**Title (in sentence case)**

**Danicamtiv increases cardiac mechanical efficiency**

**Background:** Danicamtiv is a recently‑developed cardiac‑specific myosin activator that directly increases actomyosin interaction and, thereby, increases force. It is currently widely studied pre‑clinically and has entered clinical trials. In this study, we provide the first assessment of its effects on cardiac muscle energetics.

**Method:** Ventricular trabeculae from rats were isolated and studied *in vitro*. Each of the 20 trabeculae was stimulated to produce twitch force over ranges of muscle lengths and of afterloads, with muscle heat output simultaneously measured. Each trabecula was superfused with and without danicamtiv (5 µm in Tyrode solution). In both interventions, muscles were required to undergo both isometric and work‑loop contraction protocols to quantify the components of heat output – that from muscle contraction, that from intracellular Ca2+ cycling and that from actomyosin cross‑bridge cycling. Measured mechanical and energetic parameters were evaluated over ranges of muscle lengths and afterloads.

**Results:** Danicamtiv was found to increase twitch force, muscle heat and cross‑bridge heat, with no effect on the energy expenditure associated with intracellular Ca2+ cycling. Danicamtiv slowed isometric twitch force kinetics by prolonging twitch duration and decreasing the rates of twitch rise and fall. Under work‑loop contractions, danicamtiv slowed shortening kinetics by prolonging the duration of shortening and reducing the velocity of shortening. Danicamtiv increased the extent of muscle shortening, increased muscle work output and increased mechanical efficiency, while preserving cross‑bridge efficiency.

**Conclusion:** Our results support the utility of danicamtiv as an inotropic agent not only for mechanical enhancement but, more importantly, also for energetic enhancement in increasing muscle mechanical efficiency.