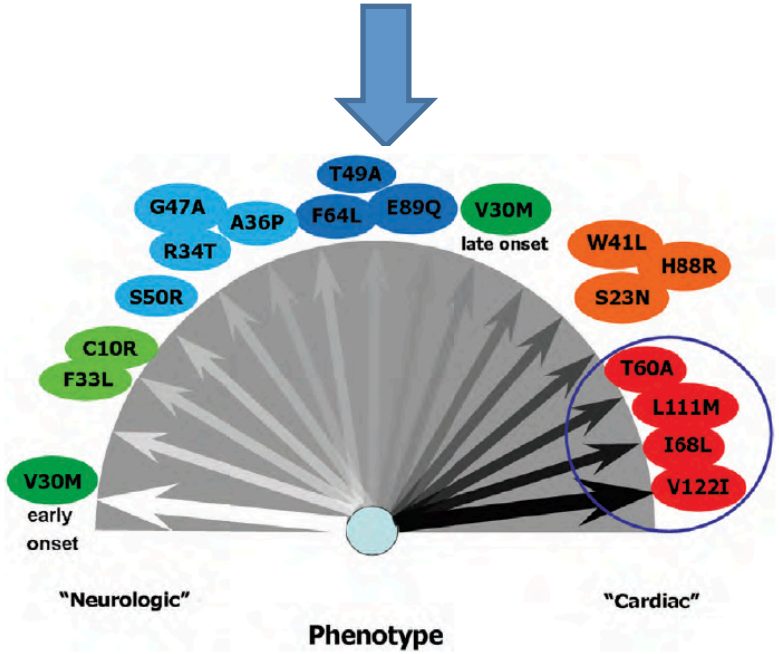
Amylose TTR

ATTR sauvage (ATTRwt)

Forme cardiaque +++

ATTR héréditaire (ATTRv)

Forme neurologique +- atteinte cardiaque



Gertz MA, *J Am Coll Cardiol* 2015;66:2451–66

Objectifs de tout traitement

Traiter les symptômes, les conséquences de la maladie

Stopper ou ralentir la progression de la maladie

Empêcher l'apparition de la maladie

Diagnostic d'amylose TTR cardiaque

Scintigraphie aux diphosphonates

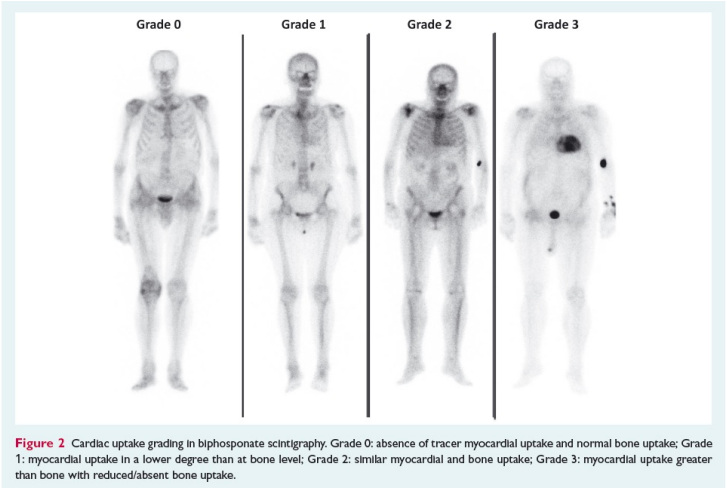
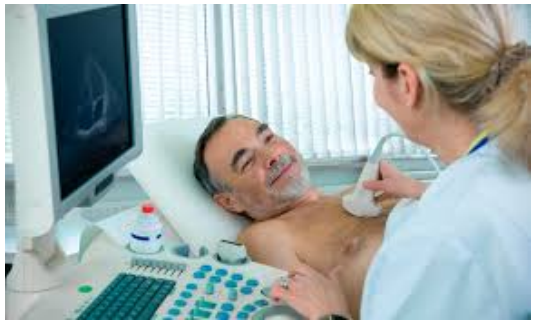
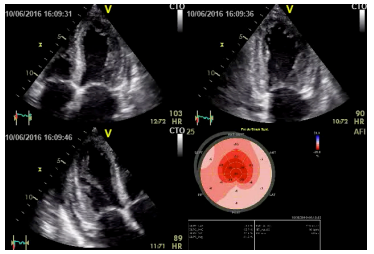


Figure 2 Cardiac uptake grading in biphosponate scintigraphy. Grade 0: absence of tracer myocardial uptake and normal bone uptake; Grade 1: myocardial uptake in a lower degree than at bone level; Grade 2: similar myocardial and bone uptake; Grade 3: myocardial uptake greater than bone with reduced/absent bone uptake.





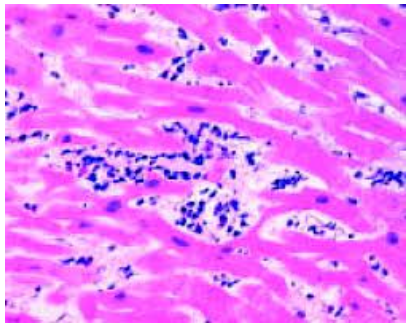
IRM

Analyse génétique

ESC European Society of Cardiology
European Journal of Heart Failure (2021) 23, 512–526
doi:10.1002/ejhf.2140
POSITION PAPER

Diagnosis and treatment of cardiac amyloidosis. A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases

Biopsie des glandes salivaires

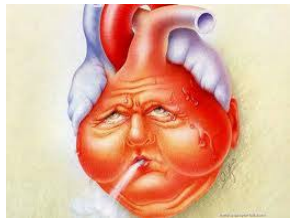


Biopsie cardiaque

Il y a 10 ans : pas de traitement spécifique de l'amylose TTR cardiaque

TTT des symptômes:

