

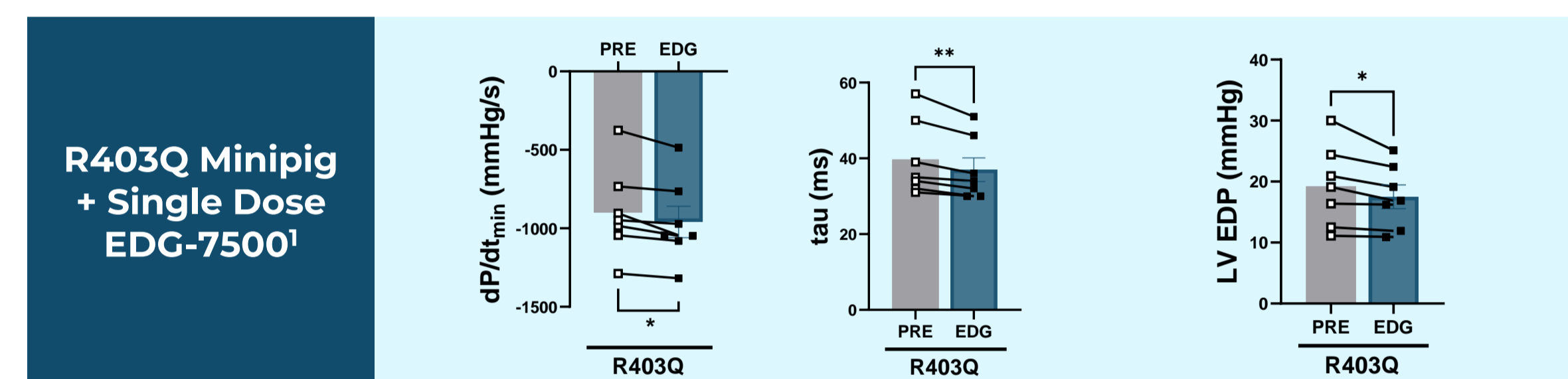
# Chronic Treatment With The Sarcomere Modulator EDG-7500 Improves Left Ventricular Distensibility and Cardiac Output Recruitment During Stress In A Minipig Genetic Model of Non-Obstructed HCM

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## BACKGROUND

Exercise intolerance due to impaired cardiac output recruitment under stress is a hallmark of hypertrophic cardiomyopathy (HCM). EDG-7500 is an oral, selective, cardiac sarcomere modulator currently under evaluation in Ph1 and Ph2 studies. Single dose administration studies of EDG-7500 in the R403Q genetic pig model showed pharmacologic driven improvement in relaxation and filling pressure (shown below).

