EVIDENCE-BASED NOVEL THERAPIES IN HCM

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European Reference Network
for rare or low prevalence complex diseases
Network Heart Diseases (ERN GUARD-HEART)

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DISCLOSURES

Relevant company relationship	
Sponsorship	Institutional research grant from BMS
Honorarium or other (financial) compensation	BMS, consultant, invited speaker Cytokinetics, consultant Pfizer, advisory board, invited speaker Sanofi Genzym, invited speaker Alnylam ,advisory board
Shareholder	-
Other	Steering committee SEQUOIA and ACACIA (Cytokinetics)

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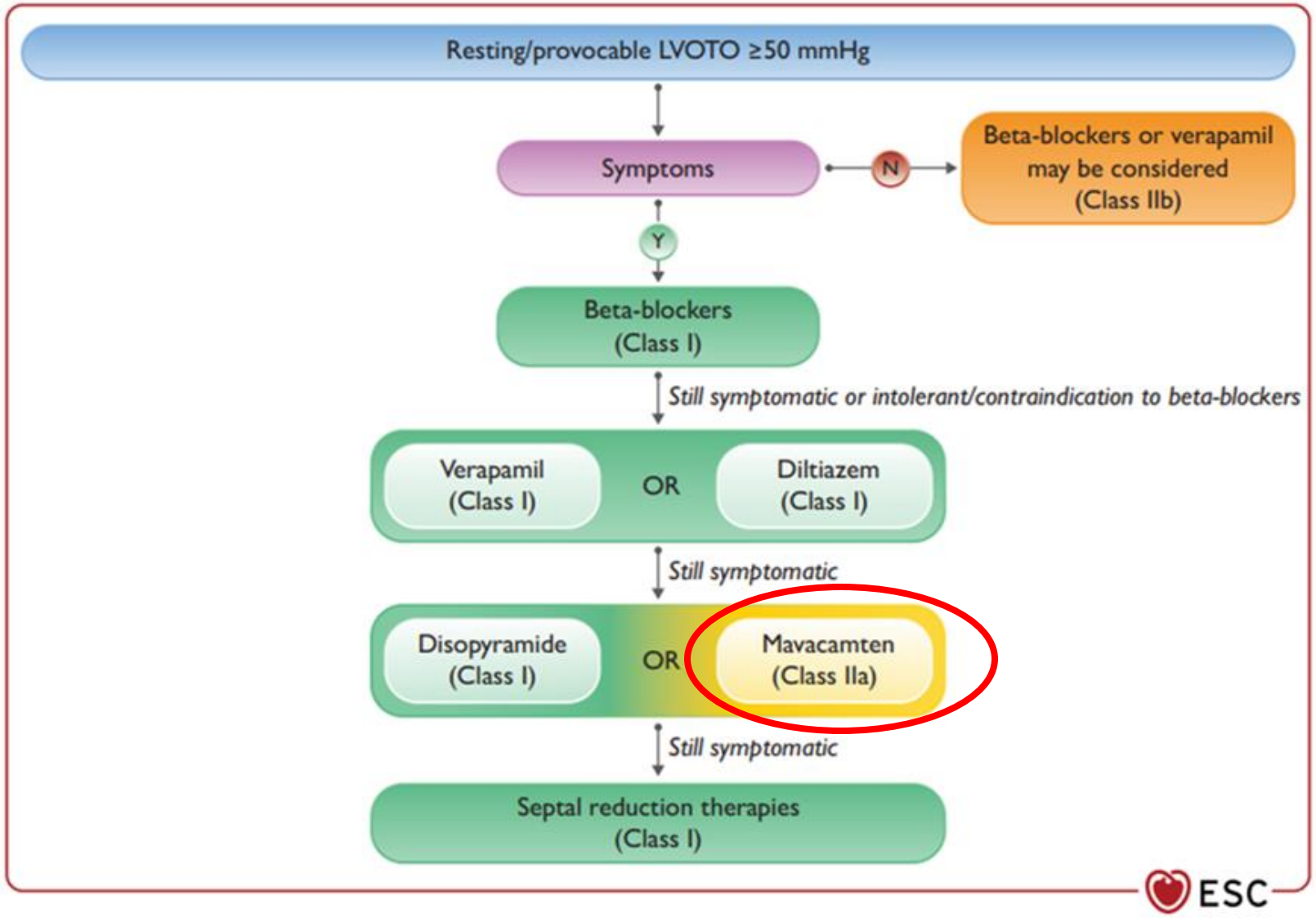
MANAGEMENT OF HCM WITH OBSTRUCTION



