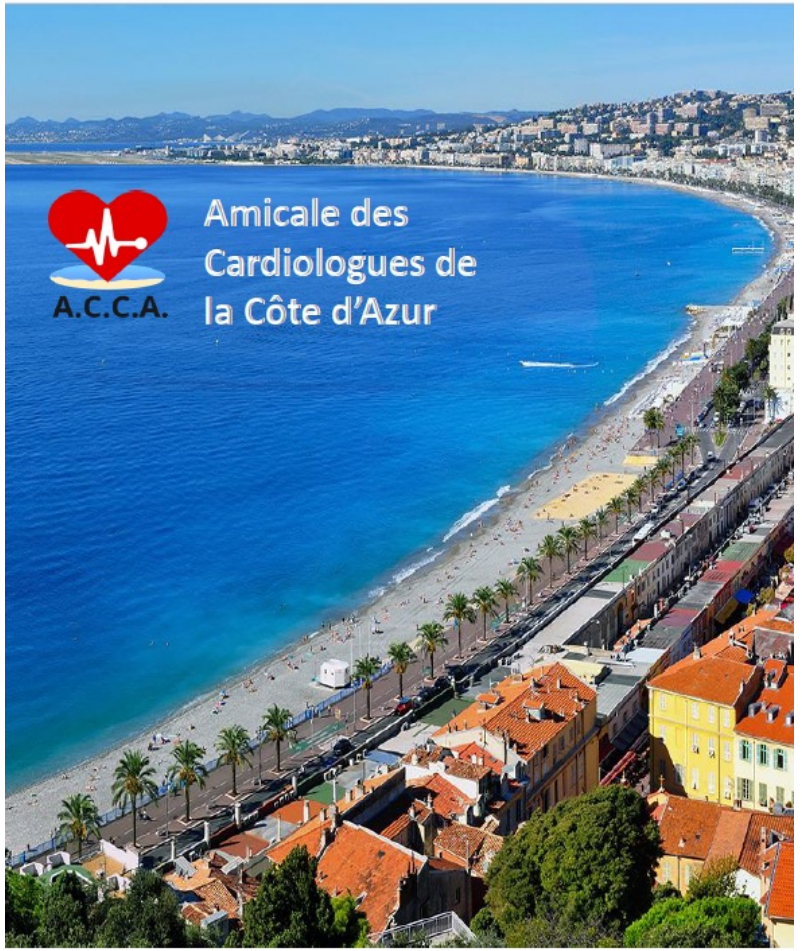
Actualités sur les nouveaux traitements des cardiomyopathies hypertrophiques



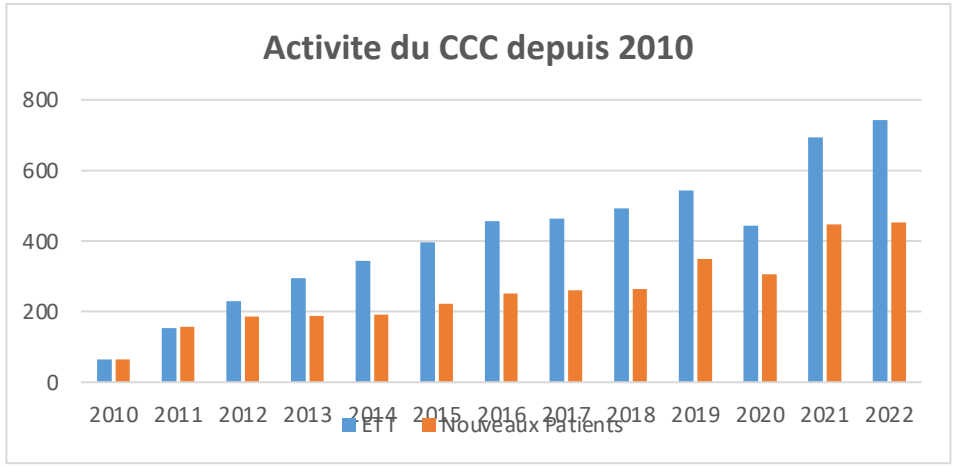
JOURNEE D'ACTUALITES THERAPEUTIQUES

Samedi 14 SEPTEMBRE 2024

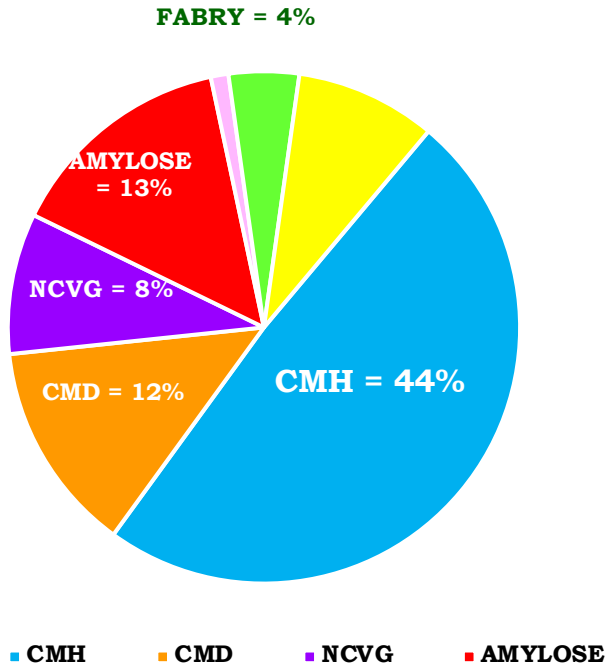
Novotel Nice Arénas

CENTRE DE COMPETENCE DES CARDIOMYOPATHIES
Activité

Depuis Avril 2010, l'activité du centre a considérablement augmenté
5320 Visites dont **3336** nouveaux patients



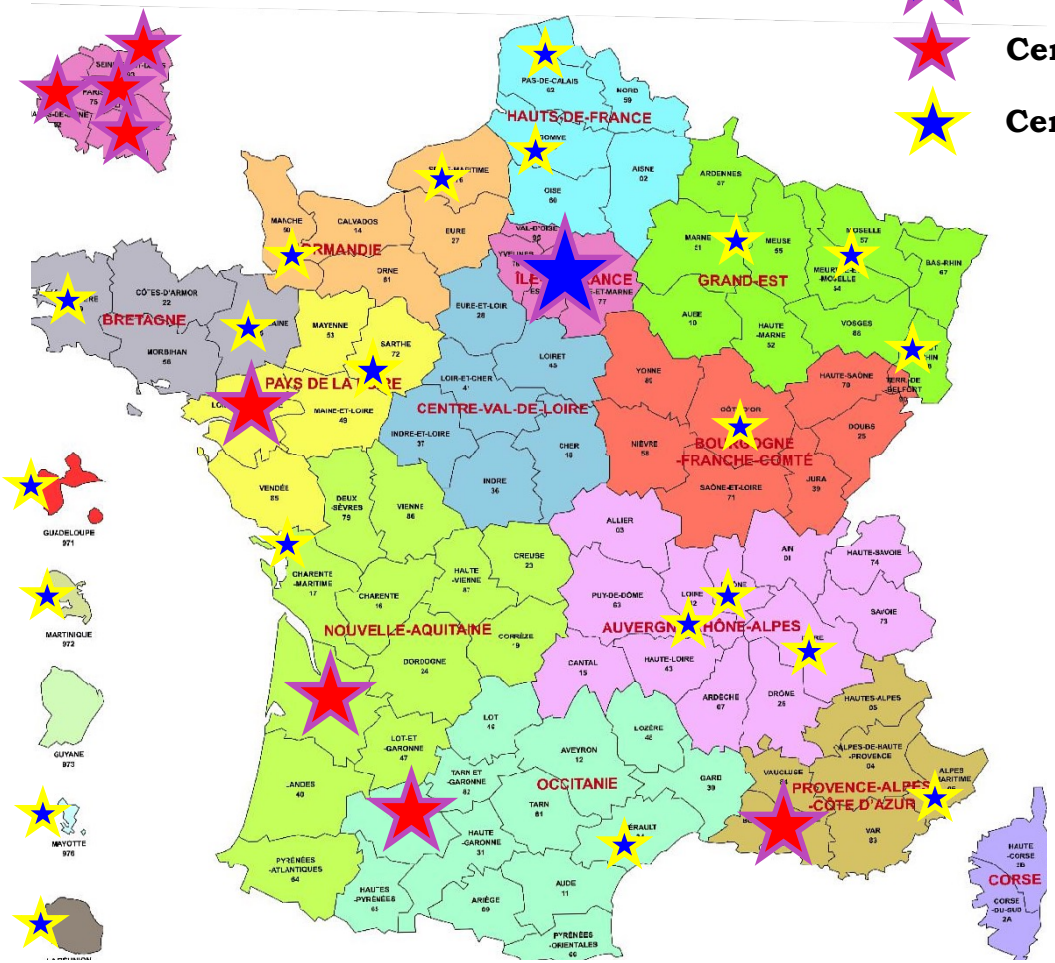
Bamara, Piramig +++
Nombre de patients vus en 2022 : 165



Centre de Référence National

Centres de Référence Constitutifs

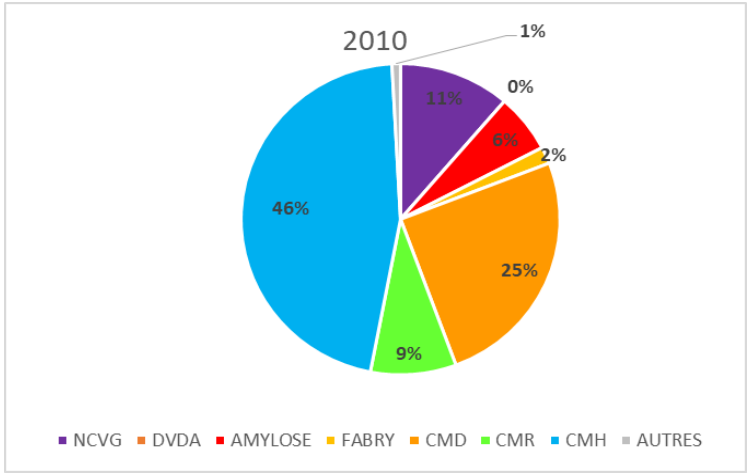
Centres de Compétence

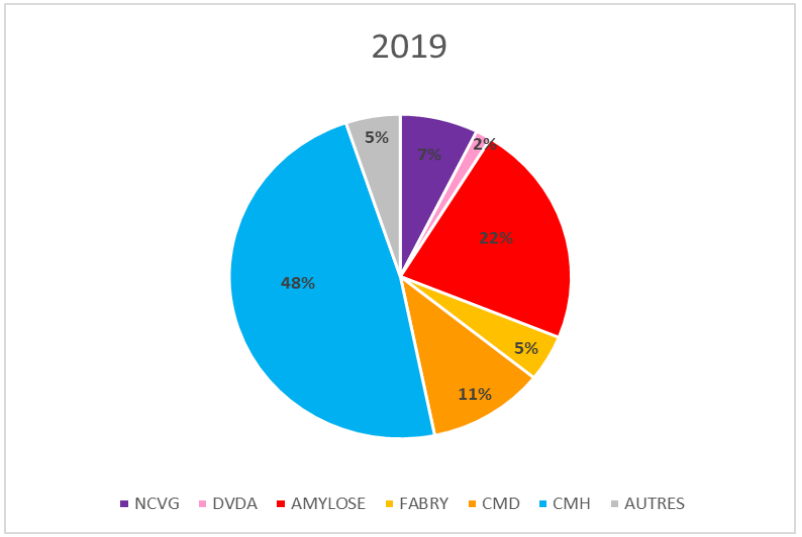


cardiogen
filière nationale de santé
maladies cardiaques héréditaires ou rares
www.filiere-cardiogen.fr

CENTRE DE COMPETENCE DES CARDIOMYOPATHIES
Activité

Répartition des motifs de consultations dans le CCC depuis 2010:





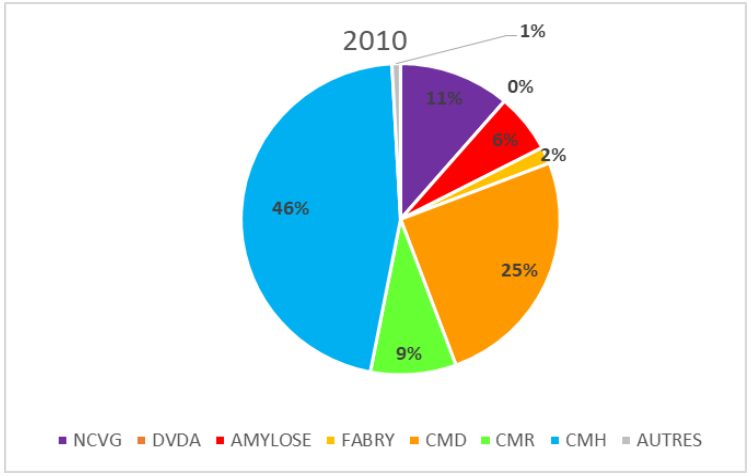
46% CMH
25% CMD
11% NCVG
6% Amylose
2% Maladie de Fabry

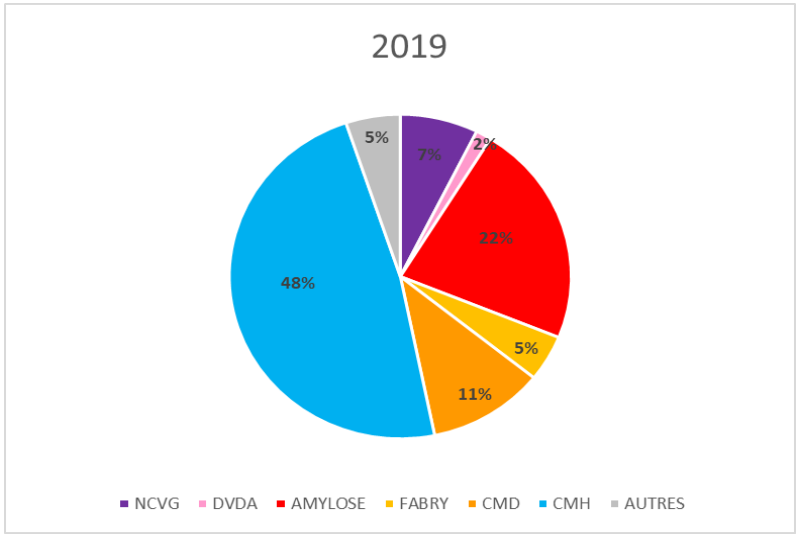
CMH 1er motif de Cs
Causes rares de CM: amylose et Fabry en augmentation

48% CMH
11% CMD
7% NCVG
22% Amylose
5% Maladie de Fabry

CENTRE DE COMPETENCE DES CARDIOMYOPATHIES
Activité

Répartition des motifs de consultations dans le CCC depuis 2010:





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CMH 1er motif de Cs
Causes rares de CM: amylose et Fabry en augmentation

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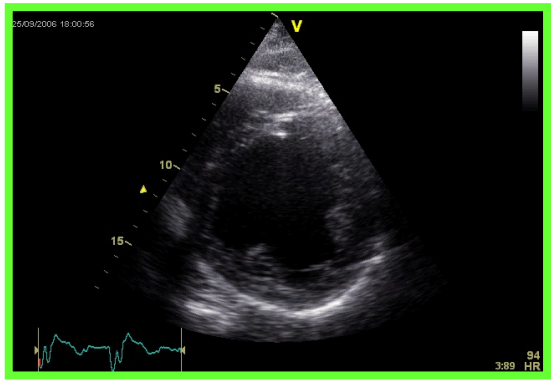
11% CMD
7% NCVG
22% Amylose
5% Maladie de Fabry