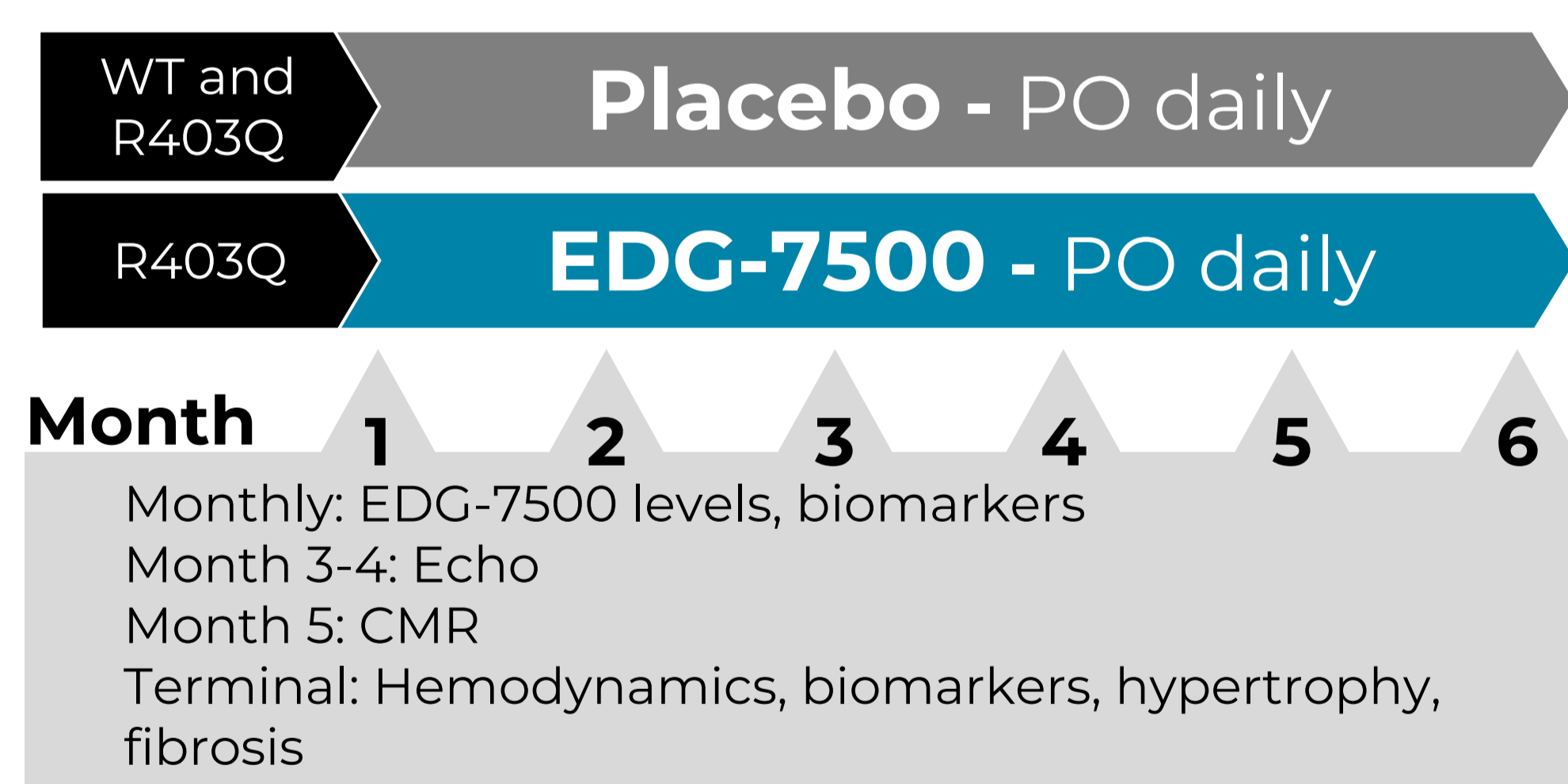


This in vivo study evaluated the chronic effects of EDG-7500 in a genetic pig model of non-obstructed HCM (nHCM).

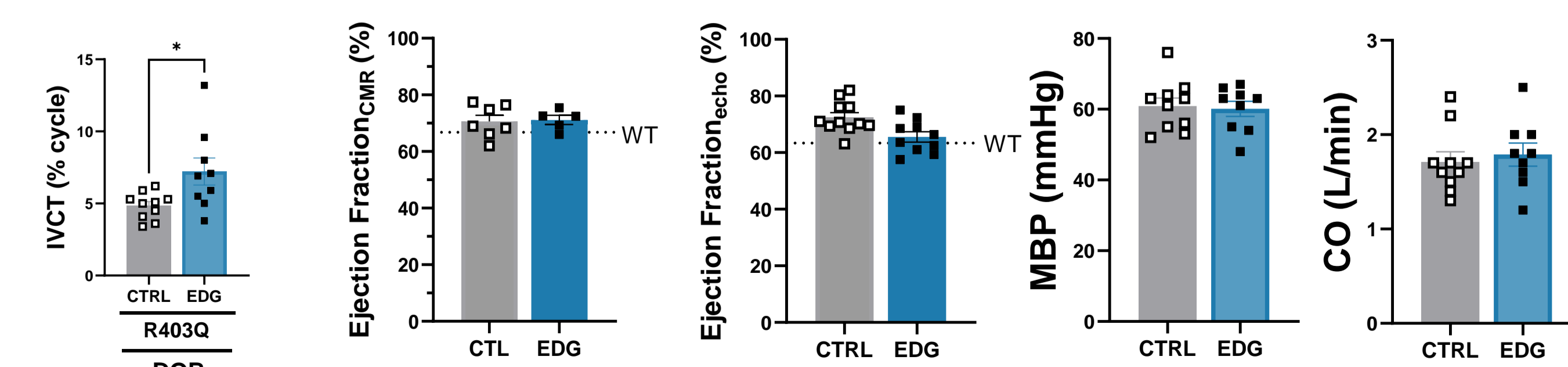
<sup>1</sup> Del Rio et al Circulation. 2023;148:A15822

## METHODS

Young (1-2M old) Yucatan mini-pigs with a heterozygous MYH7 R403Q mutation were assigned to receive either placebo (n = 10) or EDG-7500 (n = 11; PO). Untreated wild-type littermates served as disease controls (n=11). Doses were selected to target trough plasma levels between 100 and 200 ng/mL over the course of the treatment period.



