L'immunothérapie ATTR

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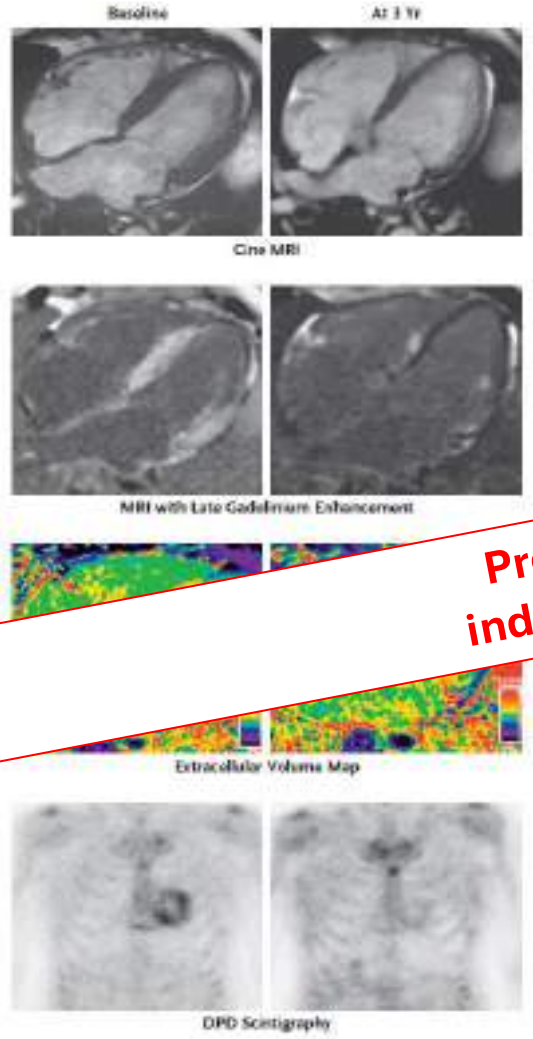
Liens d'intérêts

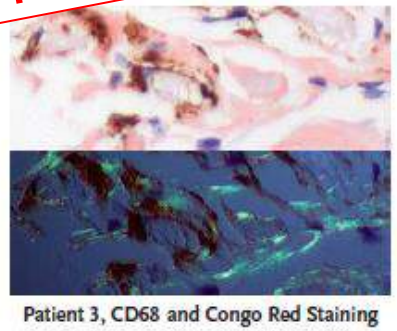
- Astra Zeneca
- Alnylam
- Bayer
- Pfizer

Trois histoires naturelles inhabituelles d'amylose TTR



Un des 3 patients
avait eu une biopsie myocardique

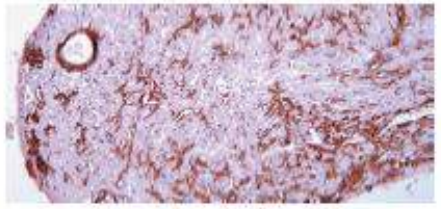
et Lymphocytes CD3



Cellule géante multinucléée phagocytant des dépots amyloïdes

**Présence d'auto-anticorps circulants IgG « anti-amylose TTR »
induisant une déplétion de la charge amyloïde dans le myocarde**

Les sérums réagissent en présence d'amylose TTR humaine exprimée sur un modèle murin transgénique et sont marqués par un anticorps anti-IgG humaine



