

# The FIX-HF-5C Study Summary

## OBJECTIVE

This randomized controlled trial is intended to show that cardiac contractility modulation (CCM) improves exercise tolerance (ET) and quality of life (QOL) in patients with moderate to severe heart failure with an EF between 25-45% (matching a subgroup of patients from the FIX-HF-5 study).

## ENROLLMENT

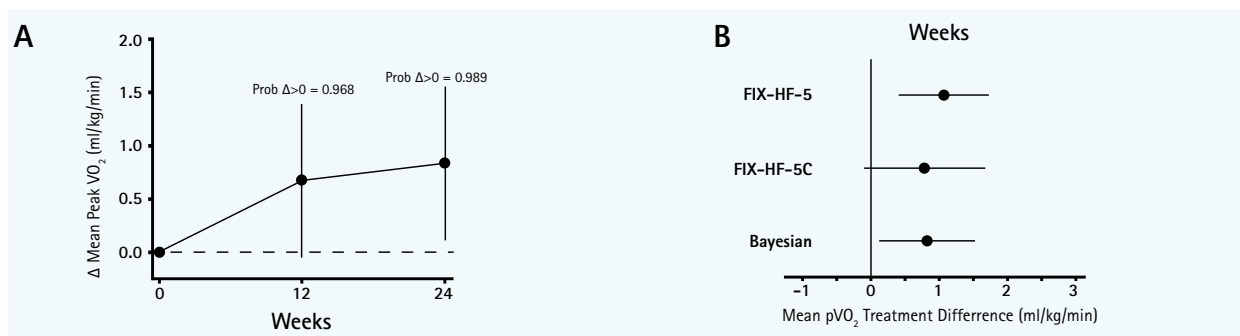
160 patients (NYHA III or IV, QRS duration <130ms, EF ≥25 and ≤45%) were randomized to control (guideline-directed medical therapy [GDMT] alone; n=86) or treatment (GDMT plus CCM; n=74) unblinded for 24 weeks.

**Primary endpoint:** Peak VO<sub>2</sub> (Figure 1)

**Secondary endpoints:** MLWHFQ, NYHA, 6 MHW. All measured at baseline, at 12 and 24 weeks (Figure 2).

## RESULTS

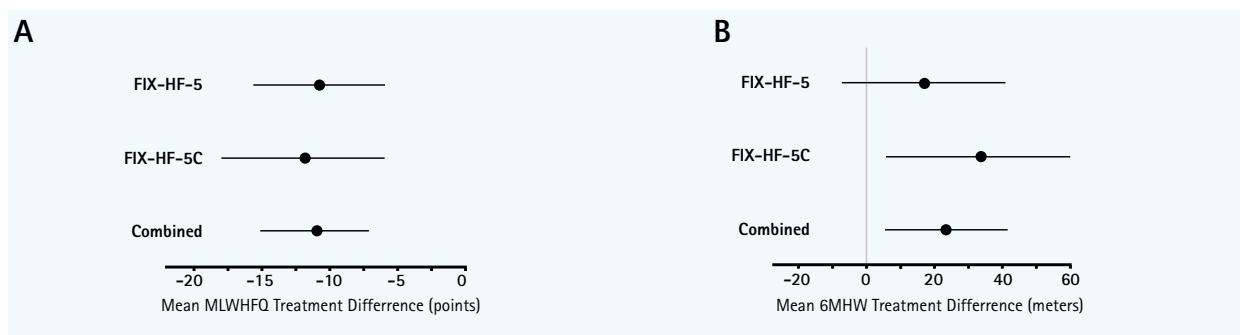
Figure 1: Primary Efficacy Results



(A) Between group-differences in peak VO<sub>2</sub> over time.

(B) 24-week between-group treatment effects in FIX-HF-5 subgroup alone, FIX-HF-5C alone, and Bayesian result.

Figure 2: Secondary Efficacy Results



Treatment effects at 24 weeks in FIX-HF-5, FIX-HF-5C separately and pooled for:

(A) Minnesota Living with Heart Failure Questionnaire (MLWHFQ)

(B) 6-min hall walk (6MHW) test.