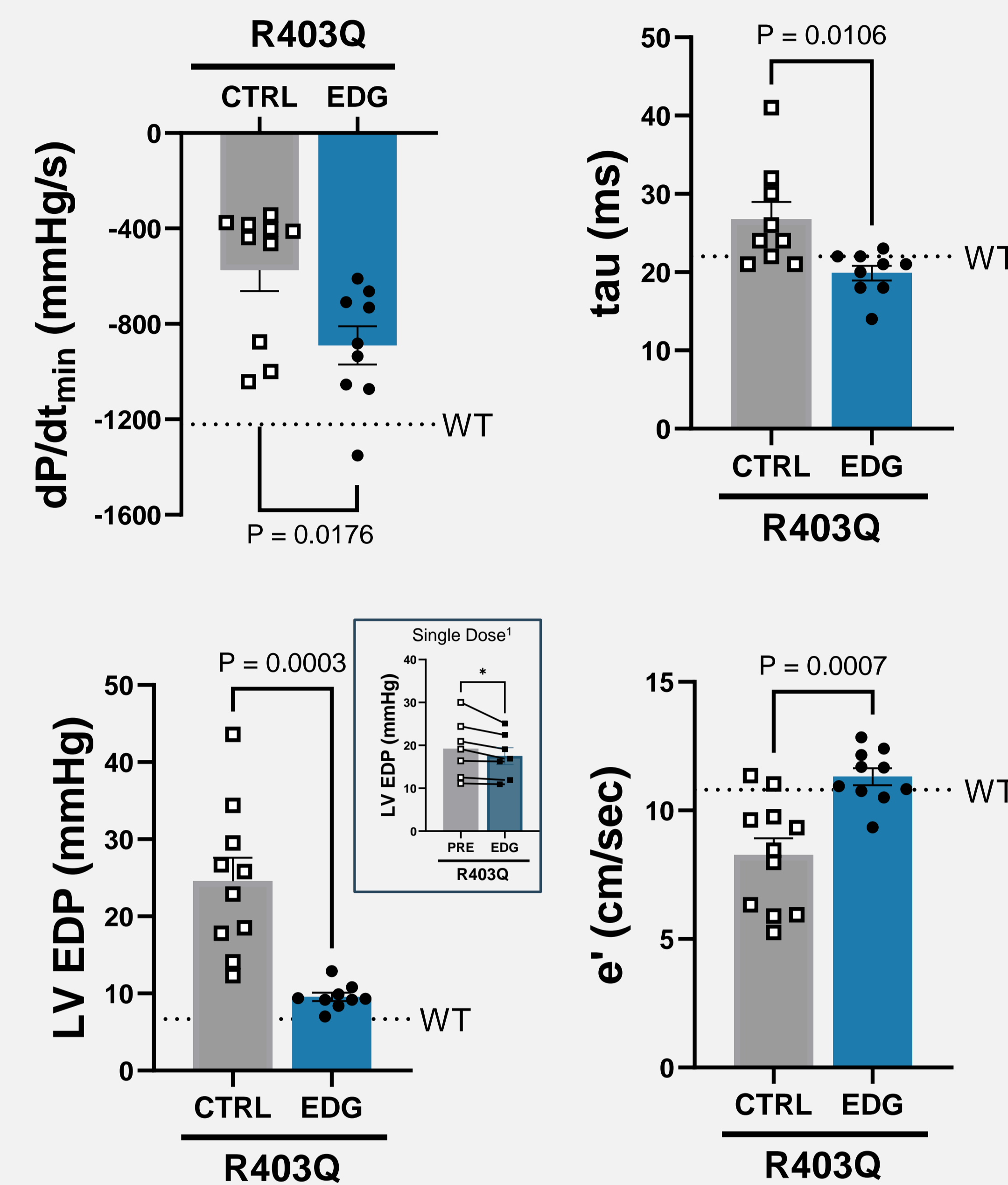
Chronic EDG-7500 treatment provided target engagement while maintaining LVEF, systemic pressure, and cardiac output @ 5-6 months



