7e MASTERCLASS AMYLOSES CARDIAQUES

ÉVÉNEMENT HYBRIDE
PRÉSENTIEL
& DISTANCIEL

Mercredi 11 décembre 2024
Fondation Biermans-Lapôtre ■ PARIS
www.masterclass-amylose.com

B- dans l'amylose : POUR

Dr Benoit LEQUEUX
CHU Poitiers

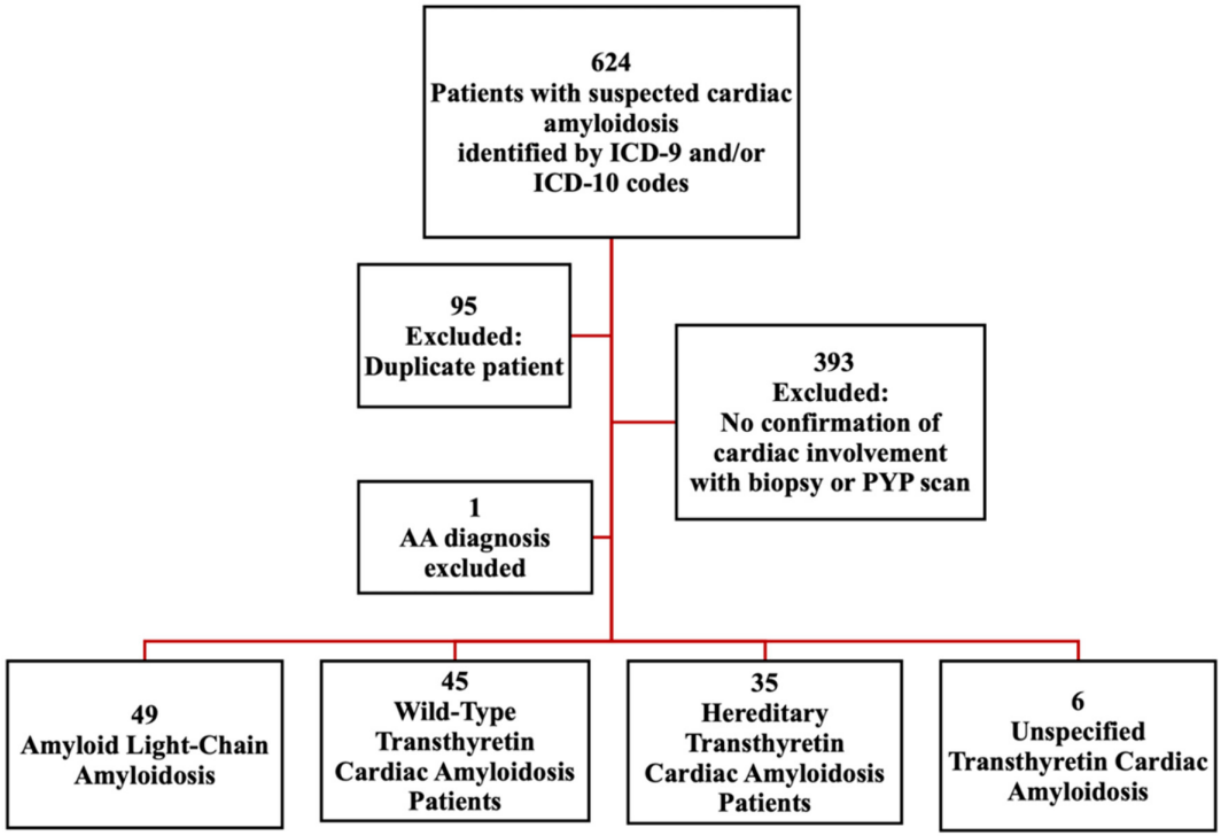
CHU Poitiers

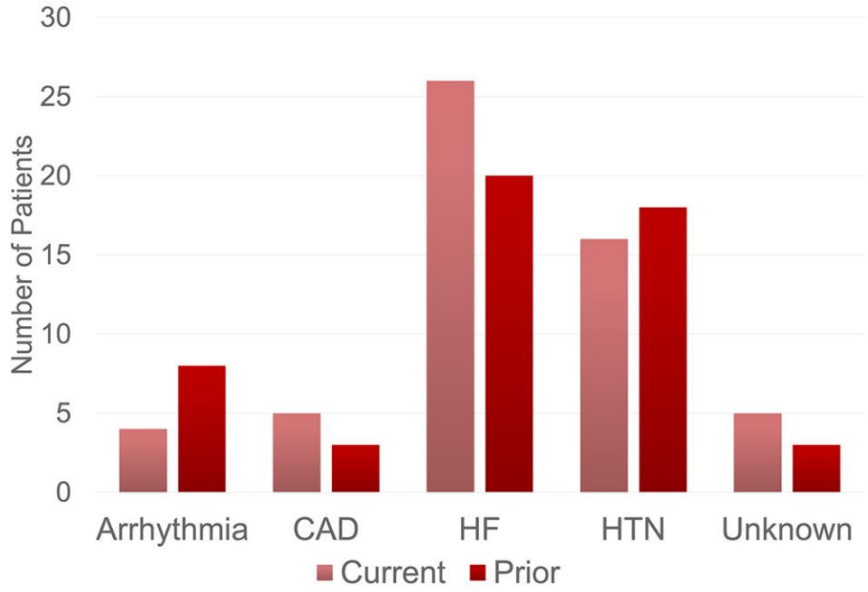
Syndicat National des Cardiologues
Médecine cardiovasculaire