- Diurétiques pour insuffisance cardiaque: essoufflement, œdèmes, fatigues
- Restriction Hydrique
- Anticoagulation dans certains cas
- Pace maker dans certains cas



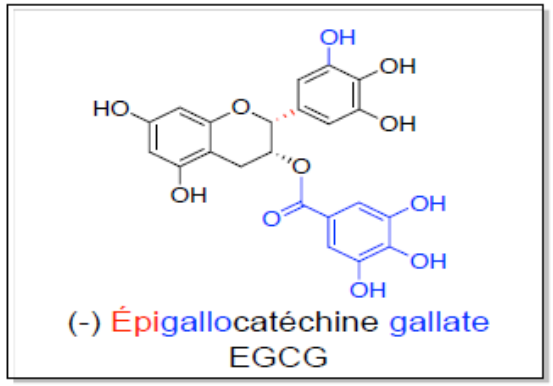
Eviter certains traitements:

- Eviter de trop ralentir le cœur
- Eviter des malaises hypotensifs

Proposer dépistage à la famille pour TTR héréditaire

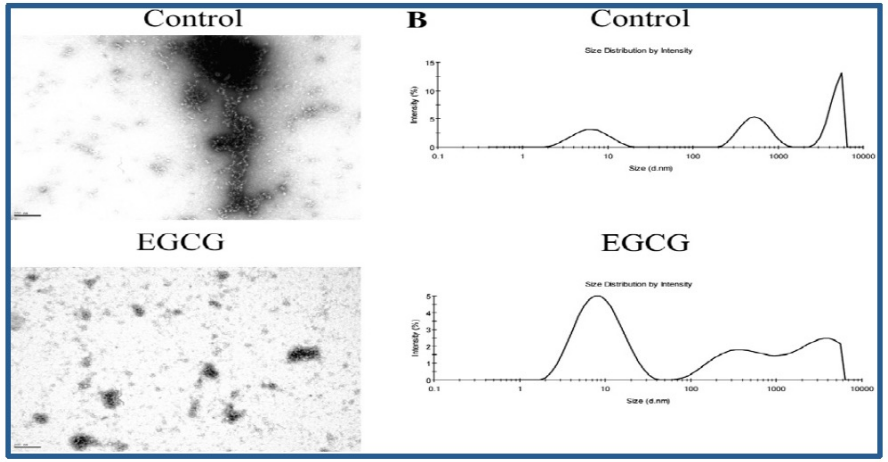
Au cas par cas: transplantation hépatique et transplantation cardiaque

Les débuts : thé vert (Camellia sinensis)



(-) Épigallocatéchine gallate
EGCG

Transformation des fibrilles préformées en petits agrégats de protéines amorphes non toxiques



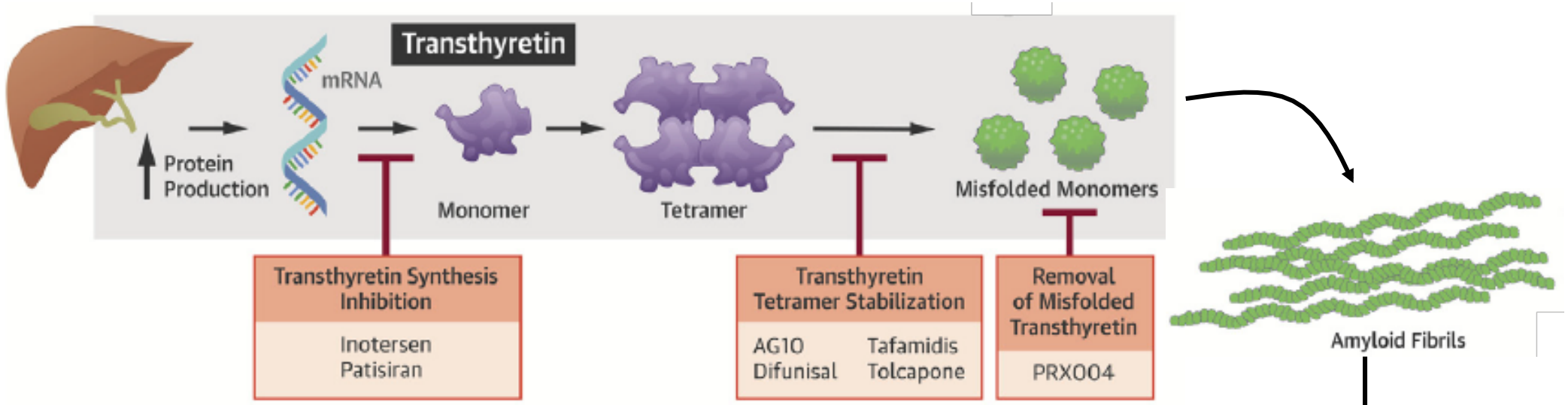
Feirera et al, FEBS Letters 585 (2011) 2424-2430

