

SUPPLEMENTAL MATERIAL

LV Ejection Fraction

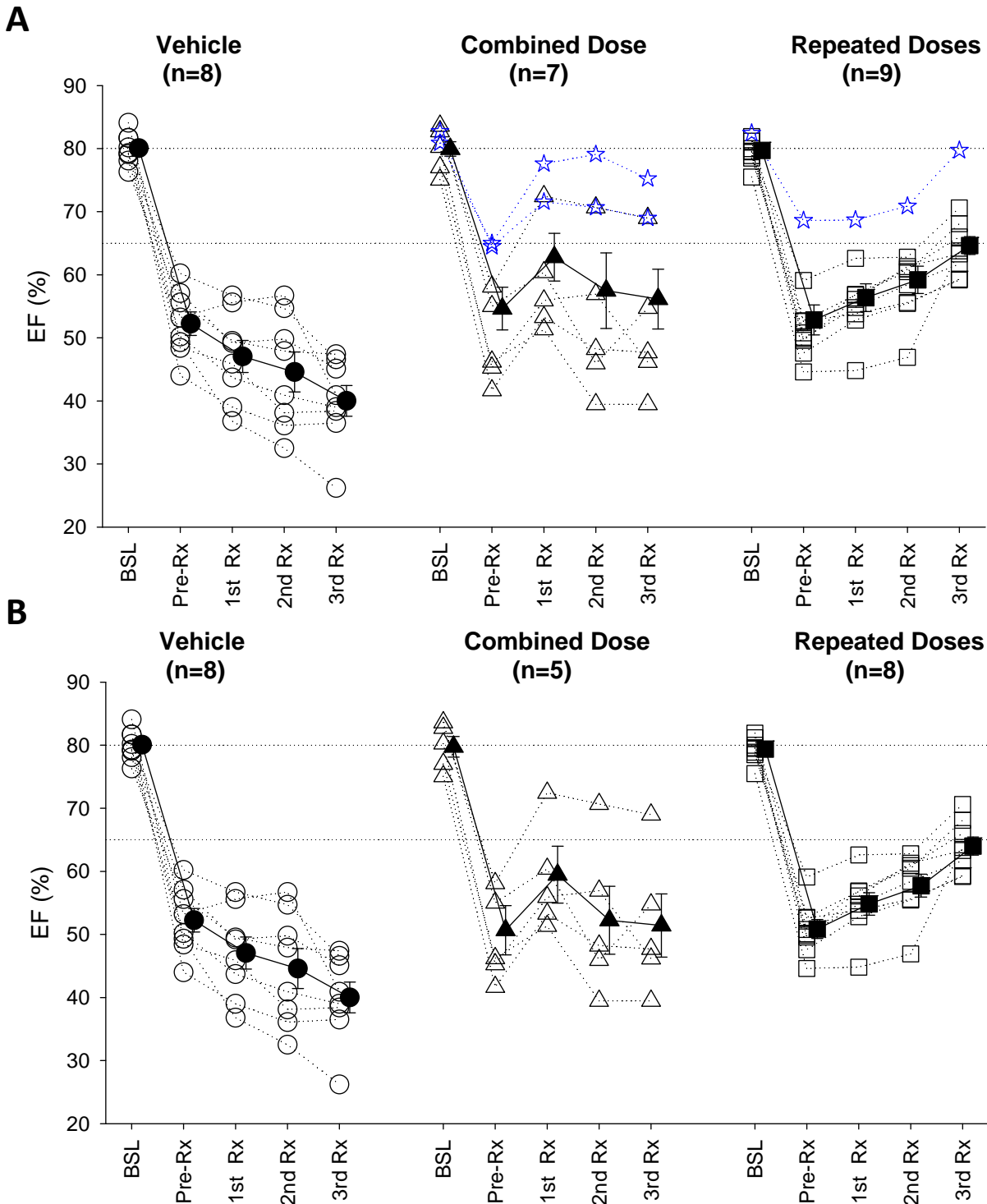


Figure S1A&B: Time course of LV ejection fraction (EF) in individual rats (dotted line with open symbols) and group means±SEM (solid line with solid symbols) in the 3 groups. The two dotted reference lines indicate baseline values (upper) and the exclusion cutoff (lower line), which is 15 EF units below baseline. **A:** All animals that completed the study protocol (with no exclusions). Blue lines denote 2 rats in the combined dose group that were excluded because of scar <10% of LV (these rats had a drop in EF = 15.5 and 16.2 units) and one rat in the repeated doses group that was excluded because of an EF drop < 15 units after MI (Pre-Rx) (specifically, 13.9 units). **B:** Animals analyzed after exclusion. BSL, baseline (before MI); Pre-Rx, pretreatment (30 days after coronary occlusion/reperfusion); 1st, 2nd, and 3rd, 35 days after the first, second, and third treatment with vehicle, combined dose (one dose of 36×10^6 CPCs) or repeated doses (three doses of 12×10^6 CPCs repeated at a 35-day interval). EF was assessed using 2D long axis images. Note that the difference in EF between the combined dose and the multiple doses groups at the end of the study is similar with and without exclusions.