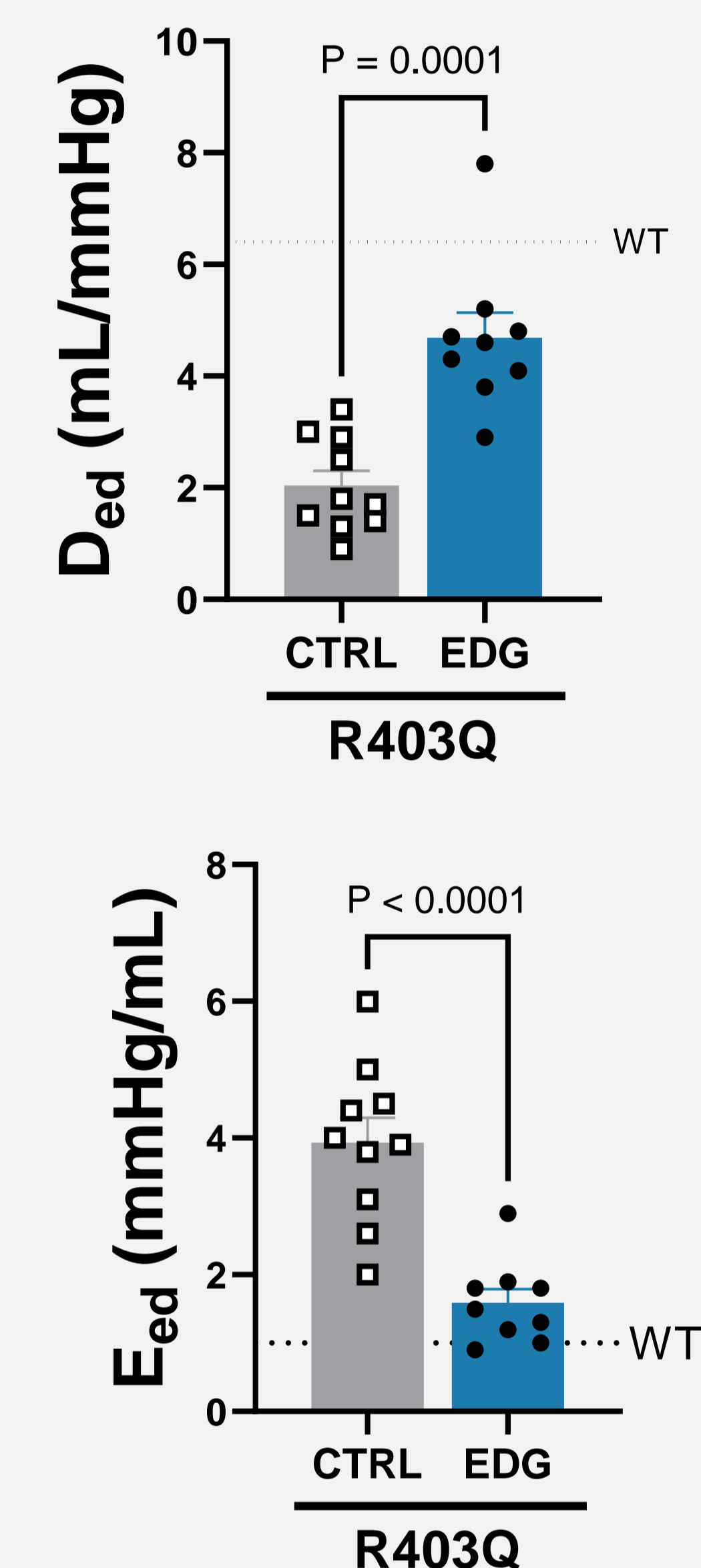
Hemodynamic assessment was performed at rest and under  $\beta$ -adrenergic ( $\beta$ -AR) cardiac stress (dobutamine, 2 ug/kg/min IV). Myocardial end-systolic and end-diastolic stiffness were determined via pressure-volume relationship generated via brief venous return occlusions.