Infusion
Extraction
Concentration
Séchage

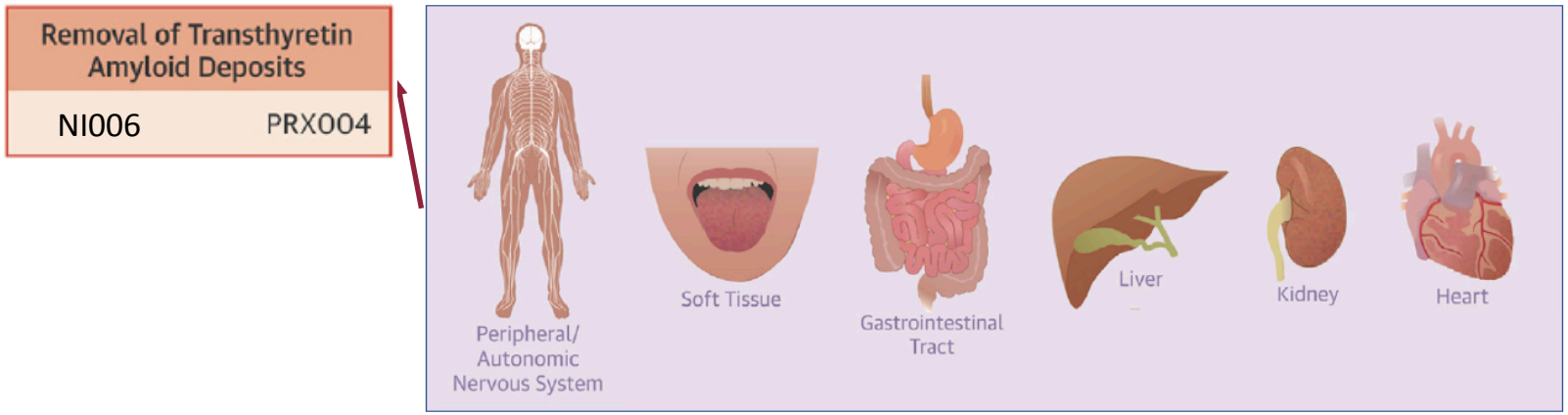
Gélules, compléments alimentaires, infusions

Mais:
1/ Teneurs très variables en EGCG
2/ Biodisponibilité médiocre par voie orale
3/ Dégradation chimique

Efficacité clinique?

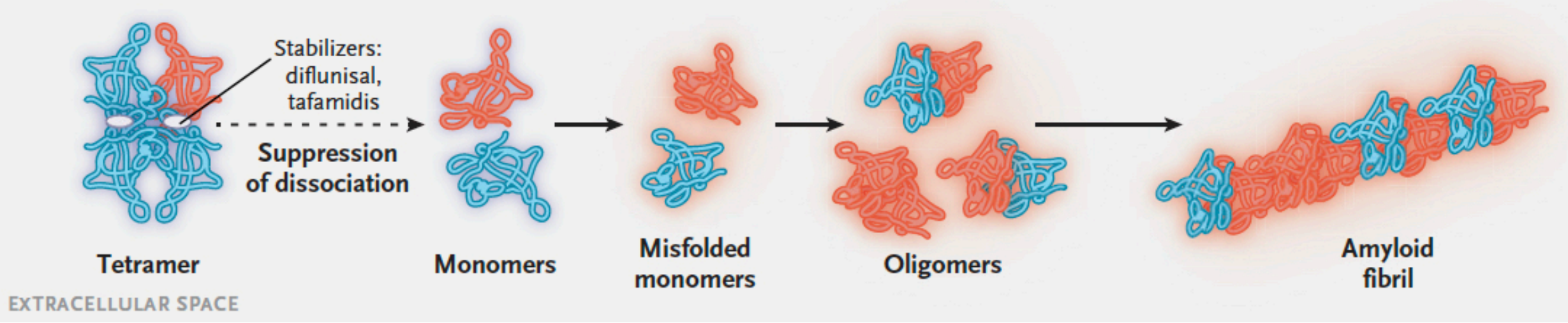


2018-2022:
L'heure des traitements spécifiques



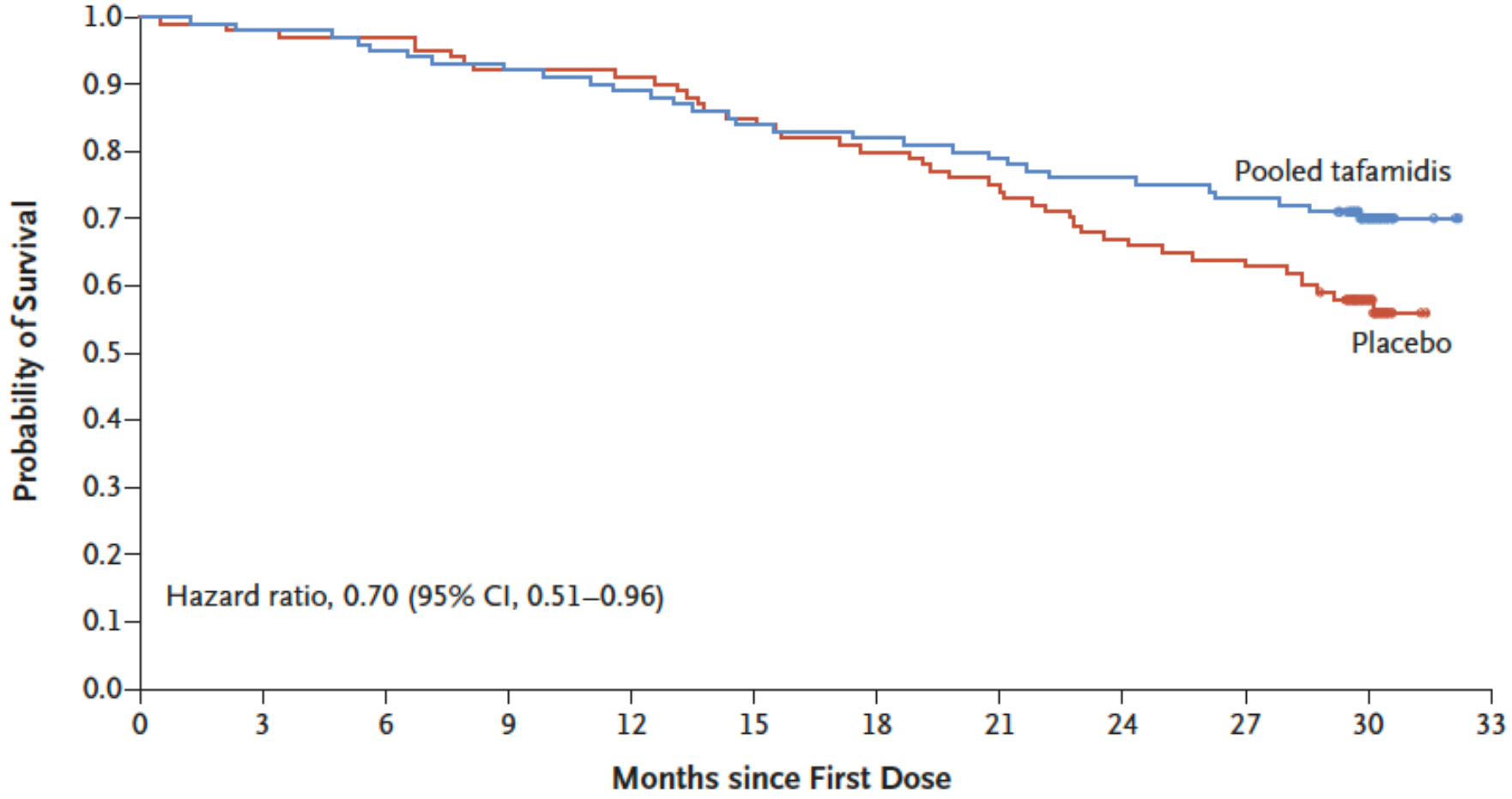
Zhang KW, et al. *JACC Basic Transl Sci.* 2019;4:438-448