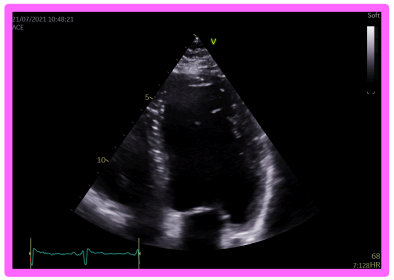
Classification of cardiomyopathies

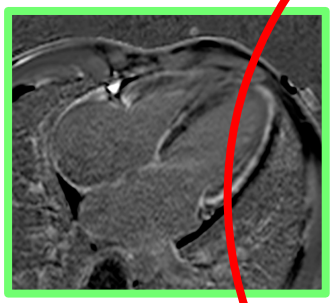
CM – ESC Guidelines 2023



DCM

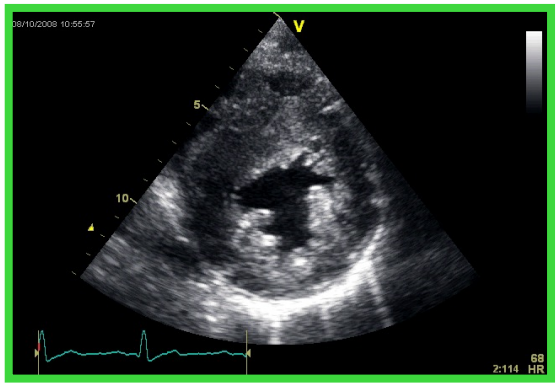
Dilated Cardiomyopathy





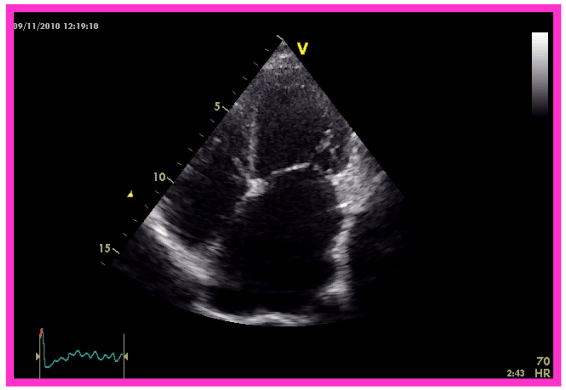
NDLVC

Non-dilated LV Cardiomyopathy



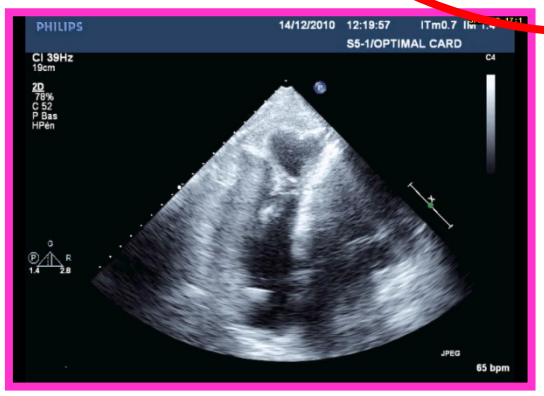
HCM

Hypertrophic Cardiomyopathy



RCM

Restrictive Cardiomyopathy



ARVC

Arrhythmogenic RV Cardiomyopathy

Traitement des CMH obstructives

1. ***Comprendre le mécanisme des symptômes***

2. **Prescrire un traitement adapté**

Les symptômes et l'obstruction dans les CMH

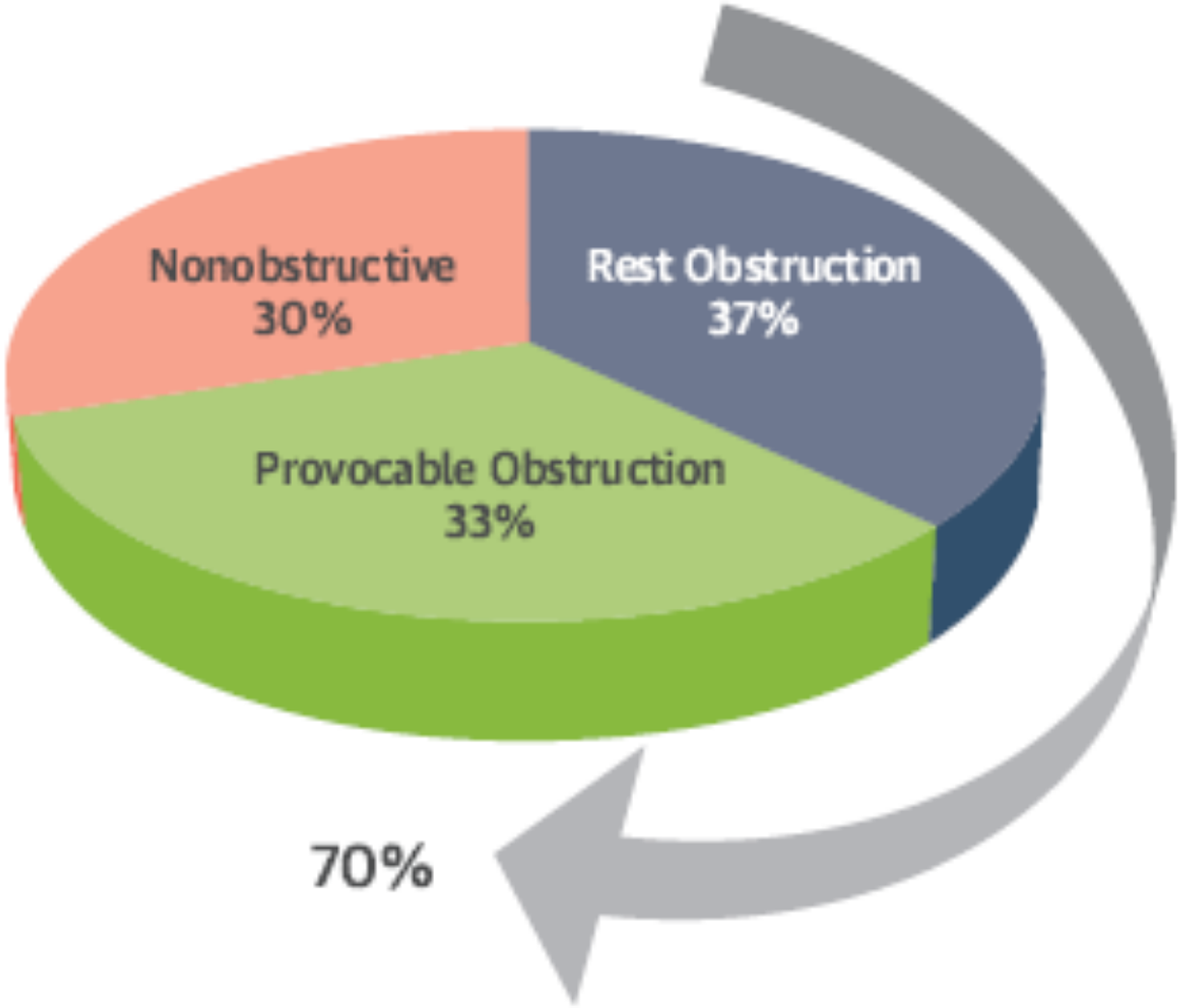
JACC STATE-OF-THE-ART REVIEW

2022

Management of Hypertrophic Cardiomyopathy

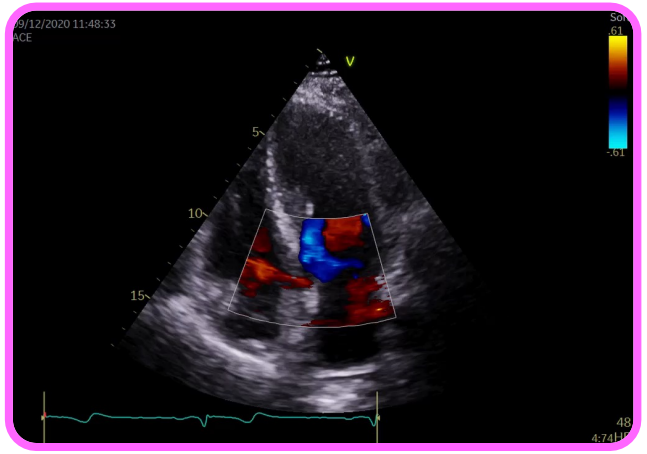
JACC State-of-the-Art Review

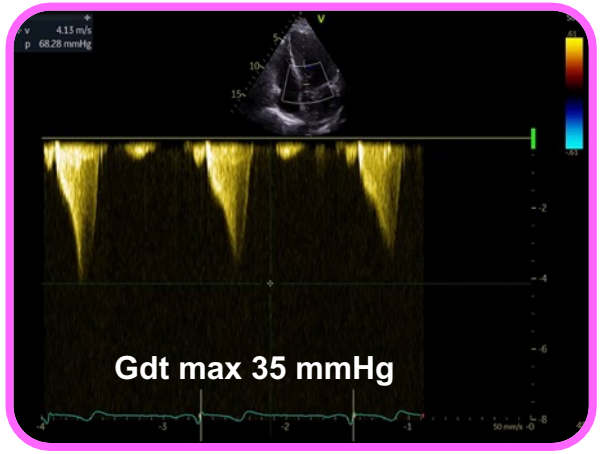
Barry J. Maron, MD,[a] Milind Y. Desai, MD,[b] Rick A. Nishimura, MD,[c] Paolo Spirito, MD,[d] Harry Rakowski, MD,[e] Jeffrey A. Towbin, MD,[f] Joseph A. Dearani, MD,[g] Ethan J. Rowin, MD,[a] Martin S. Maron, MD,[a] Mark V. Sherrid, MD[h]

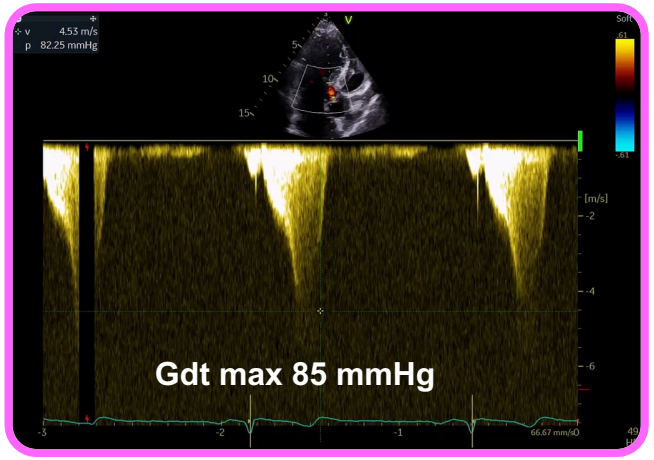


Quantification de l'obstruction intra-VG

- Manœuvres de Valsalva assis et penché en avant
- Puis debout
- Echocardiographie d'effort chez patients symptomatiques
- Echocardiographie dobutamine contre-indiquée







basal **Valsalva**

- **Obstruction = gradient maximal ≥ 30mmHg**
- **Indication thérapeutique = gradient maximal ≥ 50 mmHg**

Traitement des CMH obstructives

1. **Comprendre le mécanisme des symptômes**

2. ***Prescrire un traitement adapté***

Traitement des CMH obstructives

1. Améliorer les symptomes, réduire l'obstruction

- ✓ Traitement « classique » béta bloquants, inhibiteurs calciques, disopyramide
- ✓ Alcoolisation septale
- ✓ Chirurgie myomectomie
- ✓ Inhibiteurs de la myosine

2. Améliorer la survie, prévenir la mort subite

Traitement des CMH obstructives

ESC
European Society
of Cardiology

2023 ESC Guidelines for the management of cardiomyopathies

Developed by the task force on the management of cardiomyopathies of the European Society of Cardiology (ESC)

American
Heart
Association.

CLINICAL PRACTICE GUIDELINES

2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines

Developed in Collaboration With and Endorsed by the American Medical Society for Sports Medicine, the Heart Rhythm Society, Pediatric & Congenital Electrophysiology Society, and the Society for Cardiovascular Magnetic Resonance

Les bétabloquants

- ✓ Peu de preuves
- ✓ BB non vasodilatateurs
- ✓ AMM en France
  - ➢ *Propranolol (Avlocardyl©)*
  - ➢ *Nadolol (Corgard©)*
  - ➢ *Pindolol (Visken©)*

Non-vasodilating beta-blockers, titrated to maximum tolerated dose, are recommended as first-line therapy to improve symptoms in patients with resting or provoked[c] LVOTO.[631–633,648–650]	I	B

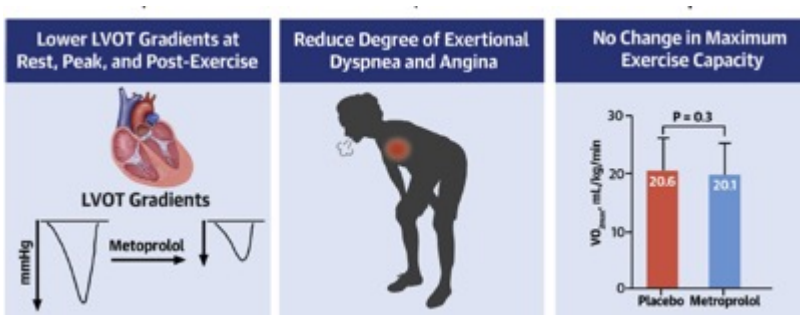
ESC European Society of Cardiology

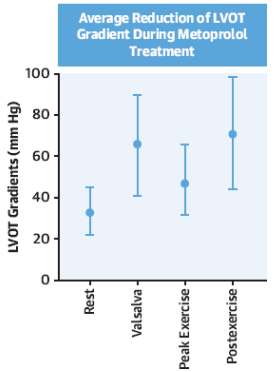
1	B-NR	1. In patients with obstructive HCM and symptoms* attributable to LVOTO, nonvasodilating beta blockers, titrated to effectiveness or maximally tolerated doses, are recommended.[1–3]

American Heart Association.

Randomized Trial of Metoprolol in Patients With Obstructive Hypertrophic Cardiomyopathy

Anne M. Dybro, MD,[a,b] Torsten B. Rasmussen, MD, PhD,[a,b] Roni R. Nielsen, MD, PhD,[a,b] Mads J. Andersen, MD, PhD,[a] Morten K. Jensen, MD, PhD,[a] Steen H. Poulsen, MD, DMSci[a,b]





Les inhibiteurs calciques bradycardisants

VERAPAMIL

Débuter 40 mg 2 ou 3/jour, jusqu'à 480 mg/jour

DILTIAZEM

Débuter 60 mg 2 ou 3/jour, jusqu'à 360 mg/jour

Attention si obstruction trop importante

(Gmax > 100 mmHg) ou HTP

Verapamil or diltiazem, titrated to maximum tolerated dose, are recommended to improve symptoms in symptomatic patients with resting or provoked[c] LVOTO who are intolerant or have contraindications to beta-blockers.[633,637–641]	I	B

ESC European Society of Cardiology

1	B-NR†	2. In patients with obstructive HCM and symptoms* attributable to LVOTO, for whom beta blockers are ineffective or not tolerated, substitution with nondihydropyridine calcium channel blockers (eg, verapamil,† diltiazem‡) is recommended.[4–6]
	C-LD‡	

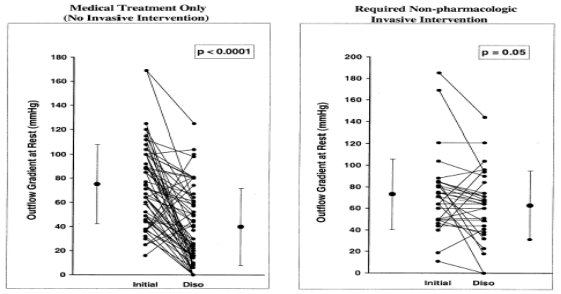
American Heart Association.

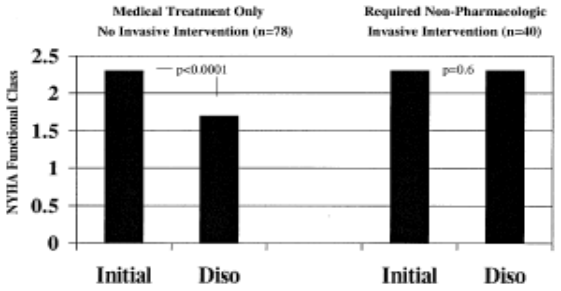
3: Harm	C-LD	7. For patients with obstructive HCM and severe dyspnea at rest, hypotension, very high resting gradients (eg, >100 mm Hg), as well as all children <6 weeks of age, verapamil is potentially harmful.[4,16]

American Heart Association.

Le disopyramide (Rythmodan®)

- ✓ 400-600 mg/j
- ✓ Attention surveillance du QT
- ✓ Association avec un bloqueur du NAV





Sherrid 2005 *JACC 2005;45:1251*

Disopyramide,[d] titrated to maximum tolerated dose, is recommended in addition to a beta-blocker (or, if this is not possible, with verapamil or diltiazem) to improve symptoms in patients with resting or provoked[c] LVOTO.[632–634]	I	B

ESC European Society of Cardiology

Disopyramide, titrated to maximum tolerated dose, may be considered as monotherapy in patients who are intolerant to or have contraindications to beta-blockers and verapamil/diltiazem to improve symptoms in patients with resting or provoked[c] LVOTO.[632]	IIb	C

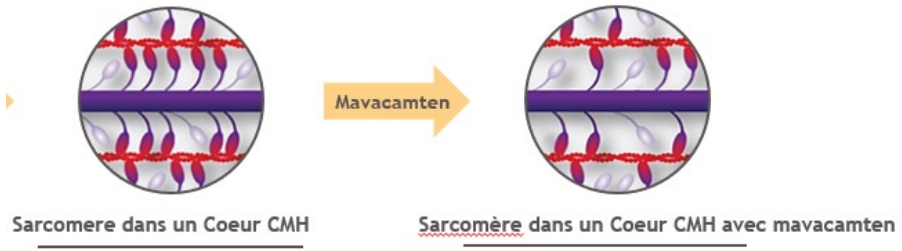
ESC European Society of Cardiology

1	B-R	3. For patients with obstructive HCM who have persistent symptoms* attributable to LVOTO despite beta blockers or nondihydropyridine calcium channel blockers, adding a myosin inhibitor (adult patients only), or disopyramide (in combination with an atrioventricular nodal blocking agent), or SRT performed at experienced centers,§ is recommended.[7–14]

American Heart Association.