Déclaration de lien d'intérêts

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

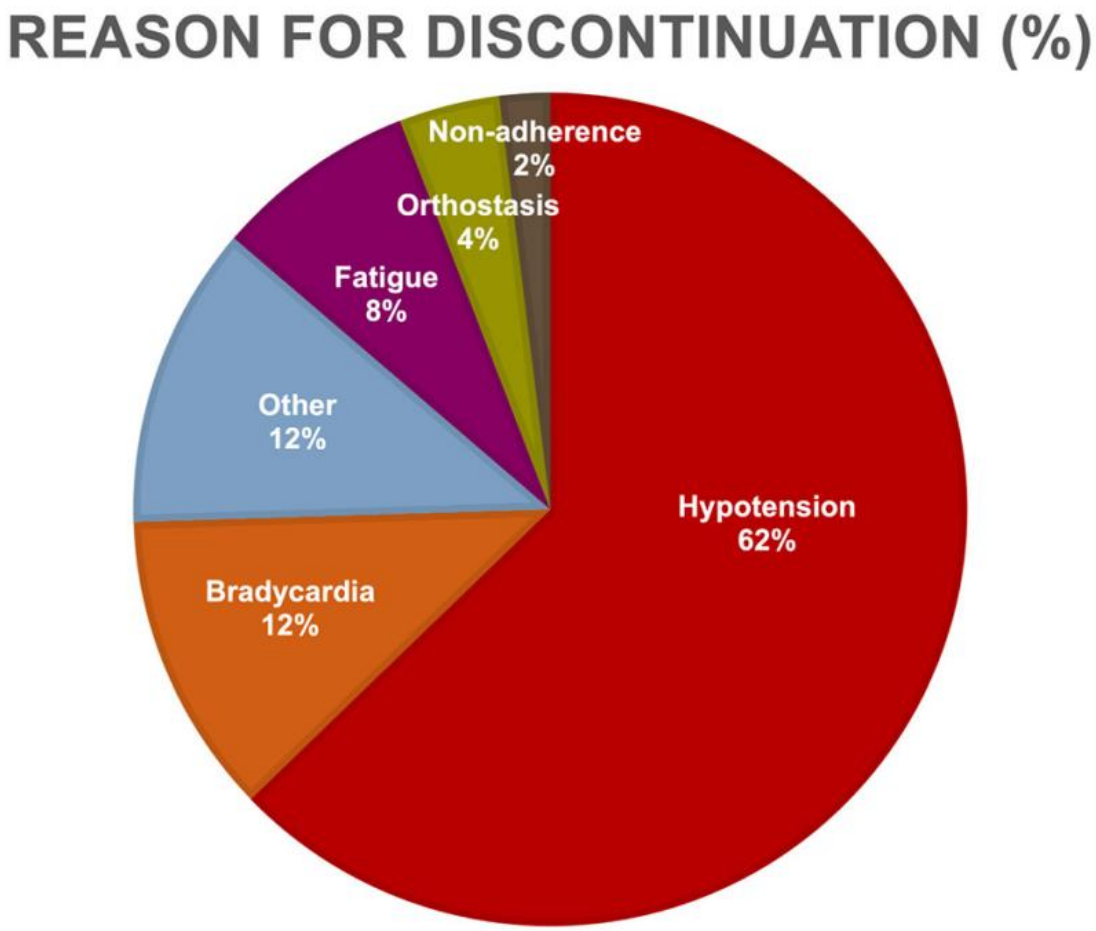
Indications du B- dans la cardiopathie amyloïde





Front Cardiovasc Med. 2022 Jul 11:9:907597. doi: 10.3389/fcvm.2022.907597. eCollection 2022.

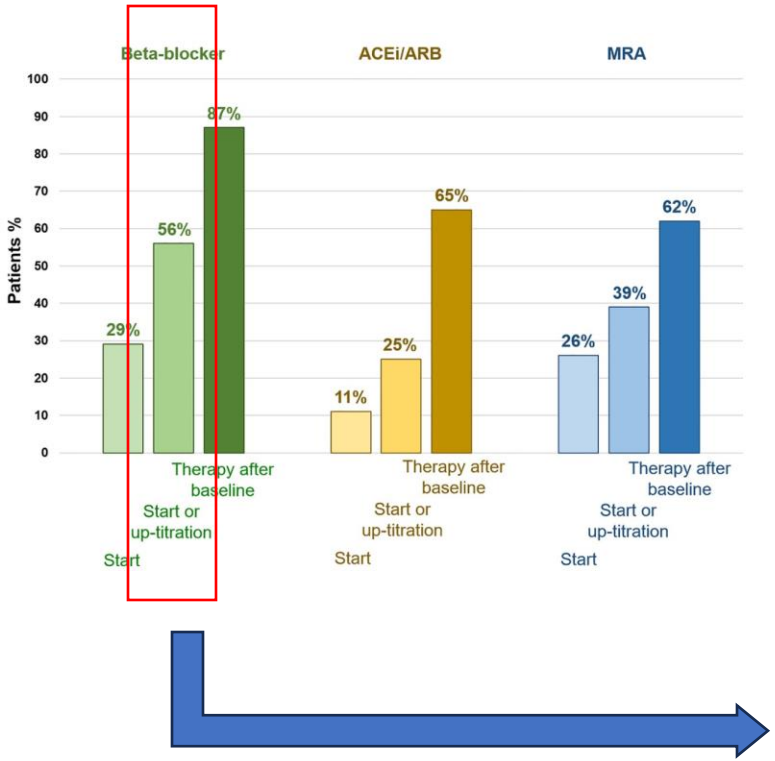
Causes d'arrêt



Front Cardiovasc Med. 2022 Jul 11:9:907597. doi: 10.3389/fcvm.2022.907597. eCollection 2022.