2023 ESC Guidelines for the management of cardiomyopathies

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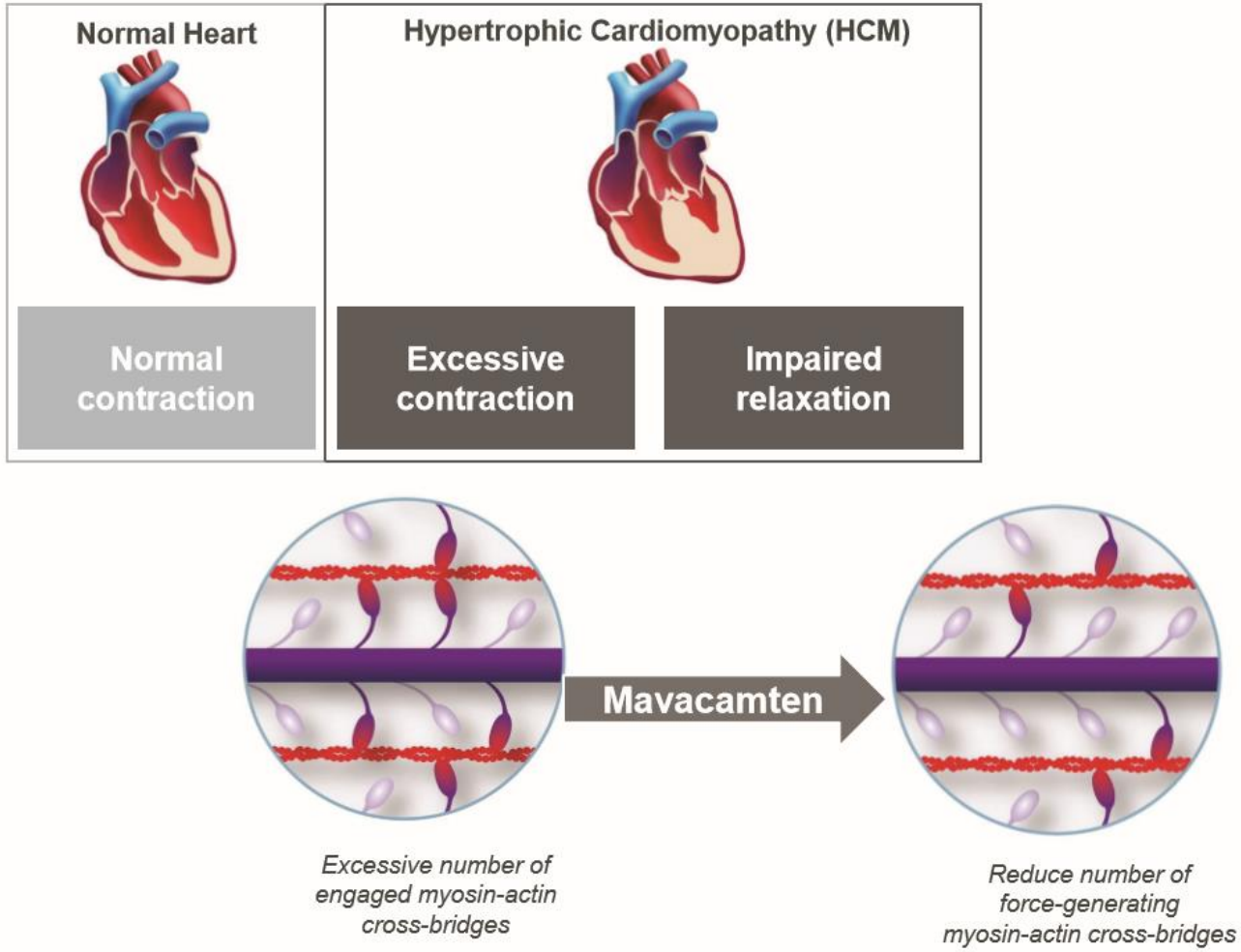
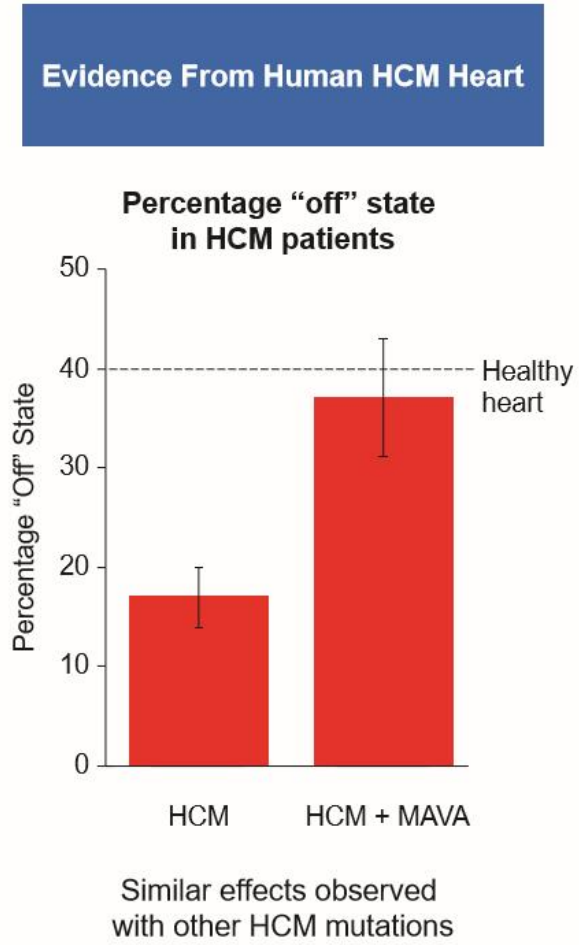
MAVACAMTEN - MYOSIN INHIBITOR