LV EDV

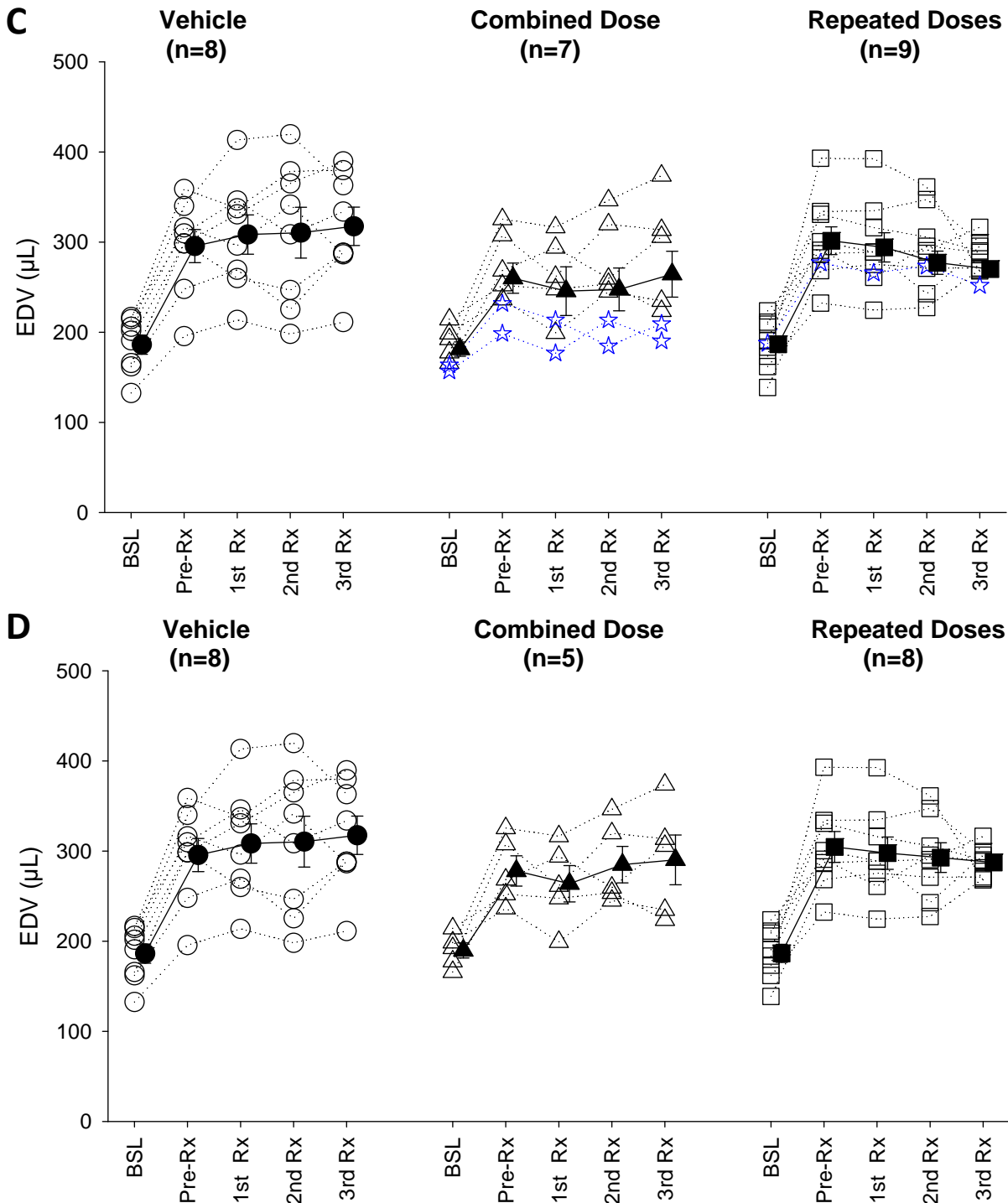


Figure S1C&D: Time course of LV end-diastolic volume (EDV) in individual rats (dotted line with open symbols) and in group mean \pm SEM (solid line with solid symbols) of the 3 groups.

C: All animals that completed the entire study protocol before exclusion. As seen in blue, 3 rats (2 in the combined dose and 1 in the repeated doses) were excluded as detailed in the previous Supplementary figure. **D:** Animals analyzed after exclusions. BSL, baseline (before MI); Pre-Rx, pretreatment (30 days after coronary occlusion/reperfusion); 1st, 2nd, and 3rd, 35 days after the first, second, and third treatment with vehicle, combined dose (one dose of 36×10^6 CPCs) or repeated doses (three doses of 12×10^6 CPCs repeated at a 35-day interval). EDV was assessed using 2D long axis images.