Tolérance du B-

Safety and Tolerability of Neurohormonal Antagonism in Cardiac Amyloidosis



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

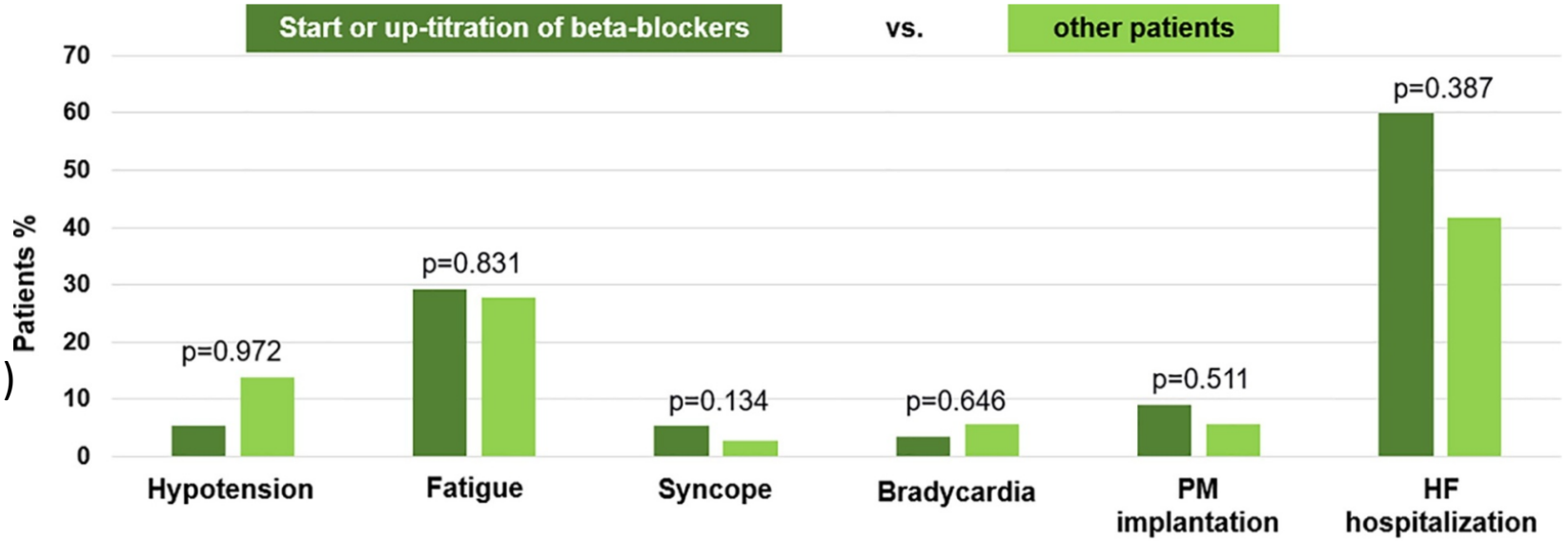
99 were evaluated (72% men, median age 80 years [72,83]).

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



Eur J Intern Med. 2020 Oct:80:66-72. doi: 10.1016/j.ejim.2020.05.015. Epub 2020 May 29.

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.

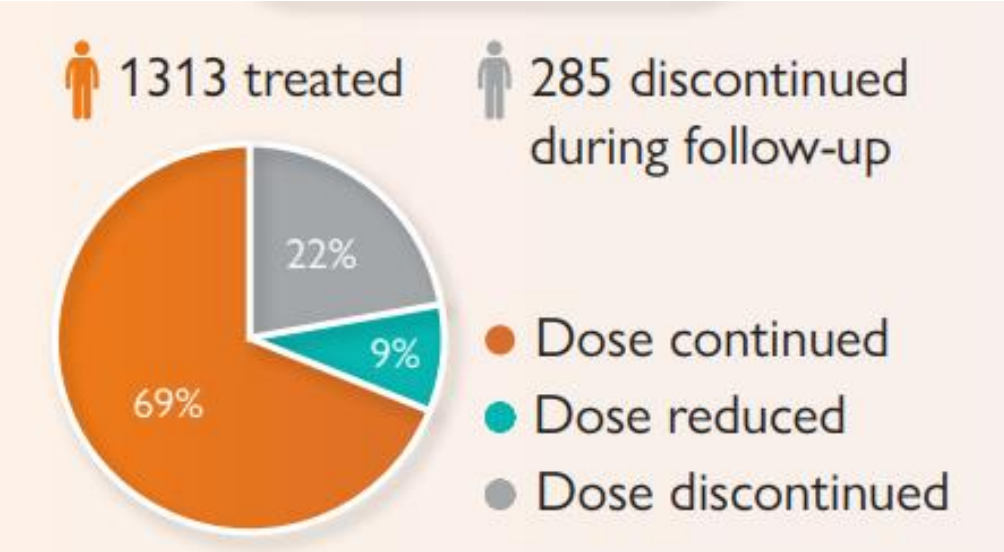
There were **no statistically significant differences in rates of potential medication side effects** in patients on the medication class compared to those who were not.