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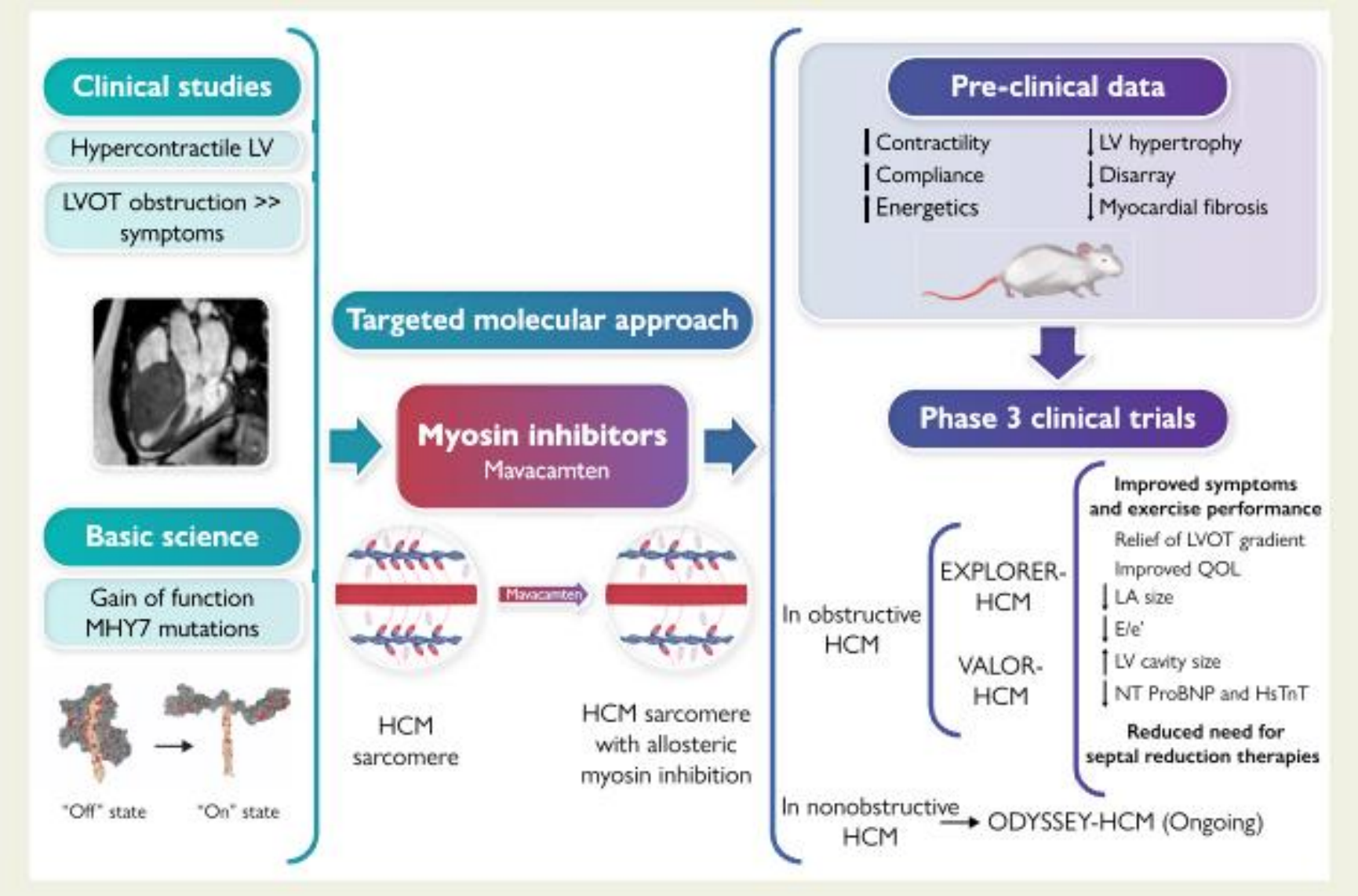
MAVACAMTEN



Braunwald et al. Eur Heart J 2023

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MAVACAMTEN IN HCM WITH OBSTRUCTION

Title (reference)	PIONEER HCM[41,42]	EXPLORER HCM[36,37]	VALOR-HCM [43]
Design	Open-label Non-randomized	Double-blind randomized	Double-blind Randomized
N	21	251	112
Duration (weeks)	12	30	16
NYHA class	II/III	II/III	III/IV
Dose (mg/day)	2–20	2.5–15	2.5–15
Primary endpoint	Change in post-exercise LVOT gradient	Exercise capacity symptom burden	Continued eligibility for SRT
OUTCOMES	↓ LVOT gradients	↓ LVOT gradients	↓ eligibility for SRT
	Improved exercise capacity and ventilatory efficiency	Improved exercise capacity	↓ LVOT gradients
	↓ NYHA class	↓ NYHA class	↓ NYHA class
	↓ NRS dyspnoea score	↓ NT-proBNP and hs-cTnI	↓ NT-proBNP and hs-cTnI
	Improved health status	Improved diastolic function	Improved health status

Braunwald et al. Eur Heart J 2023

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TOO GOOD TO BE TRUE?

