**Reference –** February 2011 – [Kadish, et al: “A randomized controlled trial evaluating the safety and efficacy of cardiac contractility modulation in advanced heart failure," American](https://impulse-dynamics.com/wp-content/uploads/2020/01/2019-Anker_et_al-2019-European_Journal_of_Heart_Failure.pdf" \t "_blank) Heart Journal

Link to trial summary - https://pubmed.ncbi.nlm.nih.gov/21315216/

**Hovering over or clicking on the reference above will cause the Abstract to appear in a popup window**

**Background:** Cardiac contractility modulation (CCM) delivers nonexcitatory electrical signals to the heart during the absolute refractory period intended to improve contraction.

**Methods:** We tested CCM in 428 New York Heart Association class III or IV, narrow QRS heart failure patients with ejection fraction (EF) ≤35% randomized to optimal medical therapy (OMT) plus CCM (n = 215) versus OMT alone (n = 213). Efficacy was assessed by ventilatory anaerobic threshold (VAT), primary end point, peak VO2 (pVO2), and Minnesota Living with Heart Failure Questionnaire (MLWFQ) at 6 months. The primary safety end point was a test of noninferiority between groups at 12 months for the composite of all-cause mortality and hospitalizations (12.5% allowable delta).

**Results:** The groups were comparable for age (58 ± 13 vs 59 ± 12 years), EF (26% ± 7% vs 26% ± 7%), pVO2 (14.7 ± 2.9 vs 14.8 ± 3.2 mL kg−1 min−1), and other characteristics. While VAT did not improve at 6 months, CCM significantly improved pVO2 and MLWHFQ (by 0.65 mL kg−1 min−1 [P = .024] and −9.7 points [P b .0001], respectively) over OMT. Forty-eight percent of OMT and 52% of CCM patients experienced a safety end point, which satisfied the noniferiority criterion (P = .03). Post hoc, hypothesis-generating analysis identified a subgroup (characterized by baseline EF ≥25% and New York Heart

Association class III symptoms) in which all parameters were improved by CCM.

**Conclusions:** In the overall target population, CCM did not improve VAT (the primary end point) but did improve pVO2 and MLWHFQ. Cardiac contractility modulation did not have an adverse effect on hospitalizations or mortality within the prespecified boundaries. Further study is required to clarify the role of CCM as a treatment for medically refractory heart failure. (Am Heart J 2011;161:329-337.e2.)