



B- dans l'amylose : POUR

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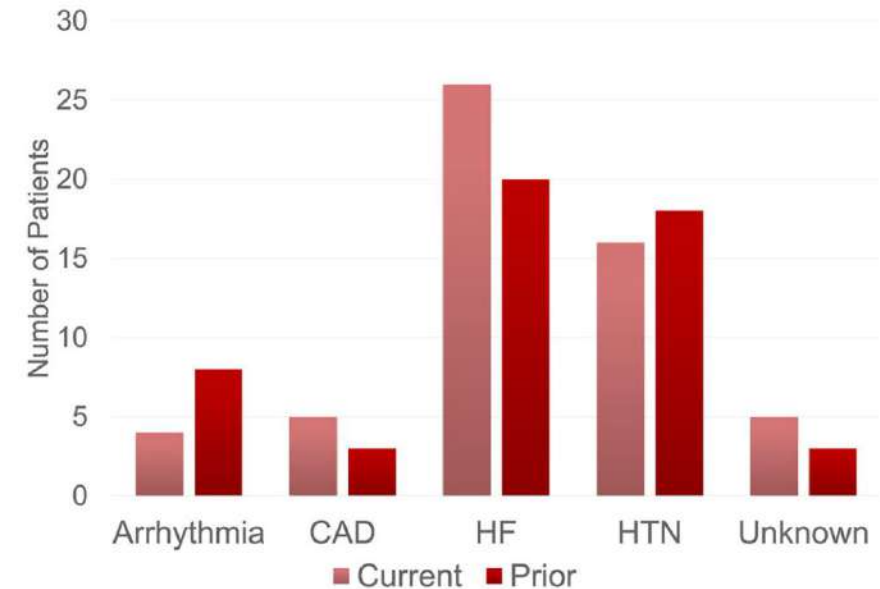
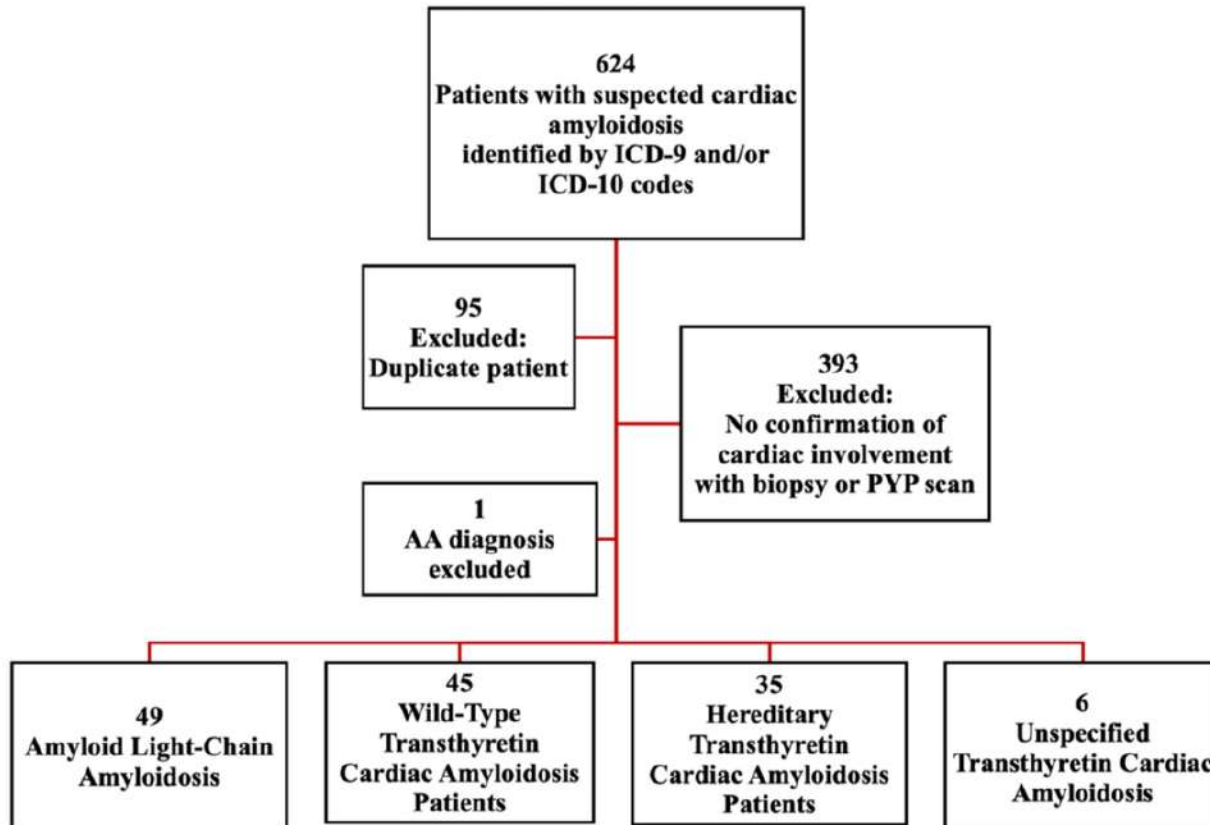


Déclaration de lien d'intérêts

- Novartis
- Pfizer
- Astra Zenecca
- Boehringer
- Servier
- Microport
- Medtronic
- Isis



