WITHDRAWal of Heart Failure Pharmacotherapy in Patients with Normalized Left Ventricular Ejection Fraction After AF Rhythm Control in AF-mediated Cardiomyopathy – The WITHDRAW-AF Randomized Trial

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Background

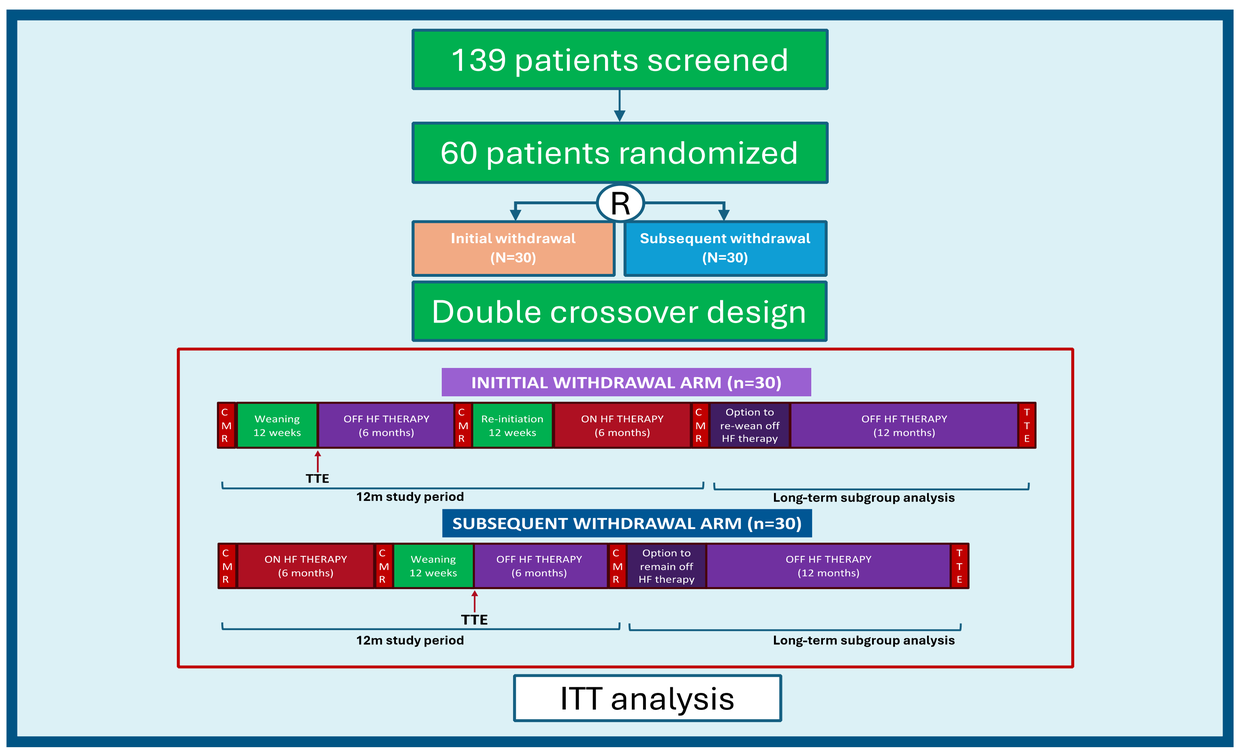
Atrial fibrillation-mediated cardiomyopathy (AFCM) represents a reversible cause of left ventricular systolic dysfunction (LVSD). Current clinical practice is indefinite heart failure (HF) pharmacotherapy despite LV ejection fraction (LVEF) normalization. However, whether this is necessary to maintain normal LVEF, in addition to rhythm control, is uncertain.

Aim

We examined the safety and feasibility of staged withdrawal of HF pharmacotherapy in AFCM following normalized LVEF and AF rhythm control.

Method

This multicenter, double crossover randomized trial examined the safety and feasibility of HF therapy withdrawal following AF rhythm control and LVEF normalization in AFCM. Participants were randomized (1:1) to initial staged withdrawal or continued medical therapy for 6 months, followed by crossover to the alternate treatment arm for a further 6 months. The primary endpoint was LVEF maintenance ≥50% following medication withdrawal. Secondary outcomes included cardiac remodeling, functional status, biomarkers, quality of life and arrhythmia recurrence on and off HF therapy.