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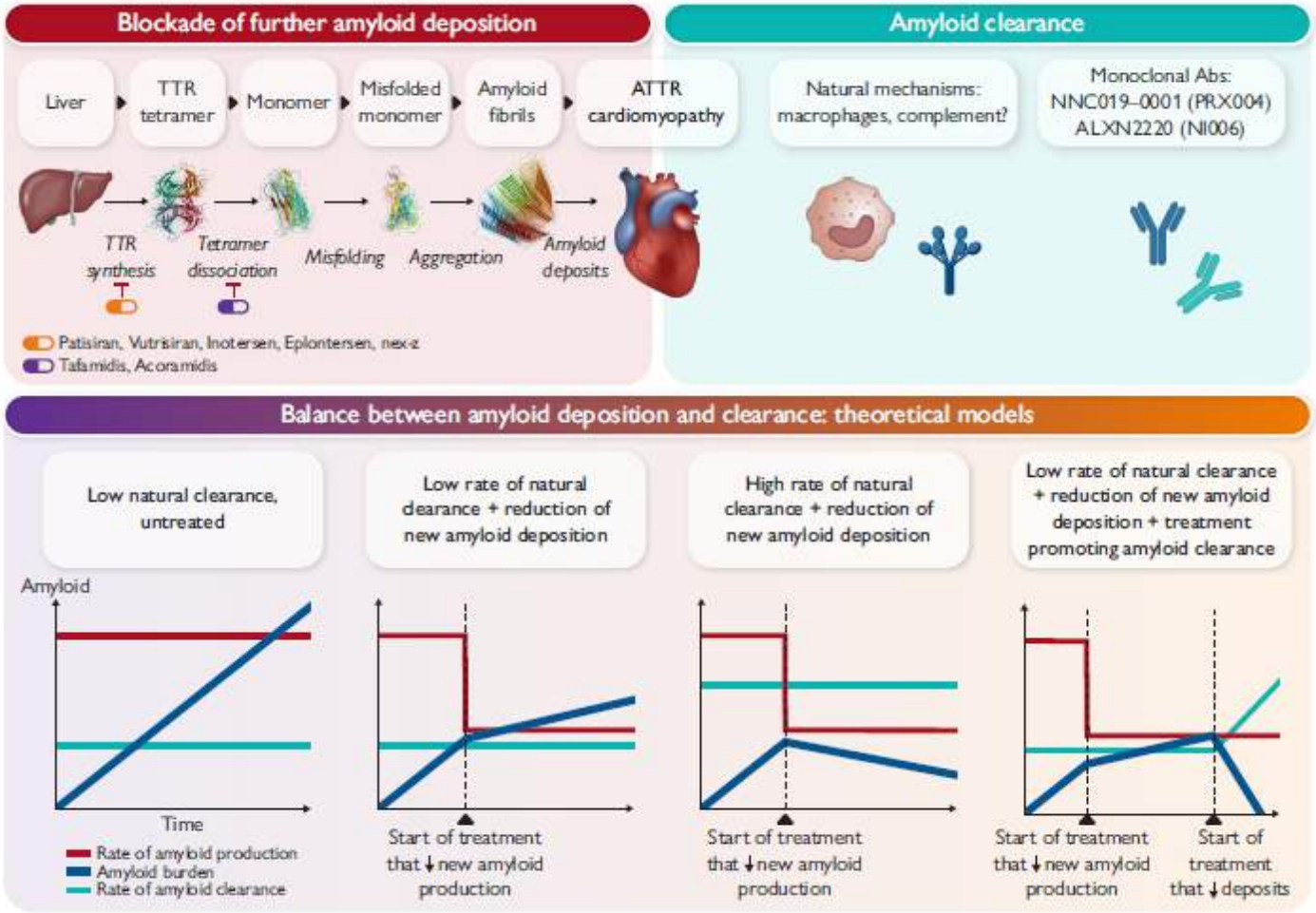
En faire une immunothérapie déplétrice de la charge amyloïde TTR ?



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Characteristic	NI006 (N = 27)	Placebo (N = 13)
Median age (IQR) — yr	74 (70–77)	68 (67–74)
Sex — no. (%) Male Female	 26 (96) 1 (4)	 13 (100) 0
Transthyretin genotype — no. (%) Variant Wild-type	 4 (15) 23 (85)	 3 (23) 10 (77)
Median NT-proBNP (IQR) — pg/ml	2029 (1433–3674)	1591 (1310–2107)

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NI006 Safety

Adverse Event	NI006, 0.3 mg/kg (N=4)	NI006, 1 mg/kg (N=4)	NI006, 3 mg/kg (N=4)	NI006, 10 mg/kg (N=5)	NI006, 30 mg/kg (N=5)	NI006, 60 mg/kg (N=5)	Placebo (N=13)
Any adverse event							
No. of patients (%)	4 (100)	4 (100)	3 (75)	5 (100)	5 (100)	5 (100)	11 (85)
No. of events	24	14	22	30	37	25	39
Severe adverse event, grade 3							
No. of patients (%)	1 (25)	2 (50)	0	1 (20)	1 (20)	0	2 (15)
No. of events	1	2	0	1	1	0	2
Serious adverse event							
No. of patients (%)	1 (25)	3 (75)	0	1 (20)	1 (20)	0	3 (23)
No. of events	1	3	0	3	1	0	3
Drug-related adverse event							
No. of patients (%)	0	1 (25)	1 (25)	1 (20)	2 (40)	1 (20)	0
No. of events	0	1	2	5	13	4	0
Adverse event leading to temporary discontinuation of NI006 or placebo — no. (%)	0	0	0	0	0	0	1 (8)
Adverse event leading to withdrawal from the trial							
Any — no. (%)	0	0	0	2 (40)	1 (20)	1 (20)	0
Coronavirus disease 2019 — no.	0	0	0	1	1	0	0
Arthralgias — no.	0	0	0	1	0	0	0
Thrombocytopenia — no.	0	0	0	0	0	1	0