# Daily administration of EDG-7500 in a model of nHCM Prevents Diastolic Dysfunction

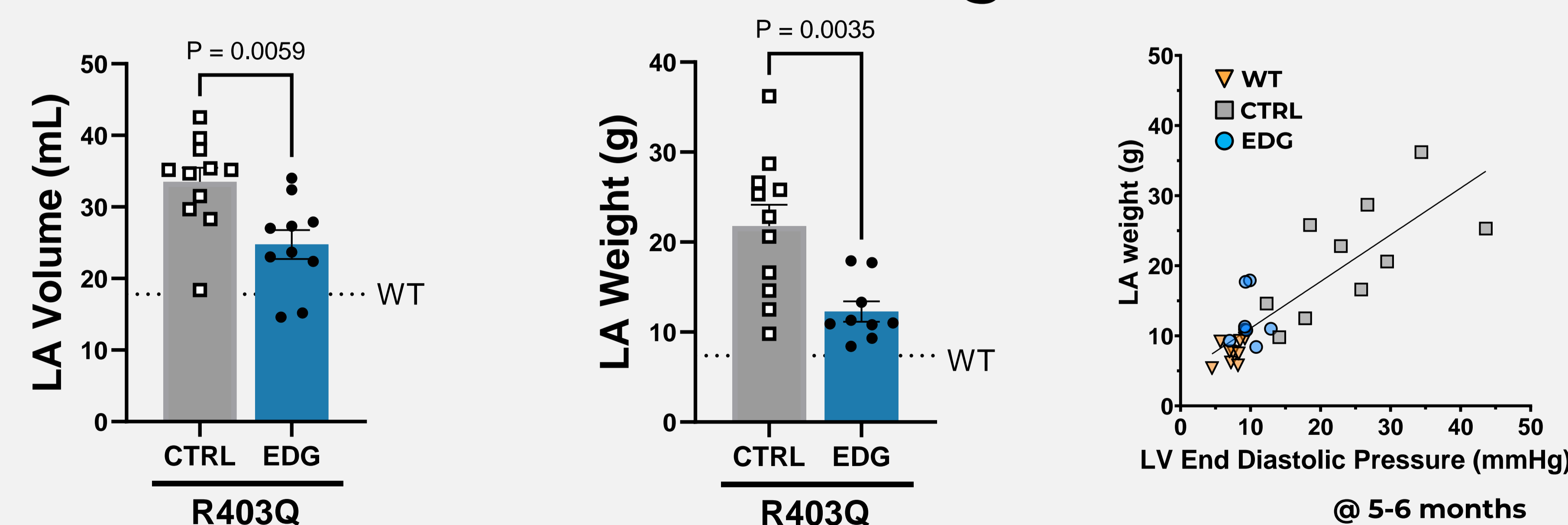
## Preserves LV diastolic filling & pressure