	Mavacamten group (n=123)	Placebo group (n=128)
Patients with ≥1 treatment-emergent adverse event	108 (88%)	101 (79%)
Total number of serious adverse events	11	20
Patients with ≥1 serious adverse event	10 (8%)	11 (9%)
Atrial fibrillation	2 (2%)	4 (3%)
Syncope	2 (2%)	1 (1%)
Stress cardiomyopathy	2 (2%)	0
Sudden death	0	1 (1%)
Transient ischaemic attack	0	1 (1%)
Cardiac failure congestive	0	1 (1%)
Diverticulitis	1 (1%)	0
Viral gastroenteritis	0	1 (1%)
Urinary tract infection	0	2 (2%)
Infection	1 (1%)	0
Rheumatoid arthritis	0	1 (1%)
Contusion	1 (1%)	0
Forearm fracture	1 (1%)	0
Dehydration	0	1 (1%)
Vocal cord polyp	0	1 (1%)
Cholesteatoma	0	1 (1%)
Prostate cancer	0	1 (1%)

Data are n (%).

Table 4: **Summary of treatment-emergent adverse events and serious adverse events**

Points of attention:

- Genotype Cytochrome P450-CYP2C19 (in Europe).
- Drug-drug interactions (CYP2C19 and CYP3A4 inhibitors).
- Contraindicated in pregnancy.
- Echocardiographic monitoring.
- Half-life 6-9 days to 23 days in poor-metabolizers.

Olivotto et al. Lancet 2020

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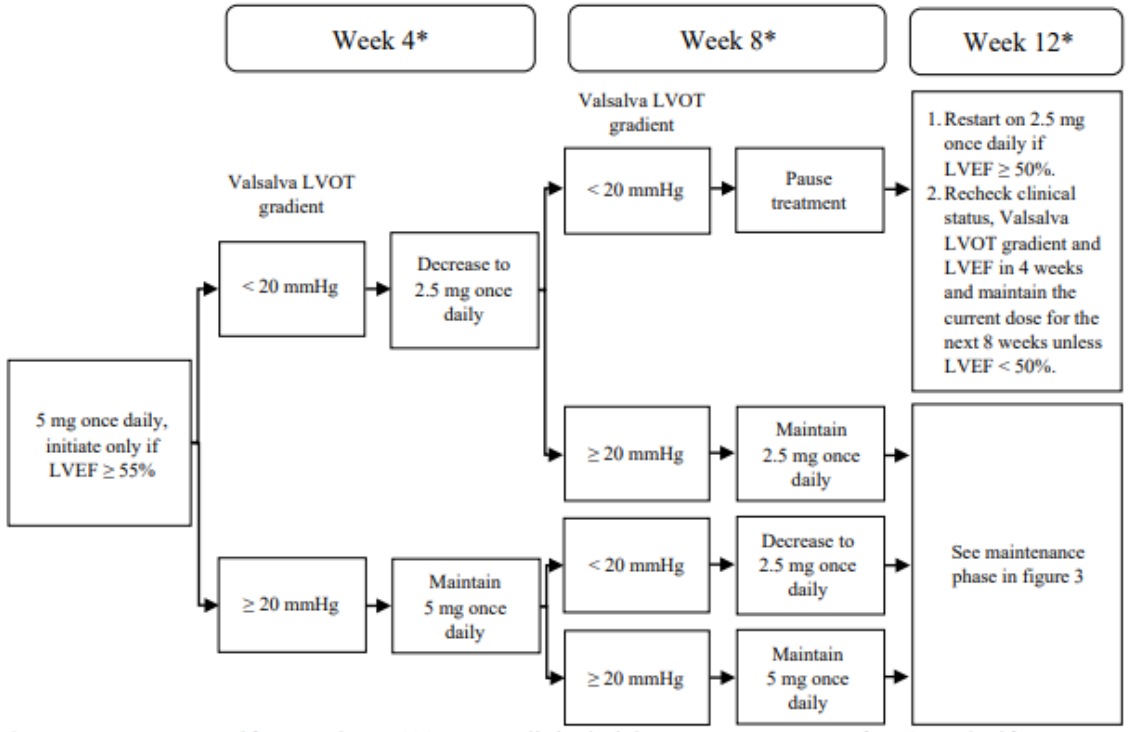
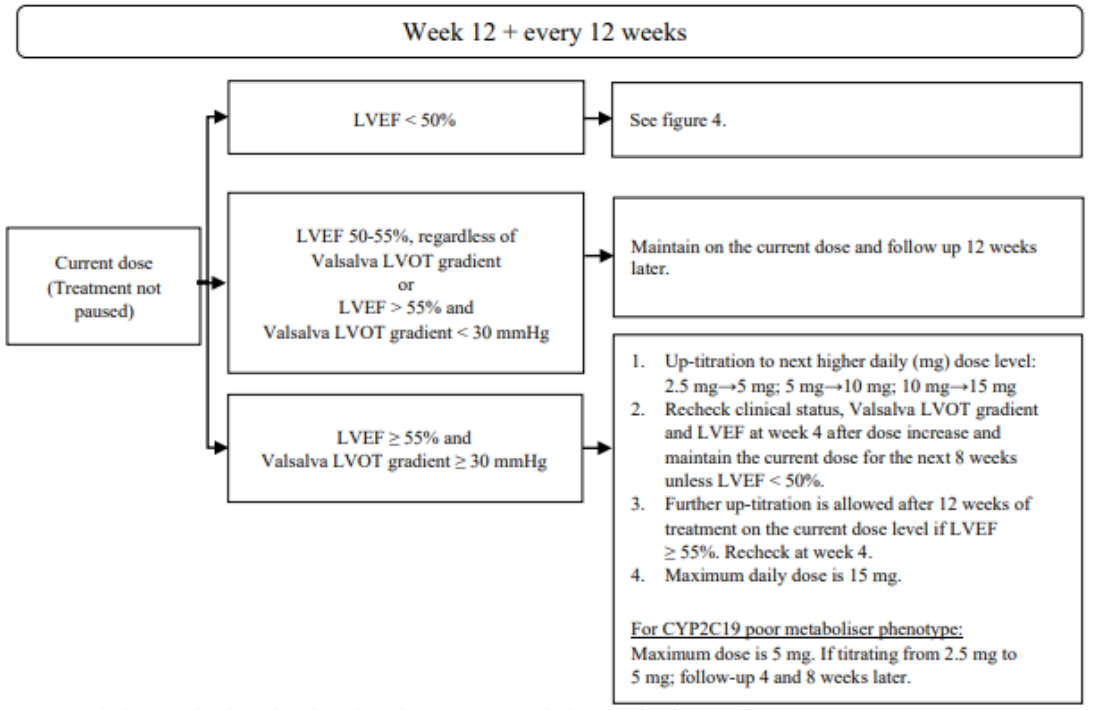
MAVACAMTEN IN PRACTICE