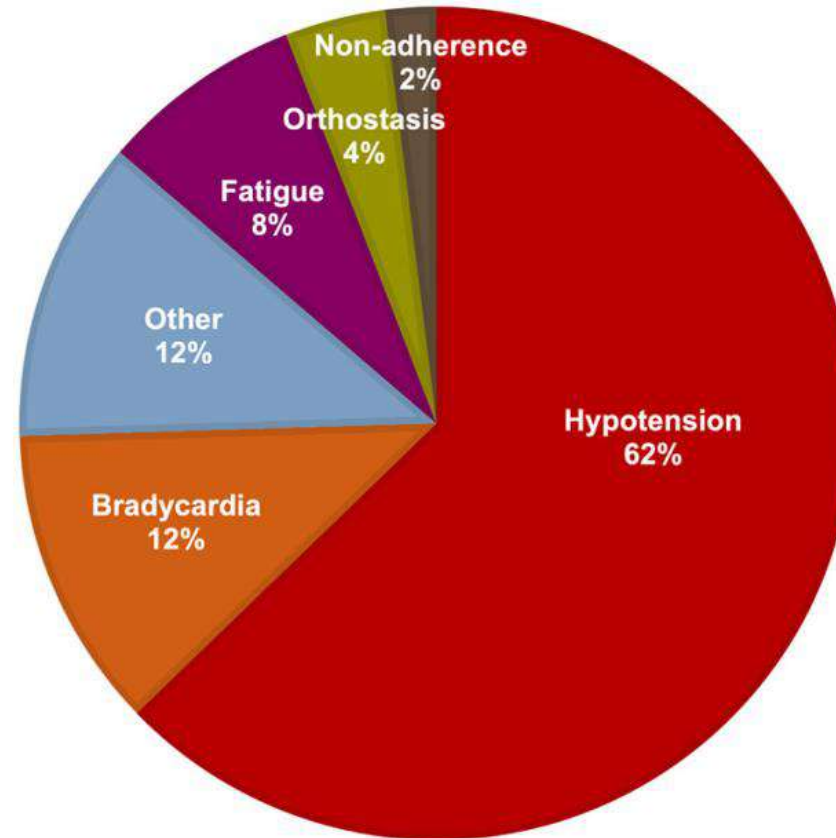
Indications du B- dans la cardiopathie amyloïde





Causes d'arrêt

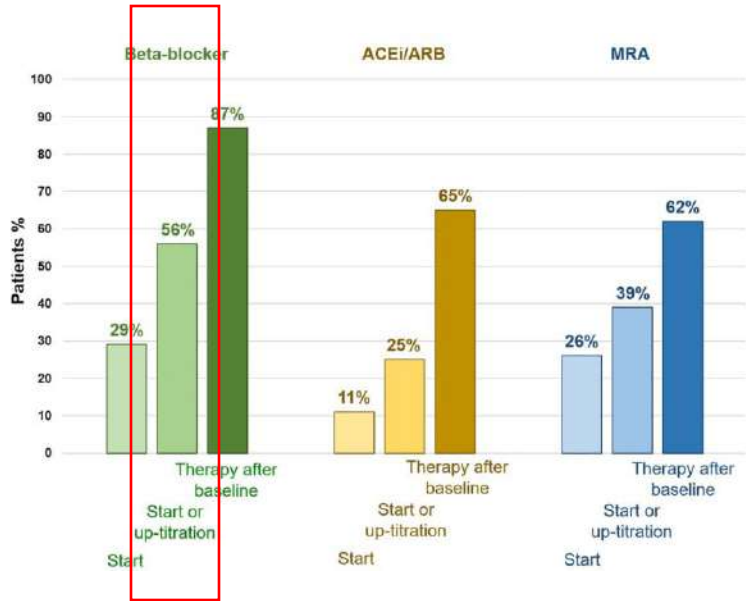
REASON FOR DISCONTINUATION (%)





Tolérance du B-

Safety and Tolerability of Neurohormonal Antagonism in Cardiac Amyloidosis



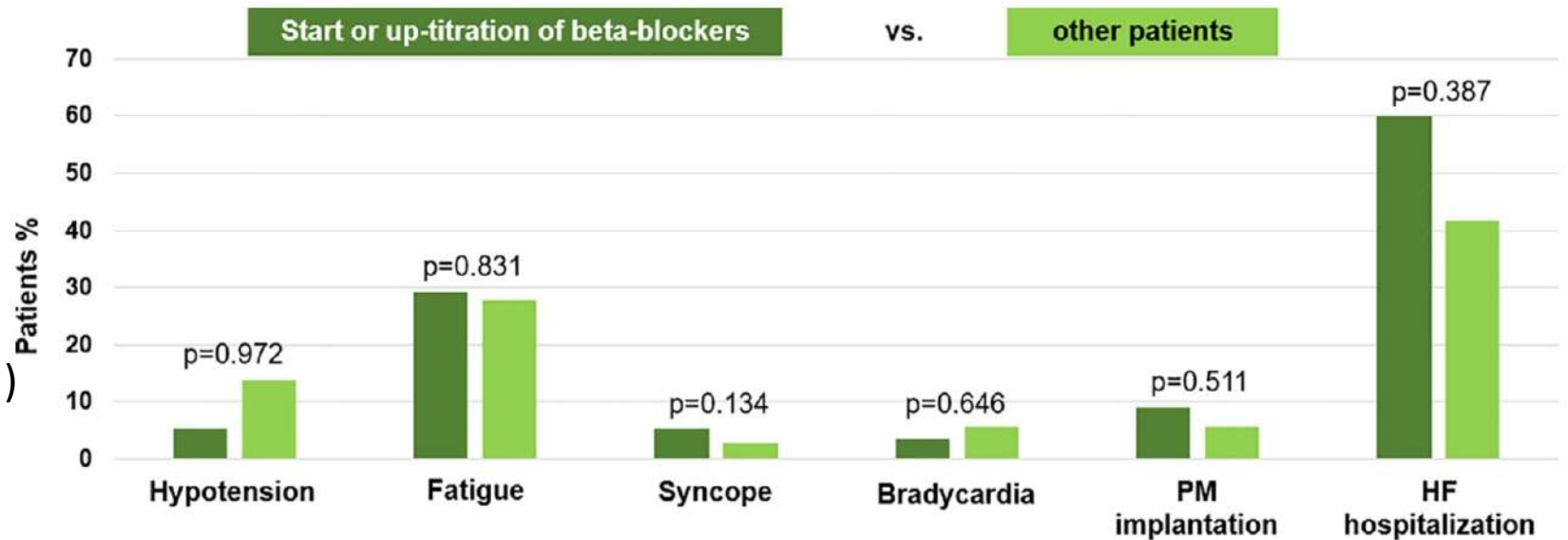
99 were evaluated (72% men, median age 80 years [72,83]).