LV ESV

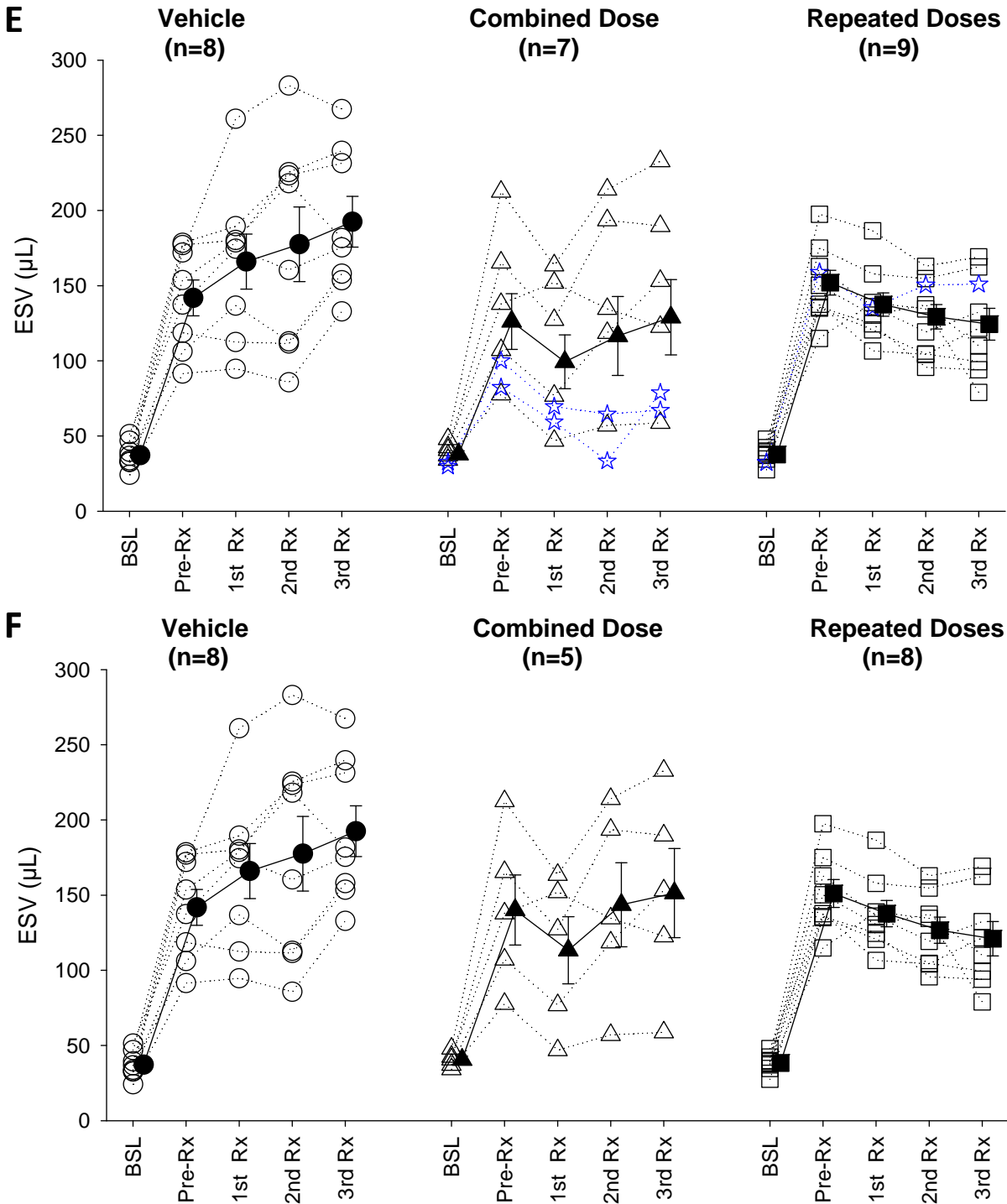


Figure S1E&F: Time course of LV end-systolic volume (ESV) in individual rats (dotted line with open symbols) and in group mean \pm SEM (solid line with solid symbols) of the 3 groups.

E: All animals that completed the entire study protocol before exclusions. As seen in blue, 3 rats (2 in the combined dose and 1 in the repeated doses) were excluded as detailed in the previous figures. **F:** Animals analyzed after exclusions. BSL, baseline (before MI); Pre-Rx, pretreatment (30 days after coronary occlusion/reperfusion); 1st, 2nd, and 3rd, 35 days after the first, second, and third treatment with vehicle, combined dose (one dose of 36×10^6 CPCs) or repeated doses (three doses of 12×10^6 CPCs repeated at a 35-day interval). ESV was assessed using 2D long axis images.