TAFAMIDIS



Buxaum JN. *N Engl J Med* 2018;379:208

Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy



Maurer MS, *N Engl J Med*. 2018;379:1007-1016

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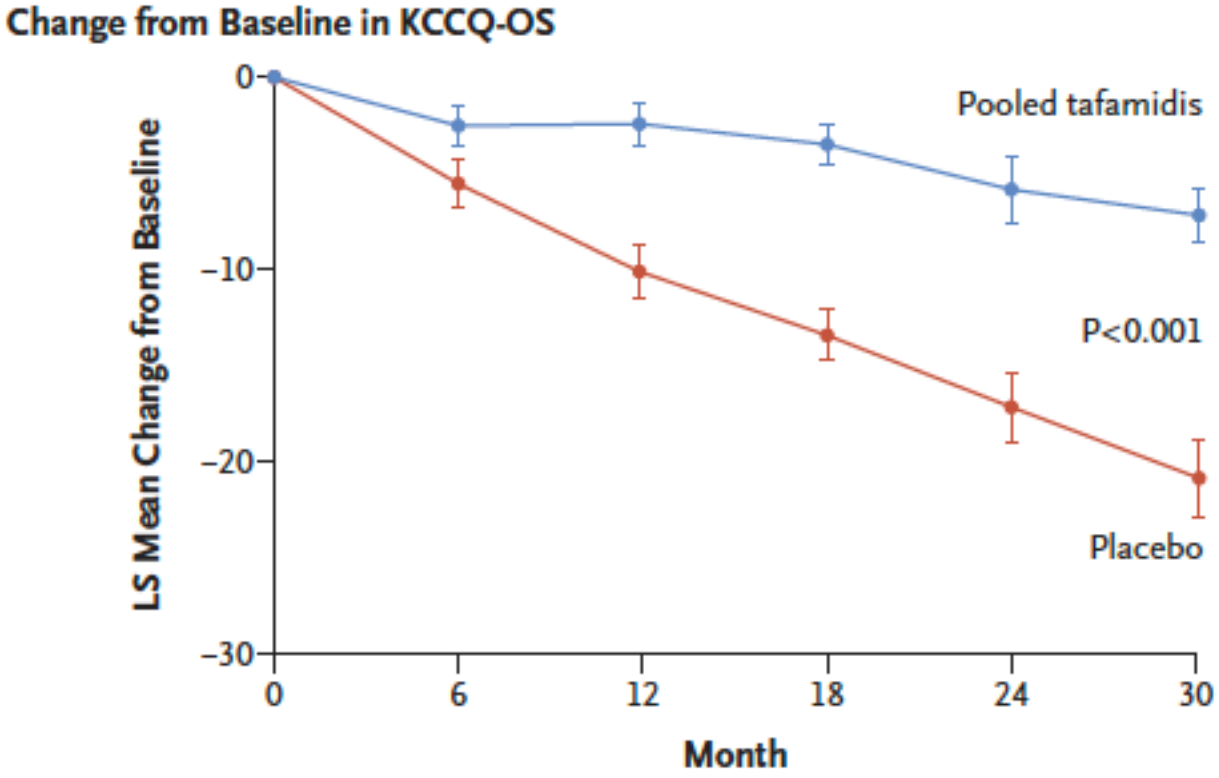
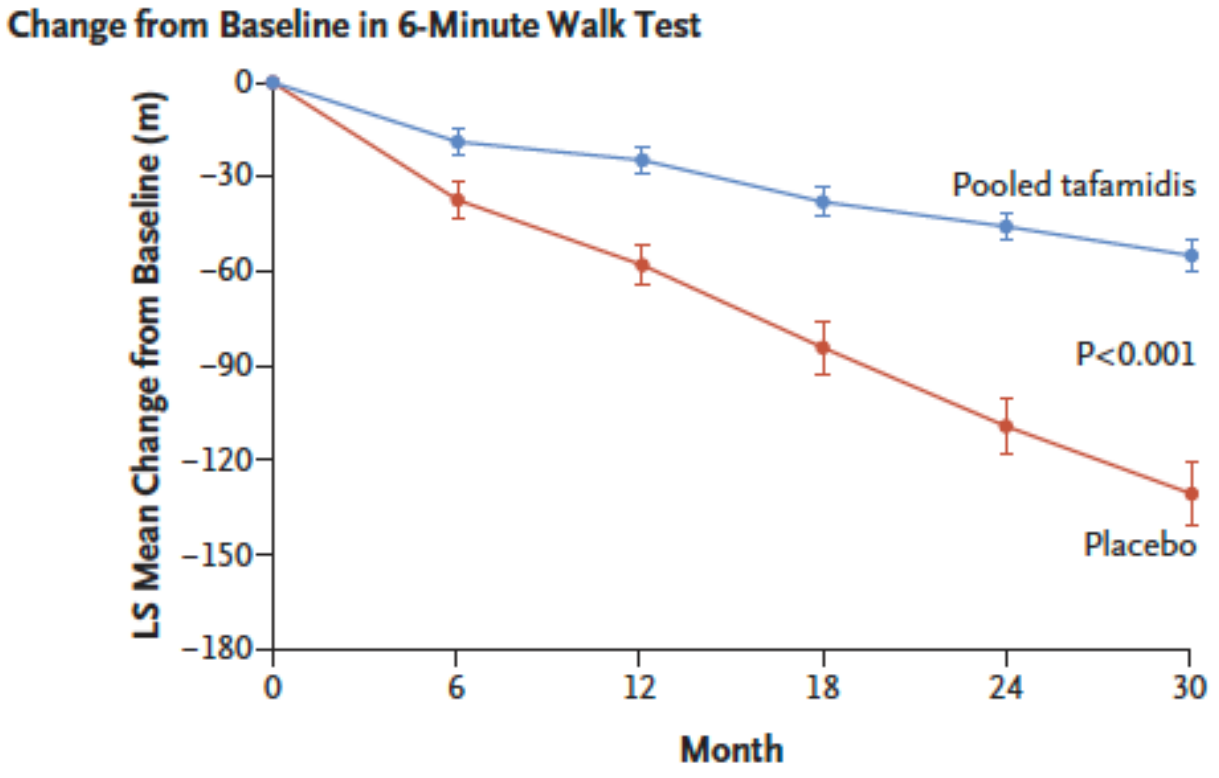
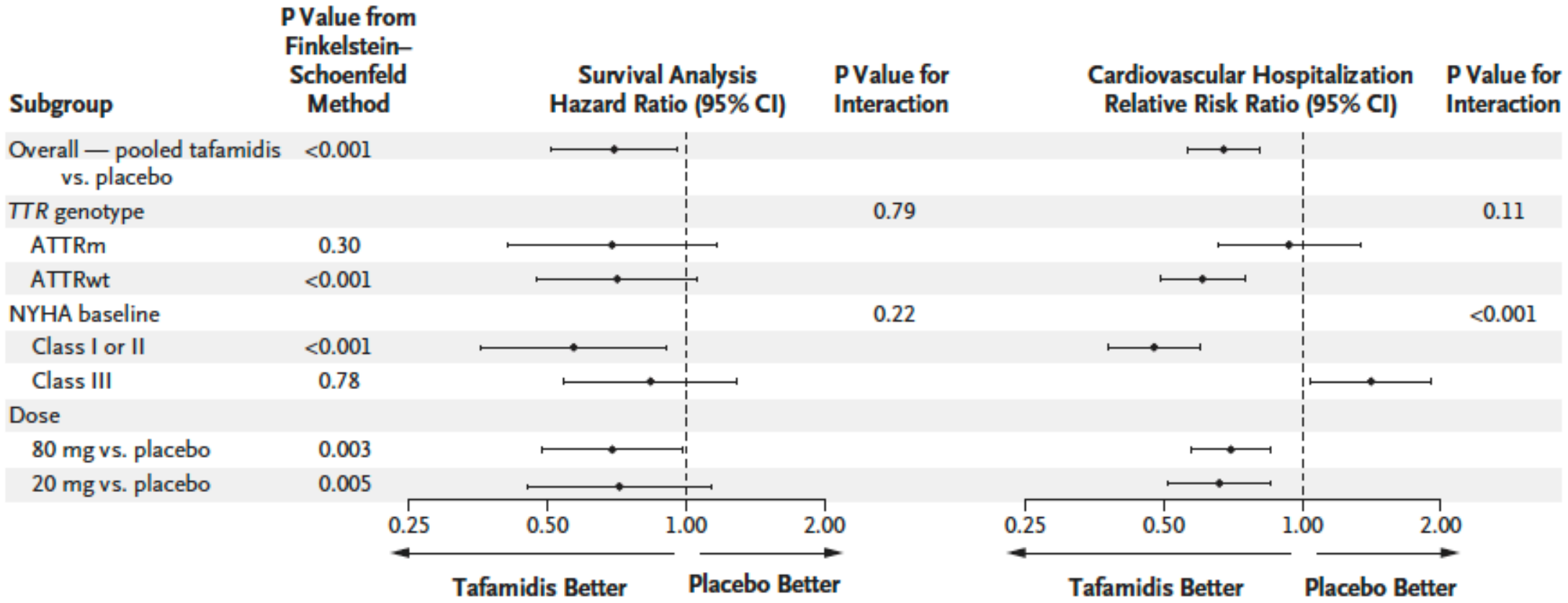