All these patients were symptomatic for dyspnoea

The majority (75%) had had previous HF hospitalizations

33 patients (33%) were diagnosed with AL amyloidosis, and 66 (67%) with ATTR amyloidosis

Median daily doses of bisoprolol after diagnosis of CA were 2.5 mg



follow-up duration (19 months [9,33])



Tolérance du B- dans l'amylose ATTR + IC

Use of Traditional Heart Failure Medications in Patients With Cardiac Amyloidosis and Heart Failure is Safe but Does Not Improve Mortality or Hospitalization

82 patients met study criteria. At time of cardiac amyloidosis diagnosis, 63.4% were on a BB, 51.2% were on an ACEI/ARB/ARNI, and 43.9% were on an MRA.

At last follow up, 51.2% were on a BB, 35.4% were on an ACEI/ARB/ARNI, and 43.9% were on a MRA.

There were **no statistically significant differences in rates of potential medication side effects** in patients on the medication class compared to those who were not.

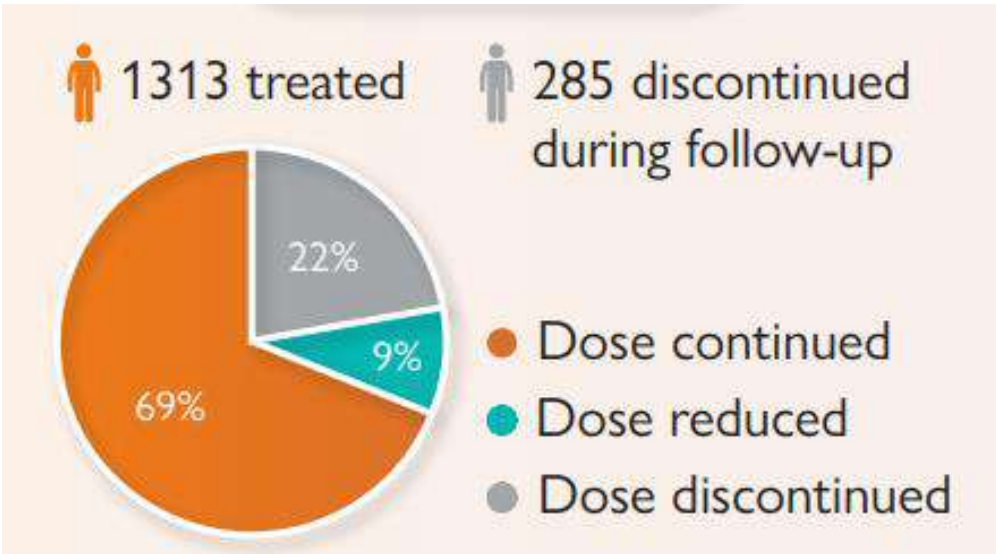
There was **no association with mortality for baseline or follow-up BB**, ACEI/ARB/ARNI, or MRA use.



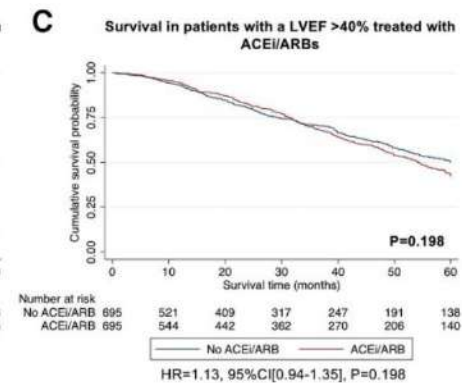
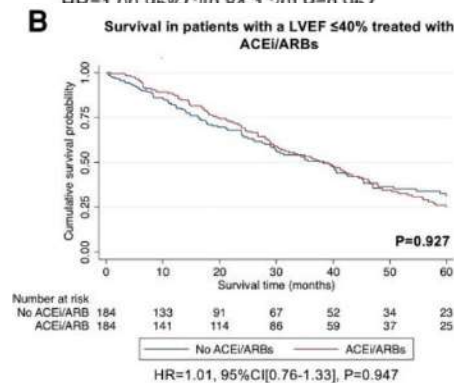
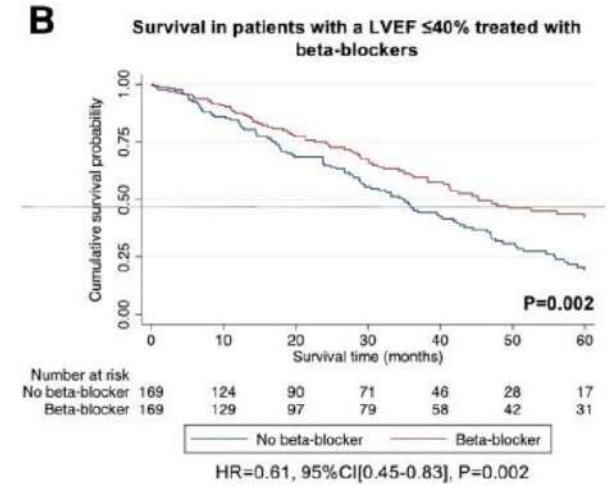
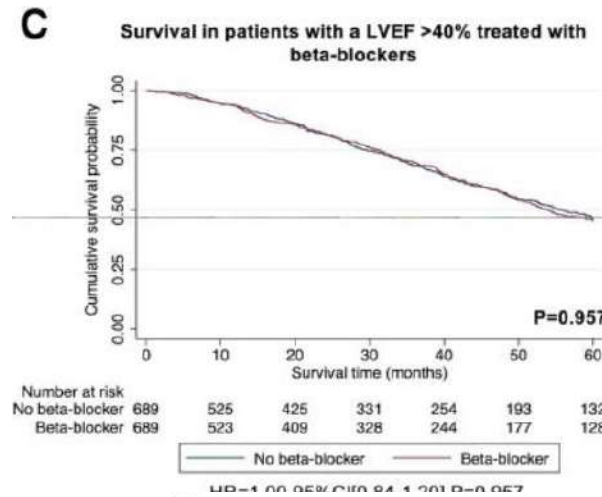
B- dans l'IC avec amylose ATTR