Composite of cardiovascular death and HF-hospitalizations

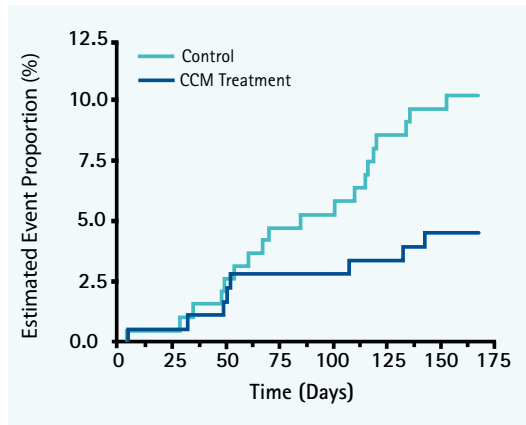


Figure 3: Comparison of estimated event proportions of the composite of cardiac death and heart failure hospitalizations between control and treatment;  $p=0.042$  by log-rank test and  $p=0.036$  when comparing 24 weeks using Greenwood's formula for the variance.

At 24 weeks, 81% (treatment group) versus 42% (control group) showed an improvement of 1 NYHA class or more. An original analysis of a small subgroup of the FIX-HF-5 study suggested particularly strong effects of CCM in patients with left ventricular EF  $\geq 35\%$ . From among the FIX-HF-5 and -5C studies, there were a total of 96 patients with EF  $\geq 35\%$  (49 in the control group and 47 in the treatment group). The effects are stronger in the  $\geq 35\%$  group.

CONCLUSIONS

The results of this study confirm results of prior studies: CCM improves exercise tolerance and quality of life in patients with EF  $\geq 25\%$  and  $\leq 45\%$ , QRS  $< 130$  ms, NSR, and NYHA class III or ambulatory class IV, despite GDMT, including medications and ICDs when indicated. The composite of cardiovascular death and heart failure hospitalizations was reduced. The clinical effects were observed across the range of EFs studied, and clinical effectiveness was even greater in patients with EFs between 35% and 45%.

References

1. Abraham WT, Kuck K-H, Goldsmith RL et al., A Randomized Controlled Trial to Evaluate the Safety and Efficacy of Cardiac Contractility Modulation. *JAm Coll Cardiol* HF 2018; in press, DOI: 10.1016/j.jchf.2018.04.010.
2. <https://www.medpagetoday.com/meeting-coverage/hrs/72819>

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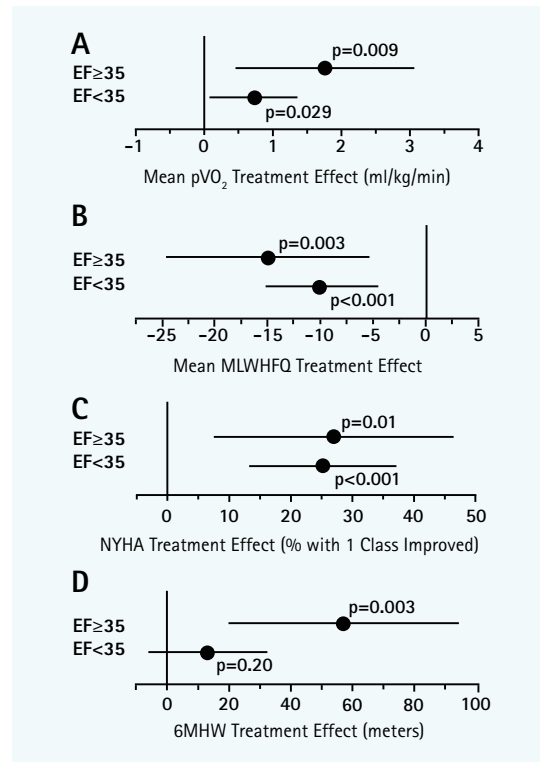
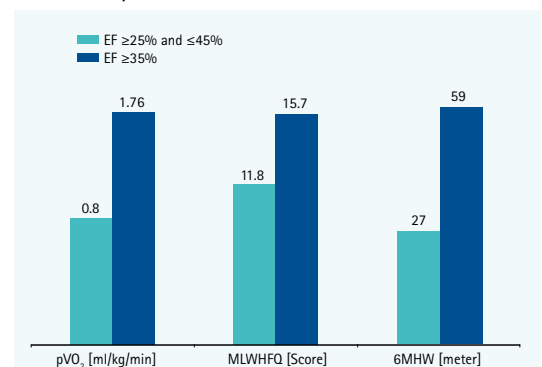


Figure 4: CCM treatment effects (difference between control and CCM groups and 95% confidence intervals) for patients with ejection fraction (EF)  $< 35\%$  versus EF  $\geq 35\%$  for (A) peak  $VO_2$ , (B) Minnesota Living with Heart Failure Questionnaire (MLWHFQ), (C) New York Heart Association (NYHA) functional class, and (D) 6-min hall walk test.

CCM efficacy



„It promises to meet a very large unmet need in the management of heart failure,“ Abraham said at a press conference at the HRS meeting in Boston [2].

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