* Interrupt treatment if LVEF is < 50% at any clinical visit; restart treatment after 4 weeks if LVEF ≥ 50% (see figure 4).
LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract



LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract

Summary of Product Characteristics mavacamten, August 2023

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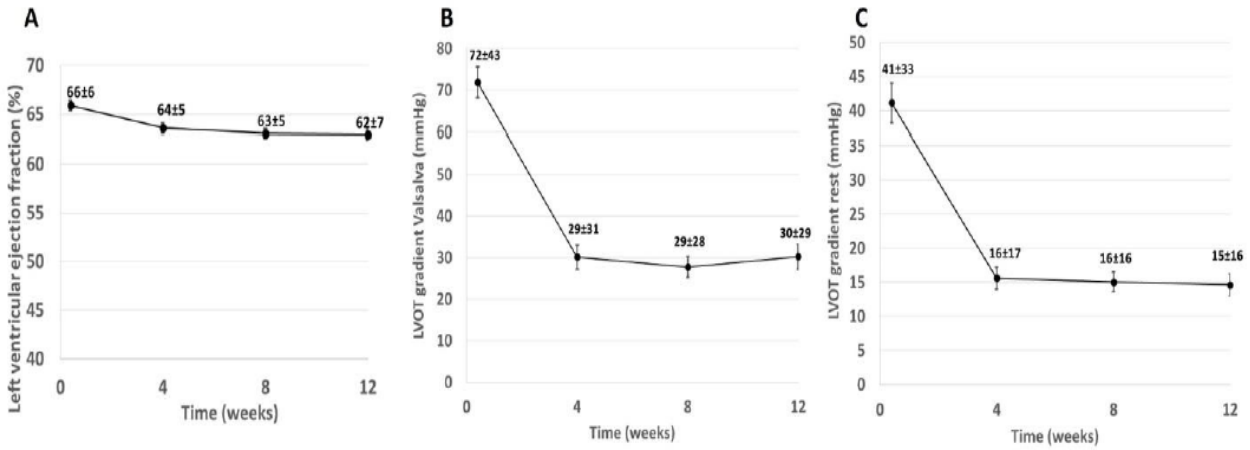
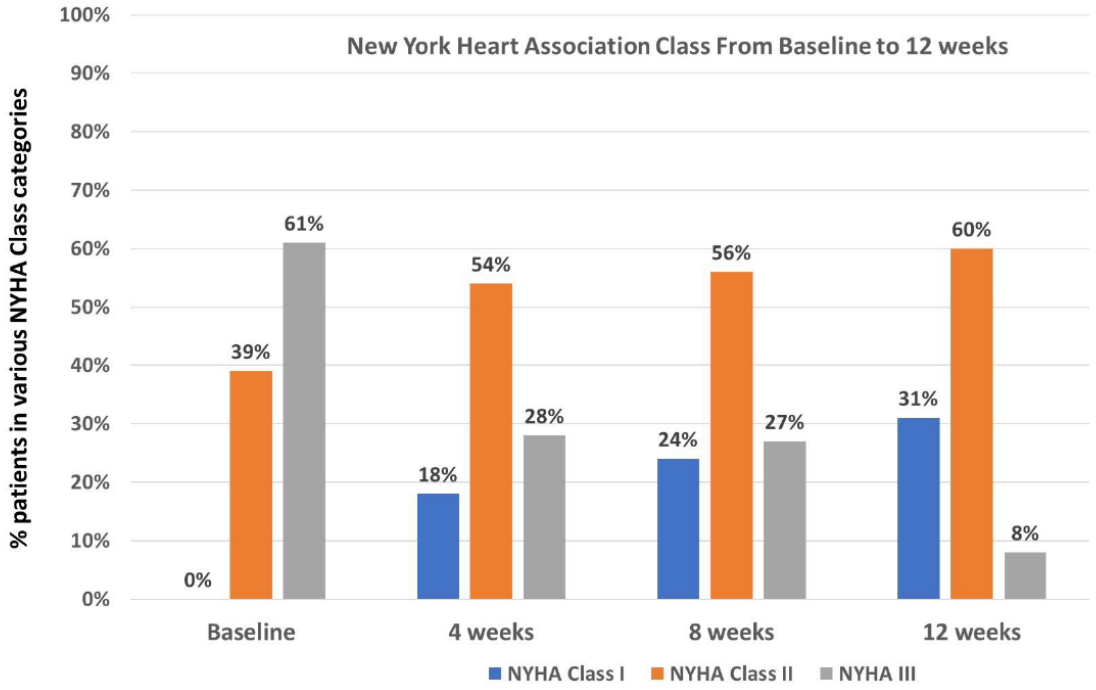
REAL WORLD DATA