HF and arrhythmias

Cytokine release syndrome
Arthralgias-arthritis

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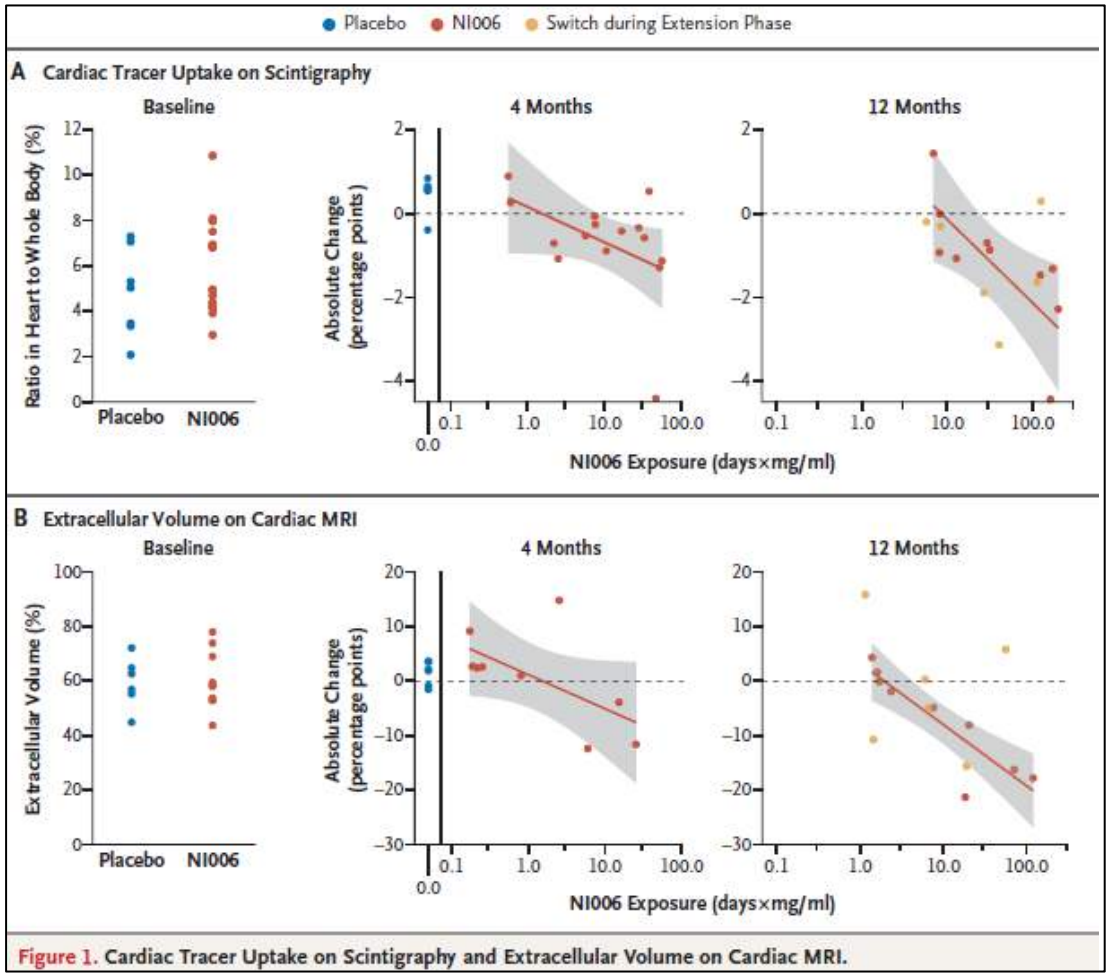
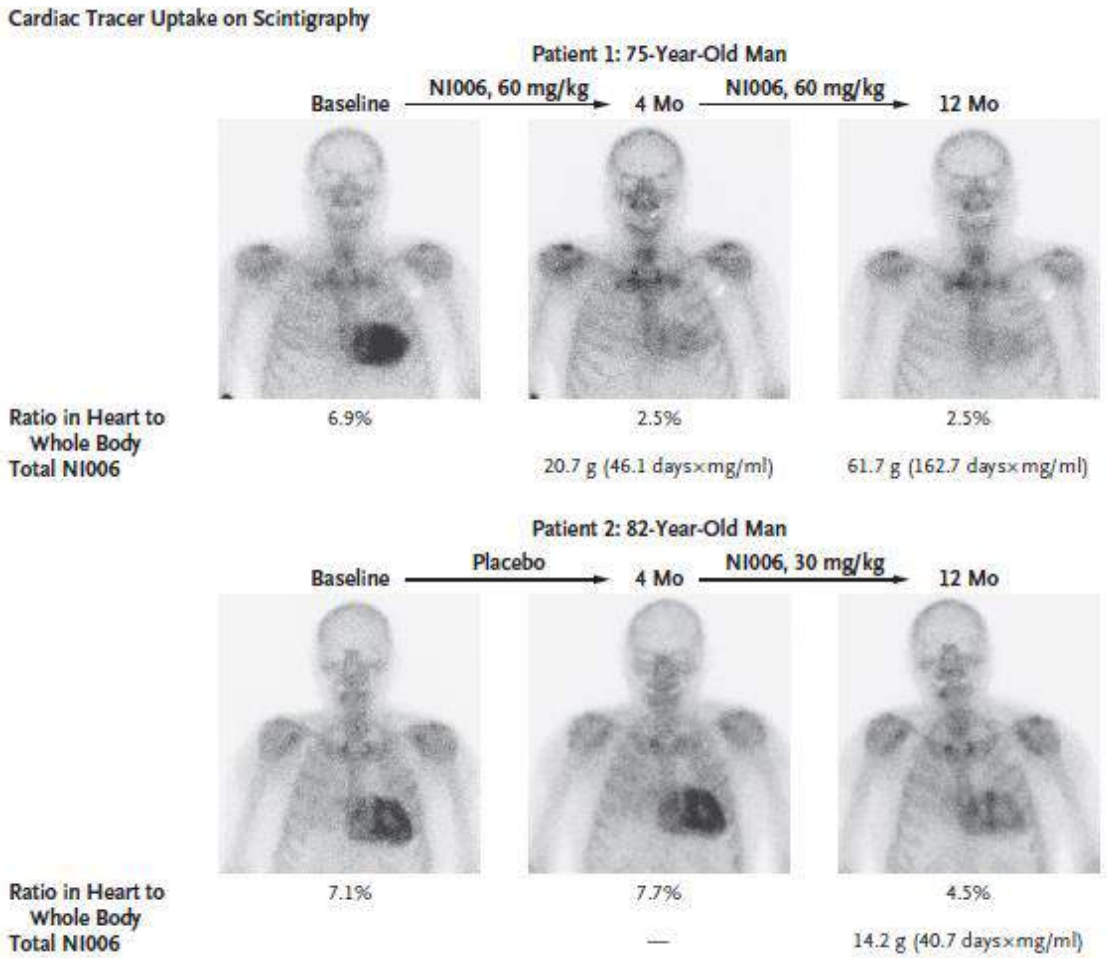