Conventional heart failure therapy in cardiac ATTR amyloidosis

2371 patients with ATTR-CA between 2000 and 2022 identified



The most commonly prescribed beta-blocker was bisoprolol ($n = 1164$, 88.7%), with the majority of patients treated with ≤ 2.5 mg per day ($n = 721$, 61.9%)



A total of 1313 (55.4%) patients were treated with beta-blockers (64.4% in patients with a LVEF $\leq 40\%$) at diagnosis. Those treated with beta-blockers had a higher prevalence of IHD, diabetes mellitus, and atrial fibrillation compared to patients not receiving this type of treatment. Those treated with beta-blockers had a more severe cardiac phenotype, with a worse functional capacity as evidenced by NYHA class and 6-min walk test (6MWT), and a higher NAC disease stage [a greater proportion of patients had stage 3 (severe) disease]. The median NT-proBNP among patients treated with beta-blockers was significantly higher, while median eGFR was significantly lower than patients not receiving beta-blockers. Patients treated with betablockers had a larger bi-atrial size, lower LVEF, lower tricuspid annular plane systolic excursion (TAPSE), and worse longitudinal strain than those not receiving this type of treatment.



POUR

A petites doses

Sur certains profils patients

Bien toléré notamment dans l'amylose ATTR

Neutre dans IC fPEF

Diminution de la mortalité sur IC rfEF < 40%

Dans l'HTA, switcher



Les controverses de la prise en charge cardiologique CONTRE les bêtabloquants



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AP-HP.
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**Réseau Amylose
Mondor** Centre de Référence National
des Amyloses Cardiaques



Contexte

Aortic Stenosis

- Severe AS confers worse prognosis.
- Concomitant ATTRwt risk factor for periprocedural AV block.
- TAVR improves outcome in amyloid-AS.

Thromboembolism

- High risk, common.
- Anticoagulate if AF, consider in selected cases in SR.
- Anticoagulate independent of CHADS-VASC score.

Conduction disorders

- PPM according to standard indications.
- Consider CRT if high paced burden expected.

Heart failure

- Control fluid.
- Diuretics.
- Deprescribe B-Blockers.
- Avoid ACEI/ARB.
- LVAD not suitable for most patients.
- Heart transplant for selected cases.

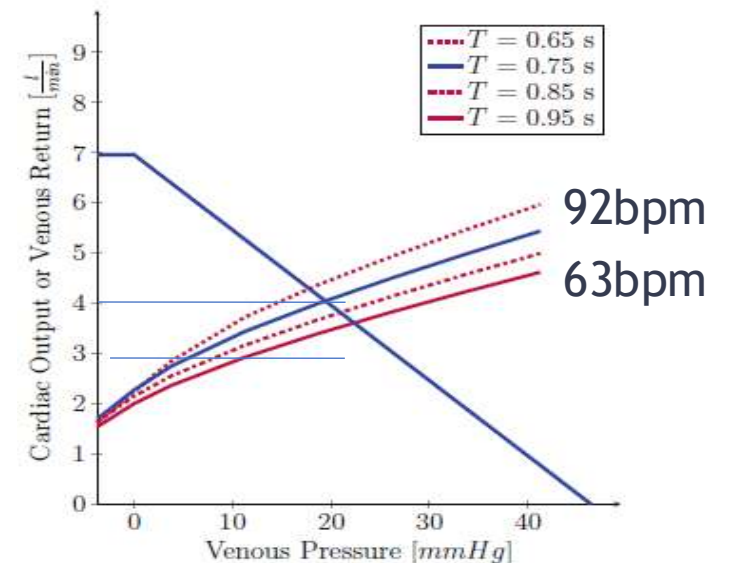
Atrial Fibrillation

- Amiodarone, preferred AA.
- Use digoxin cautiously.
- Electrical CV has significant risk of complications and AF recurrence is frequent.
- Exclude thrombi before electrical CV.
- AF ablation data scarce and controversial.

Ventricular arrhythmias

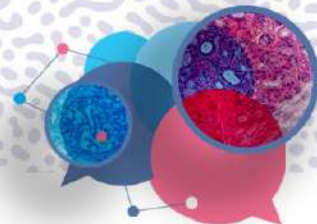
- ICD for secondary prevention.
- ICD in primary prevention usually not recommended.
- Transvenous ICD preferred over subcutaneous ICD.