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

Circulation • Volume 148, Number Suppl_1 • https://doi.org/10.1161/circ.148.suppl_1.12471

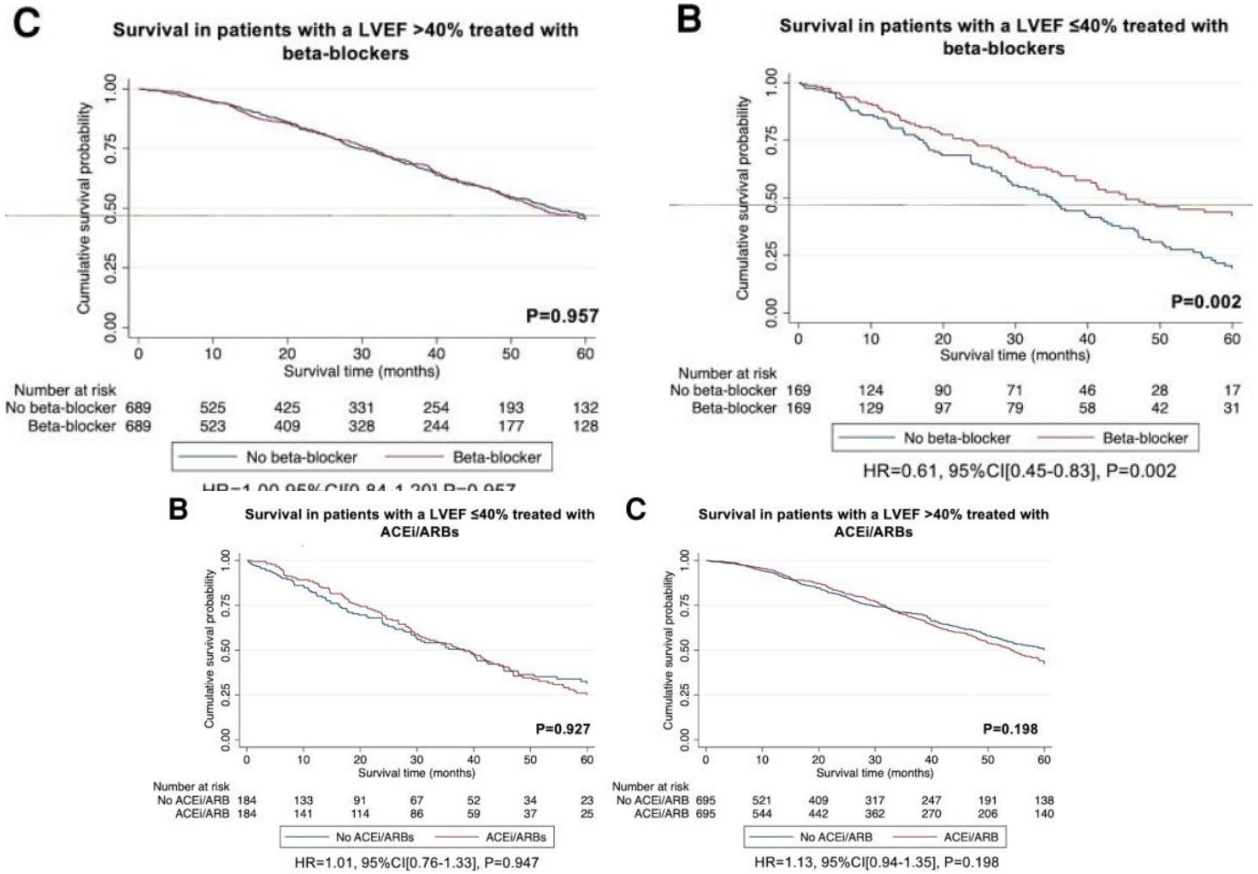
B- dans l'IC avec amylose ATTR

Conventional heart failure therapy in cardiac ATTR amyloidosis



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%)

2371 patients with ATTR-CA between 2000 and 2022 identified



A total of 1313 (55.4%) patients were treated with beta-blockers (64.4% in patients with a LVEF ≤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 receivingthis type of treatment.

Eur Heart J. 2023 Aug 14;44(31):2893-2907. doi: 10.1093/eurheartj/ehad347.

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

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Les controverses de la prise en charge cardiologique
CONTRE les bétabloquants

Dr Silvia OGHINA

Centre de référence des Amyloses Cardiaques – Filière Cardiogen
G.H.U. Henri Mondor - Créteil

AP-HP.
Hôpitaux universitaires
Henri-Mondor

cardiogen
filière nationale de santé
maladies cardiaques héréditaires ou rares
www.filiere-cardiogen.fr

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.

Heart failure

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

Thromboembolism

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

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.