Figure 1. Cardiac Tracer Uptake on Scintigraphy and Extracellular Volume on Cardiac MRI.



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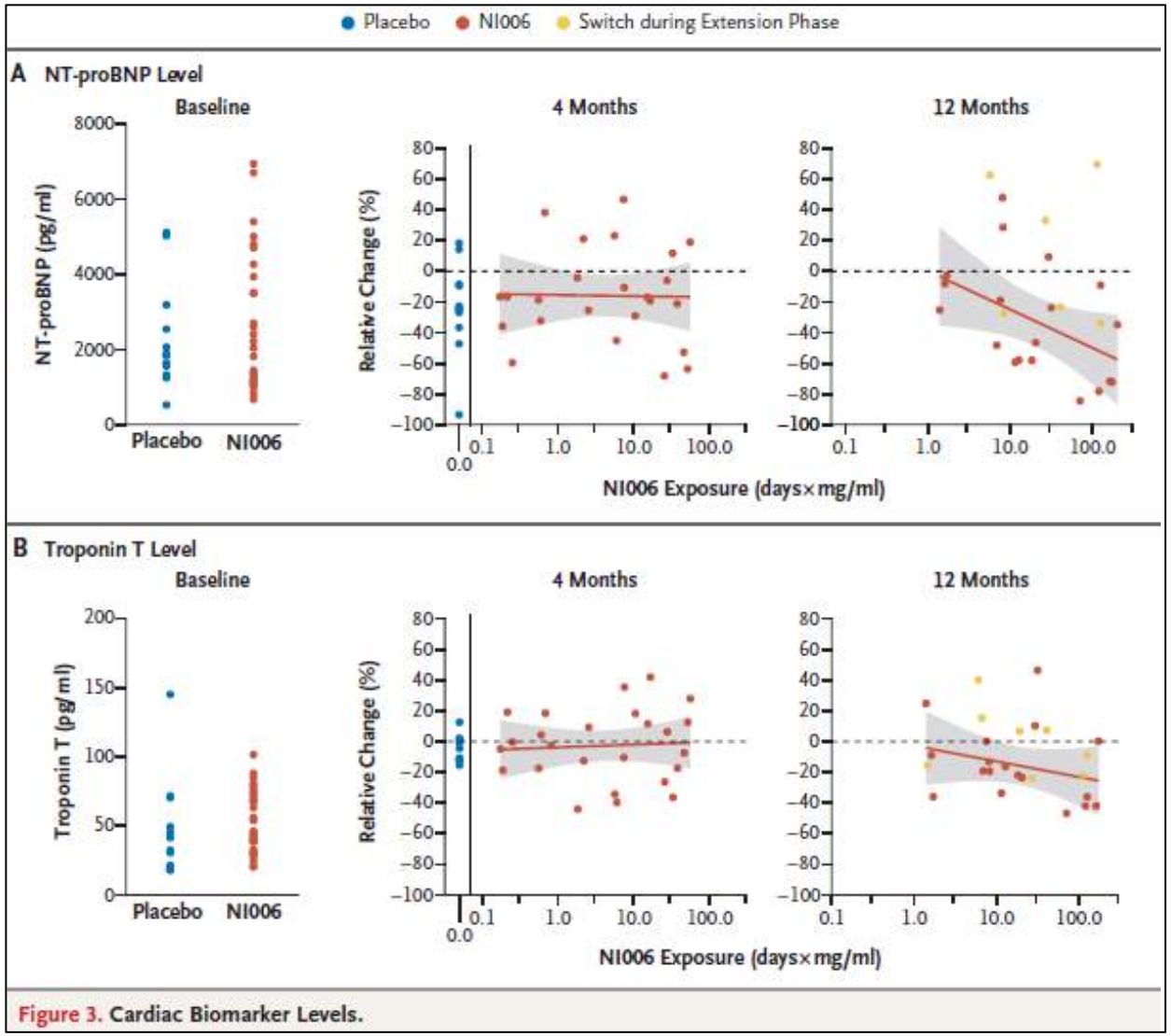

Figure 3. Cardiac Biomarker Levels.