G

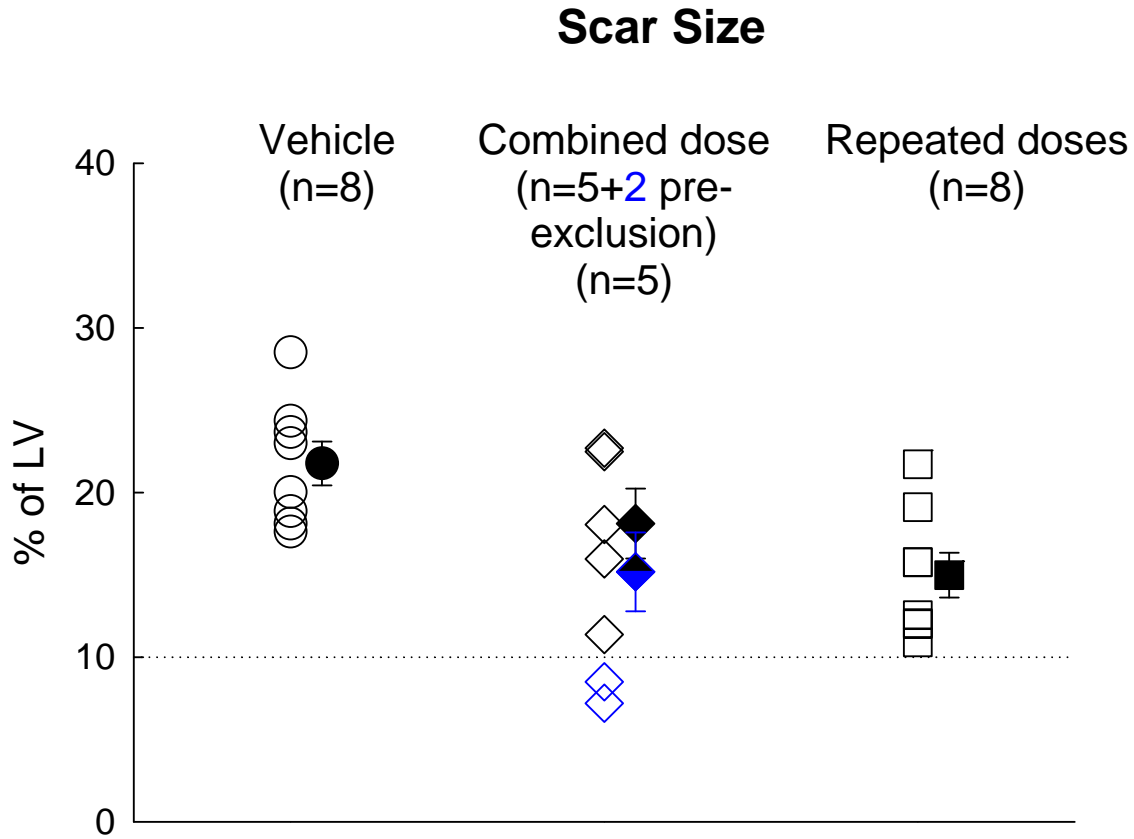


Figure S1G: Scar size (% of LV) in individual rats (open symbols) and group mean \pm SEM (solid symbols) in the 3 groups. Scar size was determined after LV sections were stained with Masson's trichrome. The solid blue diamond represents the group mean before exclusions (n=7). As seen in the blue symbols, 2 rats in the combined dose group were excluded due to small scar size (<10% of LV; 7.2 and 8.5% of LV). These two rats had also a small decrease in EF before the 1st treatment (15.5 and 16.2 EF units). No pathology analysis was performed in the rat excluded in the repeated doses group because this animal was excluded due to an EF drop <15 EF units.

Table S1. LV ejection fraction, LV volume, and scar size before and after exclusions (mean \pm SEM)