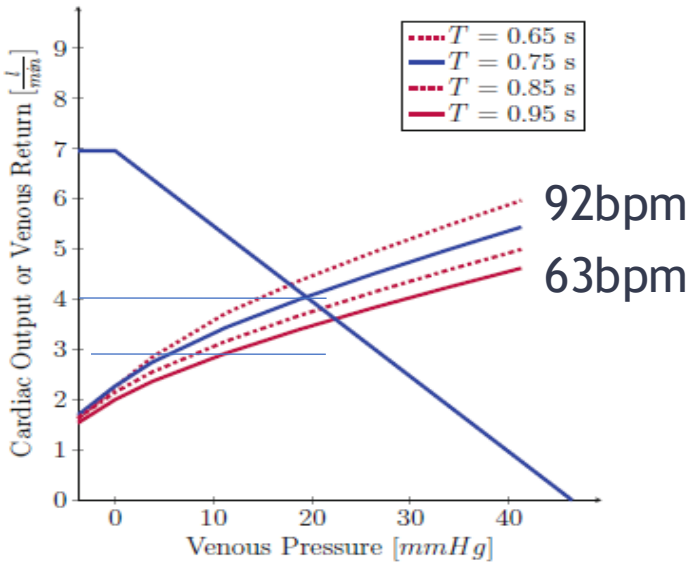
Conduction disorders

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

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



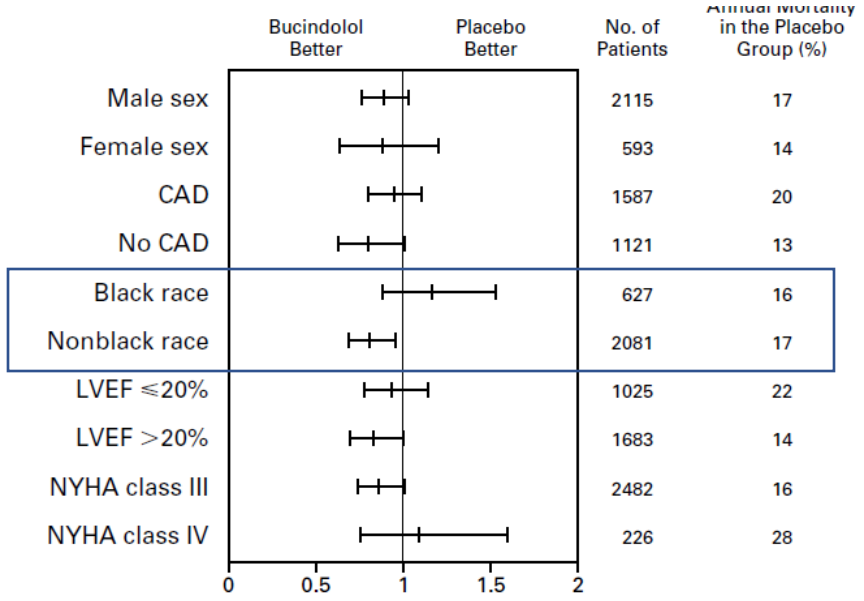
1. **Il est recommandé de dé prescrire les BB dans l'AC**
2. **Les troubles conductifs sont fréquents**
3. **Il existe des alternatives de prise en charge à la FA et aux troubles du rythme ventriculaire**

Baisse de la FC ➔ baisse du débit cardiaque

Garcia Pavia et al. European Heart Journal (2021) 42, 1554–1568 ; Chapelle et al FIMH 2015

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

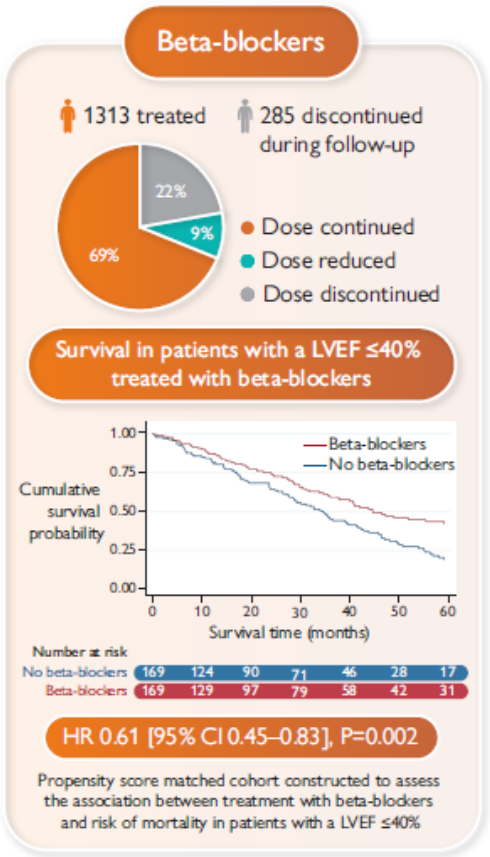
Table 1. Prevalence of the Amyloidogenic Transthyretin V122I Allele in Individuals Without Clinically Apparent Amyloidosis

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

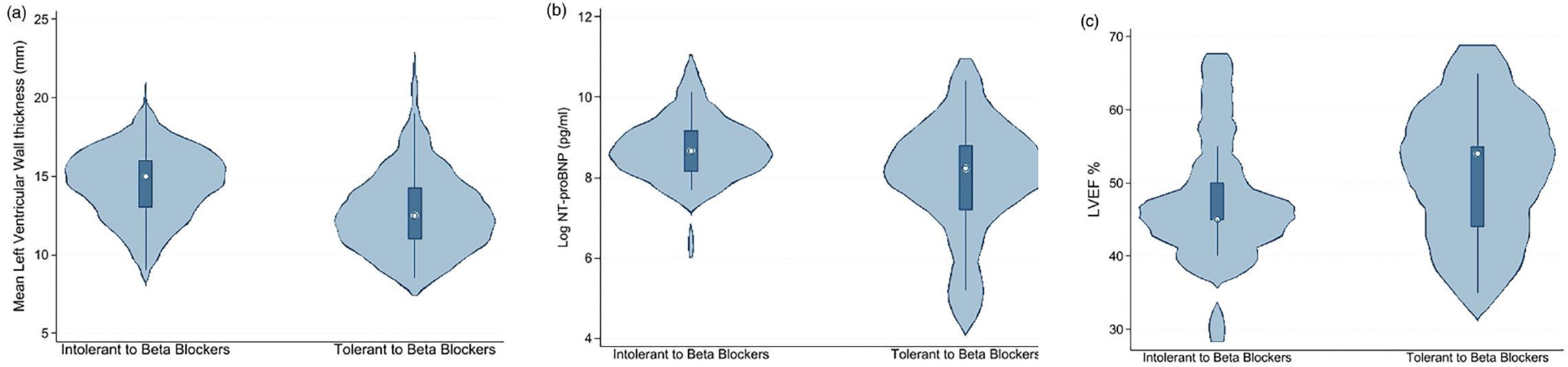
There is no longer any doubt that beta-blockers have a role in the treatment of mild-to-moderate (NYHA class II to III) chronic heart failure. Our findings raise questions about the efficacy of these agents in blacks and in patients with more advanced heart failure, as well as about the equivalency of 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.