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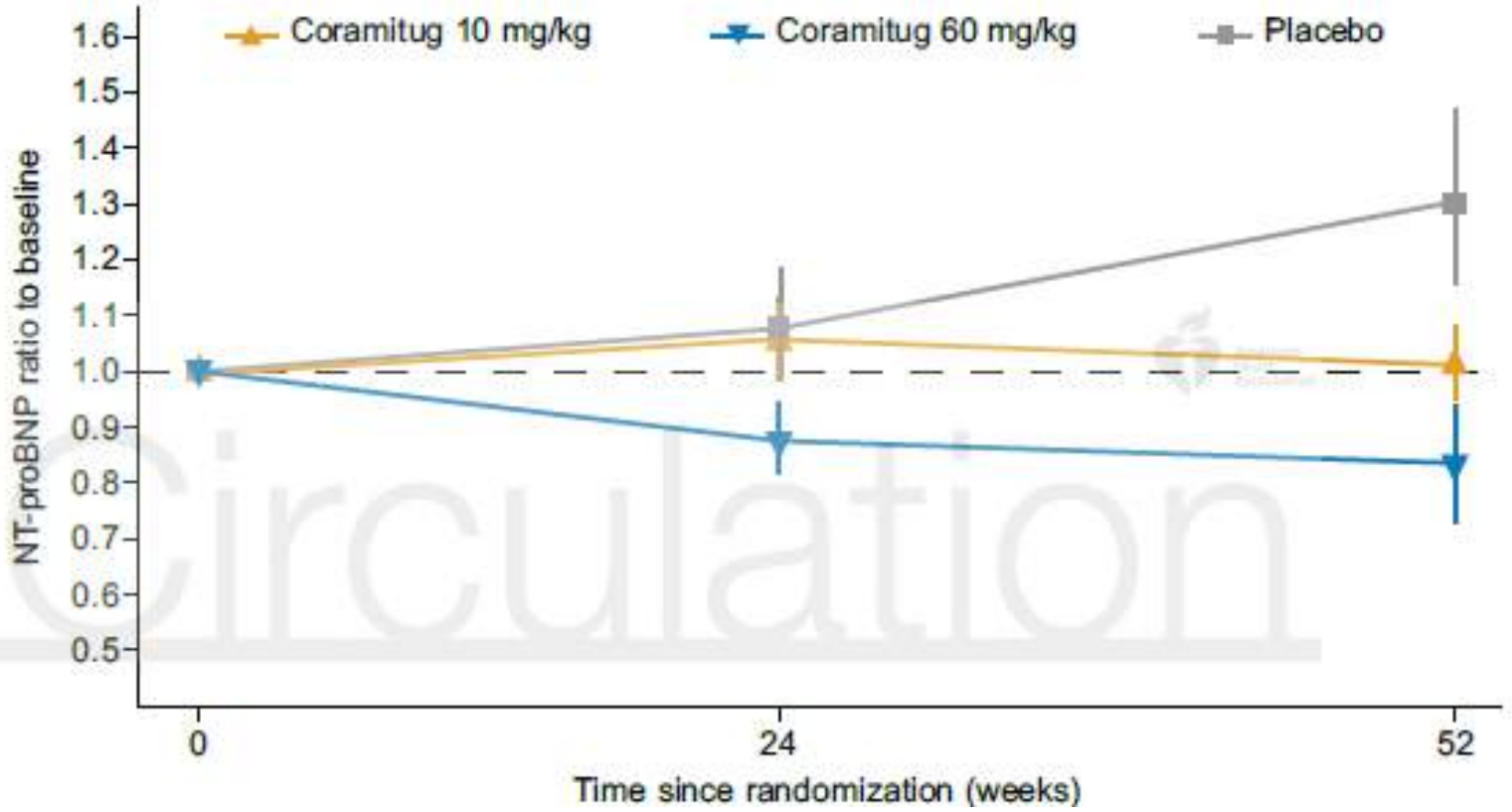
Coramitug (phase 2)



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

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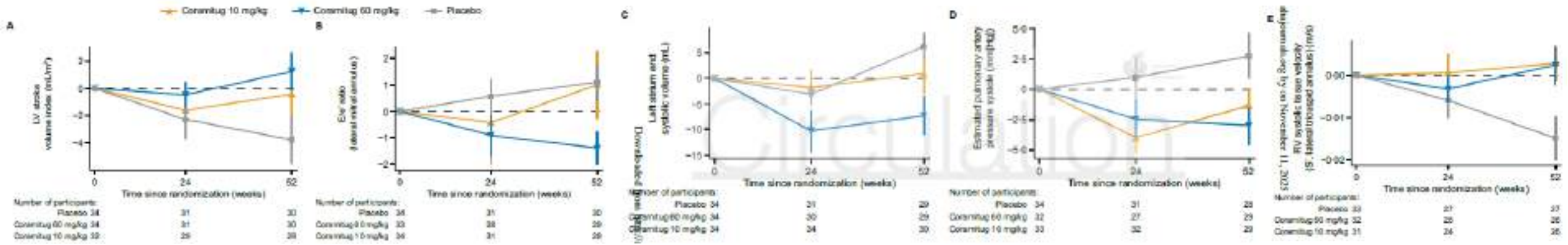