Les Inhibiteurs de la myosine

MAVACAMTEN® (Camzyos)



Cardiac myosin ATPase inhibitor (mavacamten), titrated to maximum tolerated dose with echocardiographic surveillance of LVEF, should be considered in addition to a beta-blocker (or, if this is not possible, with verapamil or diltiazem) to improve symptoms in adult patients with resting or provoked[c] LVOTO.[622,642–646]	IIa	A

ESC European Society of Cardiology

Cardiac myosin ATPase inhibitor (mavacamten), titrated to maximum tolerated dose with echocardiographic surveillance of LVEF, should be considered as monotherapy in symptomatic adult patients with resting or provoked[c] LVOTO (exercise or Valsalva manoeuvre) who are intolerant or have contraindications to beta-blockers, verapamil/diltiazem, or disopyramide.[622,644–646]	IIa	B

ESC European Society of Cardiology

1	B-R	3. For patients with obstructive HCM who have persistent symptoms* attributable to LVOTO despite beta blockers or nondihydropyridine calcium channel blockers, adding a myosin inhibitor (adult patients only), or disopyramide (in combination with an atrioventricular nodal blocking agent), or SRT performed at experienced centers,§ is recommended.[7–14]

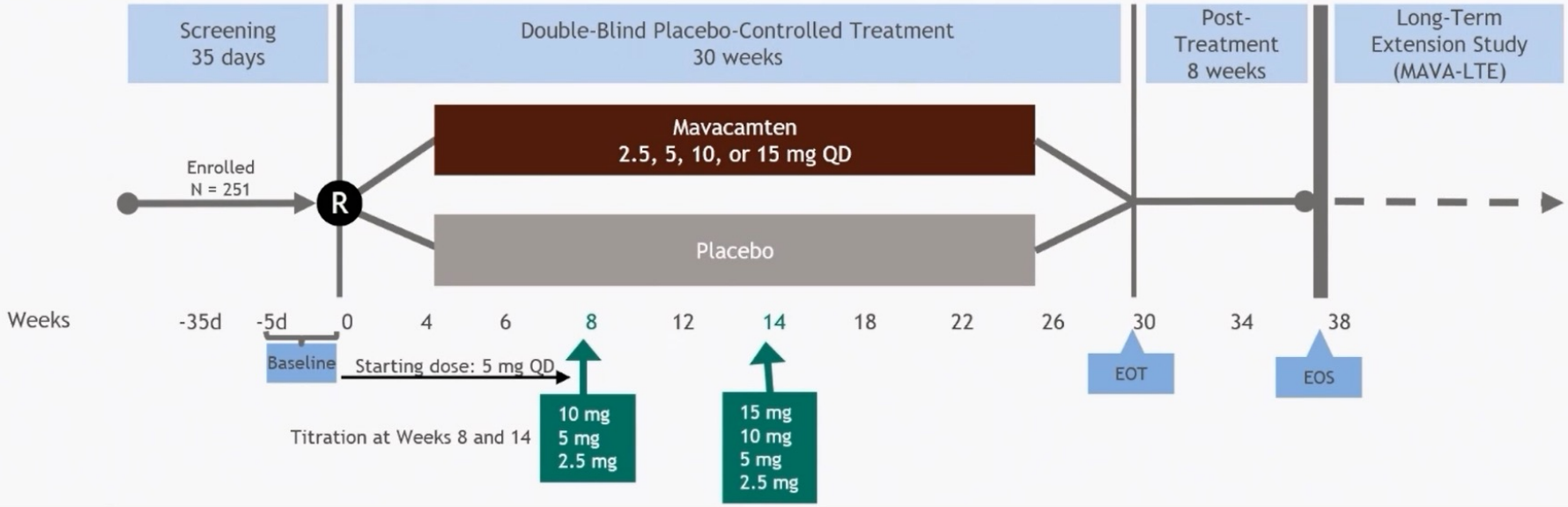
American Heart Association.

3: Harm	C-EO	11. In pregnant women, use of mavacamten is contraindicated due to potential teratogenic effects.

Inhibiteurs de la myosine – Mavacamten

EXPLORER-HCM: study design[1,2]

Patients with LVOT gradient ≥ 50 mm Hg and NYHA class II to III symptoms, LVEF ≥ 55%, were randomized 1:1 to receive once-daily oral mavacamten (starting dose of 5 mg with a 2-step dose titration) or placebo for 30 weeks



Temporary treatment discontinuation criteria: LVEF < 50% , plasma drug concentration > 1000 ng/mL, excessive QTcF prolongation

EOS, end of study; EOT, end of treatment; LVOT, left ventricular outflow tract; NYHA, New York Heart Association; QD, once daily.

1. Ho CY et al. *Circ Heart Fail* 2020;13. doi: 10.1161/CIRCHEARTFAILURE.120.006853. 2. Olivotto I et al. *Lancet* 2020;396:759–769. 3. Olivotto I, et al. Oral presentation at ESC Congress 2020 – The Digital Experience; August 29–September 1, 2020.

Inhibiteurs de la myosine – Mavacamten

Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial

Mavacamten

- First-in-class, selective inhibitor of cardiac myosin
- Reduces excessive actin-myosin cross-bridges, thus creating more favorable sarcomere function

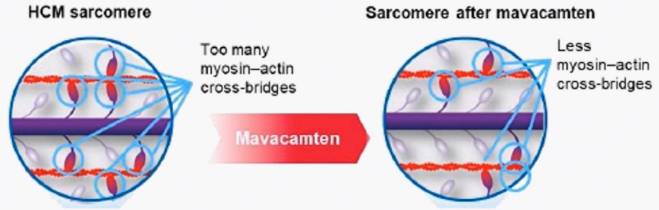
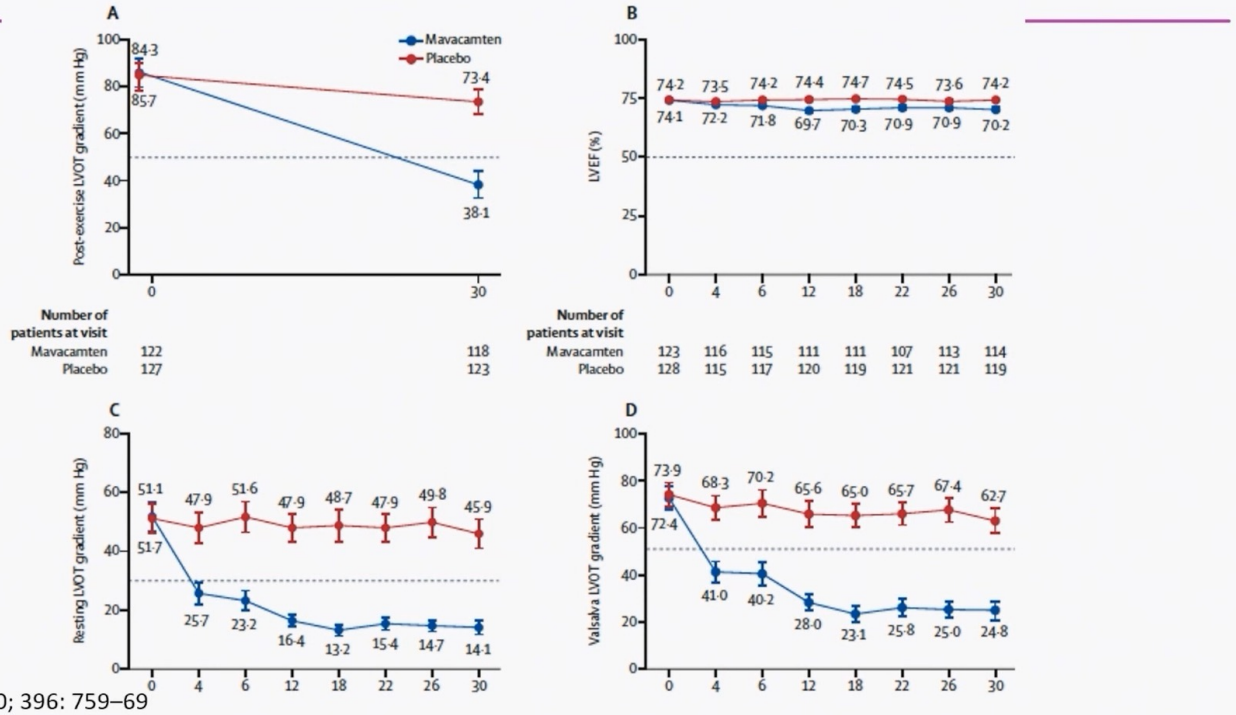


Figure 2: HCM sarcomere. Mavacamten reduces myosin-actin cross bridges.

Olivotto I. Lancet 2020; 396: 759–69

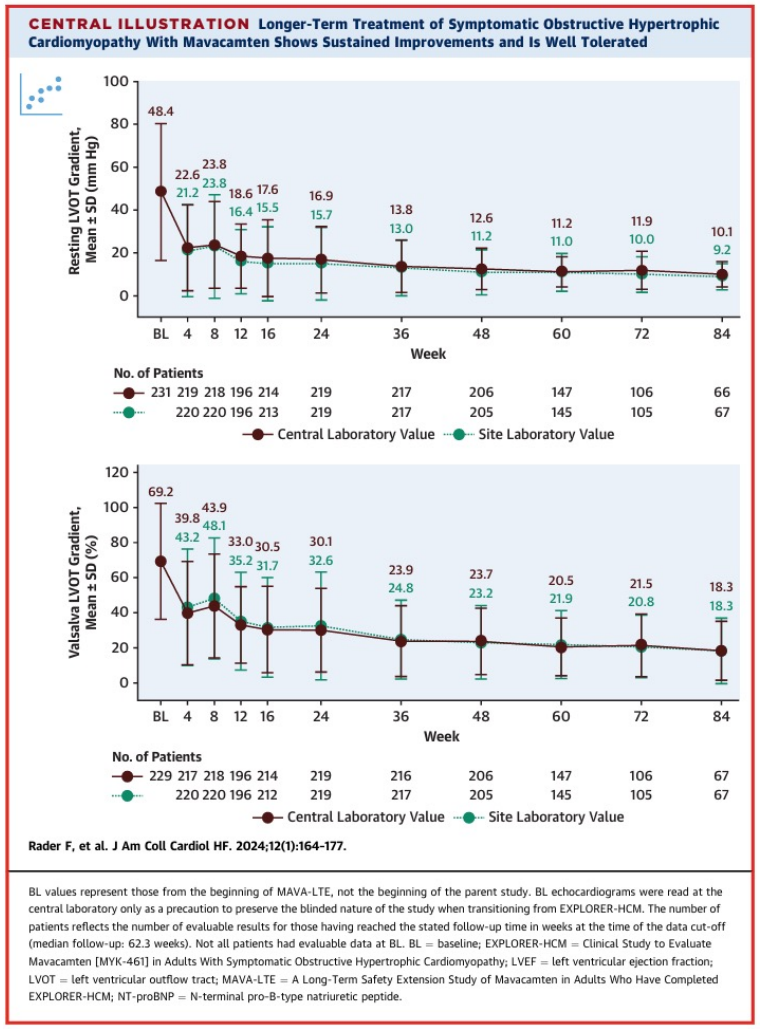
Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial

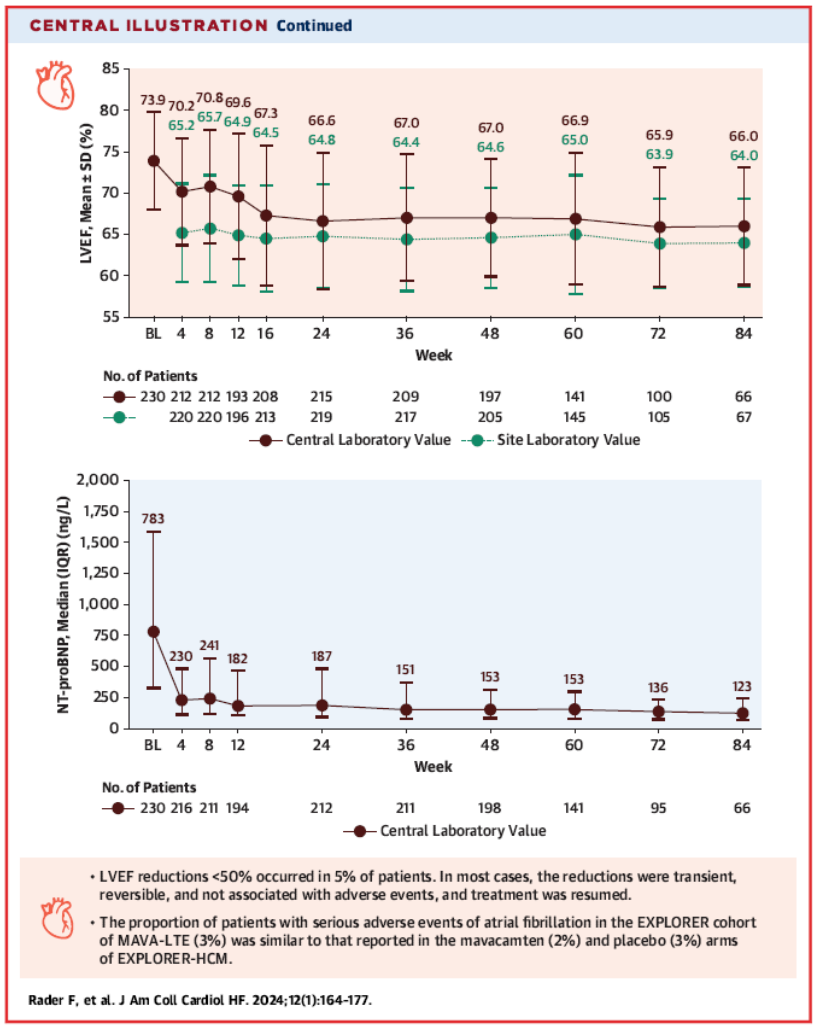


Olivotto I. Lancet 2020; 396: 759–69

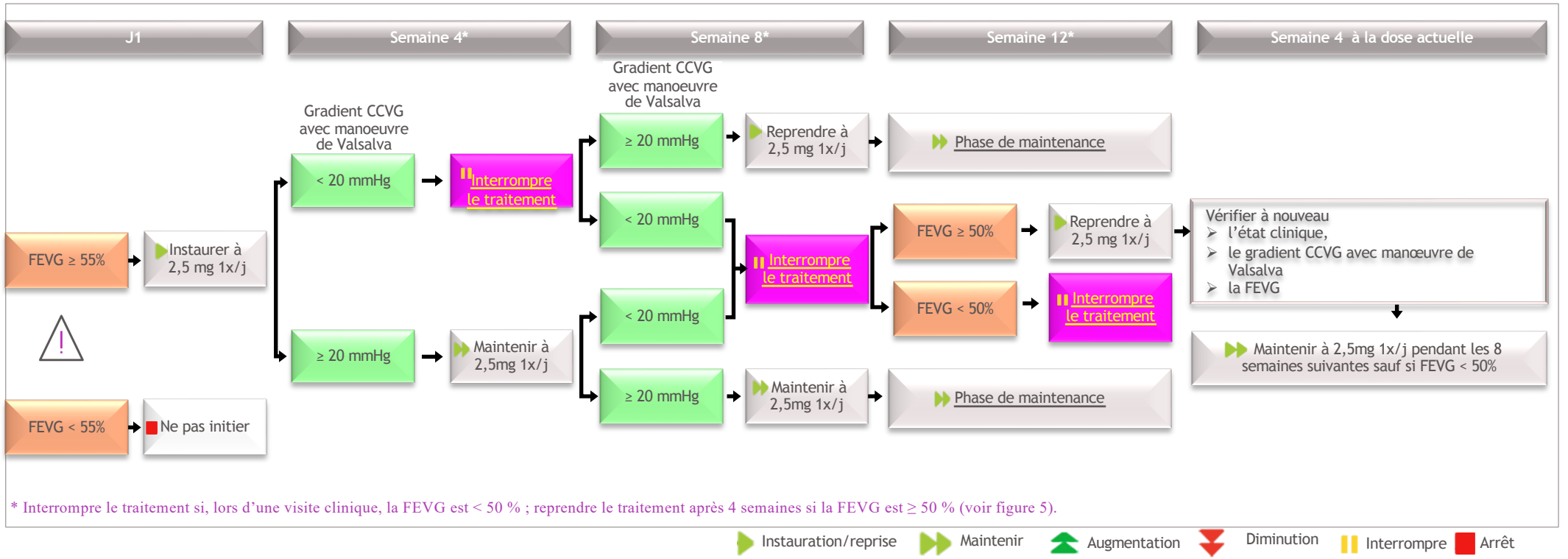
Mavacamten: résultats à long terme: MAVA-LTE