- 150 patients; 65 year, 53% female
- mavacamten 5 mg in 53%
- 16% Adjustment of treatment for drug-drug interactions
- 3 temporary interruption of mavacamten due to EF < 50%





Desai et al. Prog in Cardiovasc Dis 2024

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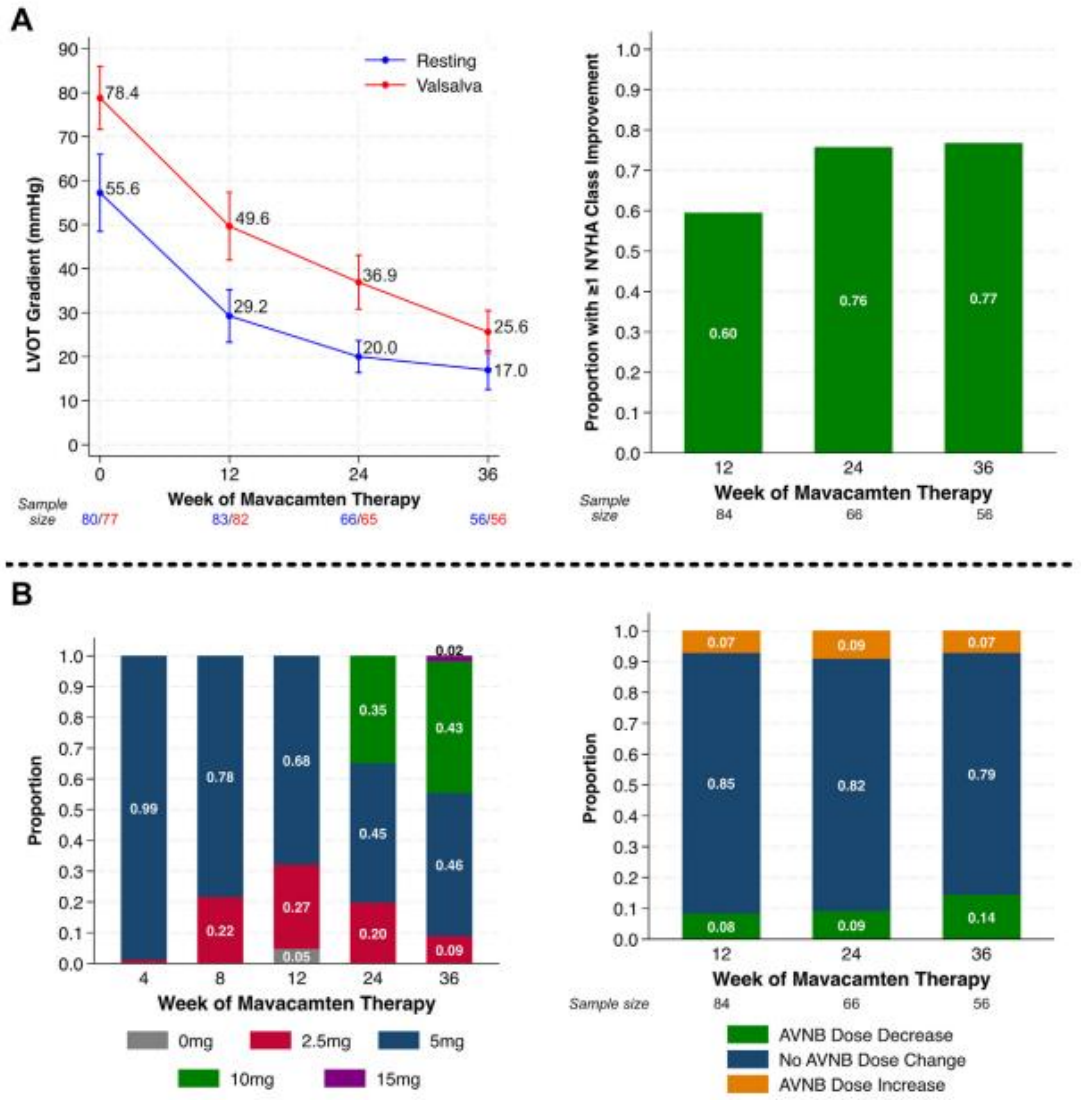
REAL WORLD DATA