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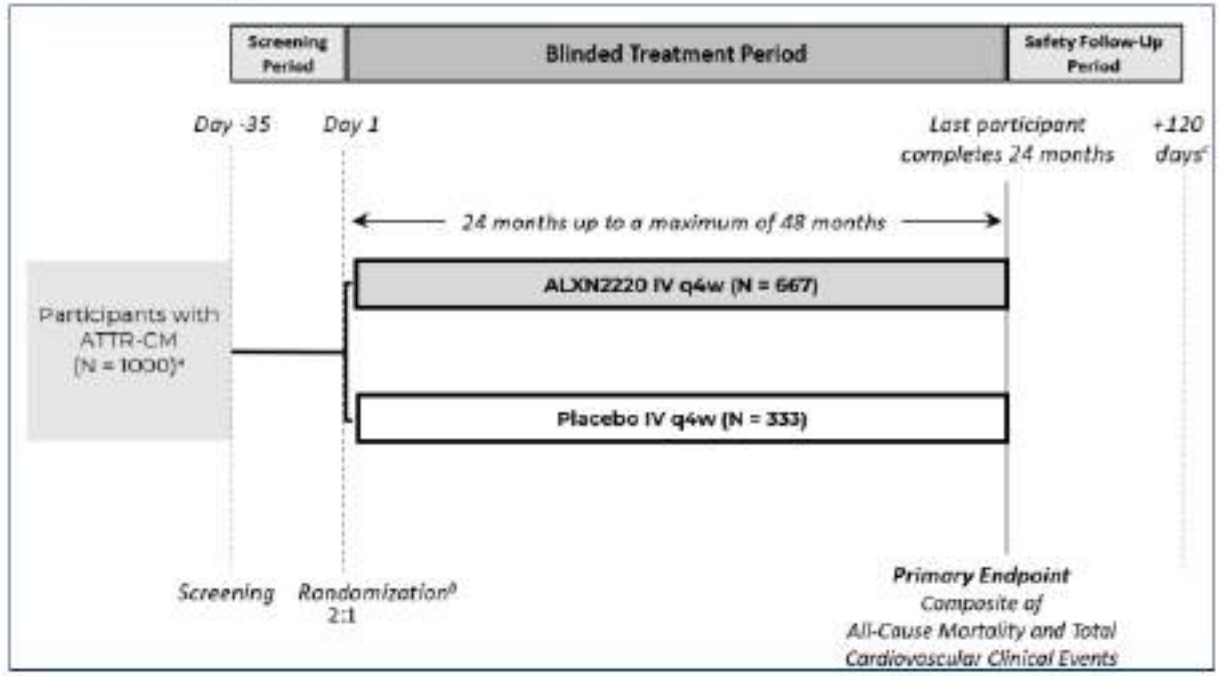
L'ère des Phase 3

DepleTTR-CM Study

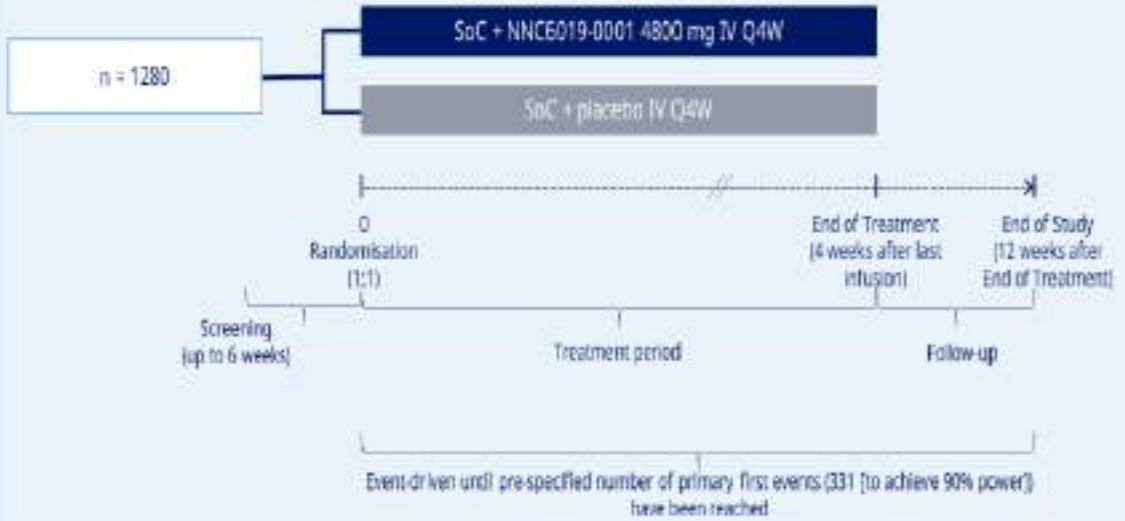


Primary objective

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)