Rader F. JACC HF 2024





Ajustement du traitement sous Mavacamten



CCVG, chambre de chasse ventriculaire gauche; FEVG, fraction d'éjection ventriculaire gauche

European Summary of Product Characteristics, CAMZYOS® (mavacamten), site EMA consulté le 07 juillet 2023: https://www.ema.europa.eu/en/documents/product-information/camzyos-epar-product-information_fr.pdf

MAVACAMTEN en pratique

CAMZYOS™ (mavacamten) 2.5, 5, 10, 15mg capsules

Indication :

CMH obstructive (>50mmHg de gradient max au repos, au Valsalva ou à l'effort)
Symptomatique (NYHA II-III)
Malgré traitement optimal (bétabloquants, inhibiteurs calciques) ou intolérance

Génotypage CYP2C19 > posologie de départ (2,5 ou 5mg)

Contre-indications :

-FEVG<55%
-Grossesse (test de grossesse négatif + contraception efficace)

Interactions médicamenteuses : avec tous les inducteurs/inhibiteurs du CYP2C19 et CYP3A4 (peu de contre-indications absolues si métaboliseur normal)

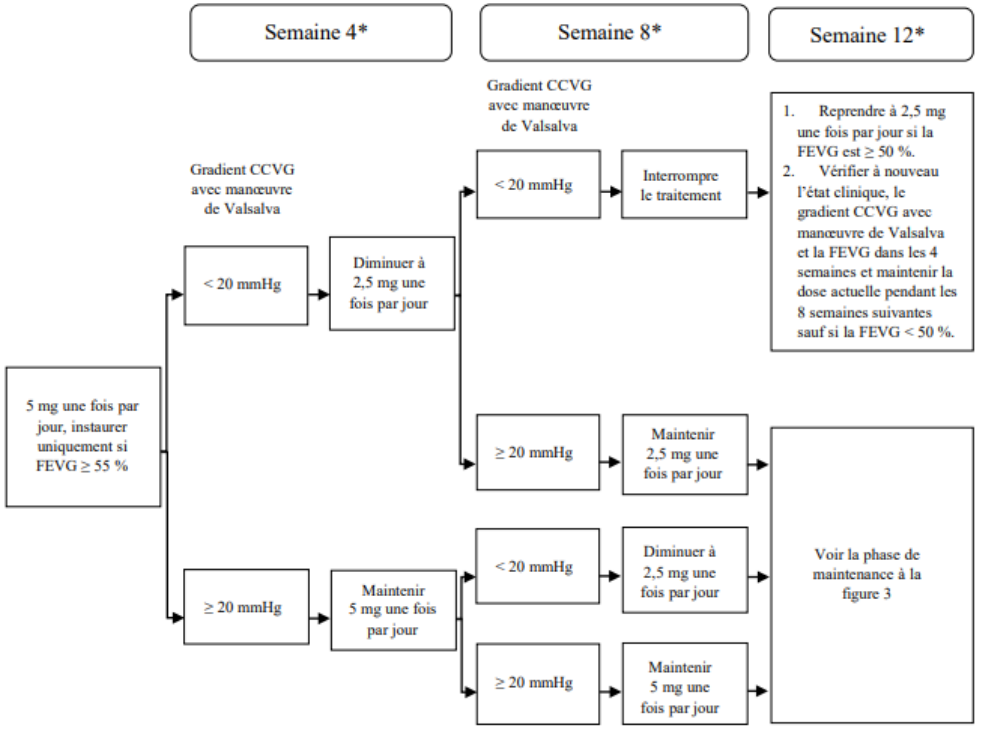
MAVACAMTEN en pratique

Suivi tous les mois pendant 3 mois

SECURITE = Vérifier que la dose n'est pas trop élevée

On ne majore jamais le traitement

Figure 2 : Instauration du traitement pour le phénotype métaboliseur intermédiaire, normal, rapide et ultrarapide du CYP2C19



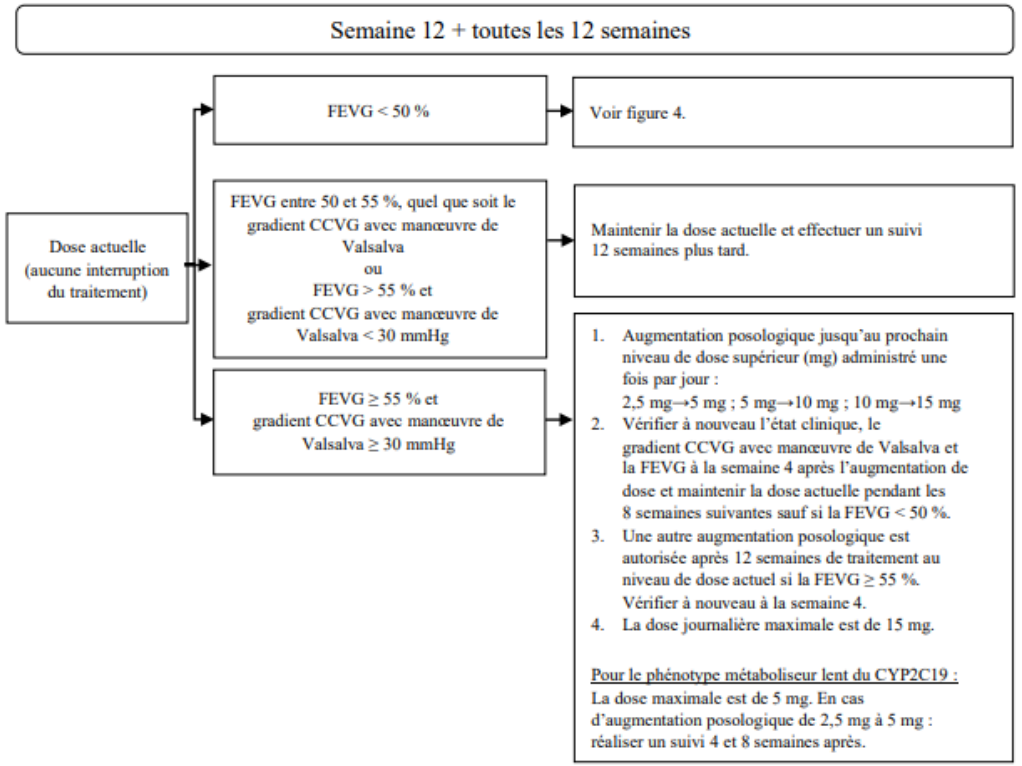
* Interrompre le traitement si, lors d'une visite clinique, la FEVG est < 50 % ; reprendre le traitement après 4 semaines si la FEVG est ≥ 50 % (voir figure 4).

MAVACAMTEN en pratique

Puis suivi tous les 3 mois pendant 1an au total

TITRATION jusqu'à posologie maximale tolérée (15mg)

Figure 3 : Phase de maintenance



CCVG = chambre de chasse ventriculaire gauche ; FEVG = fraction d'éjection ventriculaire gauche

Cohorte Marseillaise : population

60 patients éligibles au total :

-Instauration du traitement chez 36 patients

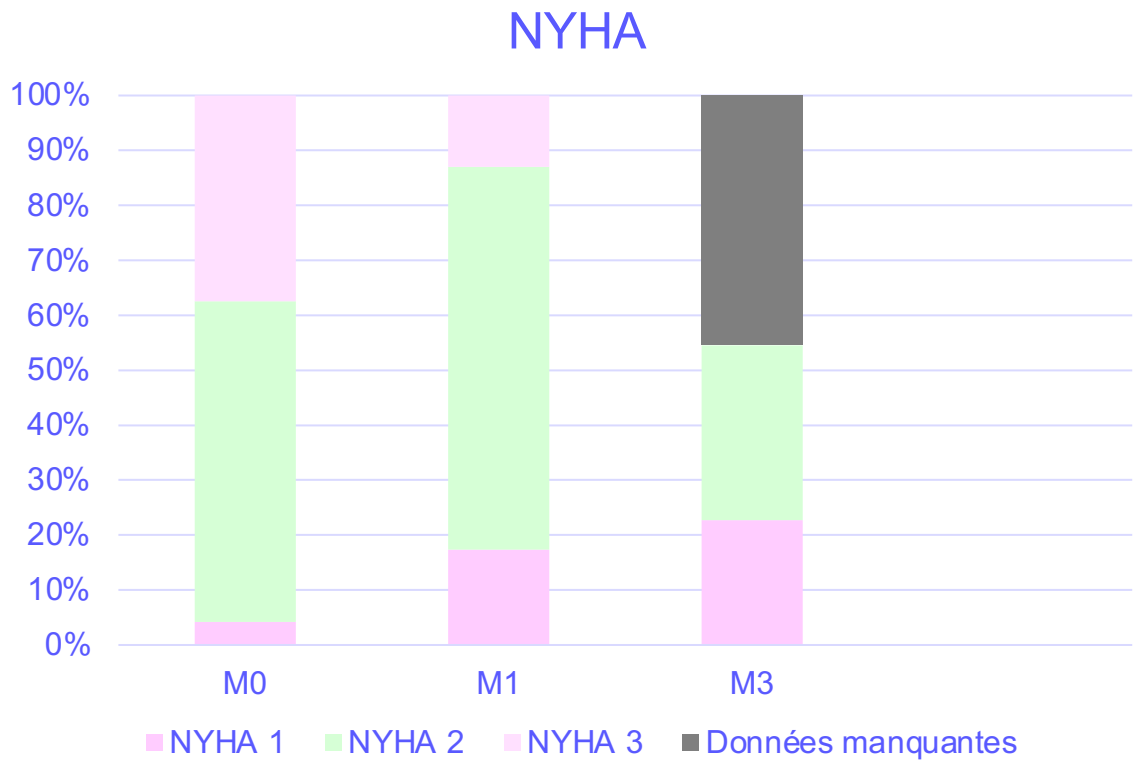
-22 patients depuis plus d'un mois (dont 12 patients depuis plus de 3 mois)

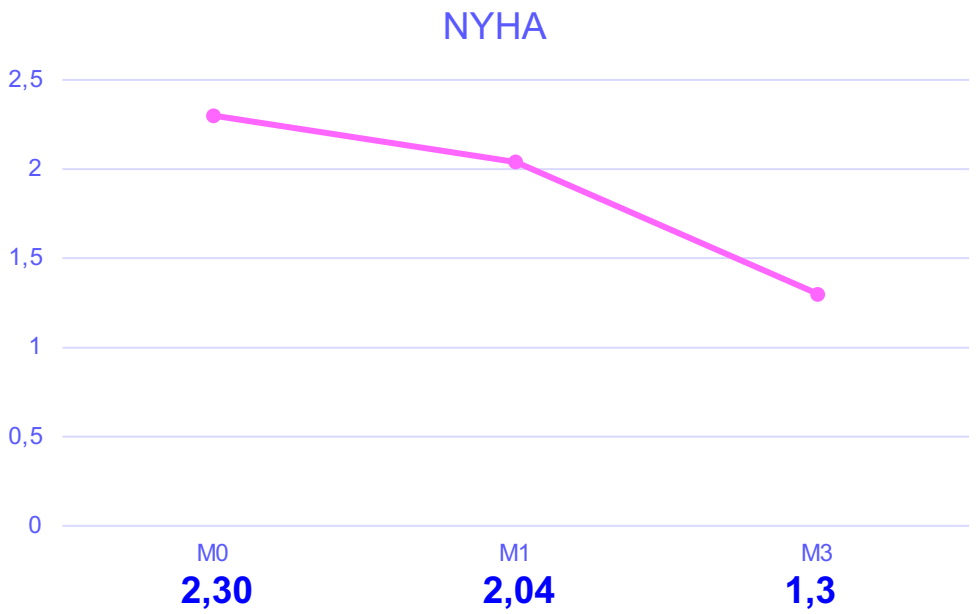
-14 patients depuis moins d'un mois

-24 patients en attente d'instauration

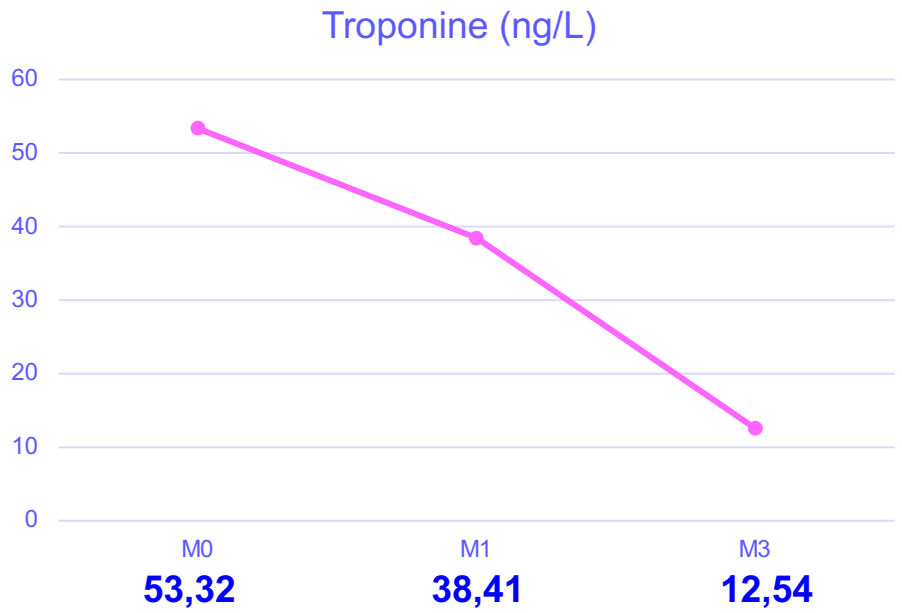
	Caractéristiques	EXPLORER (251 patients)
Age	62,09	58,5
Sexe		
Hommes	6/22 (27,27%)	59,36%
Femmes	16/22 (72,73%)	40,64%
Génétique		
Faite	22/22 (100%)	75,70%
Positive	4/22 (18,18%)	
Négative	10/22 (45,45%)	
En cours	8/22 (36,36%)	
Positive quand on a les résultats	4/14 (28,57%)	26,32%
Traitement de l'obstruction	21/22 (95,45%)	92,03%
Bétabloquants	19/21 (90,48%)	81,82%
Anticalciques	2/21 (9,52%)	18,18%
DAI	3/22 (13,64%)	22,31%