- 96 oHCM patients
- Mean age 63 years
- 54% Female
- Temporary interruption in 2 patients due to EF < 50%



Reza et al. JACC Heart Failure 2024

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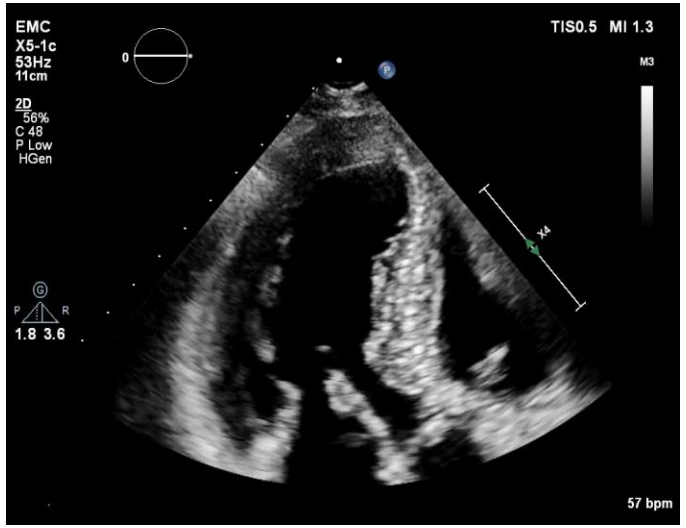
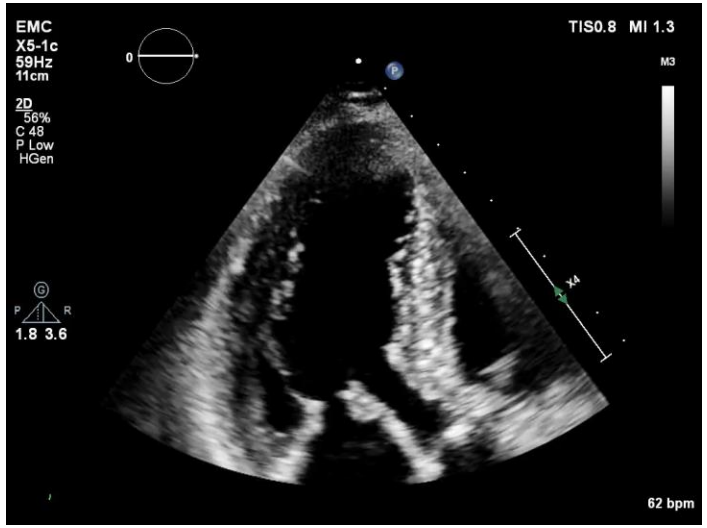
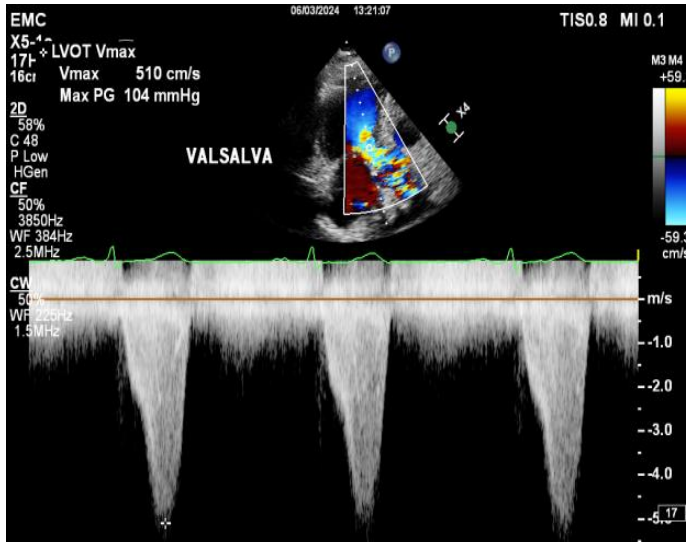
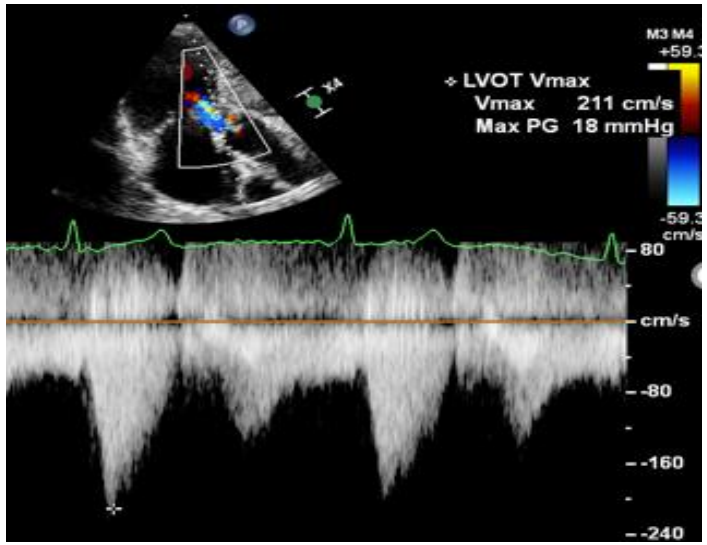
MAVACAMTEN IN PRACTICE