## Passive myocardial mechanical properties



## Left Atrial Remodeling Blunted

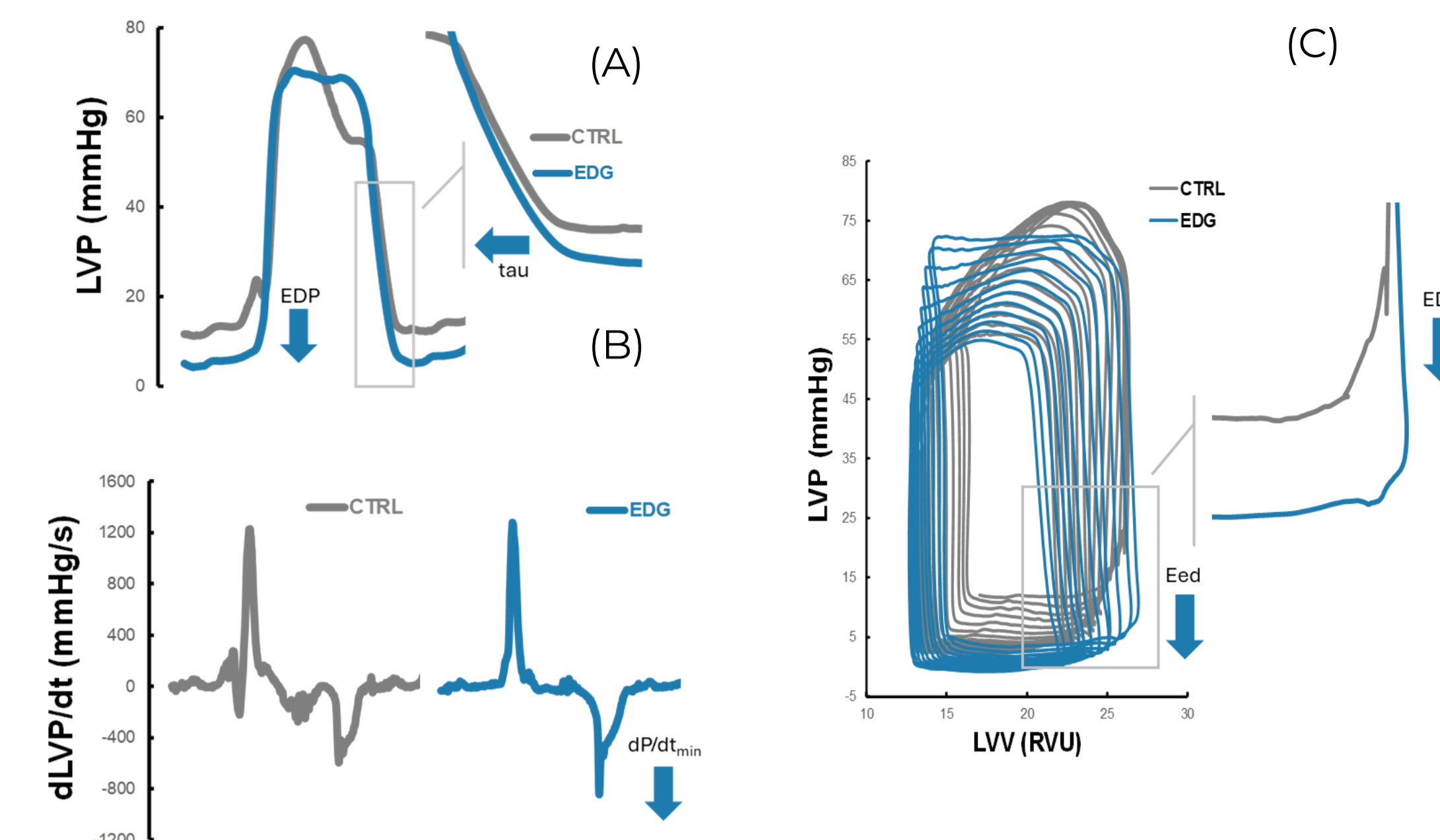


## LV relaxation and compliance preserved by chronic EDG7500 treatment @ 5-6 months

### Figure legend:

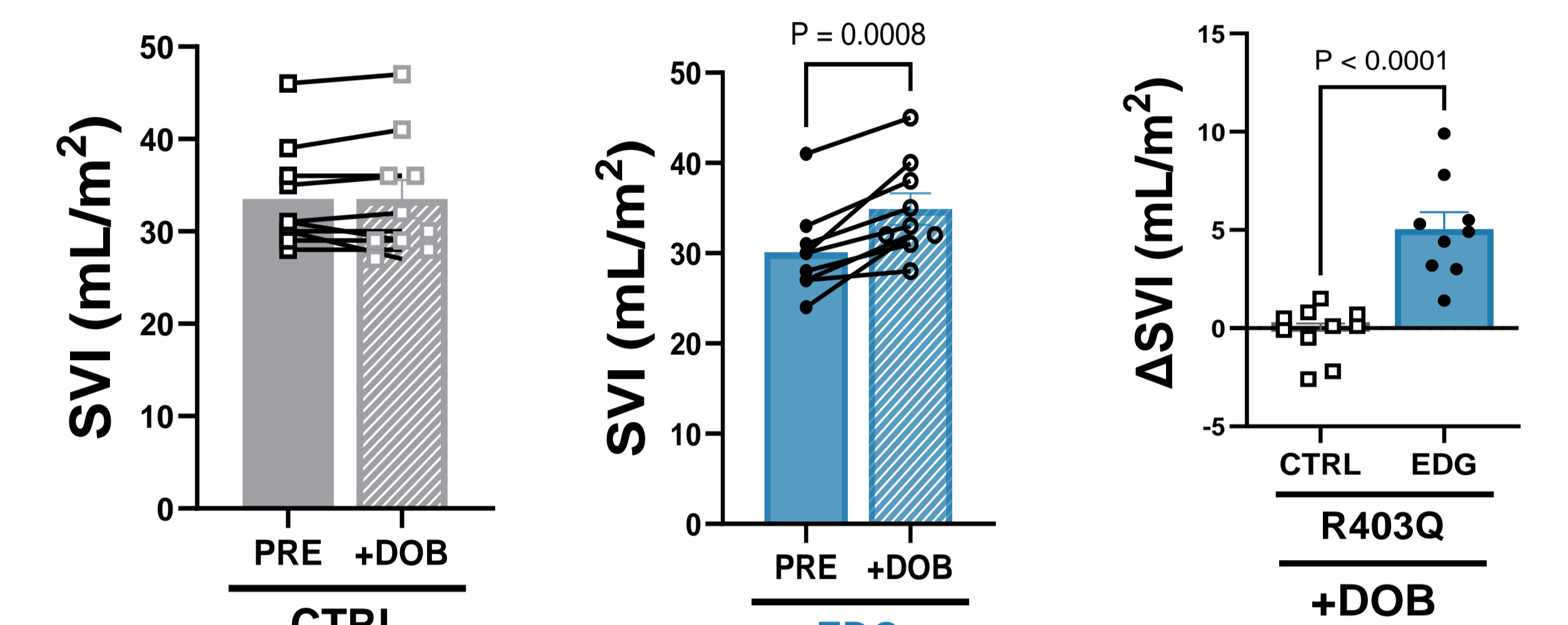
Representative traces of: Left ventricular pressure vs. time (A); Rate of change of left ventricular pressure vs. time (B); Pressure-volume loops (C).