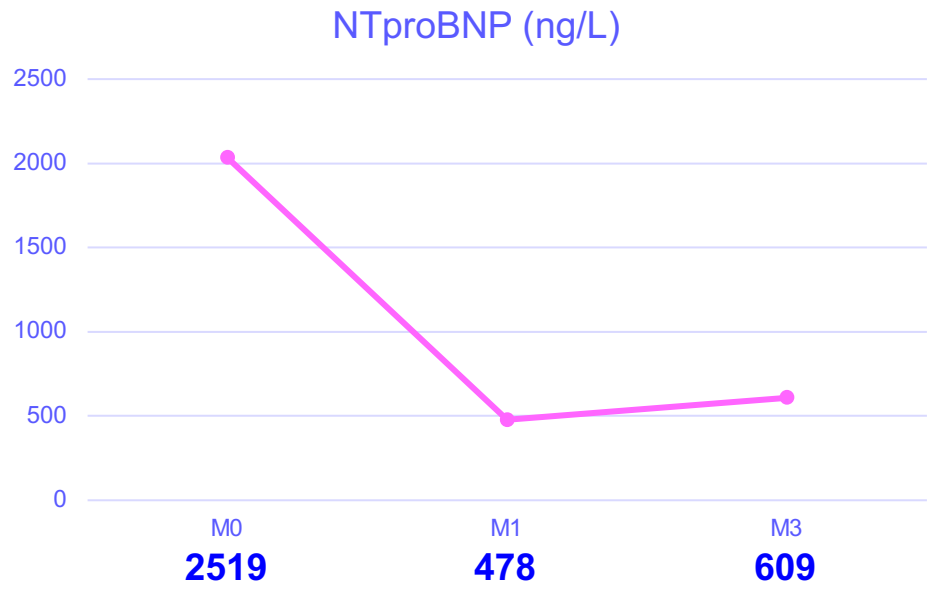
Cohorte Marseillaise : NYHA



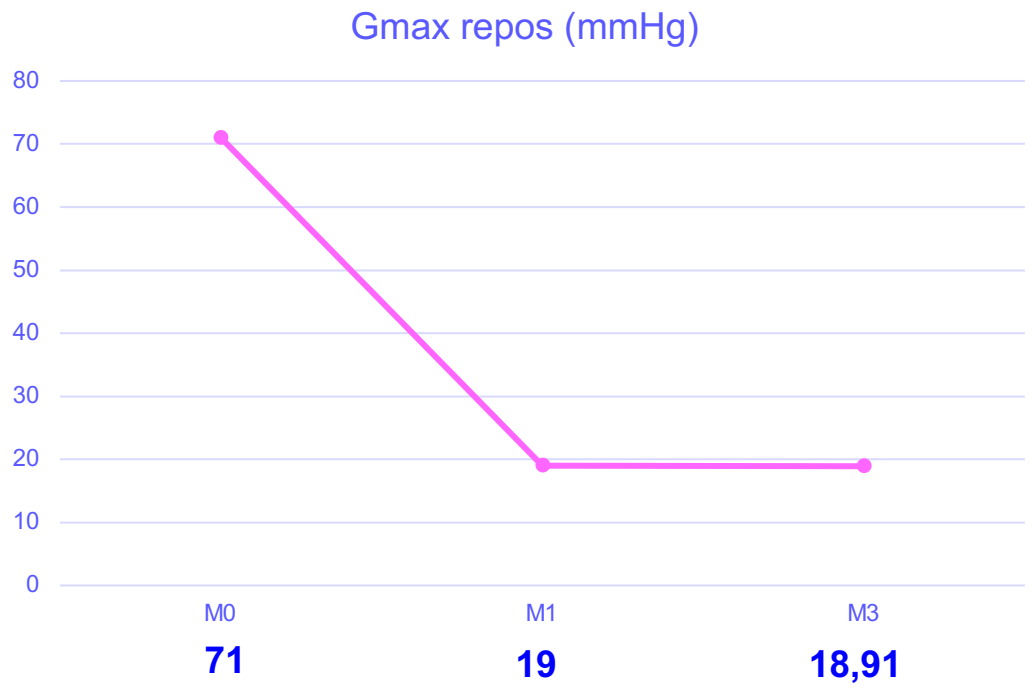


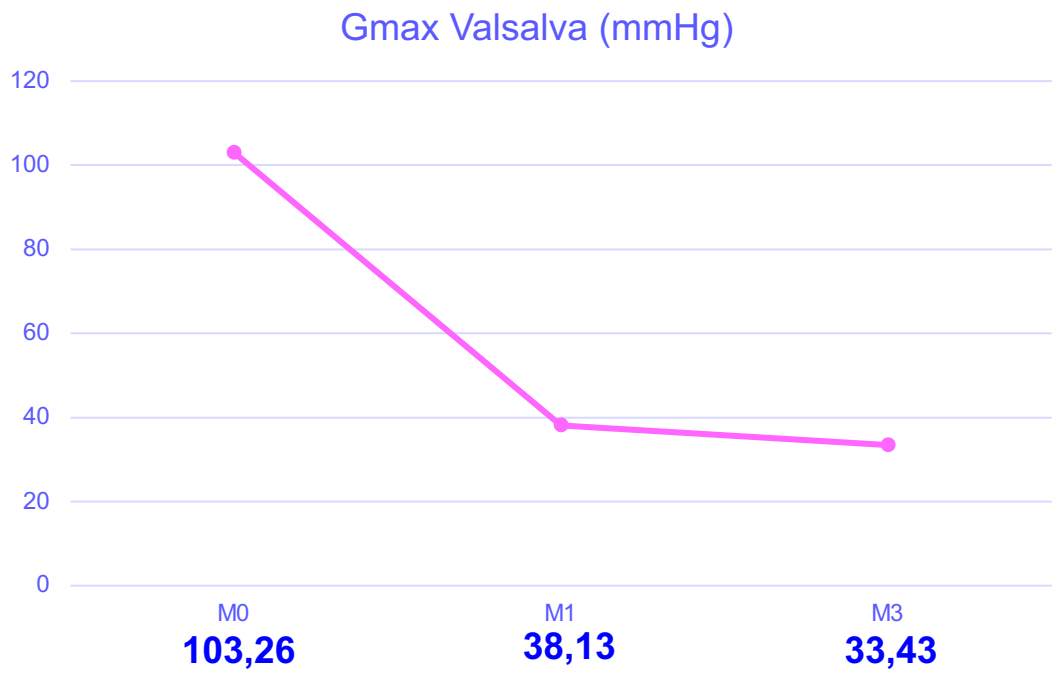
Cohorte Marseillaise : biomarqueurs





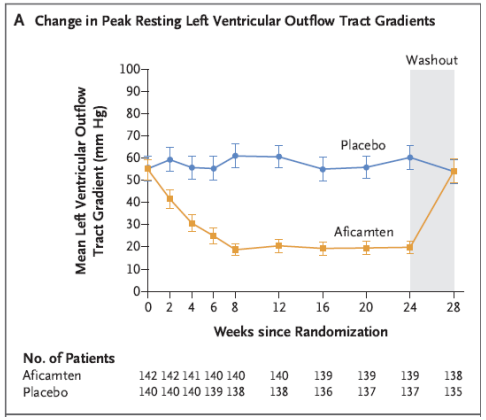
Cohorte Marseillaise : Gmax

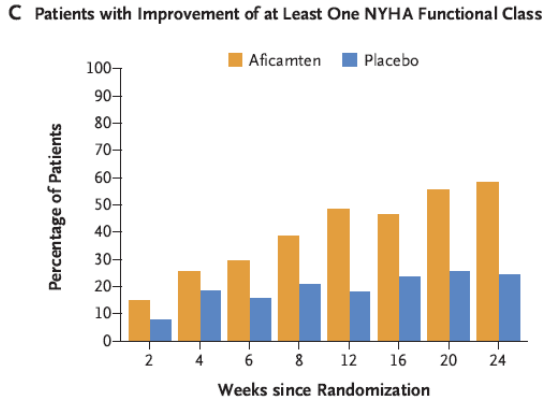




Aficamten for Symptomatic Obstructive Hypertrophic Cardiomyopathy

- ✓ 282 CMHo, 142 Aficamten vs 140 placebo
- ✓ FU 24 weeks
- ✓ Critère principal: change VO2 max à 24 semaines
- ✓ 10 critères secondaires





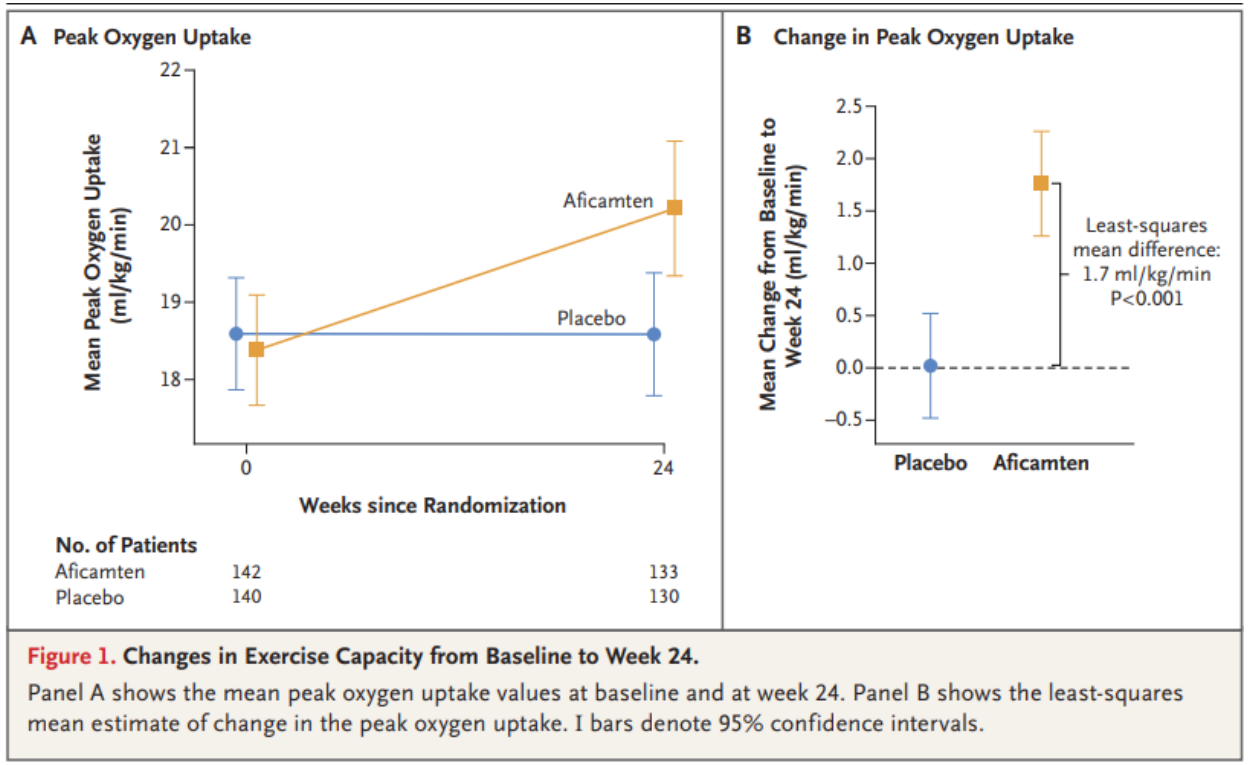


Figure 1. Changes in Exercise Capacity from Baseline to Week 24.
Panel A shows the mean peak oxygen uptake values at baseline and at week 24. Panel B shows the least-squares mean estimate of change in the peak oxygen uptake. I bars denote 95% confidence intervals.

Mavacamten

- First-in-class, selective inhibitor of cardiac myosin
- Reduces excessive actin-myosin cross-bridges, thus creating more favorable sarcomere function

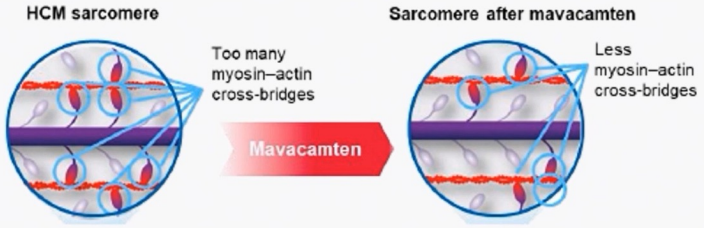


Figure 2: HCM sarcomere. Mavacamten reduces myosin-actin cross bridges.

SEQUOIA HCM

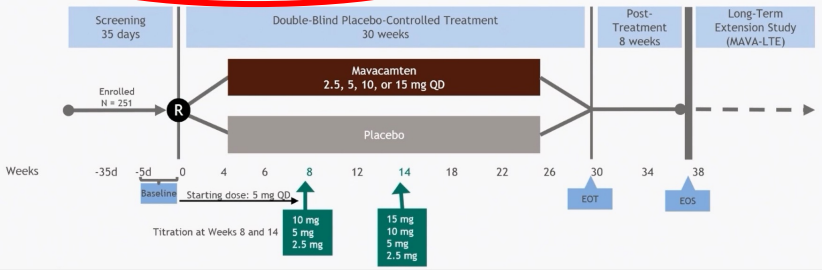
A PHASE 3, MULTI-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL TO EVALUATE THE EFFICACY AND SAFETY OF CK-3773274 IN ADULTS WITH SYMPTOMATIC HYPERTROPHIC CARDIOMYOPATHY AND LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION

Protocol Amendment 02 dated 10 December 2021

Cytokinetics

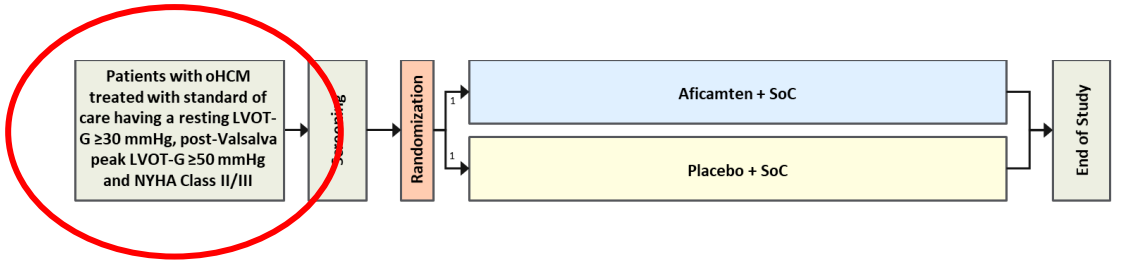
EXPLORER-HCM: study design[1,2]

Patients with LVOT gradient ≥ 50 mm Hg and NYHA class II to III symptoms, LVEF ≥ 55%, were randomized 1:1 to receive once-daily oral mavacamten (starting dose of 5 mg with a 2-step dose titration) or placebo for 30 weeks



Temporary treatment discontinuation criteria: LVEF < 50% , plasma drug concentration > 1000 ng/mL, excessive QTcF prolongation

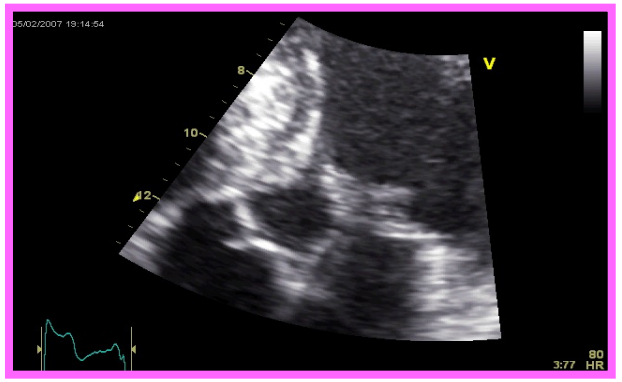
EOS, end of study; EOT, end of treatment; LVOT, left ventricular outflow tract; NYHA, New York Heart Association; QD, once daily.
1. Ho CY et al. *Circ Heart Fail* 2020;13. doi: 10.1161/CIRCHEARTFAILURE.120.006853. 2. Olivotto I et al. *Lancet* 2020;396:759–769. 3. Olivotto I, et al. Oral presentation at ESC Congress 2020 – The Digital Experience; August 29–September 1, 2020.

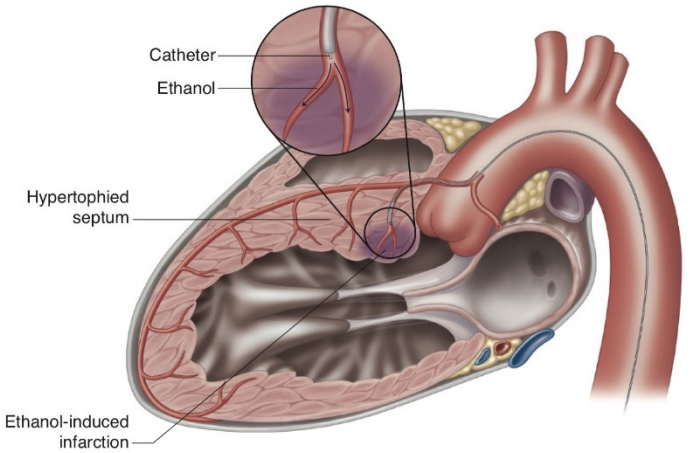


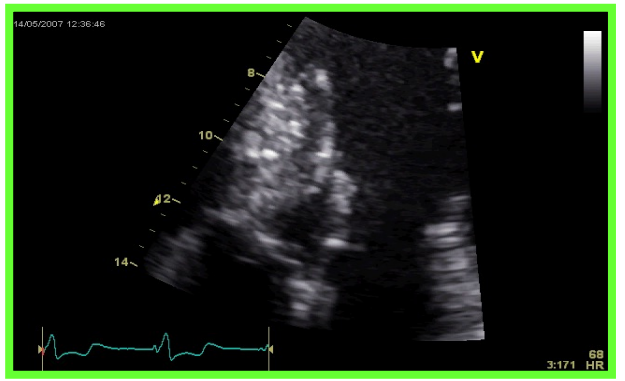
Study Visits	Screen	D1	W2	W4	W6	W8	W12	W16	W20	W24	W28
Echocardiogram	↑	↑	↑*	↑*	↑*	↑*	↑	↑	↑	↑	↑
CPET	↑									↑	
KCCQ		↑	↑	↑	↑	↑	↑	↑	↑	↑	↑
NYHA	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑	↑
Dose Titration			↑	↑	↑						

