

Acute administration of EDG-15400, a novel cardiac sarcomere modulator, improves left ventricular compliance and cardiac reserve in a genetic mini-pig model of HCM with relevance to HFpEF

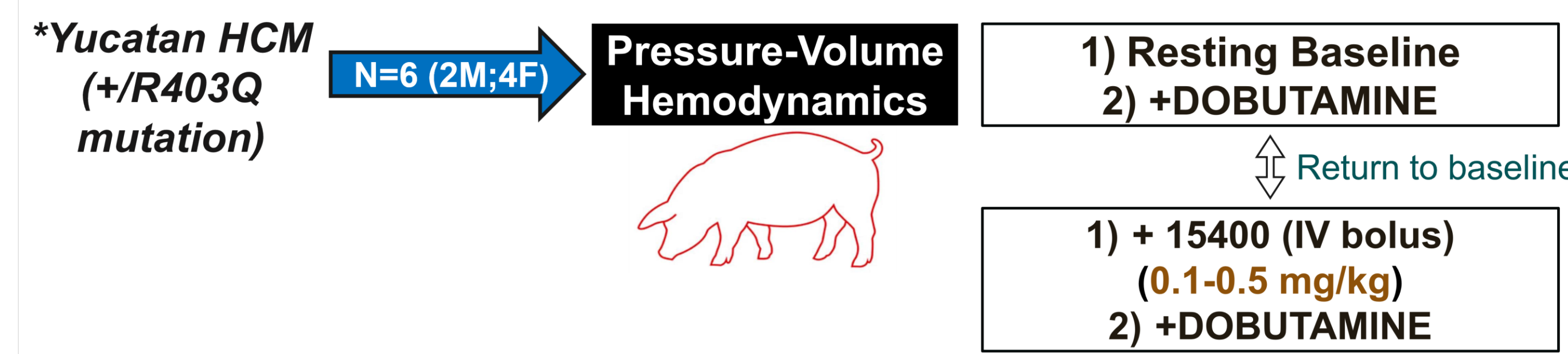
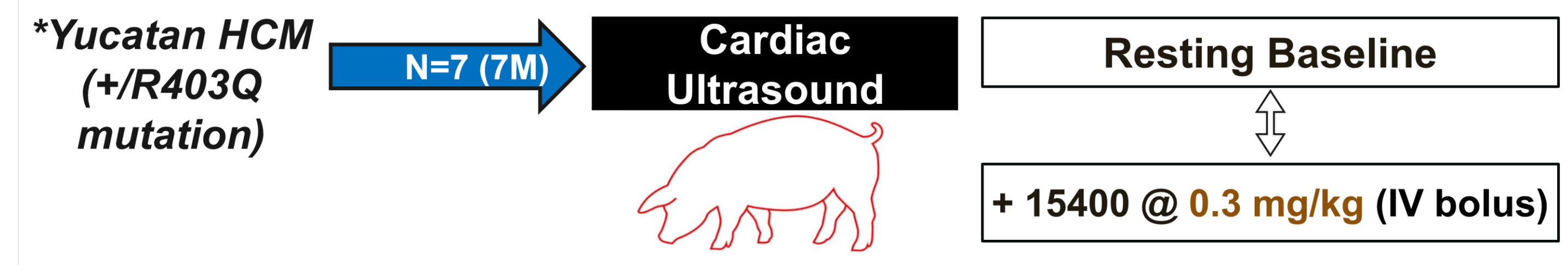
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Purpose