CTRL group (grey) and EDG-7500 daily treatment (blue)

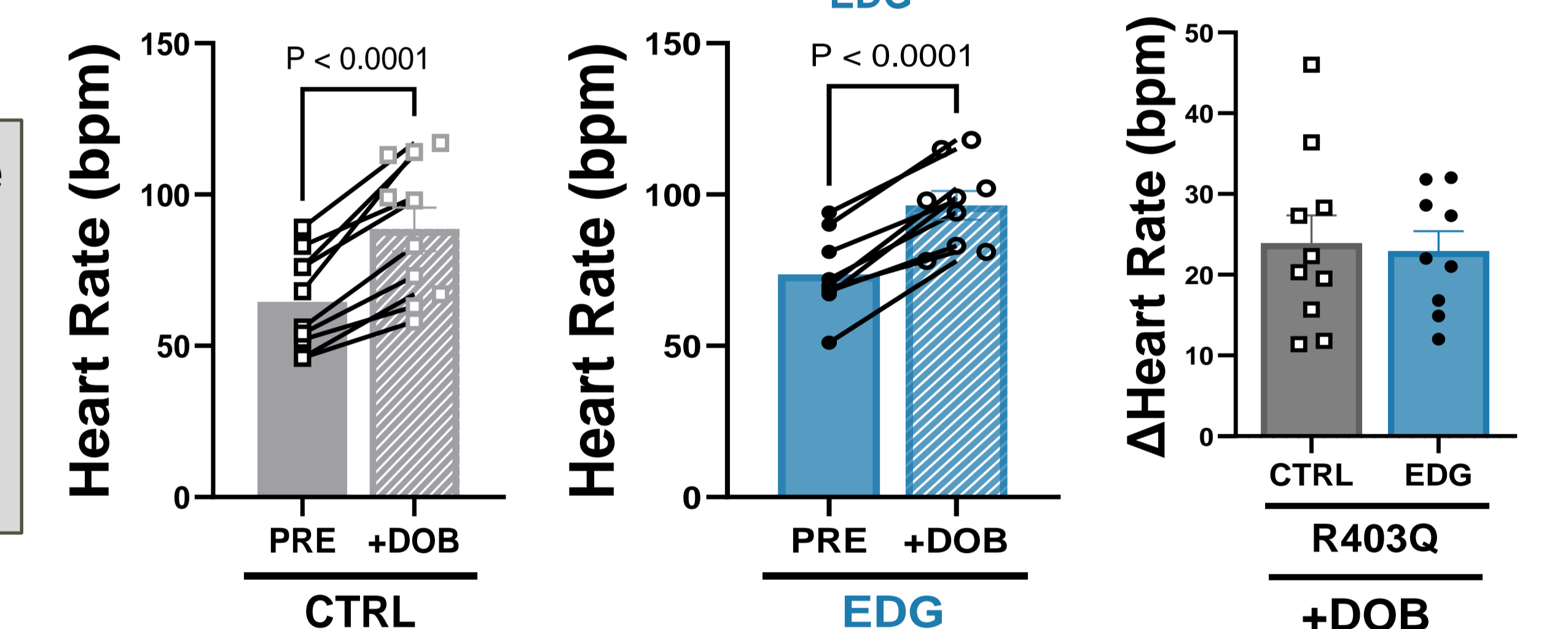


## Restoration of cardiac reserve with chronic treatment of EDG-7500 @ 5-6 months

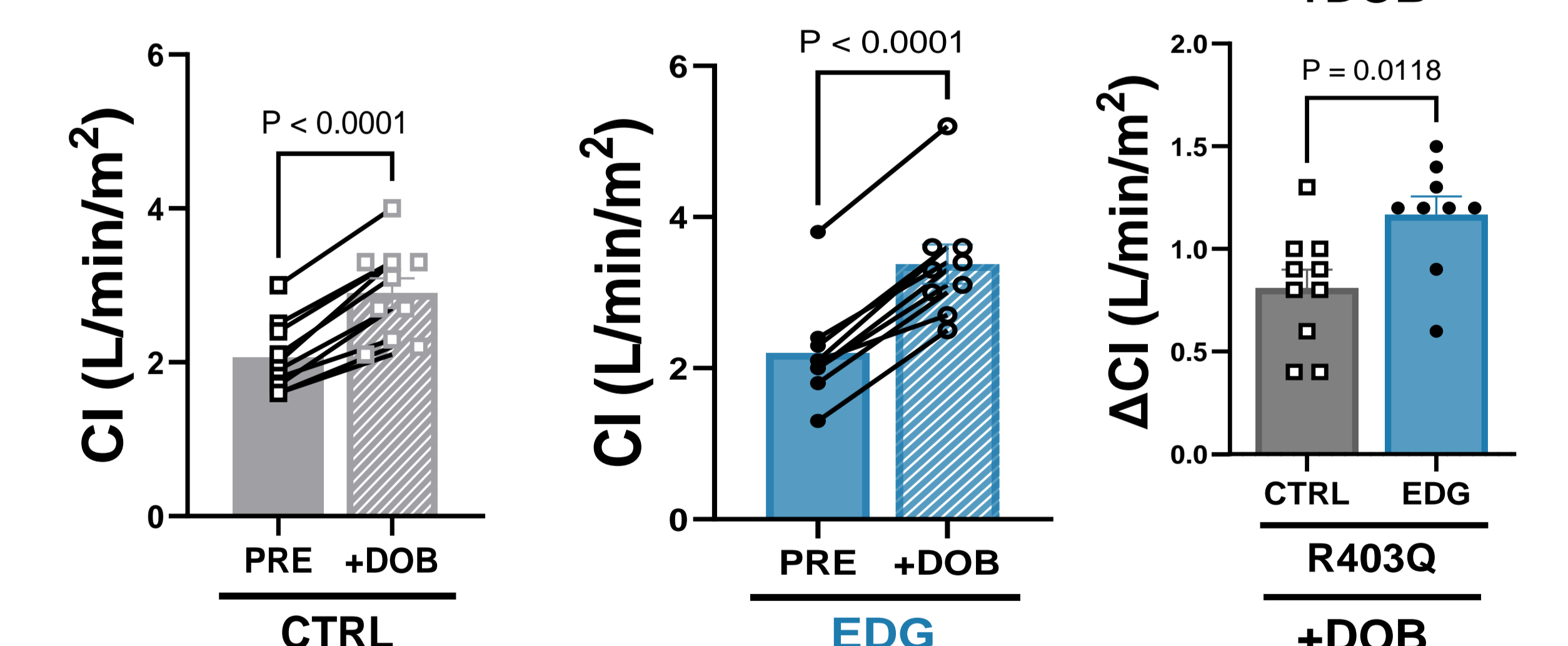
Increased stroke volume w/ 7500



Heart Rate increased in both CTRL and EDG



SV x HR yields higher CO increase in EDG treated



## CONCLUSIONS

In a minipig genetic model of nHCM:

1. EDG-7500 blunted the HCM-mediated progressive slowing of LV diastolic relaxation;
2. EDG-7500 preserved myocardial distensibility;
3. EDG-7500 maintained cardiac reserve demonstrated by SV with  $\beta$ -adrenergic stimulation

Clinical studies of EDG-7500 are underway to assess if these lusitropic benefits can be observed in patients with disorders of diastolic function.

## DISCLOSURE INFORMATION

ME, CE, ED, MH, LL, AP, AR, and MS are employees of Edgewise and own equity in Edgewise. CDR is a consultant for Edgewise and owns equity in Edgewise. SR and SSC are employees of QTest Labs.



For more information on EDG-7500 clinical studies email: [cardiacstudies@edgewisetx.com](mailto:cardiacstudies@edgewisetx.com)



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