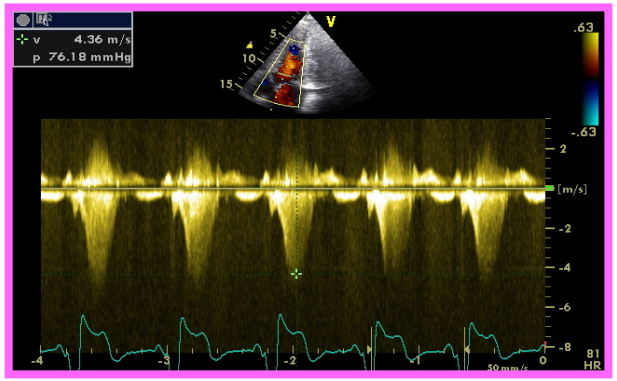
* Focused echocardiogram

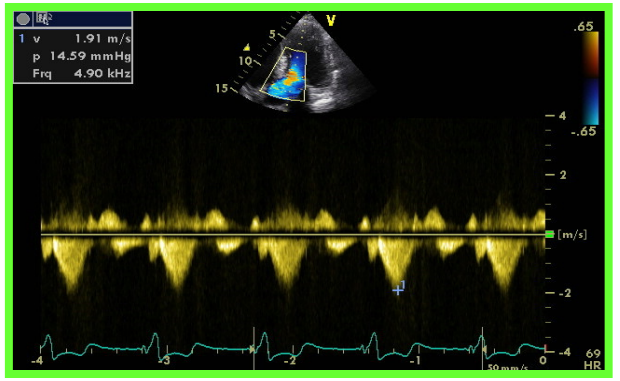
Alcoolisation septale







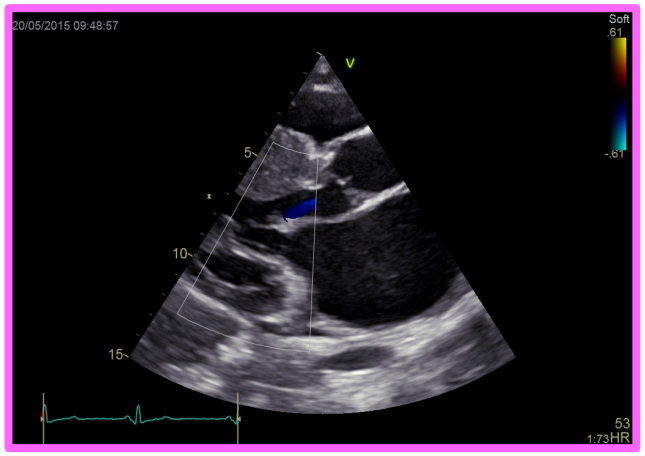


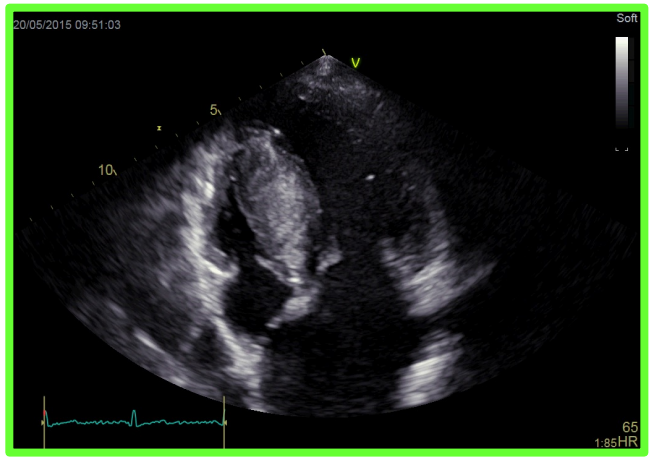


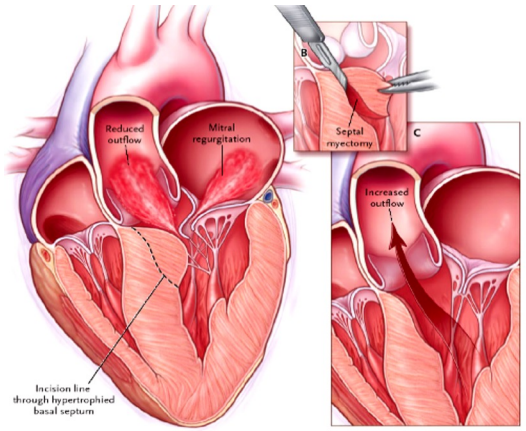
Avant alcoolisation septale

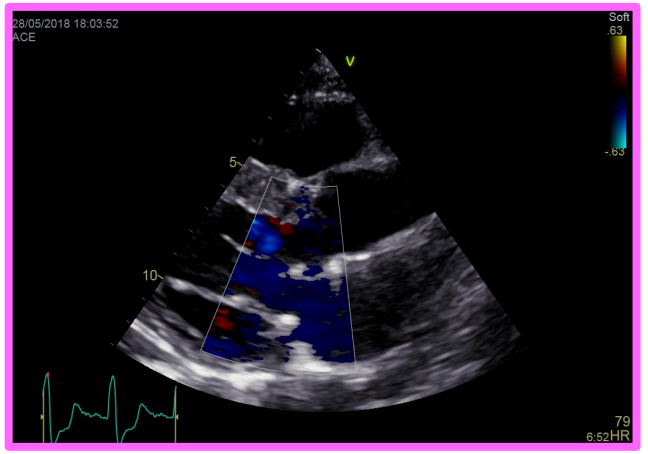
Après alcoolisation septale

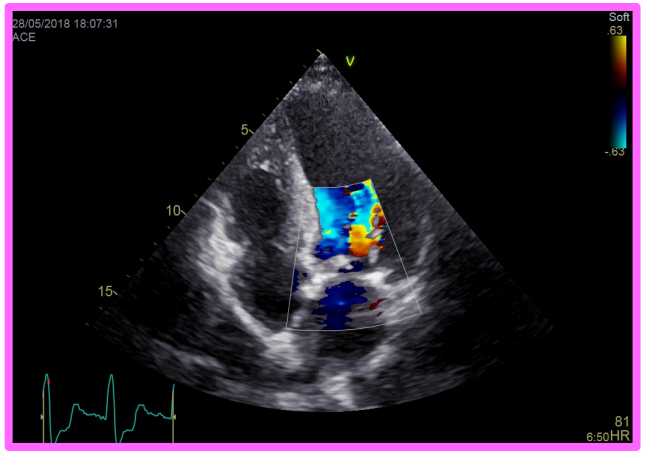
Me D., 15 ans, MYH7, myomectomie







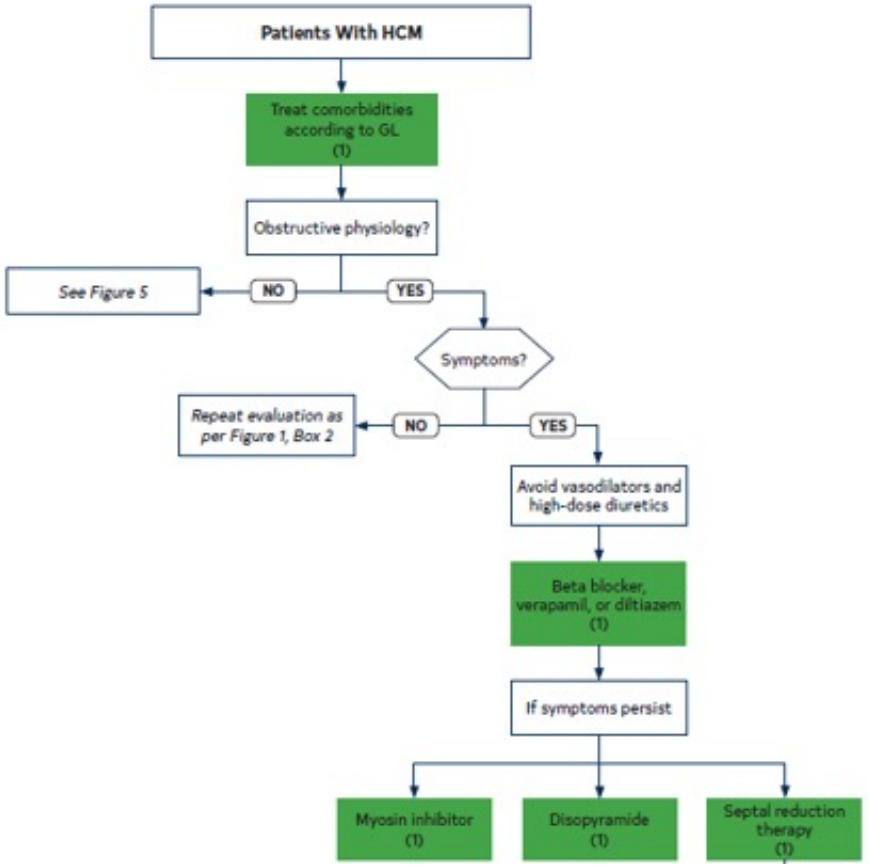




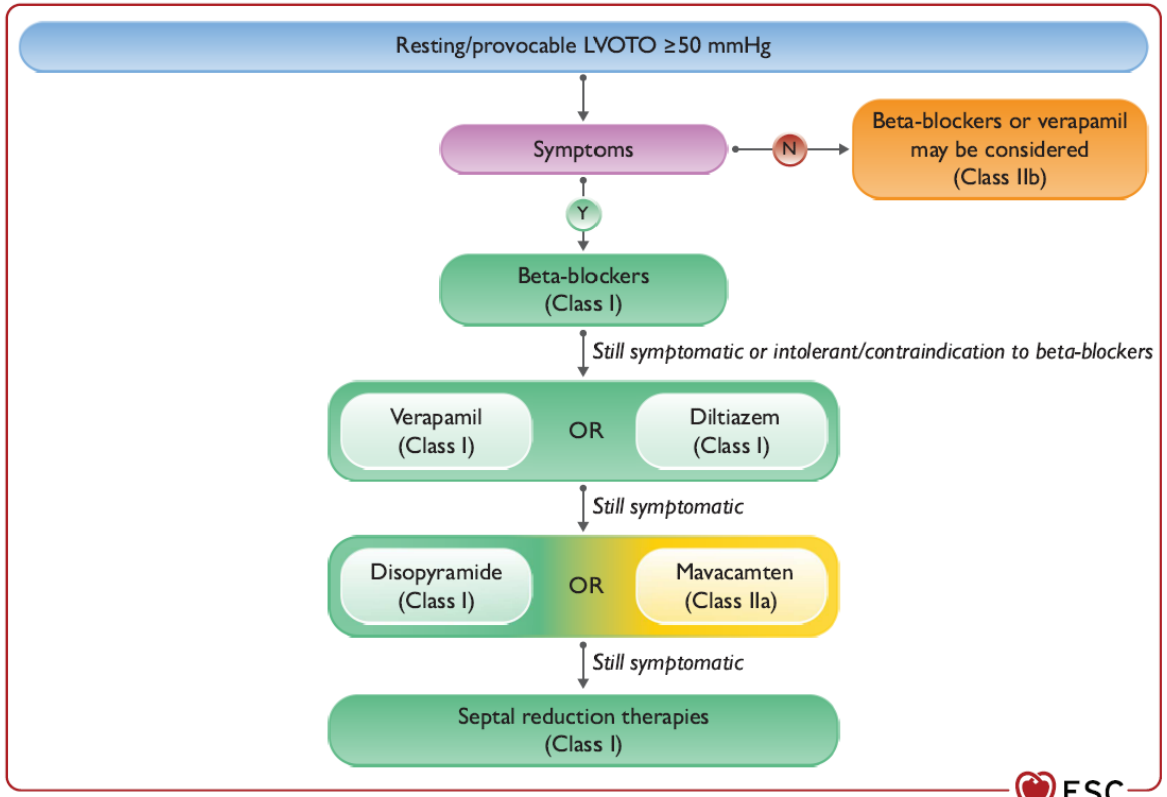
Pré-opératoire

Post-opératoire

Quel traitement pour quel patient ?



ACC/AHA 2024



CM – ESC Guidelines 2023

Etudes futures ou en cours

1. Études sur les CMH obstructives

- ✓ MAPLE-HCM - Phase 3, Randomized, Double-Blind Trial and Safety of Aficamten vs Metoprolol in oHCM
- ✓ LEXICON: Phase 3, Randomized, Double-blind, Multicenter Study of Sotagliflozin in oHCM or n-oHCM

2. Etudes sur les CMH non obstructives

- ✓ REDWOOD-HCM: Phase 2,Randomized, Double-Blind Trial and Safety of Aficamten vs placebo in n-oHCM
- ✓ ACACIA -HCM - Phase 3,Randomized, Double-Blind Trial and Safety of Aficamten vs placebo in n-oHCM
- ✓ MAVERICK-HCM: Phase 2,Randomized, Double-Blind Trial and Safety of Mavacamten vs placebo in n-oHCM
- ✓ ODYSSEY-HCM: Phase 3,Randomized, Double-Blind Trial and Safety of Mavacamten vs placebo in n-oHCM
- ✓ Ninerafaxstat: phase 2 randomized, cardiac mitotrope
- ✓ Thérapie génique 1st case of gene therapy in sarcomeric HCM (phase 1b, Cleveland 2023)

Etudes futures ou en cours CMH obstructives

- ✓ MAPLE-HCM - Phase 3, Randomized, Double-Blind Trial and Safety of Aficamten vs Metoprolol in oHCM
- ✓ LEXICON: Phase 3, Randomized, Double-blind, Multicenter Study of Sotagliflozin in oHCM or n-oHCM

MAPLE HCM

A Phase 3, Multi-Center, Randomized, Double-Blind Trial to Evaluate the Efficacy and Safety of Aficamten Compared to Metoprolol in Adults with Symptomatic Obstructive Hypertrophic Cardiomyopathy

Lexicon

SONATA-HCM: A Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Efficacy and Safety of Sotagliflozin in Patients with Symptomatic Hypertrophic Cardiomyopathy

MAPLE-HCM: Presented at the Heart Failure Society of America (HFSA) Annual Scientific Meeting | Cleveland, OH, USA | October 6–9, 2023
SONATA-HCM: Clinical Trial NCT06433050

Etudes futures ou en cours CMH non obstructives

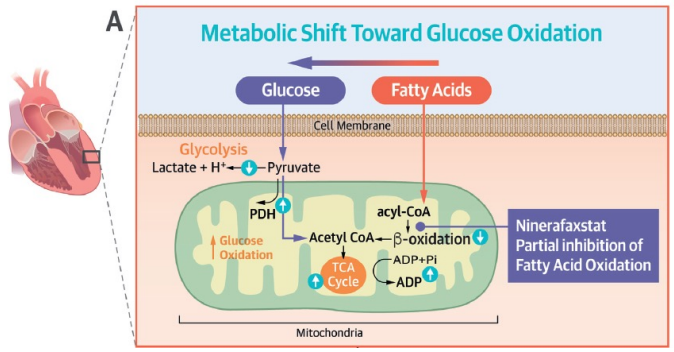
A Phase 2,Randomized, Double-Blind Trial and Safety of Aficamten vs placebo in n-oHCM

A Phase 3,Randomized, Double-Blind Trial and Safety of Aficamten vs placebo in n-oHCM

MAVERICK-HCM: Phase 2,Randomized, Double-Blind Trial and Safety of Mavacamten vs placebo in n-oHCM

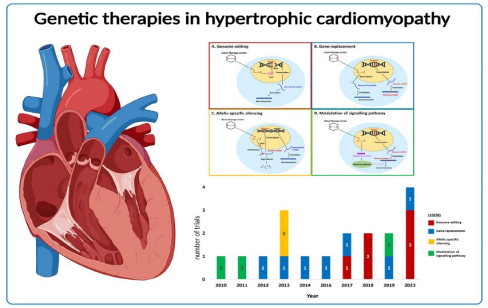
ODYSSEY-HCM: Phase 3,Randomized, Double-Blind Trial and Safety of Mavacamten vs placebo in n-oHCM

NINERAFAXSTAT: phase 2 randomized, cardiac mitotrope



THERAPIE GENIQUE:

1st case of gene therapy in sarcomeric HCM (phase 1b, Cleveland 2023)



Paratz ED, Can J Cardiol 2024

REDWOOD-HCM: Masri A, et al. J Card Fail. 2024

ACACIA-HCM: Clinical Trial NCT06433050

ODYSSEY-HCM: Desai M et al. Heart Failure Congress 2024

NINERAFAXSTAT: Maron MS, et al. J Am Coll Cardiol. 2024

MAVERICK-HCM: Ho CY, J Am Coll Cardiol. 2024

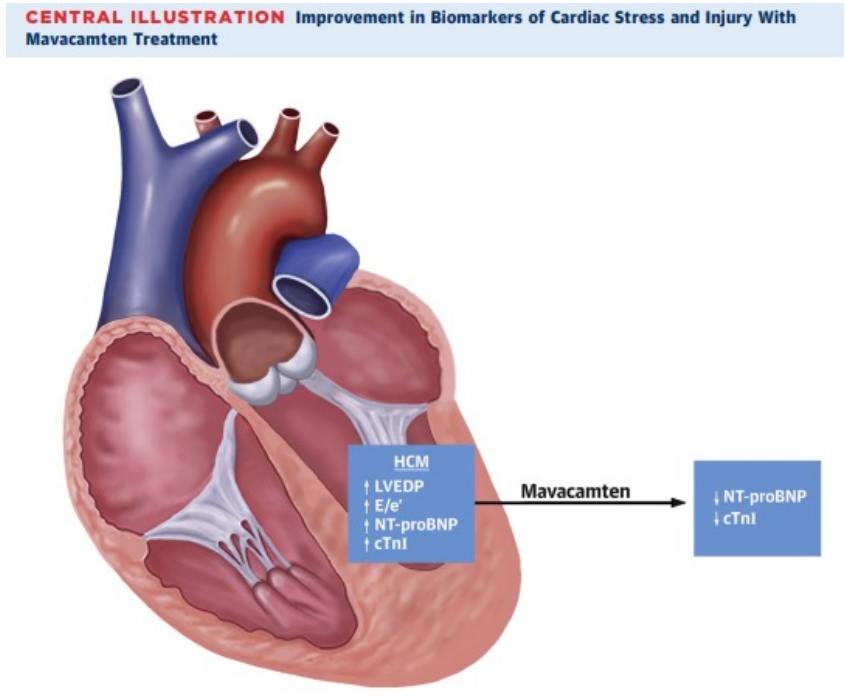
Les nouveaux traitements dans les CMH

1. Importance de documenter la cause des symptômes
2. Rechercher l'obstruction par l'échocardiographie avec manœuvre de Valsalva et effort
3. Le traitement conventionnel utilise les bétabloquants/ les anticalciques / le disopyramide
4. Les inhibiteurs de la myosine sont indiqués chez les patients qui restent symptomatiques et obstructifs
5. Le Mavacamten démontre une amélioration spectaculaire des symptomes et de l'obstruction
6. L'Aficamten semble montrer des résultats similaires
7. Leur role dans les CMH non obstructives est en cours d'étude
8. D'autres voies de recherche sont ouvertes !! (Gliflozines, mitotropes, thérapie génique)