| | | Vehicle (N=8) | Combined dose | | Repeated doses | |
|----------------------------|--------------------------------|------------------|------------------------------|-----------------------------|------------------------------|-----------------------------|
| | | | Before exclusion (n=7) | After exclusion (n=5) | Before exclusion (n=9) | After exclusion (n=8) |
| EF (%) | BSL | 80.1 \pm 0.9 | 79.9 \pm 1.1 | 79.8 \pm 1.6 | 79.7 \pm 0.7 | 79.3 \pm 0.7 |
| | Pre-Rx | 52.3 \pm 1.86 | 54.6 \pm 3.4 | 50.7 \pm 3.9 | 52.8 \pm 2.4 | 50.9 \pm 1.8 |
| | 1 st Rx | 47.1 \pm 2.53 | 62.8 \pm 3.8 | 59.5 \pm 4.5 | 56.4 \pm 2.2 | 54.8 \pm 1.8 |
| | 2 nd Rx | 44.6 \pm 3.2 | 57.5 \pm 6.0 | 52.3 \pm 5.4 | 59.2 \pm 2.2 | 57.7 \pm 1.8 |
| | 3 rd Rx | 40.0 \pm 2.4 | 56.1 \pm 4.8 | 51.4 \pm 5.0 | 64.6 \pm 1.4 | 64.0 \pm 1.4 |
| Δ EF (%) | Pre-Rx from BSL | -27.8 \pm 2.3 | -25.3 \pm 2.7 | -29.1 \pm 2.5 | -26.9 \pm 2.0 | -28.4 \pm 1.5 |
| | 1 st Rx from Pre-Rx | -5.2 \pm 1.5 | 8.2 \pm 2.1 | 8.8 \pm 2.8 | 3.5 \pm 0.8 | 4.0 \pm 0.8 |
| | 2 nd Rx from Pre-Rx | -7.7 \pm 2.0 | 2.8 \pm 3.5 | 1.6 \pm 5.1 | 6.4 \pm 1.2 | 6.9 \pm 1.2 |
| | 3 rd Rx from Pre-Rx | -12.2 \pm 1.7 | 1.5 \pm 2.2 | 0.8 \pm 3.1 | 11.8 \pm 1.8 | 13.1 \pm 1.3 |
| EDV (μ L) | BSL | 186.2 \pm 10.6 | 181.3 \pm 8.0 | 189.7 \pm 8.4 | 186.6 \pm 8.8 | 186.4 \pm 10.0 |
| | Pre-Rx | 295.6 \pm 18.4 | 259.9 \pm 18.4 | 277.9 \pm 16.8 | 301.5 \pm 15.4 | 304.6 \pm 17.1 |
| | 1 st Rx | 308.3 \pm 21.9 | 244.1 \pm 19.2 | 263.7 \pm 20.2 | 294.1 \pm 16.2 | 297.6 \pm 18.0 |
| | 2 nd Rx | 310.4 \pm 28.2 | 260.3 \pm 21.4 | 284.8 \pm 20.3 | 277.1 \pm 12.9 | 292.6 \pm 16.4 |
