

CER-001, an engineered high-density lipoprotein modulates Ischemia/Reperfusion Injury (IRI) in hypothermic and normothermic perfusion solutions through PI3K/AKT/ eNOS Ser1177 pathway

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Introduction

Machine perfusion treatments provide the opportunity to improve graft preservation and allow pre-transplant ex-vivo organ assessment. CER-001 (Abionyx), an apolipoprotein A-I (apoA-I)-containing HDL mimetic, has shown clinical and pre-clinical anti-inflammatory, vascular and reno-protective effects. Given the role of the cytokine storm, innate immune activation and endothelial dysfunction during renal Ischemia/Reperfusion Injury (IRI), this study aims to evaluate the ability of CER-001 supplementation in perfusion solution to modulate IRI.

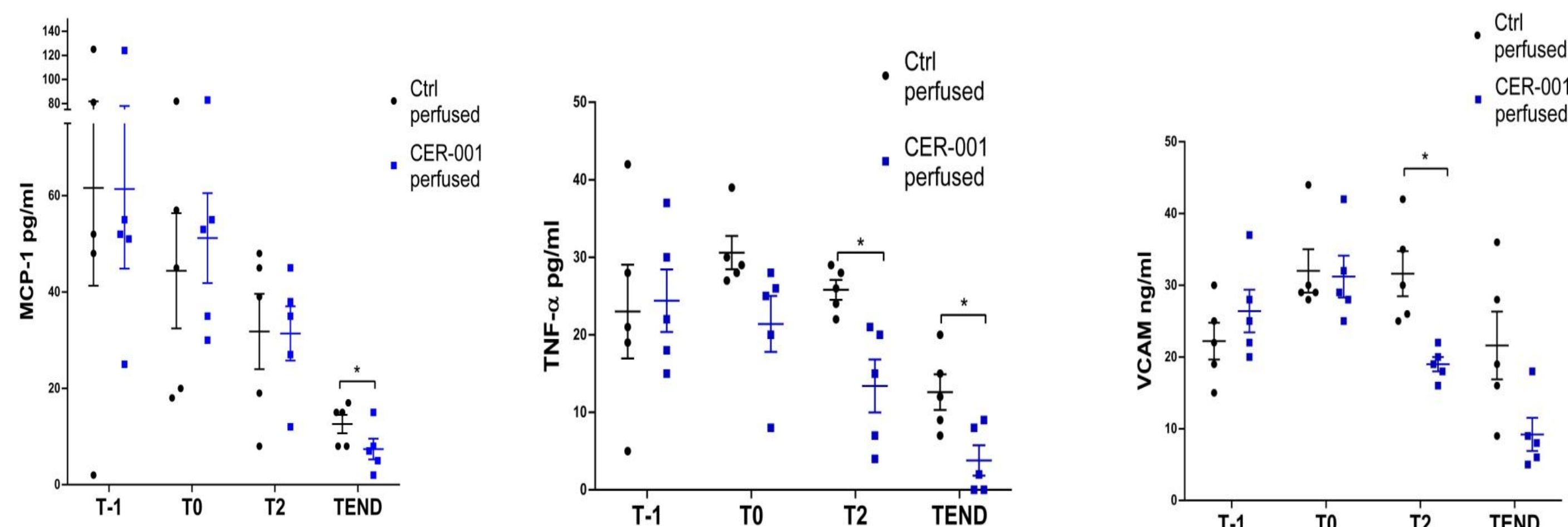
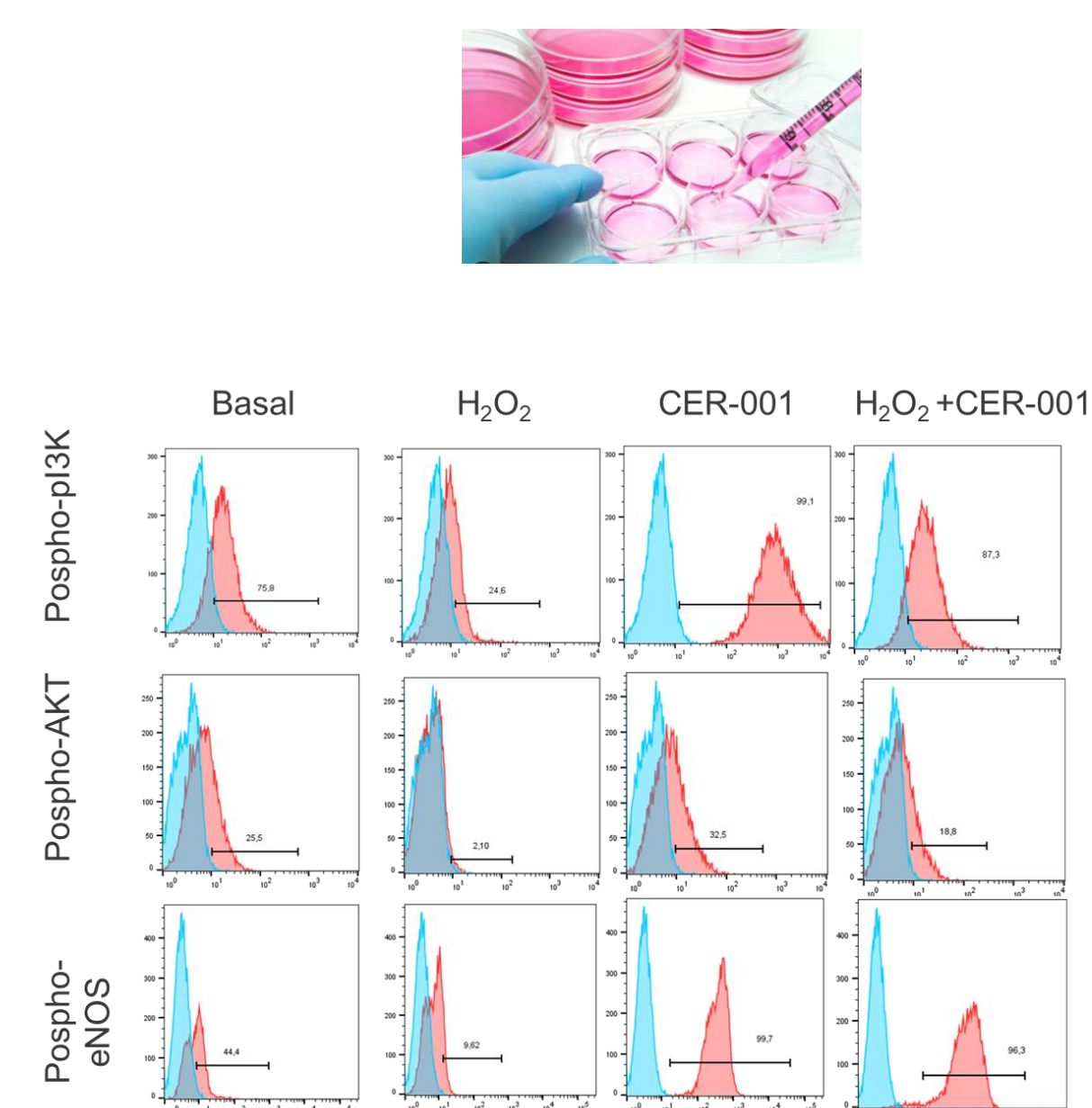
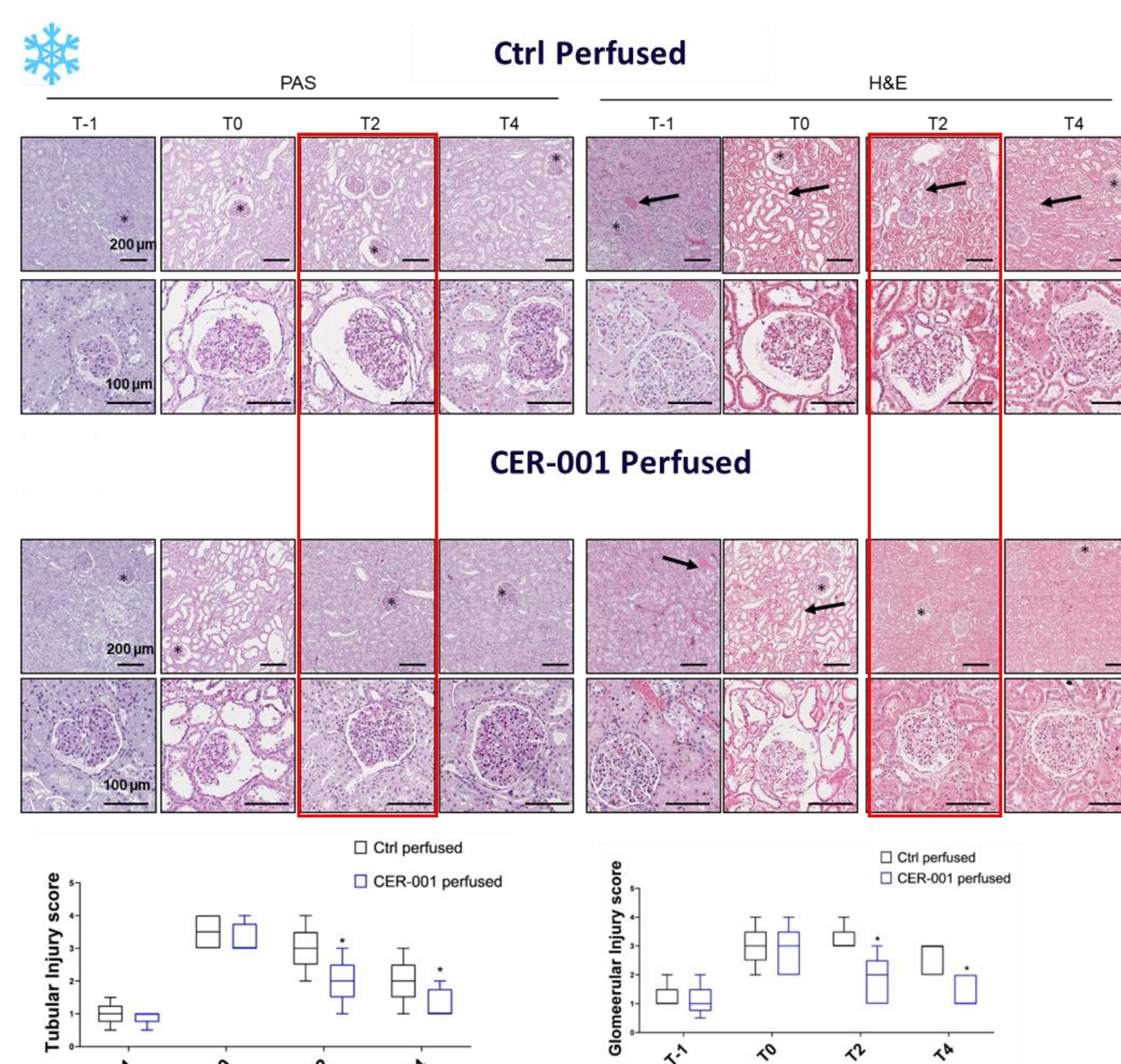
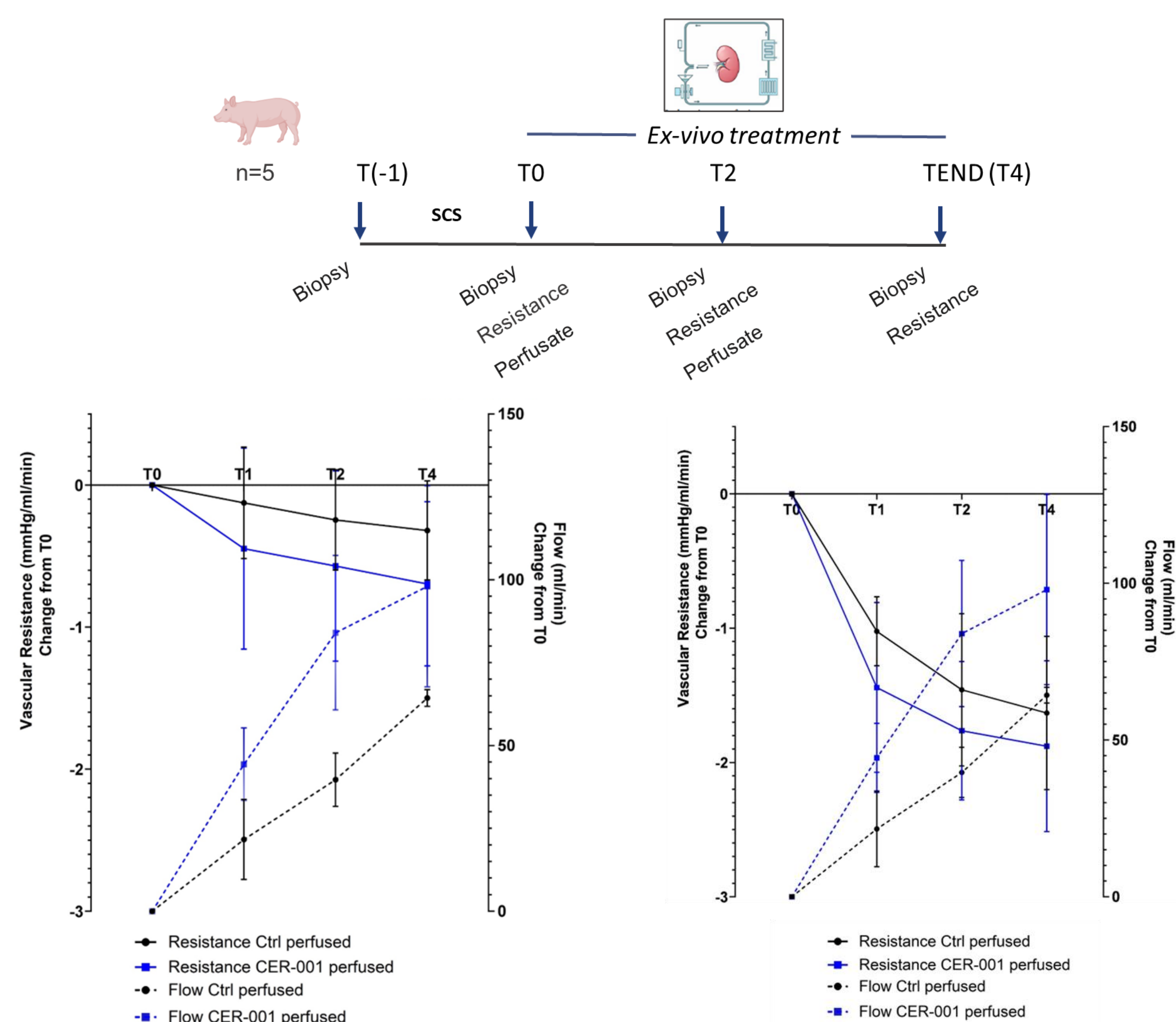
METHODS

In an experimental model of donation after cardiac death (DCD), renal graft were perfused in oxygenated manner at low temperature (4-6°C, HMP) or at 32 °C (NMP) by Perkidney, Perlife Device From Aferetica Purification Therapies. Kidneys (n=20) underwent to 60 min of warm ischemia and 15h of static cold storage. During the perfusion we collected biopsies, perfusates and registered renal resistance. Graft from the same pigs were perfused with standard solution with or without CER001. For NMP we supplemented a solution a plasma volume expander enriched with autologous red blood cells leucodepleted as oxygen carrier. Endothelial cells exposed to H2O2, C5a and CER-001 (50-100 µg/mL) were assessed by MTT and FACS.

RESULTS

During HMP and NMP, CER-001 group expressed significant amelioration of vascular resistances, flows and cytokines levels (CER-001 vs CONTROL, p<0.05). CER-001 promoted the activation of pAkt-eNOS pathway leading to the release of protective nitric oxide through eNOS Serine 1177 phosphorylation.

In vitro, CER-001 prevents apoptosis and endothelial dysfunction.



Conclusion

The use of CER-001 in MP counteracted vasoconstriction and inflammation, improving renal resistance during the treatment.