La Timone Hospital; Marseille, France

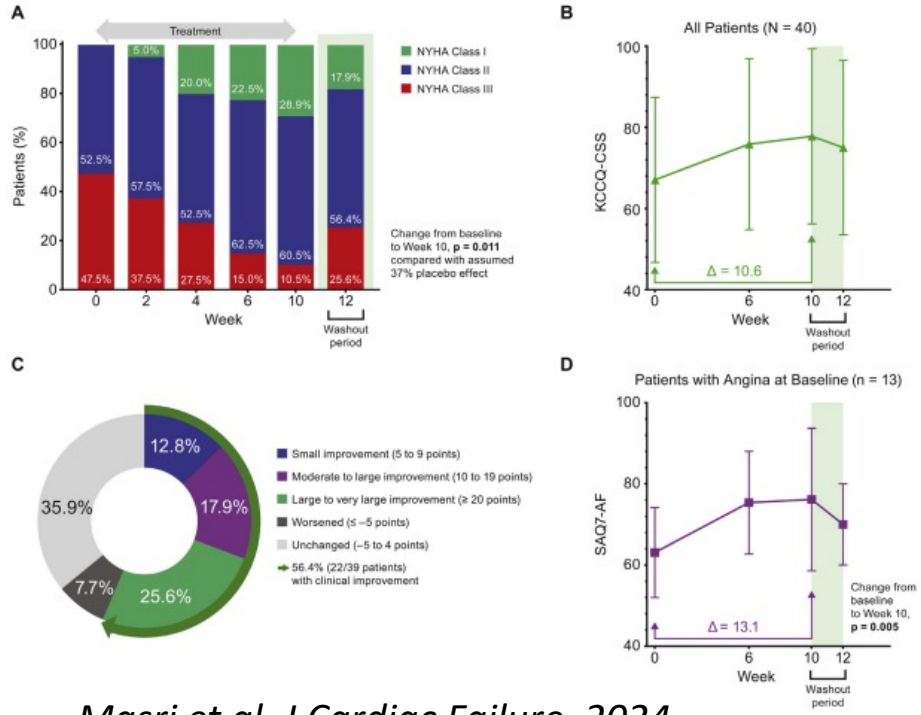
Et la CMH Non-Obstructive symptomatique?

- Mavacamten MAVERICK-HCM phase 2 trial



Ho et al, JACC, 2020

- Aficamten REDWOOD-HCM cohort 4, phase 2 trial



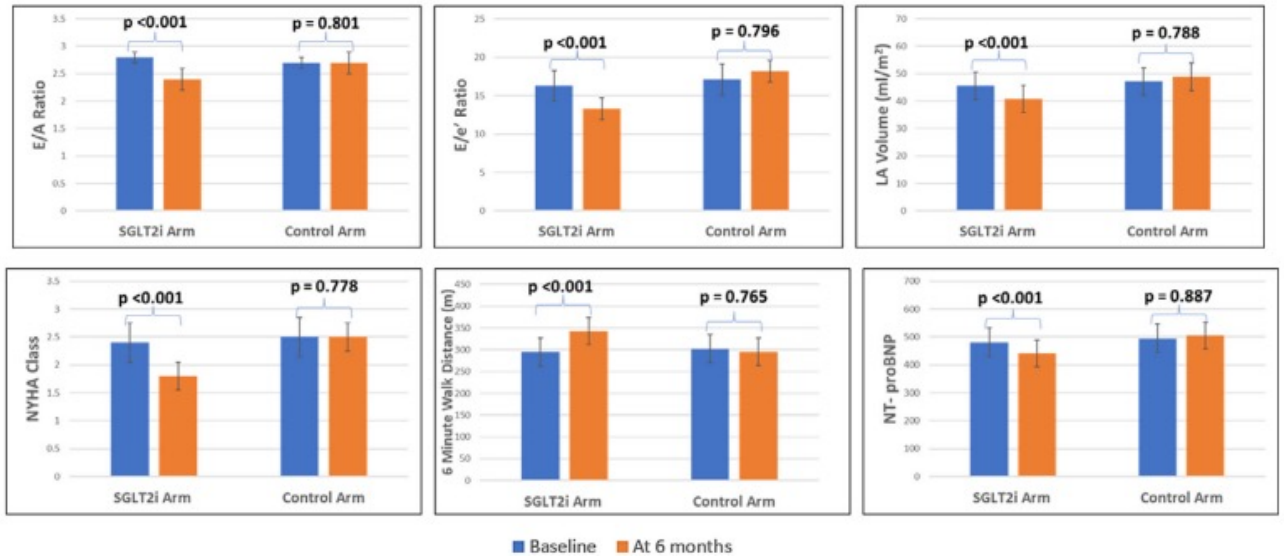
Masri et al, J Cardiac Failure, 2024

→ Mavacamten phase 3 trial **ODYSSEY**, under way

→ Aficamten phase 3 trial **ACACIA**, coming soon

Autres médicaments de la CMH Non-Obstructive?

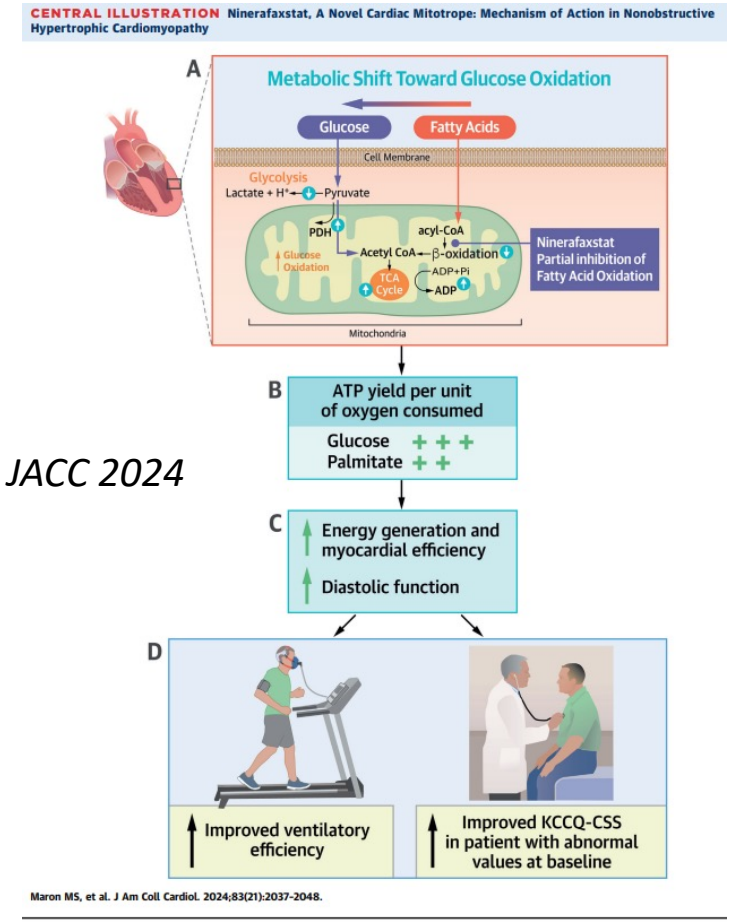
- Sotagliflozin SGLT1i & SGLT2i in diabetic pts with noHCM (44 pts, open-label, 6 months)



Subramanian et al, AJC, 2023

→ Sotagliflozin phase 3 trial **(Lexicon lab)**, coming soon

- Ninerafaxstat phase 2 trial, a novel cardiac mitotrope, enhances cardiac energetics, 67 pts FU 12 w

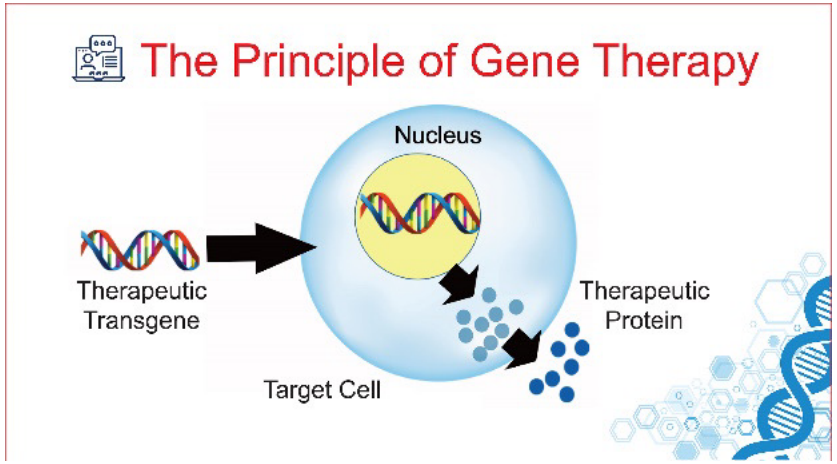


Maron MS et al, JACC 2024

Et l'édition génique / thérapie génique ?

New therapeutic strategies

ARNi, microRNA, ASO antisense oligonucleotide, gene therapy



TENAYA™ THERAPEUTICS

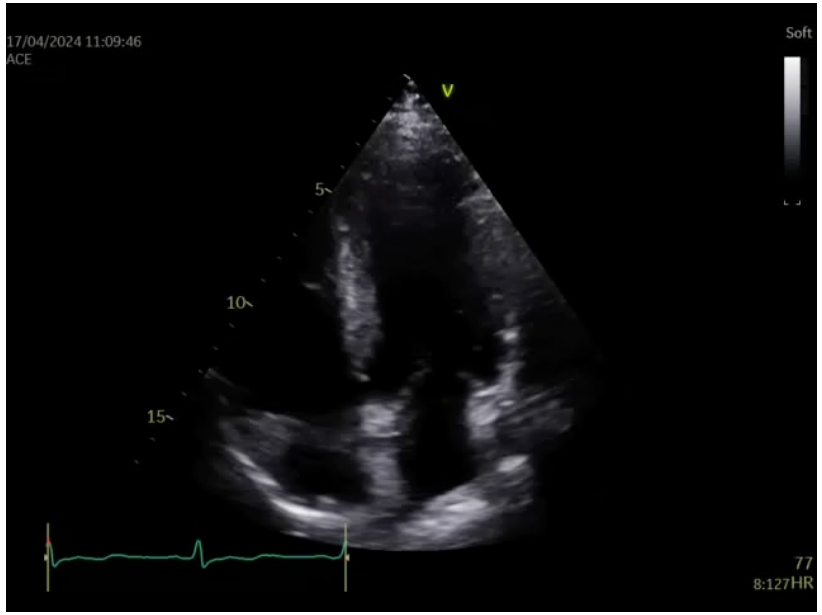
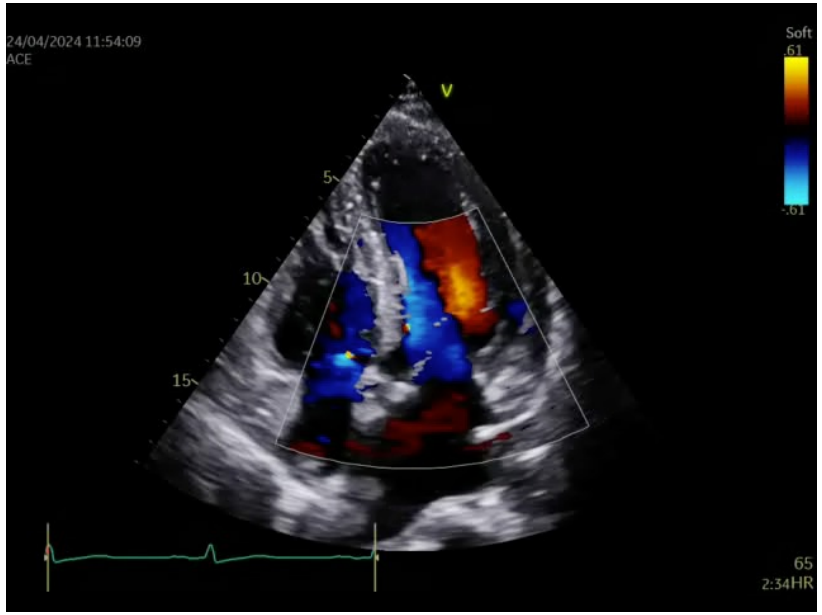
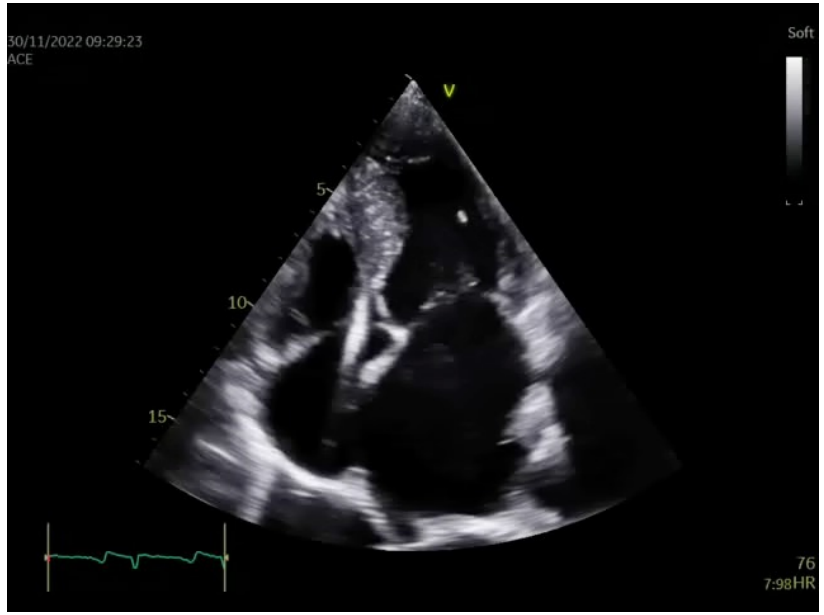
Tenaya Therapeutics Doses First Patient in the MyPeak-1™ Phase 1b Clinical Trial of TN-201 for the Treatment of MYBPC3-Associated Hypertrophic Cardiomyopathy

October 5, 2023

→ ***1st case of gene therapy in sarcomeric HCM (phase 1b, Cleveland) in human, October 2023 ++***

→ Towards precision medicine related to etiology-directed therapy

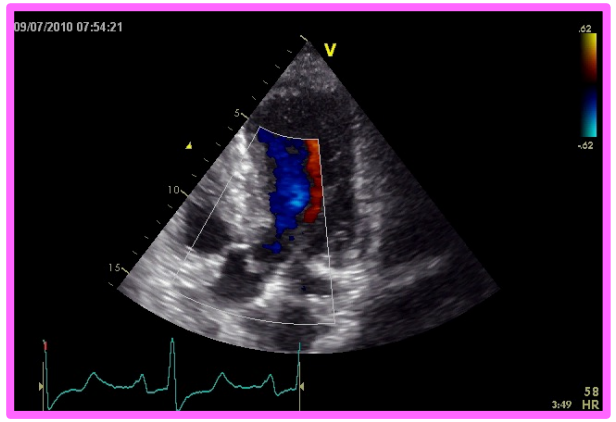
CONCLUSION : IC dans la CMH

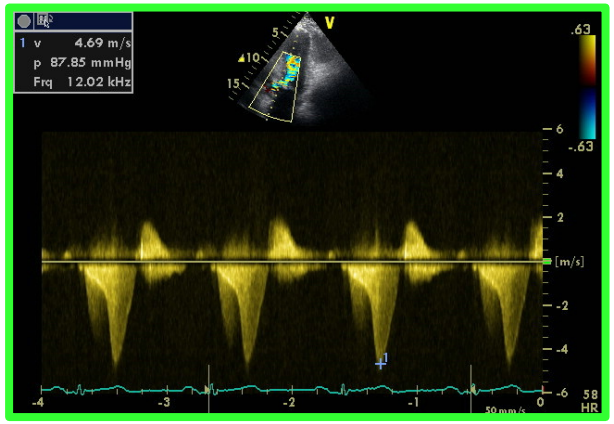
CMH « simple »	CMH obstructive	CMH restrictive / dysfonction VG
		