Physiopathologie Débit cardiaque = FC x VES



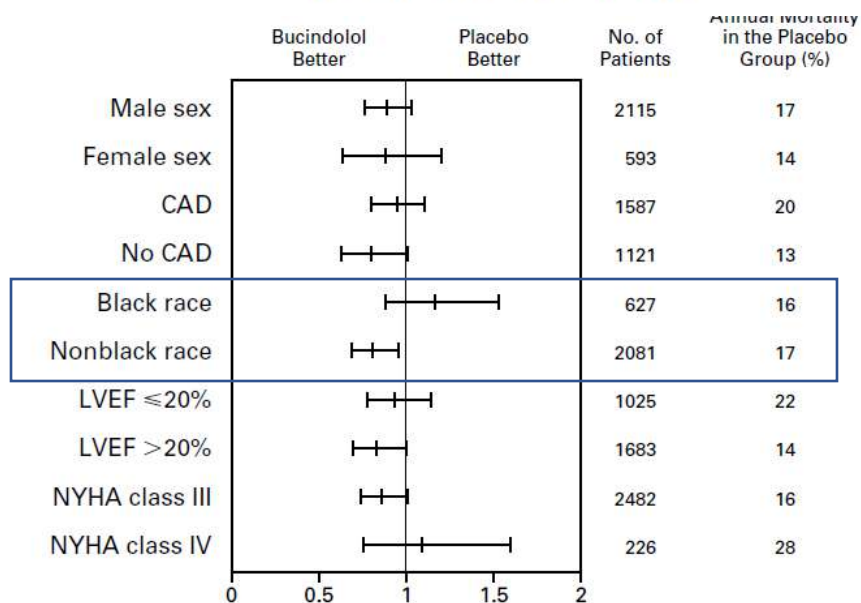
1. Il est recommandé de déprescrire les BB dans l'AC
2. Les troubles conductifs sont fréquents
3. Il existe des alternatives de prise en charge à la FA et aux troubles du rythme ventriculaire

Baisse de la FC → baisse du débit cardiaque



Contexte historique

A TRIAL OF THE BETA-BLOCKER BUCINDOLOL IN PATIENTS WITH ADVANCED CHRONIC HEART FAILURE



Transthyretin V122I in African Americans With Congestive Heart Failure

Table 1. Prevalence of the Amyloidogenic Transthyretin V122I Allele in Individuals Without Clinically Apparent Amyloidosis

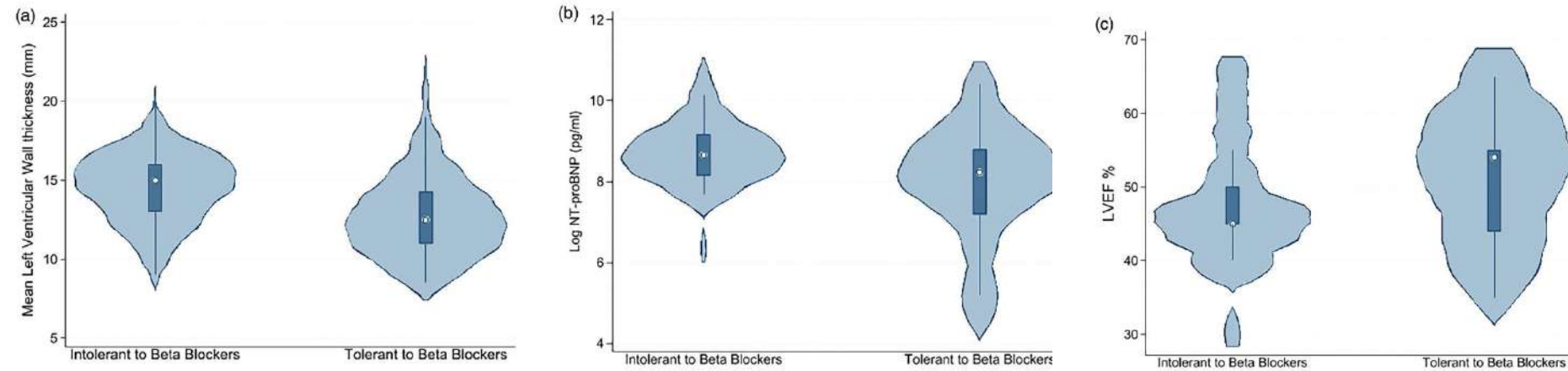
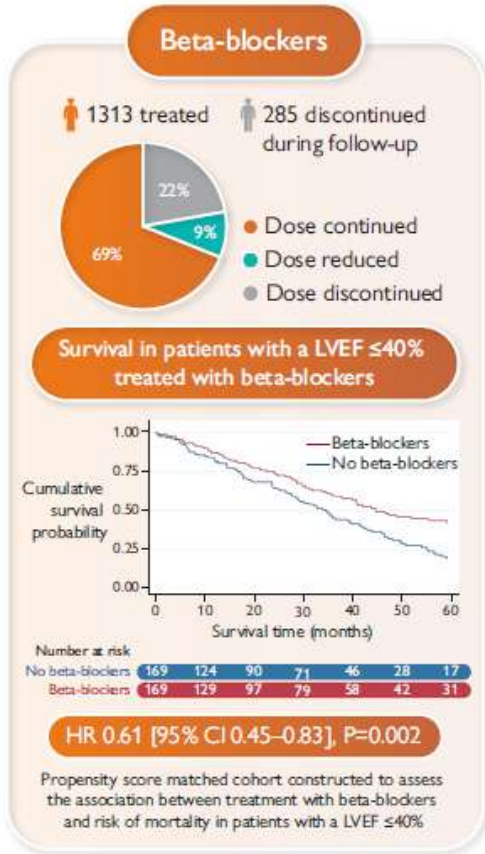
Sample	Number	Age (yrs)	Prevalence (%)	Allele Frequency
Caucasian (convenience) (2)	86	Not noted	<1.2 (0/86)	<0.006
Caucasian (3)	453	Newborn	0.4 (2/453)	0.002
African American*	1,219	Newborn	3.3 (40/1219)	0.016
African American (3)	1,000	Newborn	3.0 (30/1000)	0.015
African American (CHS)*	802	Community >65	2.12 (17/802)	0.011
BEST: NYHA class III and IV heart failure*	207	19–93	6.3 (13/207)	0.032
Under age 60 yrs	116	<60	3.5 (4/116)	0.018
Age 60 yrs or over	91	>60	10 (9/91)	0.05