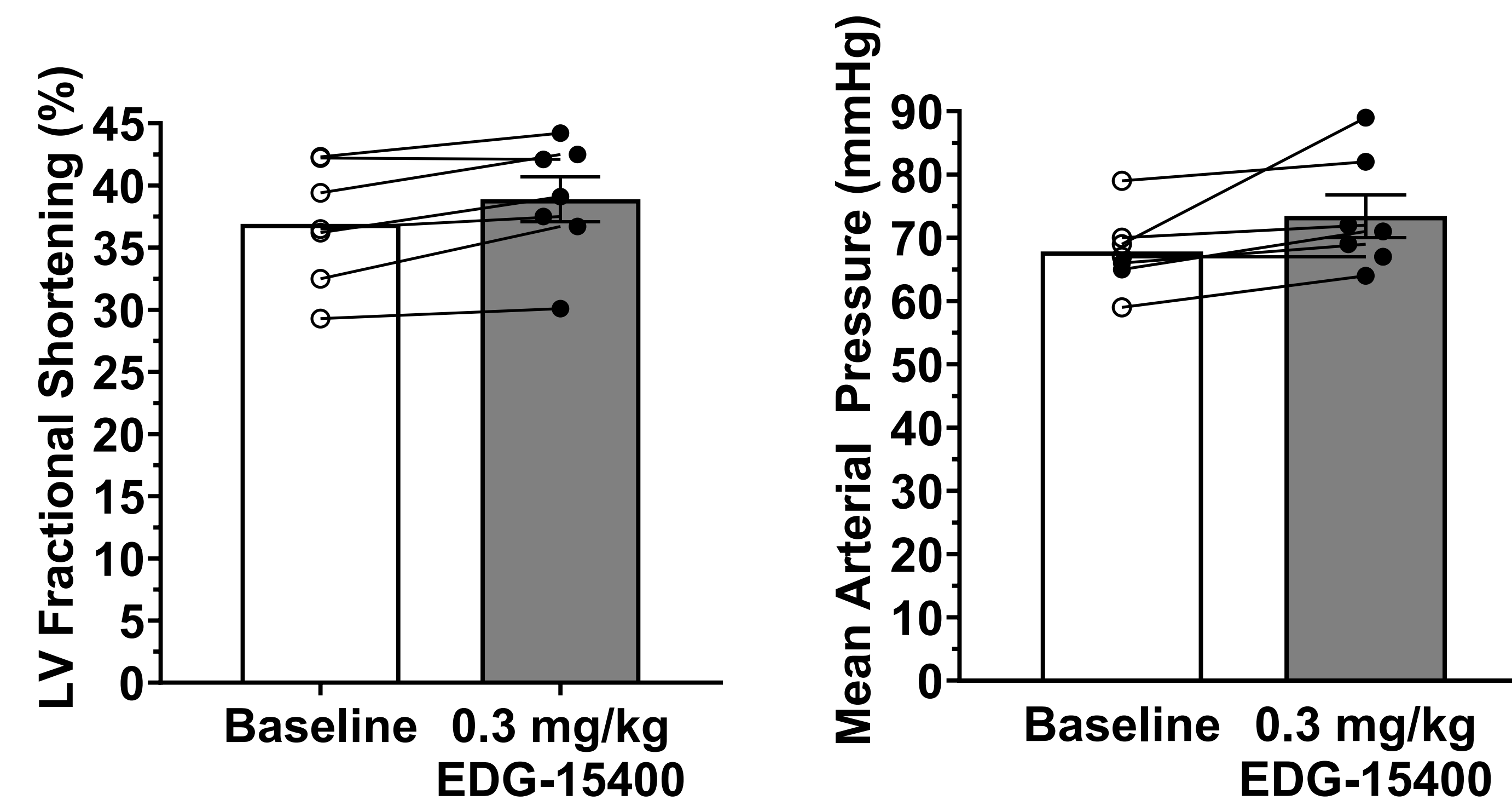
- To determine if EDG-15400 improves left ventricular (LV) diastolic function and cardiac reserve under stress without impairing systolic function in a mini-pig model of non-obstructive hypertrophic cardiomyopathy (nHCM) with translational relevance to HFpEF, including preserved resting ejection fraction and diastolic dysfunction evident as increased LV end diastolic pressure, impaired early diastolic filling velocities, and enlarged left atria.