Eichhorn EJ et al Engl J Med. 2001 May 31;344(22) ; Buxbaum J, et al. J Am Coll Cardiol. 2006.

Oui, mais .. !



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



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

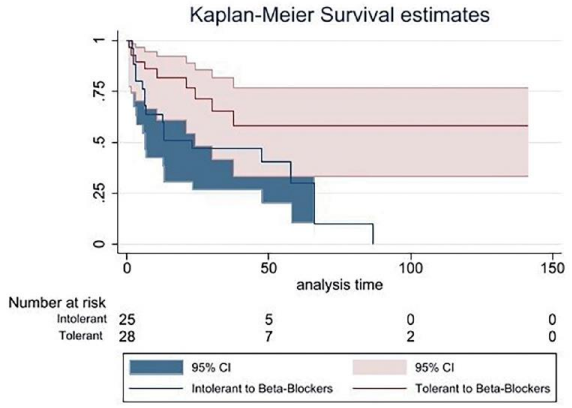


Figure 3. Differences in survival based on BB tolerance with the use of Cox-regression models with adjustment for patient characteristics.

> Les patients « intolérants » ont un pronostic plus sombre

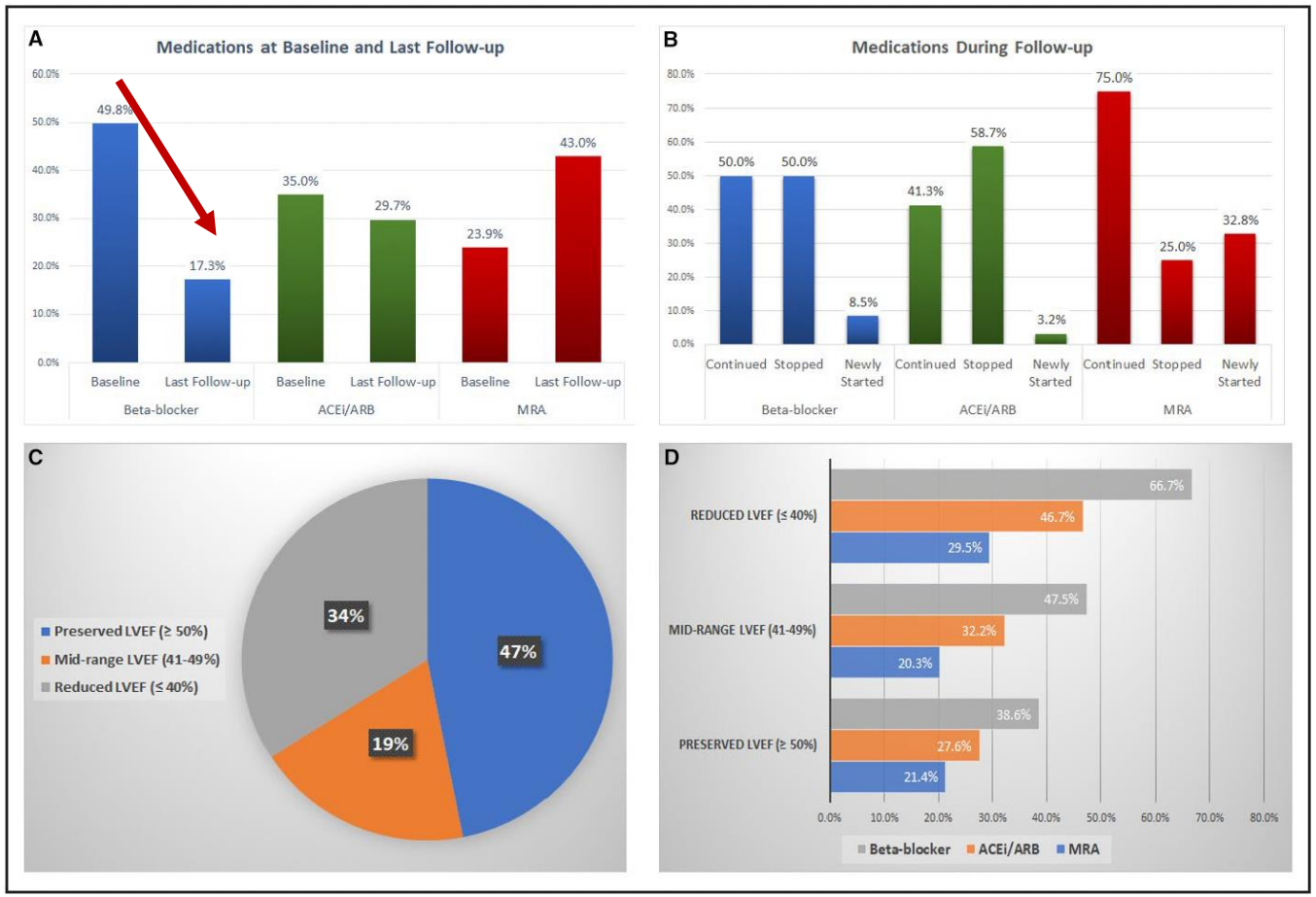
Etude rétrospective

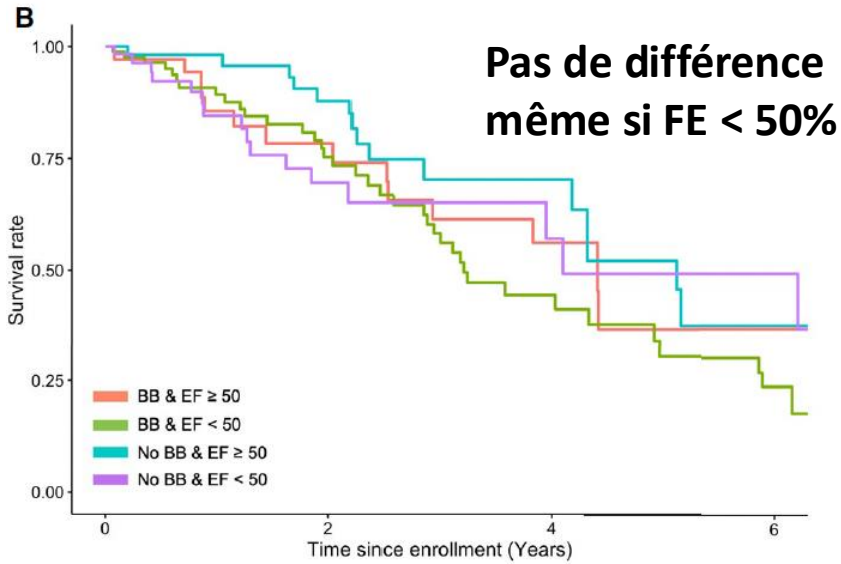
1. **BB :**
   - **Arrêtés ou réduits 31%**
   - **< 2,5 mg Bisoprolol chez 62%**

