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PATHOPHYSIOLOGICAL BASIS OF RESOLUTION OF ACUTE-ON-CHRONIC LIVER FAILURE (ACLF) INDUCED BY THE NOVEL LIVER DIALYSIS DEVICE, DIALIVE (ALIVER CONSORTIUM)

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Background In ACLF, systemic inflammation (SI) due to pathogen and damage associated molecular patterns (PAMPs and DAMPs), albumin and endothelial dysfunction results in organ failure. DIALIVE, a liver dialysis device replaces dysfunctional albumin and removes PAMPs and DAMPs. In a randomised controlled trial, DIALIVE resolved ACLF faster and in a greater proportion of patients compared with standard of care (SOC). This substudy aimed evaluated the effect of DIALIVE on pathophysiological processes that are causally associated with ACLF.

Methods Study included patients with ACLF 1–3a, randomized to DIALIVE or SOC. End points were evaluated at Day 10. DIALIVE group received treatments in the first 3-days (range 1–6). Plasma samples were obtained on Days 0, 5 and 10. A post-hoc inferential Mixed Models for Repeated Measurements analysis was performed to evaluate the statistically significant

differences between groups at the Day 10. Changes in variables from baseline in the groups is shown in the figure 1 SAS system v.9.4 used.

Results 32 ACLF patients were randomised to DIALIVE (N=17; CLIF-OFs: 10.3 (1.6)) or SOC (n=15;CLIF-OFs: 9.9 (1.2)). 30-evaluable patients (n=15 each group) comprised this substudy. PAMPs: Endotoxin activity: The patient-level pre-defined reduction goals were 20%. Marked advantage seen for DIALIVE (80%) vs SOC (36.4%) at Day 5. LAL assay. Significant reduction in DIALIVE group (p=0.005). Albumin Function: DIALIVE increased human mercaptalbumin (p<0.001) and reduced human nonmercaptalbumins 1 and 2 (p=0.003 and p=0.203); improved binding capacity (p=0.073; EPR spectroscopy) and reduced ischemia modified albumin ratio (p=0.014) vs SOC. DAMPs: M30 and M65 components of cytokeratin 18 (p=0.079; p=0.192) and RIPK3 (marker of necroptosis) (p=0.624) were reduced in the DIALIVE group. SI: IL-8, IL-18 and TNFα were reduced in the DIALIVE compared with SOC group (p=0.021; p=0.021; p=0.08). Endothelial function: ADMA and Factor VIII were markedly reduced in the DIALIVE patients (p<0.001; p=0.070). TLR4 and Inflammasome ligands: Incubation of plasma with a 1L1b/IL18 Inflammasome cell line reduced signalling significantly (p=0.021); favourable reductions were also seen with TLR4 reporter cell line (p=0.403), in favour of DIALIVE vs SOC.

Conclusions DIALIVE impacts significantly on DAMPs, PAMPs, albumin and endothelial function, markers of SI and, reduces TLR4 and inflammasome ligands that collectively contribute to its ability to resolve ACLF.

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READMISSIONS POST LIVER TRANSPLANTATION: A 10 YEAR STUDY

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Introduction Short-term readmissions post liver transplantation (LT) are a marker of patient care and a high-cost burden. Studies from the U.S. suggest a 30–45% readmission rate at

Abstract P077 Figure 1 Impact of DIALIVE on the pathophysiological processes deranged in ACLF - change from baseline at Days 5 and 10 for DIALIVE (green) and SOC (red) group