mavacamten 5 mg







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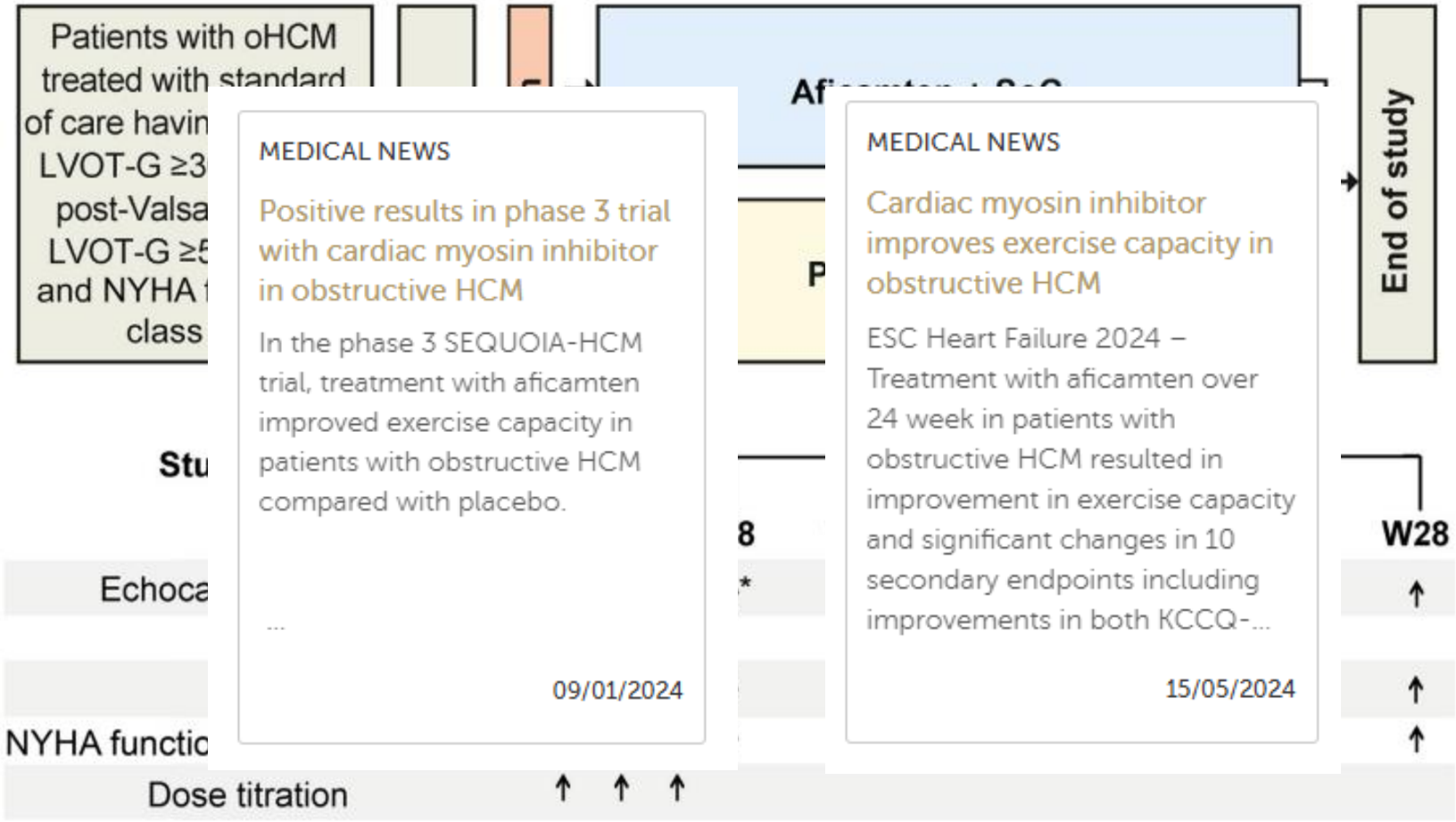
SEQUOIA-HCM STUDY



Coats et al. JACC; Heart Failure 2024

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Thanks for your attention

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