Pas de complication Dysfonction diastolique	Obstruction / IM Dyspnée ++ / angor	Evolution insuffisance cardiaque réfractaire
Pas de traitement ++ Inhibiteur calcique / BB / diurétique	TRT OBSTRUCTION (med ou invasif) Attention volémie / vasodilatation	TRT de la dysfonction VG Transplantation ++
Très bon pronostic	Bon pronostic	Mauvais pronostic

L'insuffisance cardiaque dans les CMH

- **Obstruction symptomatique – FEVG normale**

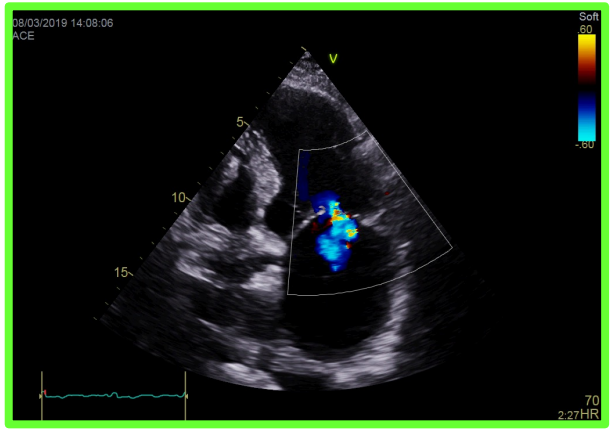
  - ✓ *obstruction sous-aortique*
  - ✓ *dysfonction diastolique*
  - ✓ *insuffisance mitrale*





- **CMH évoluée « restrictive »**

  - ✓ *Fibrose myocardique*
  - ✓ *Régression de l'hypertrophie*
  - ✓ *Régression de l'obstruction*
  - ✓ *Diminution de la FEVG*
  - ✓ *Dilatation OG*
  - ✓ *Profil restrictif et HTAP*
  - ✓ *Elévation du BNP / NT-proBNP*



CMHo: indications d'un traitement interventionnel

- ✓ Patient toujours symptomatique
- ✓ Sous traitement maximal
- ✓ Avec obstruction persistante

SRT to improve symptoms is recommended in patients with a resting or maximum provoked LVOT gradient of ≥50 mmHg who are in NYHA/Ross functional class III–IV, despite maximum tolerated medical therapy.[697–702]	I	B

ESC European Society of Cardiology

SRT should be considered in patients with recurrent exertional syncope caused by a resting or maximum provoked LVOTO gradient ≥50 mmHg despite optimal medical therapy.[686,711–713]	IIa	C

ESC European Society of Cardiology

1	B-NR	1. In patients with obstructive HCM who remain symptomatic despite GDMT, SRT in eligible patients,* performed at experienced HCM centers,† is recommended for relieving LVOTO (Tables 4 and 5).[1–3]

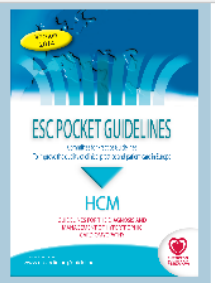
American Heart Association.

Et le risque rythmique alors?

ESC guidelines 2023

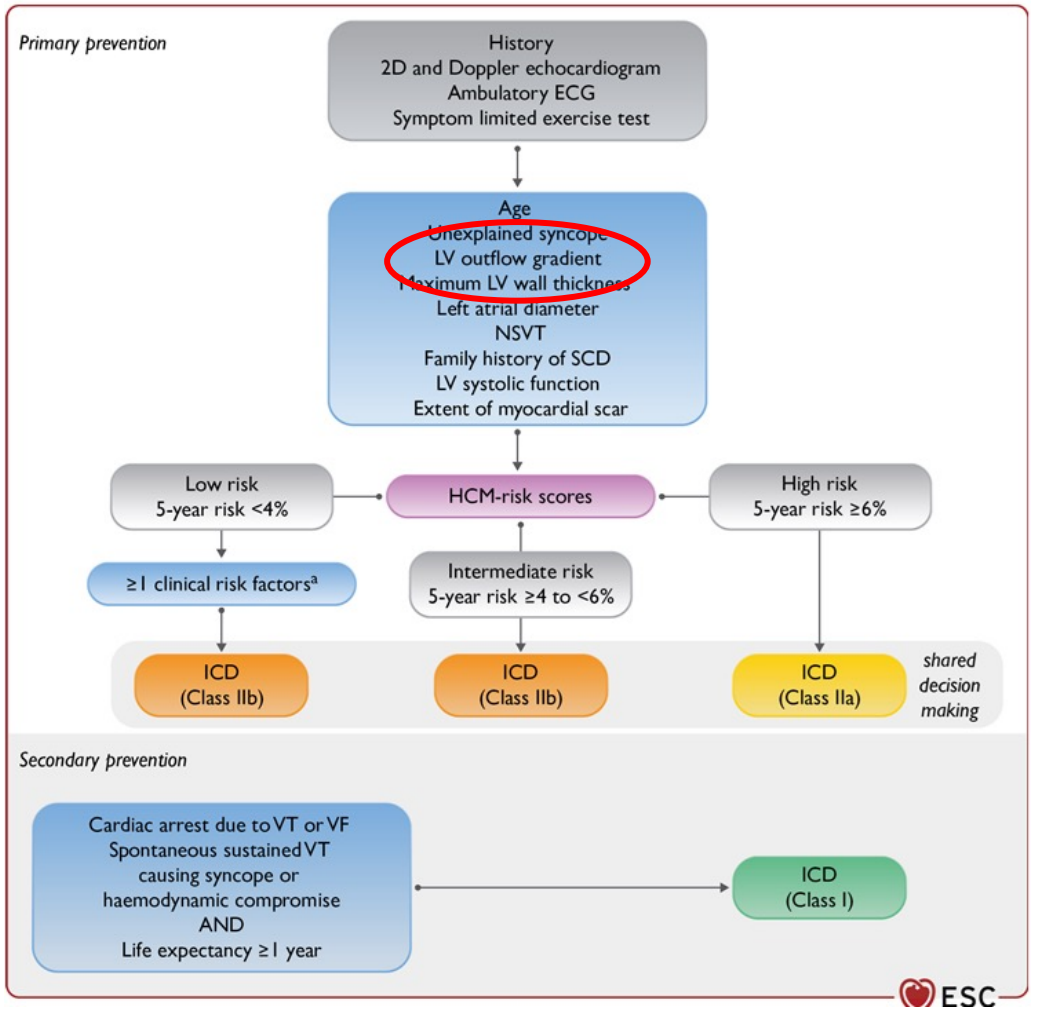
HCM Risk-SCD Calculator

EUROPEAN SOCIETY OF CARDIOLOGY®



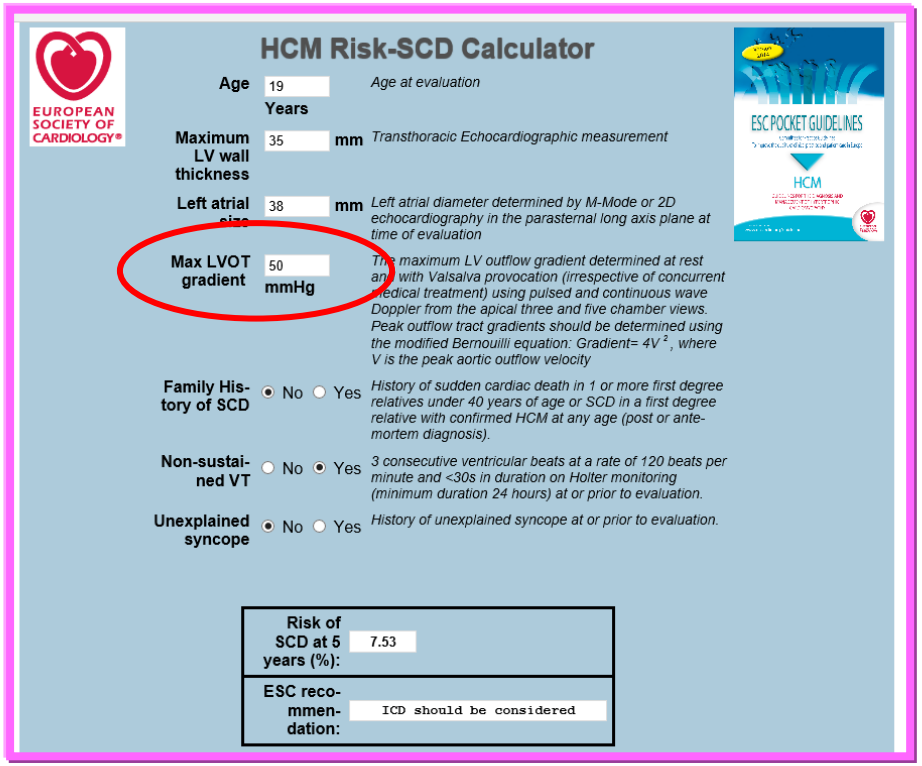
Age	19 Years		*Age at evaluation*
Maximum LV wall thickness	35	mm	*Transthoracic Echocardiographic measurement*
Left atrial size	38	mm	*Left atrial diameter determined by M-Mode or 2D echocardiography in the parasternal long axis plane at time of evaluation*
Max LVOT gradient	50 mmHg		*The maximum LV outflow gradient determined at rest and with Valsalva provocation (irrespective of concurrent medical treatment) using pulsed and continuous wave Doppler from the apical three and five chamber views. Peak outflow tract gradients should be determined using the modified Bernouilli equation: Gradient= $4V^2$, where V is the peak aortic outflow velocity*
Family History of SCD	◉ No ○ Yes		*History of sudden cardiac death in 1 or more first degree relatives under 40 years of age or SCD in a first degree relative with confirmed HCM at any age (post or ante-mortem diagnosis).*
Non-sustained VT	○ No ◉ Yes		*3 consecutive ventricular beats at a rate of 120 beats per minute and <30s in duration on Holter monitoring (minimum duration 24 hours) at or prior to evaluation.*
Unexplained syncope	◉ No ○ Yes		*History of unexplained syncope at or prior to evaluation.*

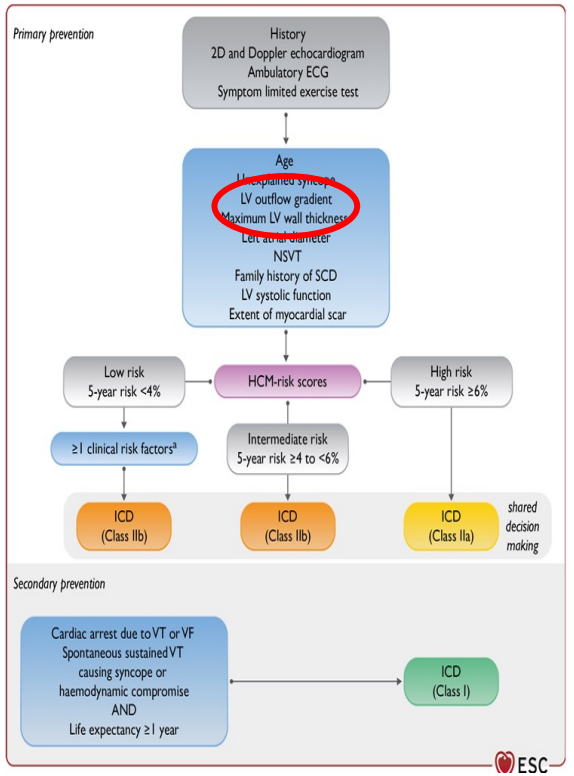
Risk of SCD at 5 years (%):	7.53
ESC recommendation:	ICD should be considered



Traitements de la CMHo : questions non résolues

1. Quel médicament pour quel patient ?
2. Cardiomyopathies non obstructives ?
3. Amélioration du pronostic rythmique par les inhibiteurs de la myosine ?





VALOR-HCM (Mavacamten)

Myosin Inhibition in Patients With Obstructive Hypertrophic Cardiomyopathy Referred for Septal Reduction Therapy

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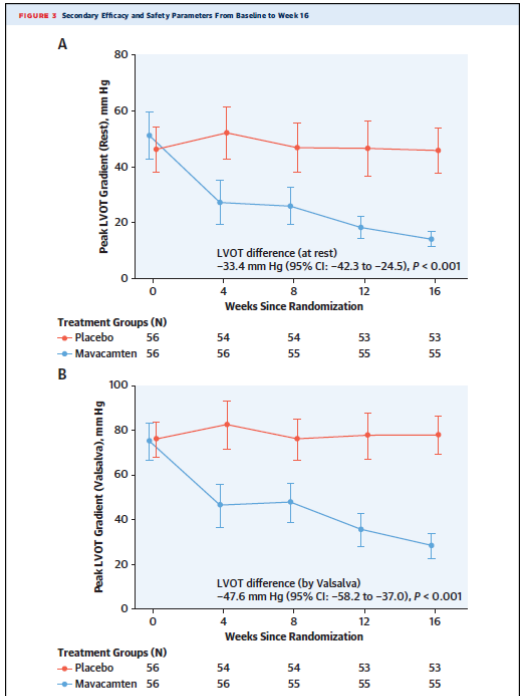

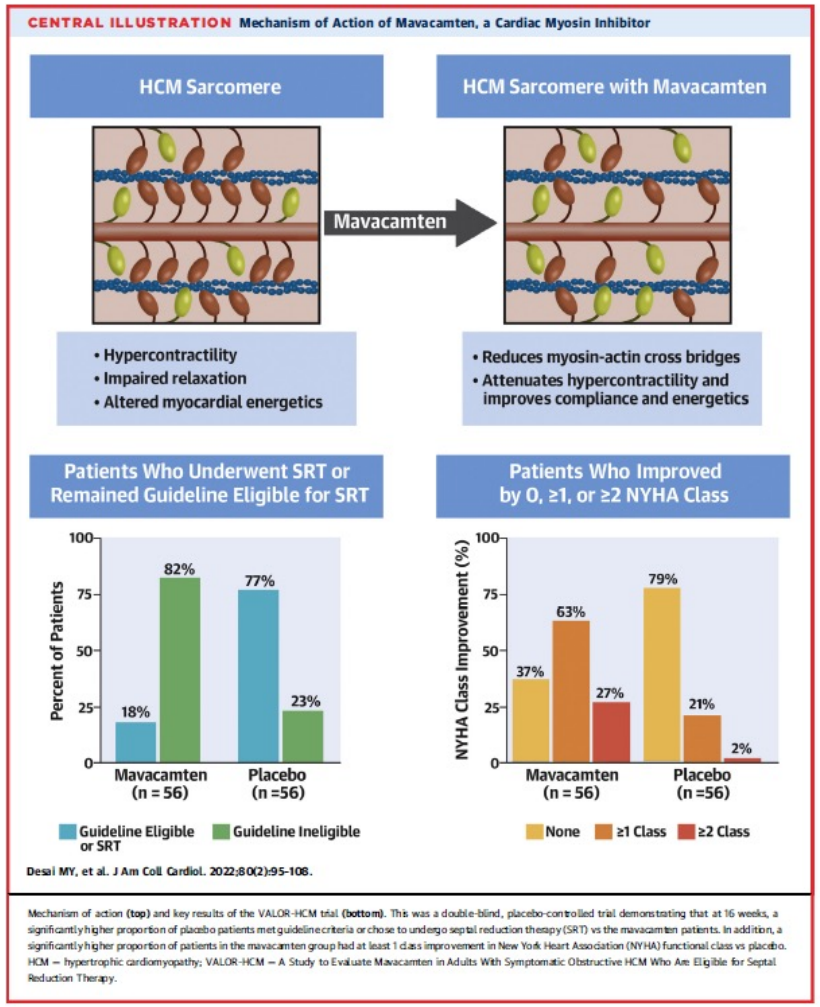

Mechanism of action (**top**) and key results of the VALOR-HCM trial (**bottom**). This was a double-blind, placebo-controlled trial demonstrating that at 16 weeks, a significantly higher proportion of placebo patients met guideline criteria or chose to undergo septal reduction therapy (SRT) vs the mavacamten patients. In addition, a significantly higher proportion of patients in the mavacamten group had at least 1 class improvement in New York Heart Association (NYHA) functional class vs placebo. HCM = hypertrophic cardiomyopathy; VALOR-HCM = A Study to Evaluate Mavacamten in Adults With Symptomatic Obstructive HCM Who Are Eligible for Septal Reduction Therapy.