| | 3 rd Rx | 317.4 \pm 21.3 | 264.4 \pm 25.4 | 290.2 \pm 27.6 | 270.1 \pm | 287.3 \pm 6.0 |
| Δ EDV (μ L) | Pre-Rx from BSL | 109.4 \pm 9.8 | 78.7 \pm 16.2 | 88.2 \pm 21.3 | 114.9 \pm 16.0 | 118.1 \pm 17.7 |
| | 1 st Rx from Pre-Rx | 12.7 \pm 13.1 | -15.9 \pm 8.9 | -14.2 \pm 12.7 | -7.4 \pm 3.7 | -6.9 \pm 4.2 |
| | 2 nd Rx from Pre-Rx | 14.8 \pm 15.4 | 0.4 \pm 8.7 | 6.9 \pm 5.0 | -24.4 \pm 11.2 | -12.0 \pm 7.1 |
| | 3 rd Rx from Pre-Rx | 21.8 \pm 12.6 | 4.4 \pm 10.9 | 12.3 \pm 13.8 | -31.5 \pm 15.8 | -17.8 \pm 17.8 |
| ESV (μ L) | BSL | 37.2 \pm 3.0 | 37.9 \pm 2.4 | 40.5 \pm 2.3 | 37.7 \pm 2.0 | 38.4 \pm 2.1 |
| | Pre-Rx | 141.9 \pm 12.0 | 126.2 \pm 18.5 | 140.1 \pm 23.3 | 152.0 \pm 8.2 | 151.1 \pm 9.3 |
| | 1 st Rx | 166.0 \pm 18.3 | 99.4 \pm 17.9 | 113.3 \pm 22.3 | 137.4 \pm 7.7 | 132.7 \pm 8.7 |
| | 2 nd Rx | 177.6 \pm 24.8 | 116.5 \pm 26.2 | 143.6 \pm 28.0 | 129.3 \pm 8.2 | 126.7 \pm 8.7 |
| | 3 rd Rx | 192.5 \pm 16.9 | 129.0 \pm 25.1 | 151.4 \pm 29.6 | 124.4 \pm 10.6 | 121.0 \pm 11.4 |
| Δ ESV (μ L) | Pre-Rx from BSL | 104.6 \pm 10.7 | 88.3 \pm 16.4 | 99.6 \pm 21.1 | 114.2 \pm 10.7 | 112.7 \pm 10.0 |
| | 1 st Rx from Pre-Rx | 24.2 \pm 10.7 | -26.8 \pm 7.5 | -26.8 \pm 10.8 | -19.0 \pm 3.1 | -18.4 \pm 3.4 |
| | 2 nd Rx from Pre-Rx | 35.7 \pm 14.04 | -9.6 \pm 10.2 | 3.4 \pm 8.1 | -22.7 \pm 4.8 | -24.5 \pm 5.1 |
| | 3 rd Rx from Pre-Rx | 50.6 \pm 10.2 | 2.8 \pm 10.6 | 11.2 \pm 12.4 | -27.6 \pm 4.9 | -37.6 \pm 9.2 |
| Scar size (% of LV) | | 21.8 \pm 1.3 | 15.2 \pm 2.4 | 18.1 \pm 2.1 | * | 14.9 \pm 1.4 |

* No pathology analysis was performed in the rat that was excluded due to EF drop < 15 EF units.