Maurer MS, *N Engl J Med*. 2018;379:1007-1016

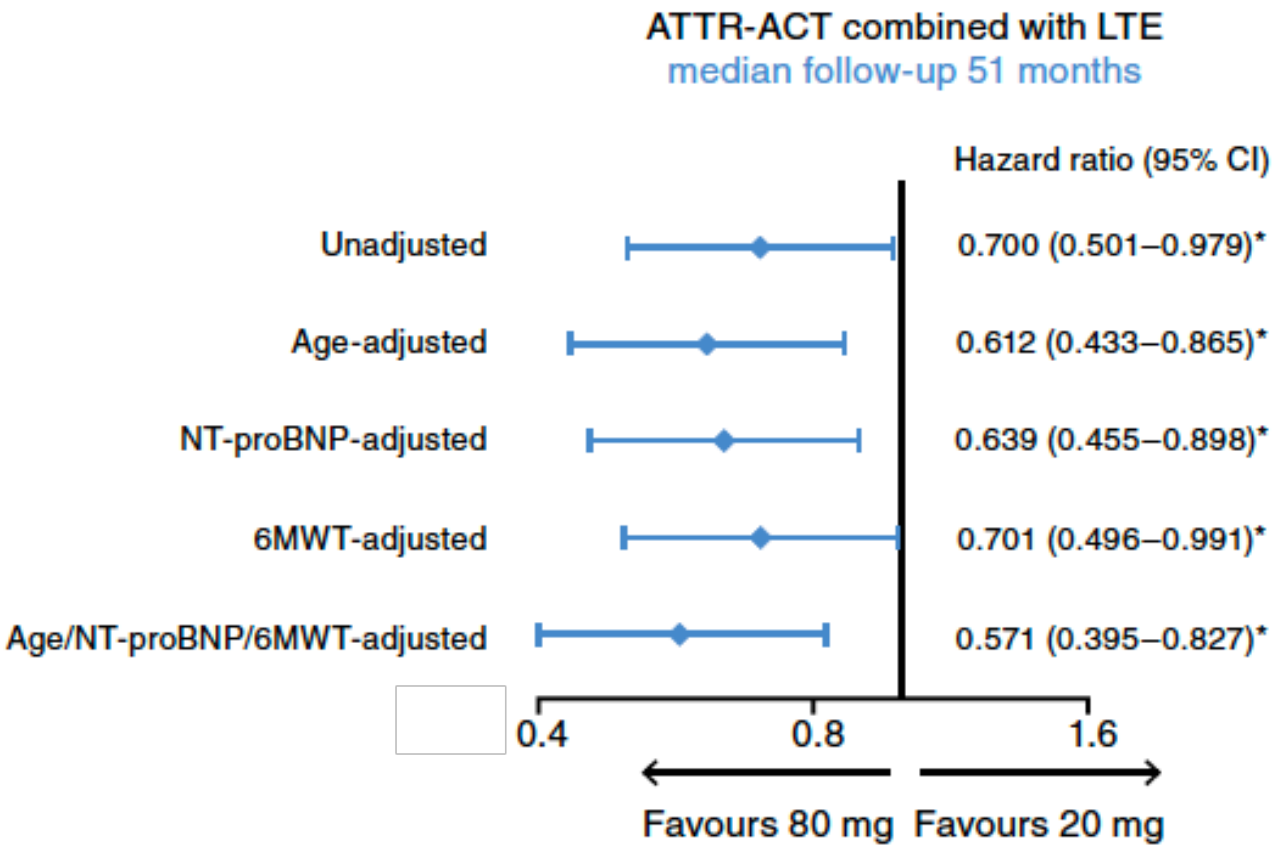
Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy

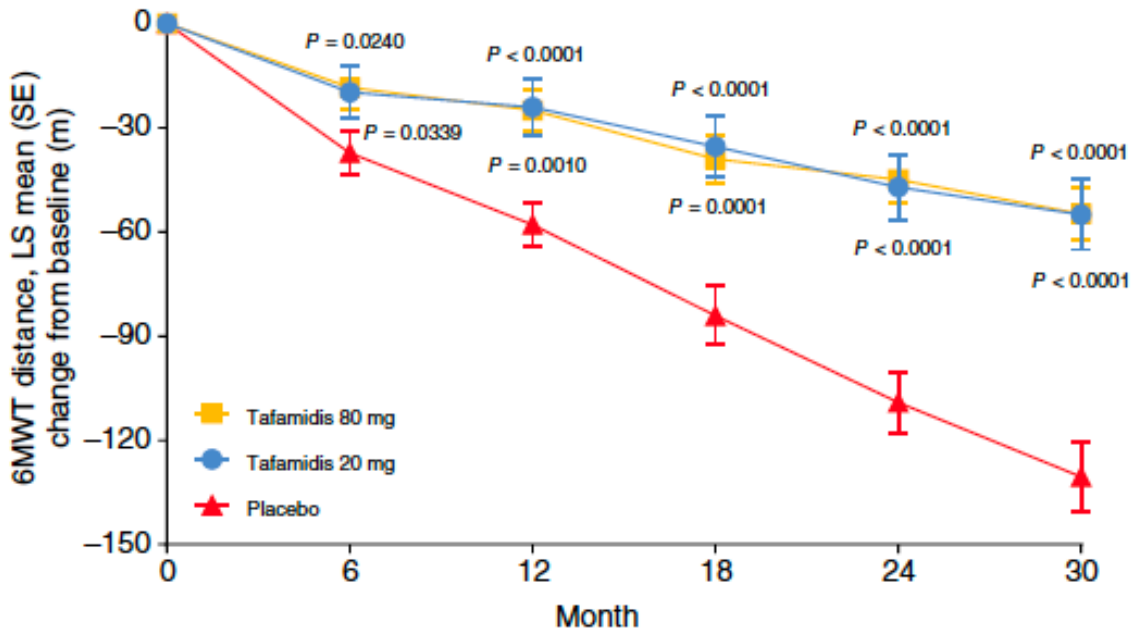


Maurer MS, *N Engl J Med*. 2018;379:1007-1016

Efficacy and safety of tafamidis doses in the Tafamidis in Transthyretin Cardiomyopathy Clinical Trial (ATTR-ACT) and long-term extension study