Ionnaou et al, Eur Heart J. 2023 Aug 14;44(31):2893-2907.
Briasoulis et al. Amyloid. 2022 Mar;29(1):31-37.

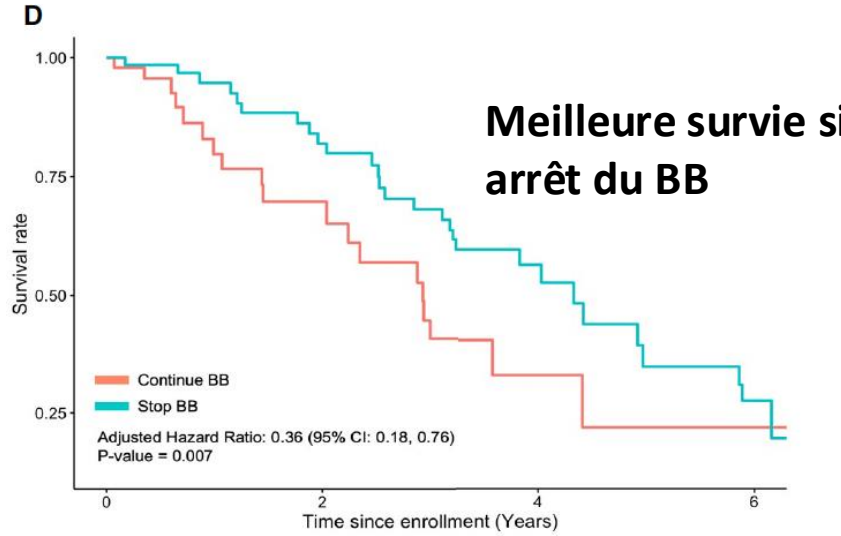
Quel bénéfice sur la survie ?

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%





Pas de différence même si FE < 50%



Meilleure survie si arrêt du BB

Cheng et al. J Am Heart Assoc. 2021 Dec 21;10(24):e022859.

Quel bénéfice fonctionnel ?

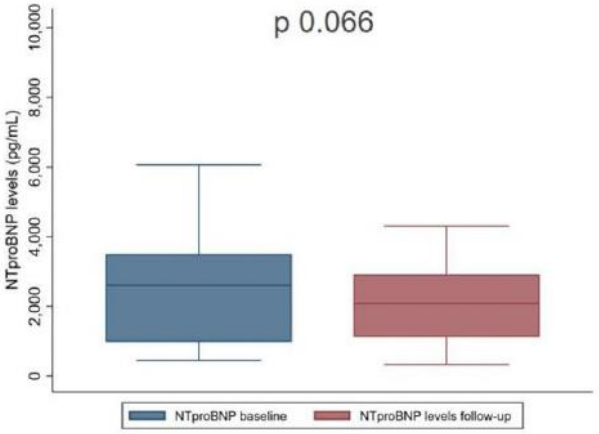
106 ATTR-CM traités par BB
> Arrêt des BB sauf si FA incontrôlée

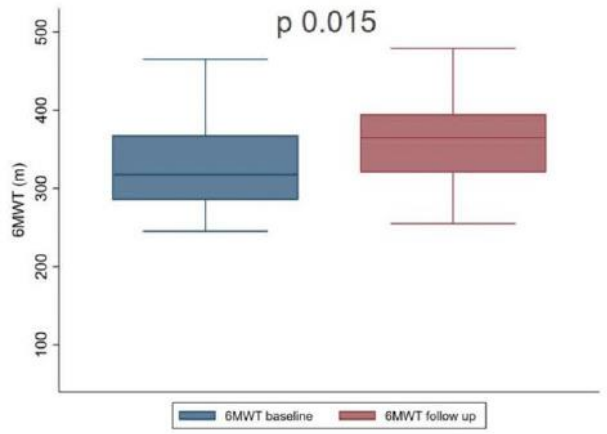
26 ATTR-CM étudiés :
23 hommes, 77.5 ± 5.0 ans, 24 ATTRwt, FEVG 52.7 ± 8.2%, 15 en FA