Methods



Results

EDG-15400 has no left ventricular systolic impact with acute administration

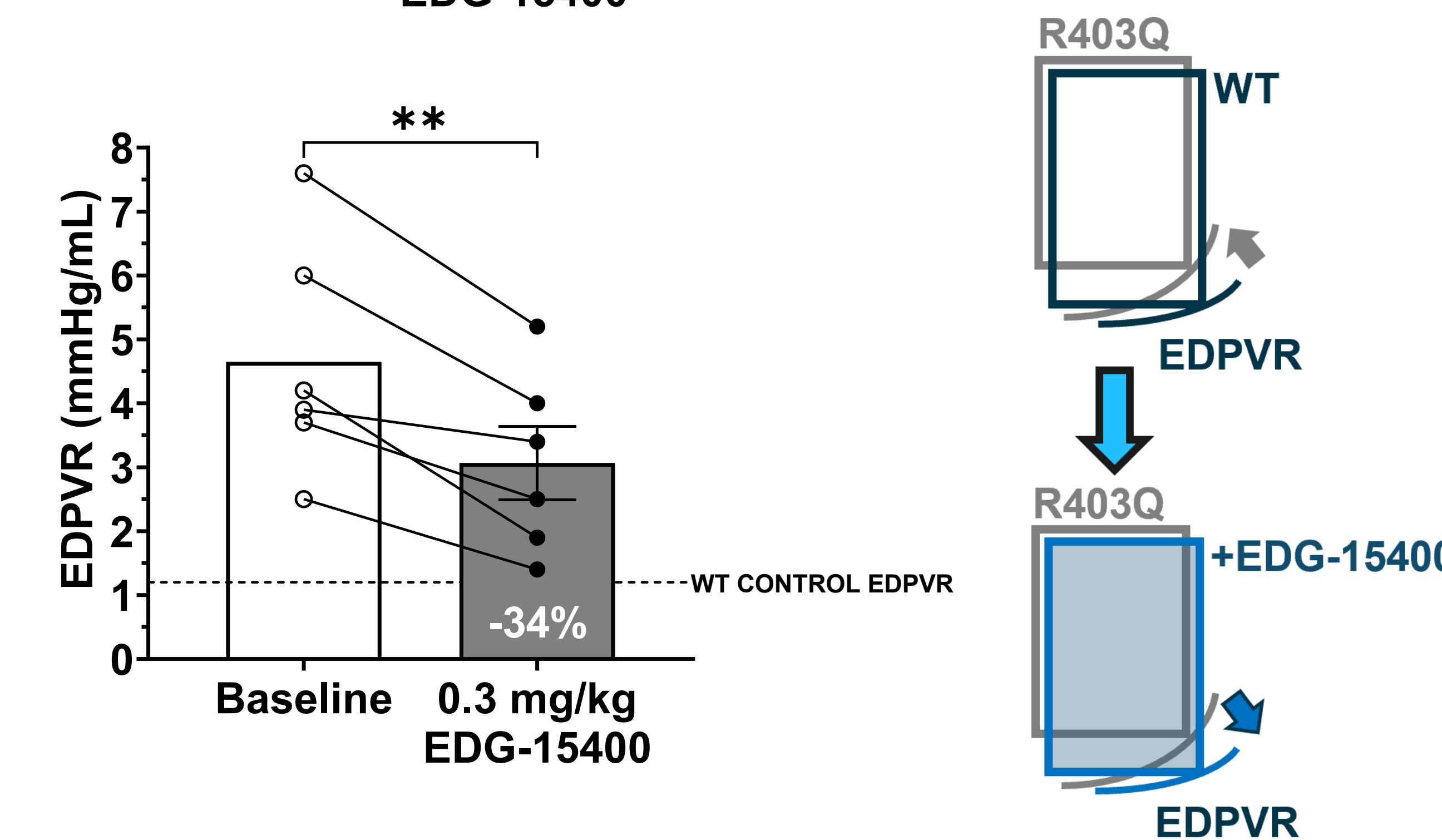
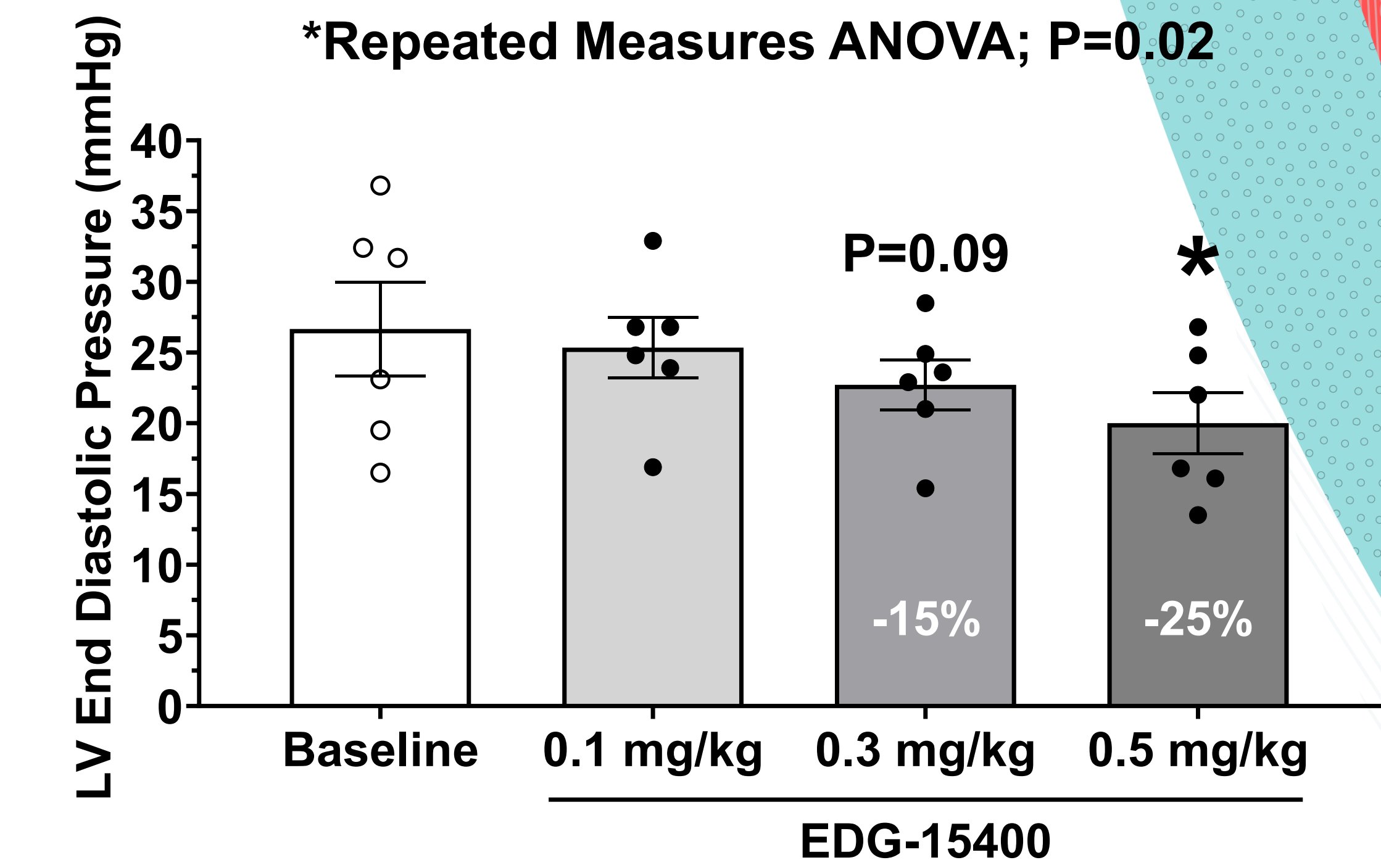
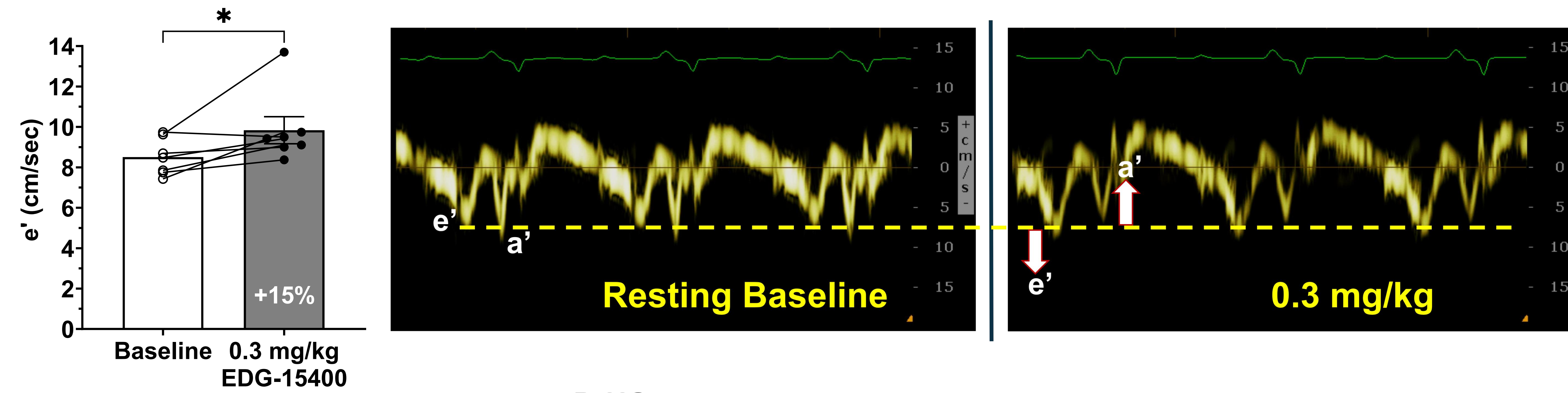