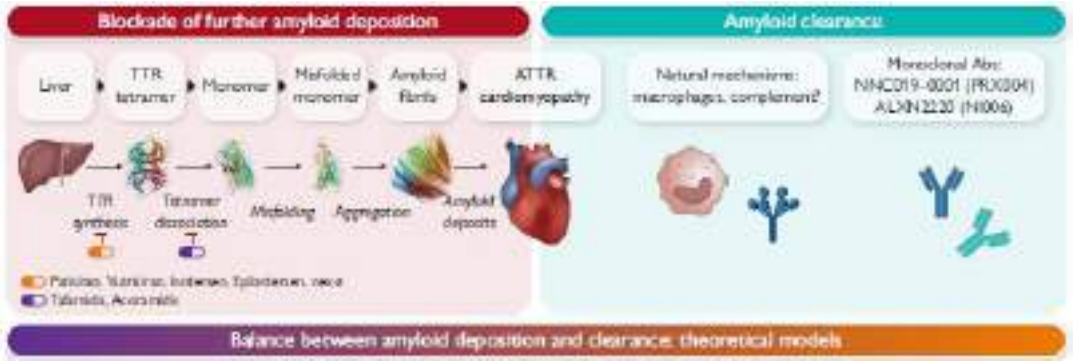
Acronym: CLEOPATTRA

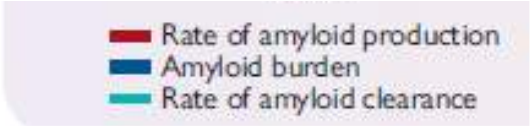
Short Title: CLEOPATTRA: A research study to look at the effects of treatment with a medicine called coramitug (NNC6019-0001) in people with heart failure due to ATTR amyloidosis.

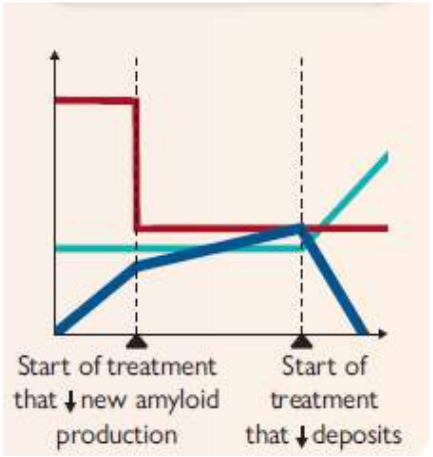


Objectives	Endpoints	
Primary	Title	Time frame
To demonstrate superiority of NNC6019-0001 versus placebo, both added to SoC [a], in reducing the CV death & morbidity in participants with ATTRwt-CM or ATTRv-CM	Primary:	
	The composite outcome of: • CV death [b] • Recurrent CV events (CV hospitalisation [b,c] and urgent HF visits [b])	From baseline (week 0) up to EOS [d]

Puis l'ère des combinaisons silenceurs - Ac dépléteurs ?

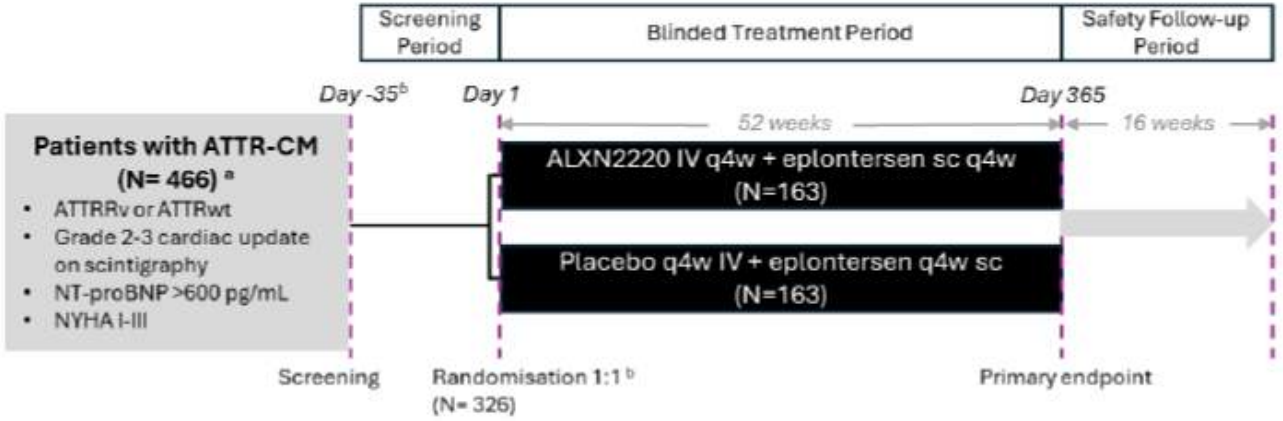






A Phase 2b, Randomized, Double-blind, Active-controlled, Multicenter Study to Evaluate the Efficacy and Safety of Eplontersen and ALXN2220 Compared to Eplontersen and Placebo in Adult Participants with Transthyretin-Mediated Amyloid Cardiomyopathy (ATTR-CM)

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



L'immunothérapie ATTR

- Un formidable espoir de réverser la charge amyloïde au sein de l'organe (cœur, autres organes cibles ?)
- A confirmer dans les études de phase 3 en cours
- Quelle place dans la stratégie thérapeutique ? Combinaison ? Usage séquentiel Dépléteur – silenceur/stabilisateur ?