Evaluation :
- **Baseline**
- **A 1 mois**

NTproBNP

2604 pg/mL baseline
(IQR: 980 - 3507)
to
2080.5 pg/mL follow up
(IQR: 1120 - 2920)



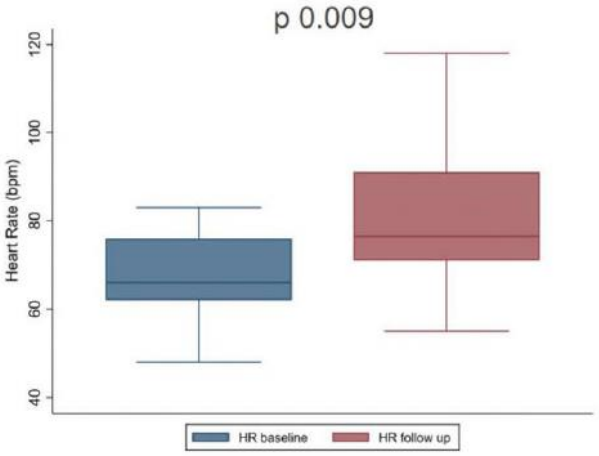


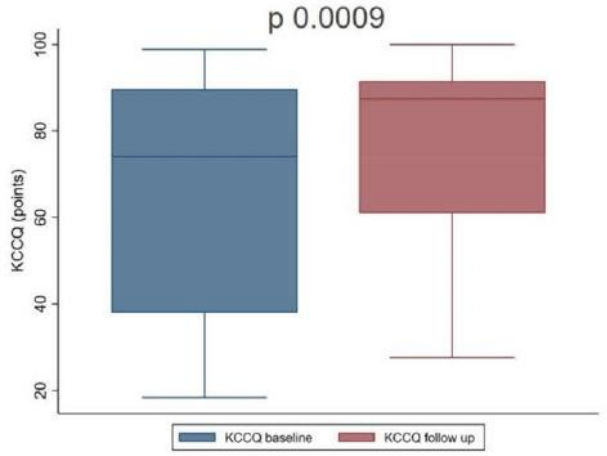
6MWT

317.5 meters baseline
(IQR: 285 - 368)
to
365 meters follow up
(IQR: 320 - 395)

Heart Rate

66 bpm baseline
(IQR: 62 - 76)
to
76.5 bpm at follow up
(IQR: 71 - 91)





KCCQ

74 points baseline
(IQR 38 - 90)
to
87.4 points follow up
(IQR: 61 - 92)

Cabrera Romero et al. Amyloid. 2024 Nov 20:1-3.

Conclusion

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

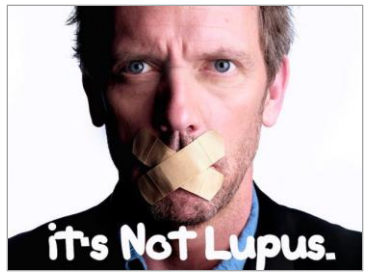
Physiopathologie et histoire naturelle de la maladie plutôt à la défaveur des BB dans les amyloses cardiaques

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 !

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Merci à l'ensemble du RÉSEAU AMYLOSE Mondor !

Cardiac Amyloidosis Referal Center (Rare Disease Network)

Cardiologists Team

Cardiologist: T Damy, S Oghina, A Zaroui, S Guendouz, A Galat, S Mallet, GDS Chadha, M Hentati, E Charbonneau, S Odouard, A Copie, E Teiger
Rythmologist: N Lellouche, T Moulin, K Ramoul, N Elbaz, S Rouffiac, V Ouazana

Coordination - Quality of Life

Healthcare pathway: C Henrion, Anaïs
Referral center secretariat: I Vallat
IDE amyloidosis coordination: S Maupou
Psychology: J Pompougnac

cardiogen
filière nationale de santé
maladies cardiaques héréditaires ou rares

Clinical Research Team/HEAR

Study engineer: M Kharoubi,
Research assistant: Ani, Dilan, Saafa, Sarah, Benoît, Lola

Medicine Multidisciplinary Network

Neurology: V Planté-Bordeneuve, T Gendre
Neuromuscular disease: S Souvannanorath
Nephrology: V Audard, H Sakhi
Haematology: F Lemmonier, K Belhadj, J Dupuis, F Le Bras, R Gounot, M Van Den Akker
Internal medicine: M Michel
Hepatology: V Leroy, A Sessa
Geriatry: A Broussier, N Liu, N Marie Nelly
Genetic: B Funalot, B Hébrard, C Nativelle
Rhumato : S Guignard
Orthopédie : O Pidet

Amyloidosis Diagnosis and Monitoring Platforms

Electrophysiology: JP Lefaucheur
Pathology: E Poullot, C Charpy, A Moktefi
Sequencing: P Fanen, M Konyukh
Immuno-biology: V Frenkel, H Abroud, A Beldi Ferichou
Radiology: V Tacher, I Sifaoui
Nuclear medicine: E Itti, L Lerman

HF Telemonitoring

Coordination: E Sarre, A Duchenne
Nurses: A Gauchard, M Frelat, S Dias, C Lecerf
Cardiologist : L Hittinger

INSERM U955 Clinial Epidemioloy in Aging

Florence Canoui-Poitrine
Etienne Audureau
Charlotte Lafont

UMR CNRS 8256, INSERMU1164

Onnik Agbulut
Ekaterinii Kordeli
France Lam

Oncopole - Toulouse: Mass spectometry: M Colombat - NGS cytogenetic: H Loiseau