There is no longer any doubt that beta-blockers have a role in the treatment of mild-to-moderate (NYHA class II to III) chronic heart failure. Our findings raise questions about the efficacy of these agents in blacks and in patients with more advanced heart failure, as well as about the equivalency of beta-blockers. In doing so, it makes clear the need for studies that examine the mechanism of the heterogeneity of response to beta-blockers and for clinical trials that directly evaluate beta-blockers in blacks and in patients with NYHA class IV heart failure.



Oui, mais .. !

236 AL, 53 patients traités par BB (22.5%)



> Les patients « intolérants » aux bêtabloquants sont plus sévères (épaisseur, NTproBNP, FEVG)

Etude rétrospective

1. BB :

- Arrêtés ou réduits 31%
- < 2,5 mg Bisoprolol chez 62%

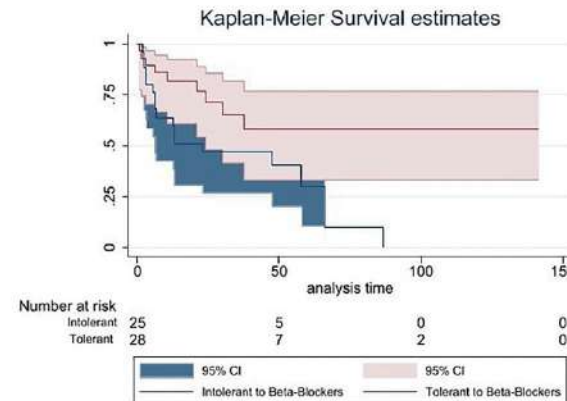


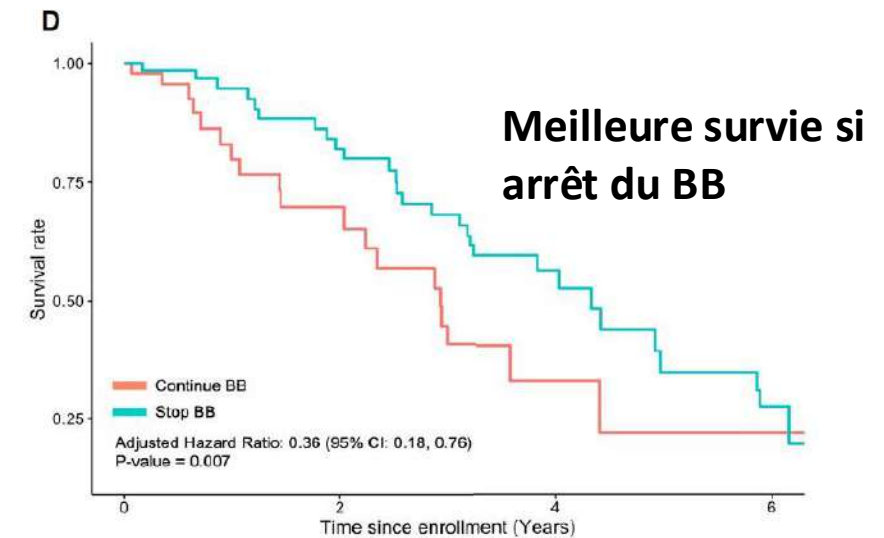
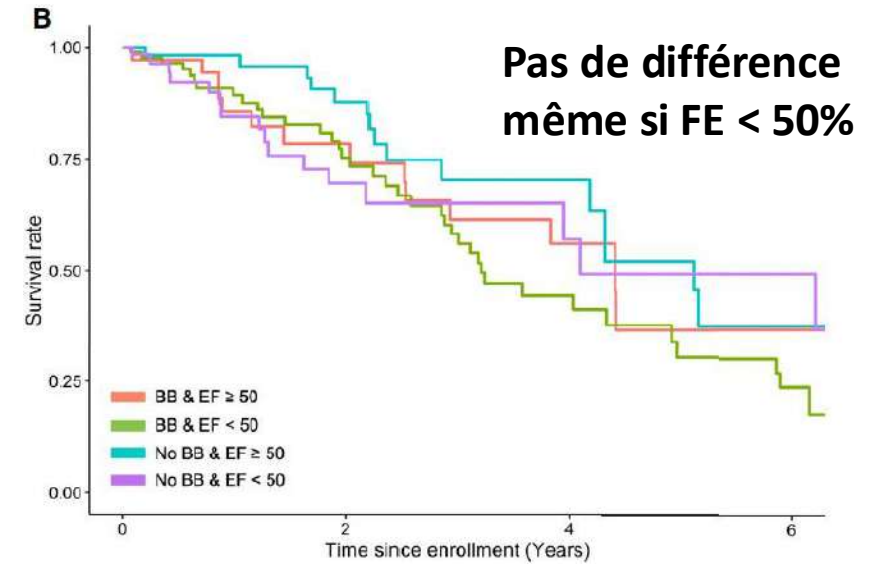
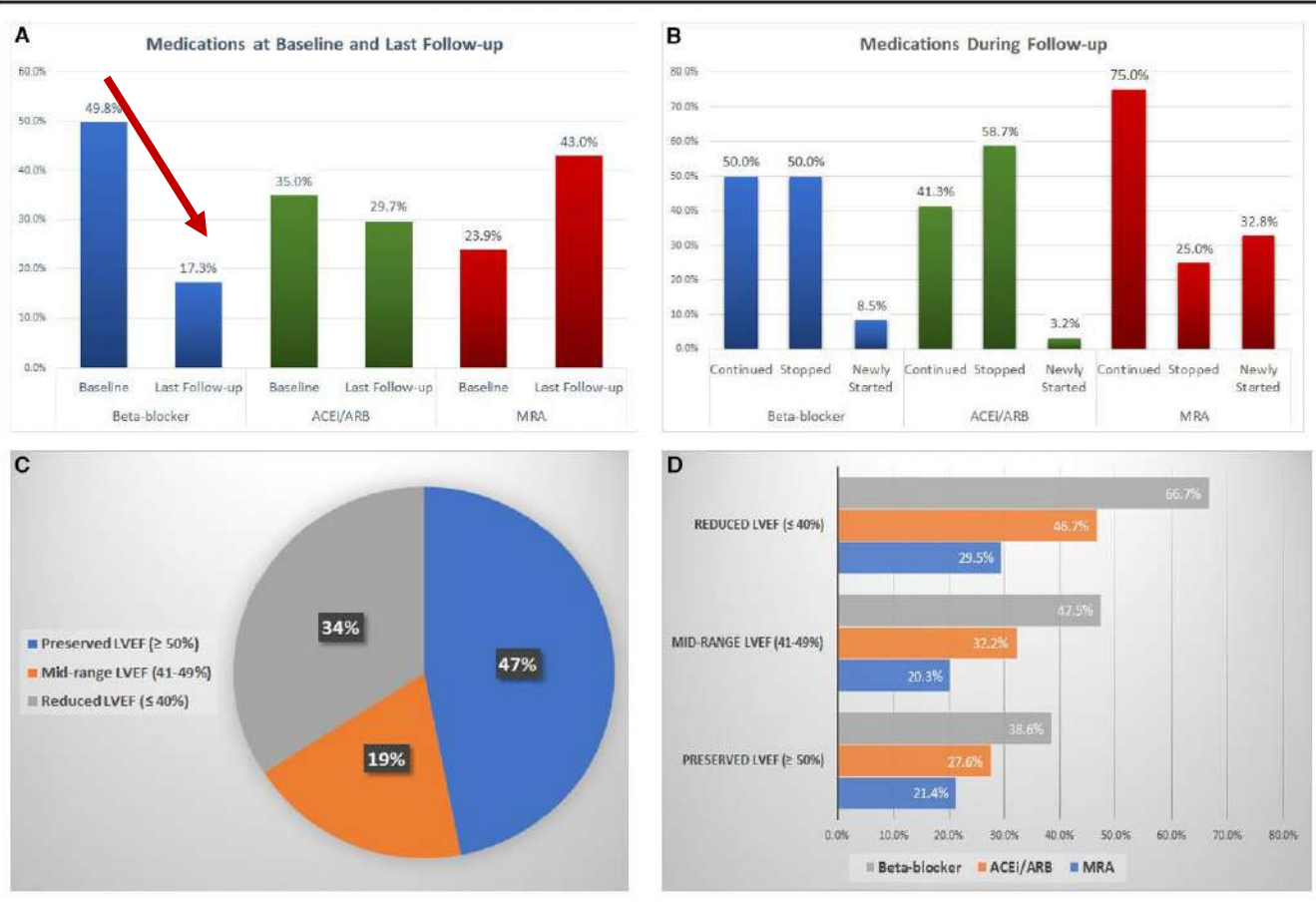
Figure 3. Differences in survival based on BB tolerance with the use of Cox-regression models with adjustment for patient characteristics.

> Les patients « intolérants » ont un pronostic plus sombre



Quel bénéfice sur la survie ?