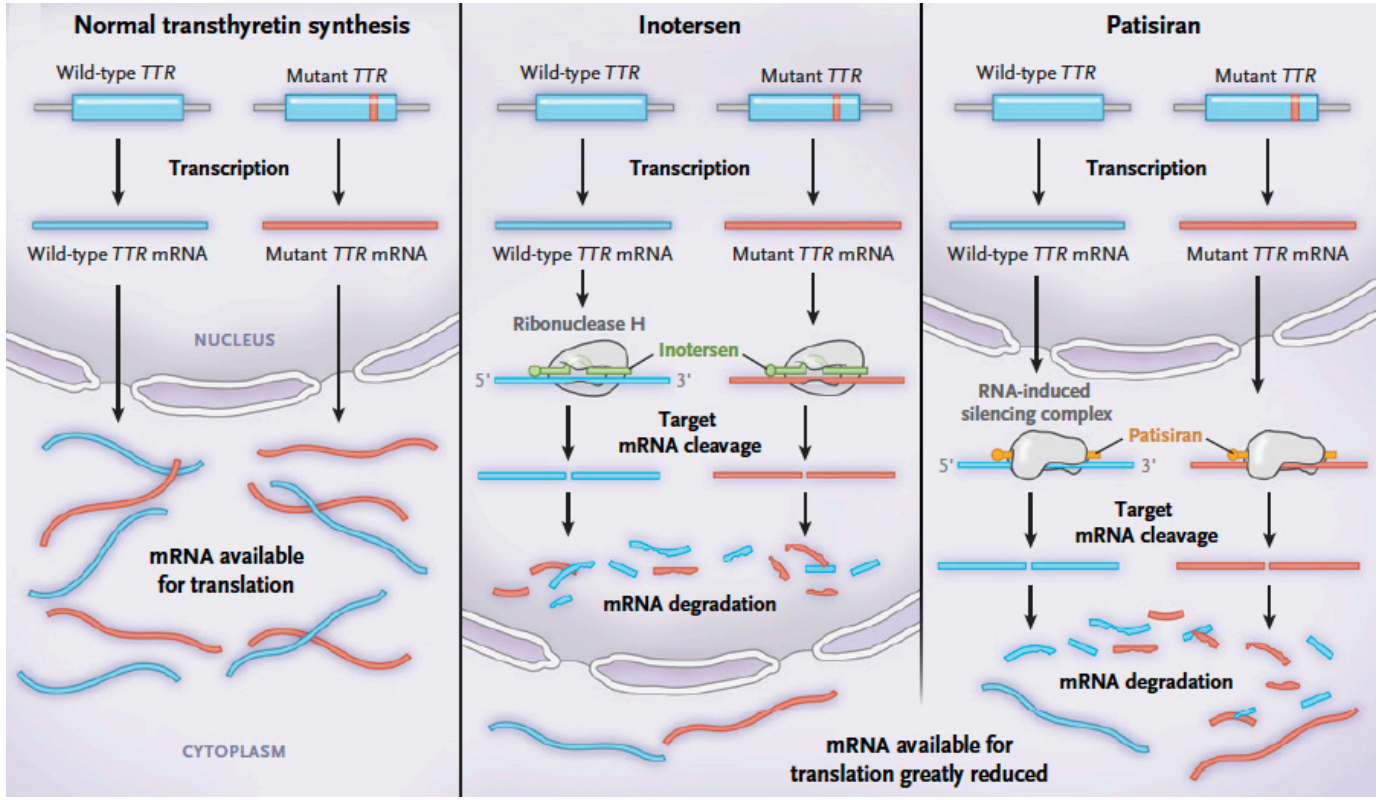
Mortalité totale



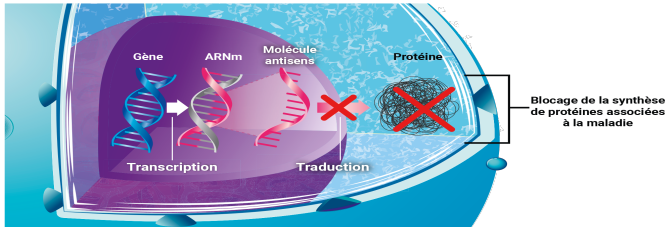


Damy T, et al. *Eur J Heart Fail.* 2021;23:277-285

OLIGONUCLÉOTIDES



Modèle « anti-sens »



La molécule agit **avant** la synthèse de la protéine.