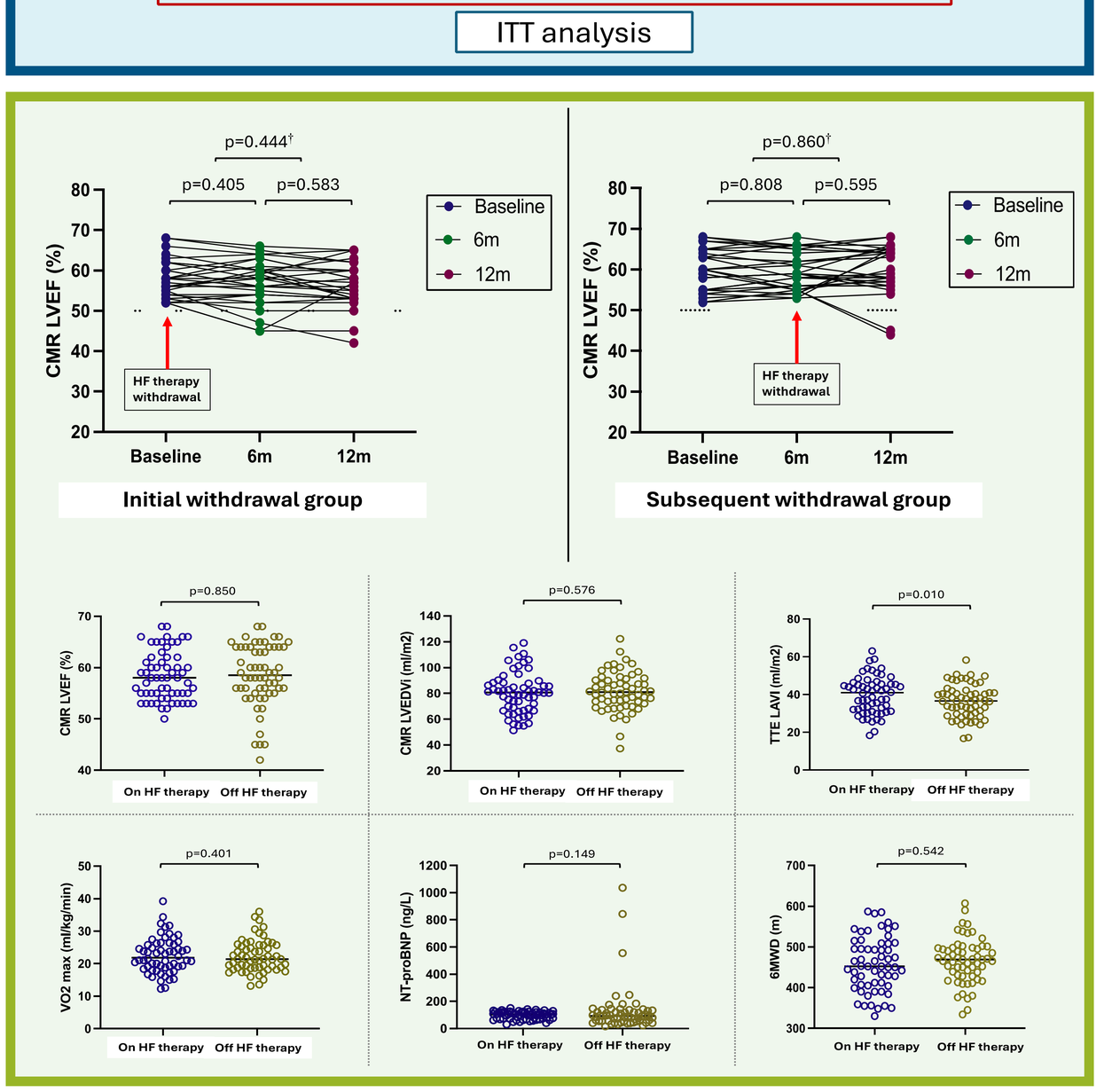
Results

Between July 2021 to May 2024, 60 patients were enrolled. Treatment withdrawal and 12-month follow up was completed in all participants.

HF therapy was safely withdrawn with LVEF maintenance in the majority (91.7%) 6 months post medication withdrawal compared to continued medical therapy (OR 1.61, 95% CI 0.26-3.86,p=0.609) with no clinical HF or adverse sequelae in 5/60 (8.3%) who experienced a relapse in LVSD.

CMR LVEF was comparable between randomization groups and across study time-points (mixed effects p=0.370). TTE parameters, NT-proBNP, functional status, QoL and AF burden were comparable on and off HF therapy.

Enrolment LVEF ≤55% was the only predictor of LVSD relapse; other clinical, functional and imaging parameters did not predict primary outcome failure.



Conclusion

Withdrawal of HF therapy following AF rhythm control is feasible and safe in the majority with AFCM following LVEF normalization with LVEF surveillance and rhythm control.