309 ATTR-CM, 73.2±9.8 ans, 84.1% hommes, 34.0% ATTRv.
45.3% NYHA II et 41.7% NYHA III. FEVG médiane 45.1%±15.2%. 17.2%



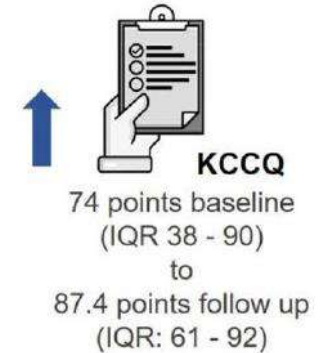
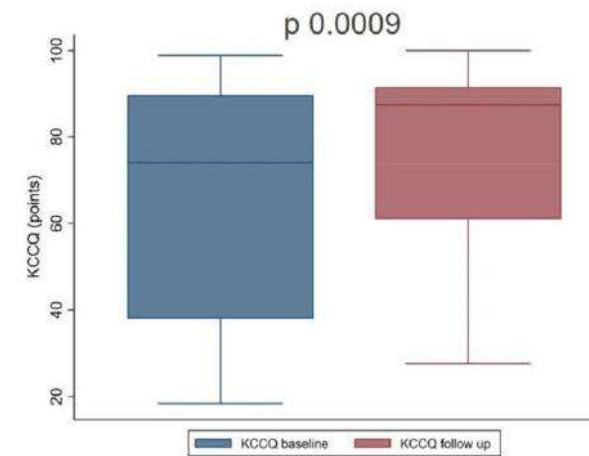
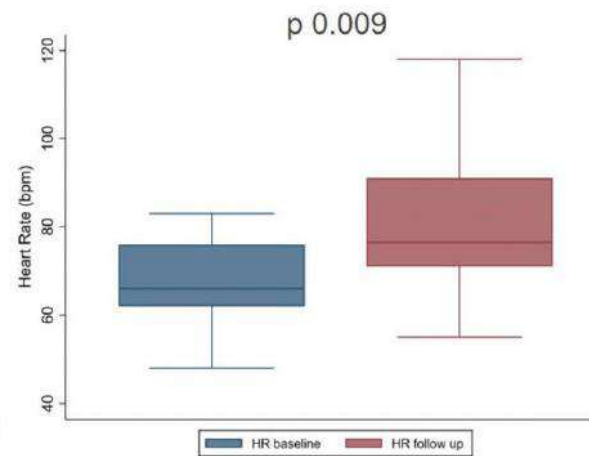
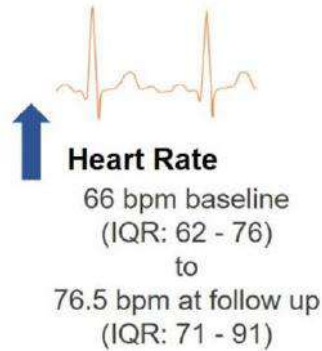
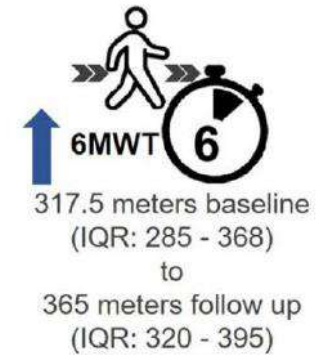
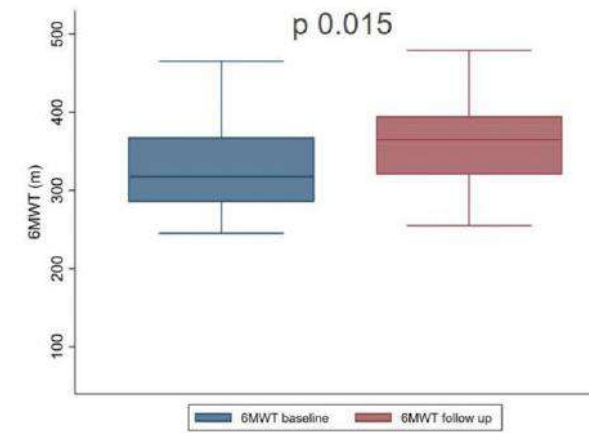
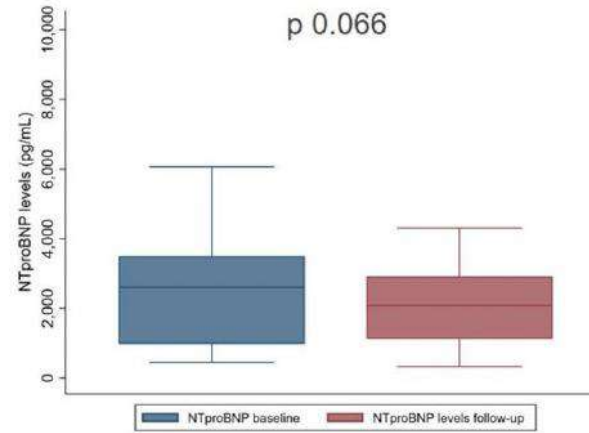
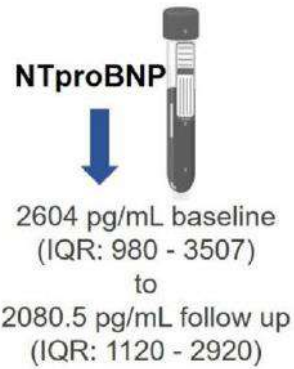


Quel bénéfice fonctionnel ?

106 ATTR-CM traités
par BB
> Arrêt des BB sauf si
FA incontrôlée

26 ATTR-CM étudiés :
23 hommes, 77.5 ± 5.0
ans, 24 ATTRwt, FEVG
52.7 ± 8.2%, 15 en FA

Evaluation :
- Baseline
- A 1 mois





Conclusion

Consensus d'expert plutôt en défaveur des BB dans les amyloses cardiaques

Physiopathologie et histoire naturelle de la maladie plutôt à la défaveur des BB dans les amyloses cardiaques

Etudes montrant un bénéfice sur la survie biaisées par la meilleure tolérance des BB chez les patients les moins sévères (qui meurent moins) ?

Bénéfice fonctionnel précoce à l'arrêt des BB

D'ailleurs, l'intolérance des BB n'est-elle pas un « red flag » ?

La seule étude randomisée sur le sujet serait-elle BEST ?



**It's
amyloidosis !**



Merci à l'ensemble du RÉSEAU AMYLOSE Mondor !

Cardiac Amyloidosis Referral Center (Rare Disease Network)

Cardiologists Team

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Referral center secretariat: I Vallat
IDE amyloidosis coordination: S Maupou
Psychology: J Pompougnac



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Nephrology: V Audard, H Sakhi
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Hepatology: V Leroy, A Sessa
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