Acute EDG-15400:

- Does NOT change LV fractional shortening
- Does NOT change mean arterial pressure

Results

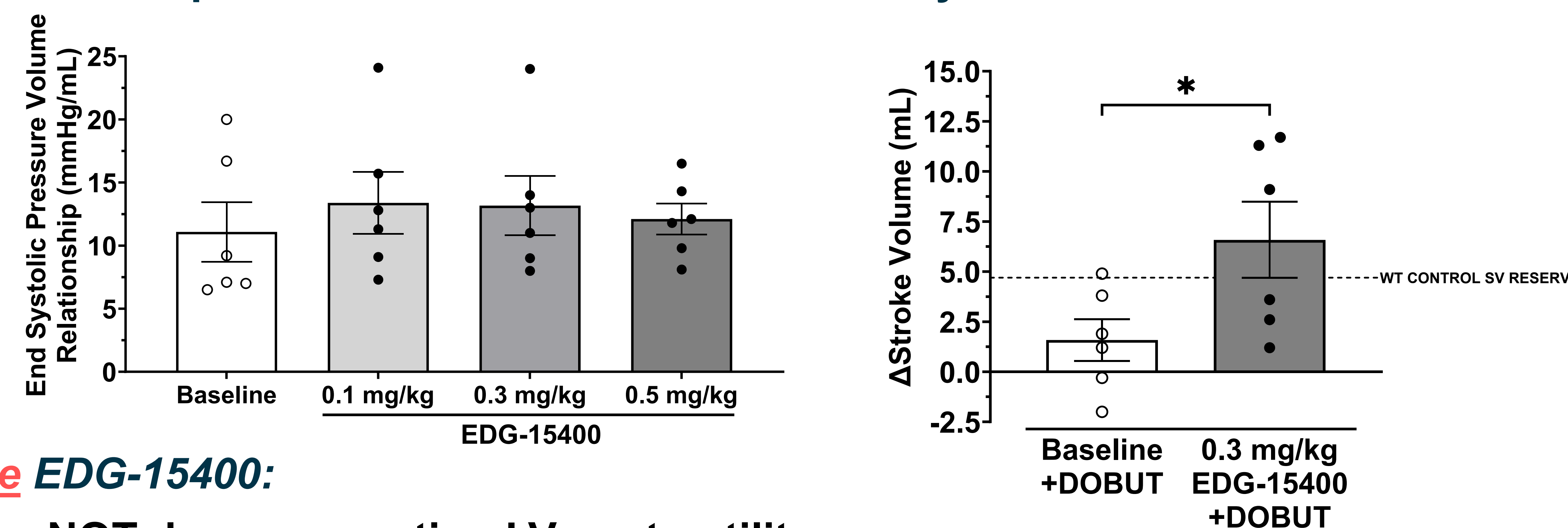
EDG-15400 improves left ventricular diastolic function



Acute EDG-15400 improves diastolic function marked by:

- Increased mitral annulus velocity during early filling (e')
- Dose-dependent decrease in LV end diastolic pressure
- Decrease in the end diastolic pressure volume relationship (EDPVR)

EDG-15400 preserves left ventricular contractility and restores cardiac reserve



Acute EDG-15400:

- Does NOT decrease resting LV contractility
- Increases stroke volume reserve to normal levels

Conclusions

- Acute EDG-15400 demonstrates potent improvement in LV early relaxation, diastolic filling pressures, and compliance
- Diastolic efficacy does not come at the cost of impaired systolic performance
- Unlike CMIs, beneficial effects on diastolic function do not occur with a parallel decrease in LV contractility
- These findings support the ongoing development of EDG-15400 in HFpEF beyond supranormal ejection fractions

Disclosures
EDG-15400 is an investigational agent that is not approved for use by any regulatory authority in any territory. This study is funded by Edgewise Therapeutics. Craig Emter, Marcus Henze, Natalie Hawryluk, Emily DiNatale, and Alan Russell are employees of and hold shares of Edgewise Therapeutics.