Buxaum JN. *N Engl J Med* 2018;379:208

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis

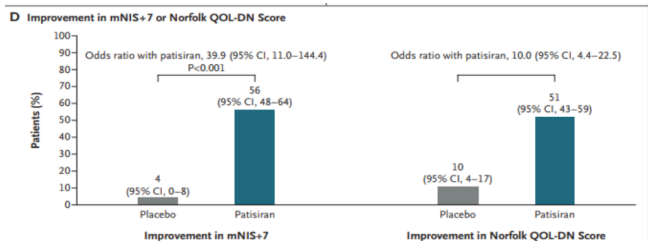
M.D. Benson, M. Waddington-Cruz, J.L. Berk, M. Polydefkis, P.J. Dyck, A.K. Wang, V. Planté-Bordeneuve, F.A. Barroso, G. Merlini, L. Obici, M. Scheinberg, T.H. Brannagan III, W.J. Litchy, C. Whelan, B.M. Drachman, D. Adams, S.B. Heitner, I. Conceição, H.H. Schmidt, G. Vita, J.M. Campistol, J. Gamez, P.D. Gorevic, E. Gane, A.M. Shah, S.D. Solomon, B.P. Monia, S.G. Hughes, T.J. Kwoh, B.W. McEvoy, S.W. Jung, B.F. Baker, E.J. Ackermann, M.A. Gertz, and T. Coelho

mNIS+7: - 19,7
NORFOLK-QOL-DN Score: -11,7

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JULY 5, 2018 VOL. 379 NO. 1

Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis

D. Adams, A. Gonzalez-Duarte, W.D. O'Riordan, C.-C. Yang, M. Ueda, A.V. Kristen, I. Tournev, H.H. Schmidt, T. Coelho, J.L. Berk, K.-P. Lin, G. Vita, S. Attarian, V. Planté-Bordeneuve, M.M. Mezei, J.M. Campistol, J. Buades, T.H. Brannagan III, B.J. Kim, J. Oh, Y. Parman, Y. Sekijima, P.N. Hawkins, S.D. Solomon, M. Polydefkis, P.J. Dyck, P.J. Gandhi, S. Goyal, J. Chen, A.L. Strahs, S.V. Nochur, M.T. Sweetser, P.P. Garg, A.K. Vaishnaw, J.A. Gollob, and O.B. Suhr



Traitements indiqués dans formes neurologiques de l'amylose TTR héréditiare

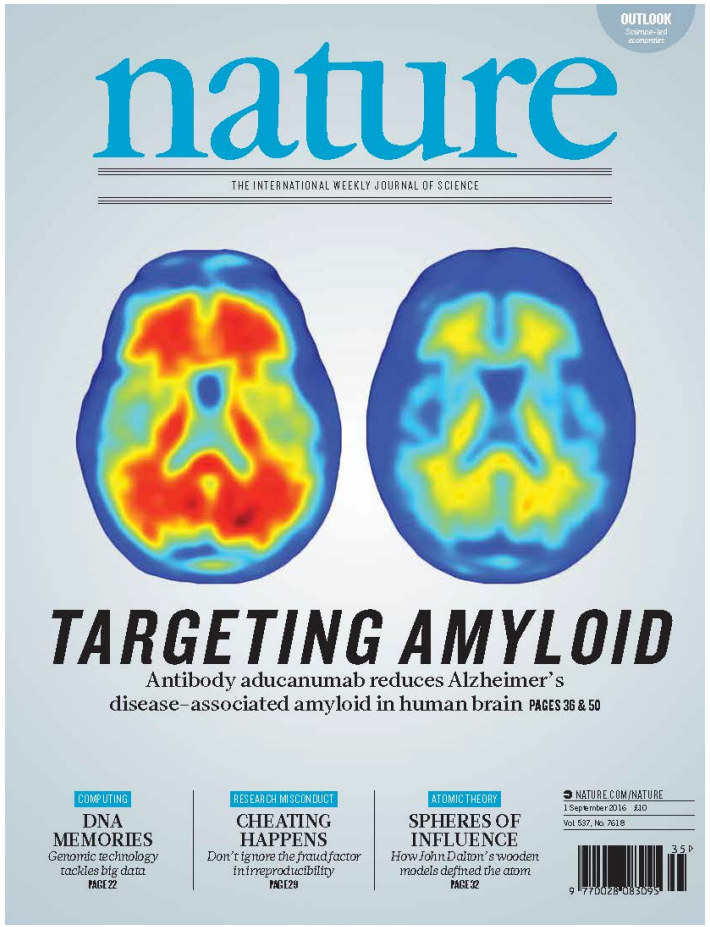
Etudes en cours pour application aux formes cardiaques des amylose TTR sauvages et héréditaires

APPOLO B

HELIOS B

IONIS

Anticorps monoclonaux contre fibrilles amyloïdes TTR



PRX004

Anticorps monoclonal anti-transthyrétine

A Study of PRX004 in Subjects With Amyloid Transthyretin (ATTR) Amyloidosis

ClinicalTrials.gov Identifier: NCT03336580

Recruitment Status : Terminated (Because of the impact of COVID-19 pandemic)
First Posted : November 8, 2017
Last Update Posted : August 20, 2020

NI006

Anticorps monoclonal anti-transthyrétine

First-in-Human Study of NI006 in Patients With Amyloid Transthyretin Cardiomyopathy

ClinicalTrials.gov Identifier: NCT04360434

Recruitment Status : Recruiting
First Posted : April 24, 2020
Last Update Posted : August 10, 2021

Sevigny J, et al. *Nature.* 2016;537:50-6

www.clinicaltrials.gov

2012

Traiter les symptômes, les conséquences de la maladie21

2018

Stopper ou ralentir la progression de la maladie

2022

Empêcher l'apparition de la maladie?

Diurétiques, Pace Maker, Anticoagulation, restrictions hydriques…

Tafamidis, Inotersen et Patisiran (formes neuros, en étude formes cardio)

Anticorps? Nouvelles thérapeutiques?

Scintigraphies osseuses pour le diagnostic d'amylose par an