This project has received funding from the European Union's Horizon 2020 research and innovation programme under agreement No. 733057

ALIVER

ALIVER
DIALIVE Summary Results*

*Produced from the report dated 150920, preliminary results based on October 22, 2020 Investigator Meeting

CONSORTIUM

Germany

France

Switzerland

Spain

Belgium

Ireland

United Kingdom

Spain

Germany

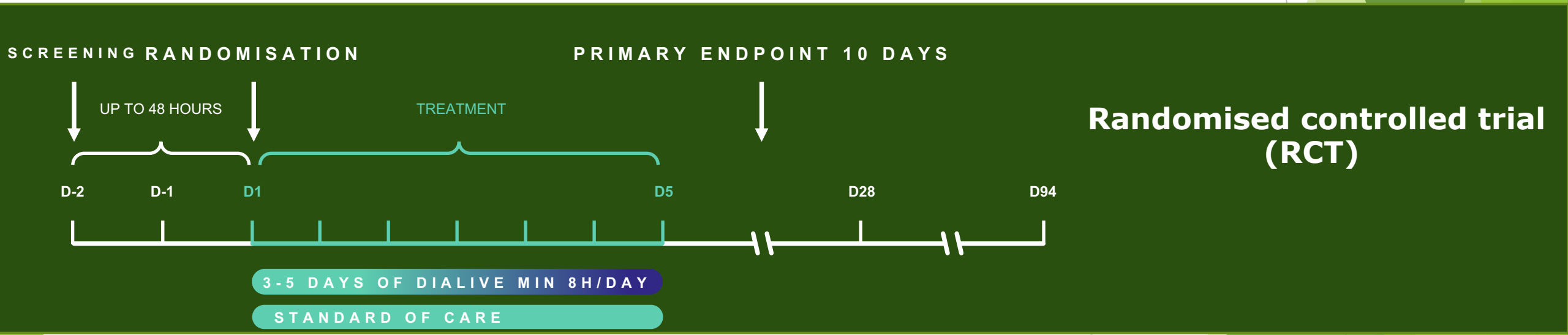
United Kingdom

United Kingdom

This project has received funding from the European Union's Horizon 2020 research and innovation programme under agreement No. 733057

DIALIVE Trial Design

Primary endpoint	**Safety at 10 days** after 3-5 sessions of 8-12 hours DIALIVE treatment in ICU
Population	ACLF 1 - 3. **n= 30 randomised 1:1 to standard of care**
Key inclusion criteria	m/f ≥ 18. History indicative of **alcohol-related cirrhosis.** History of **acute decompensating event**

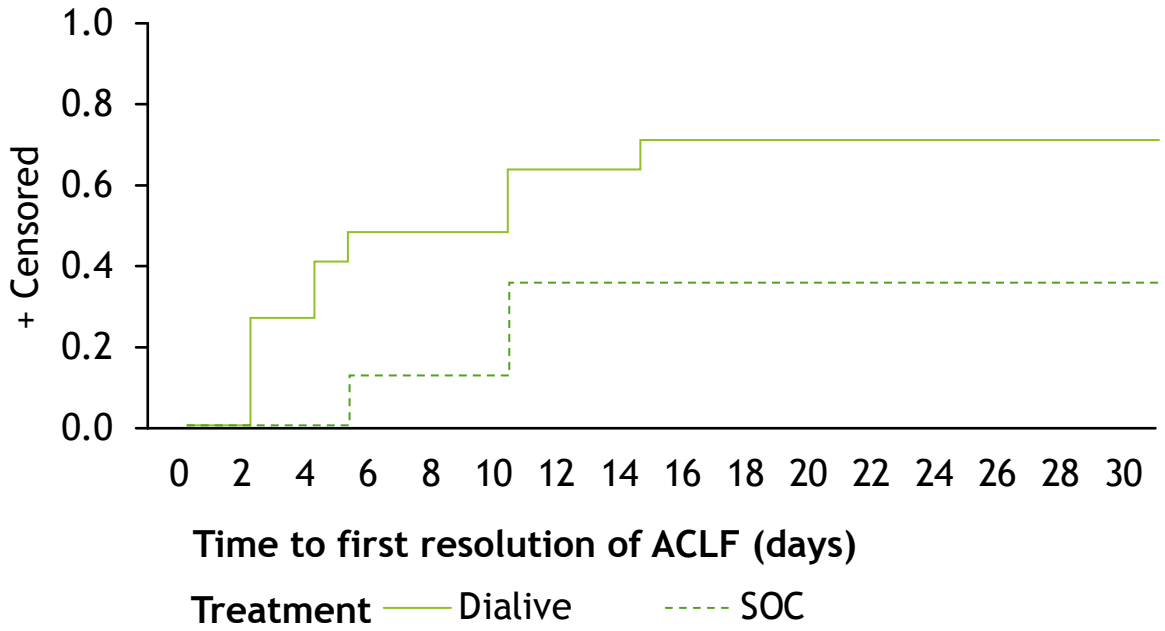


Randomised controlled trial (RCT)

This project has received funding from the European Union's Horizon 2020 research and innovation programme under agreement No. 733057

RCT Demonstrates Significantly Faster 'Time to Resolution of ACLF' Compared with Standard of Care[1]

SURVIVAL CURVES FOR TIME TO RESOLUTION OF ACLF



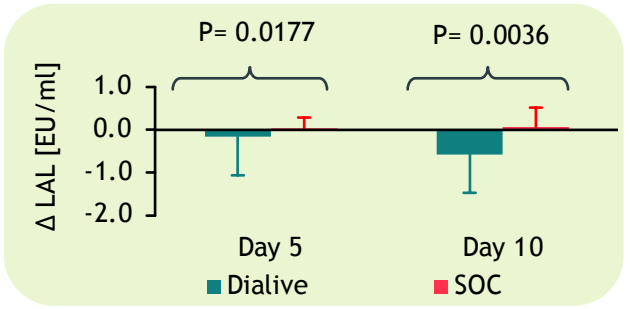
Group	Total	ACLF resolved	Time-to-resolution (p25 ; median time)	P-value (Logrank)
DIALIVE	15	10 (66.7%)	2 days ; 10 days	0.0307
SOC	15	5 (33.3%)	10 days ; not reached	

1. The above-presented conclusions were presented at the Dialive Investigators' meeting held on 22 October 2020 and are based on preliminary analyses that may change. Remains subject to finalizing the remaining statistical report and clinical study report, and completion of data collection for extended post-hoc study.

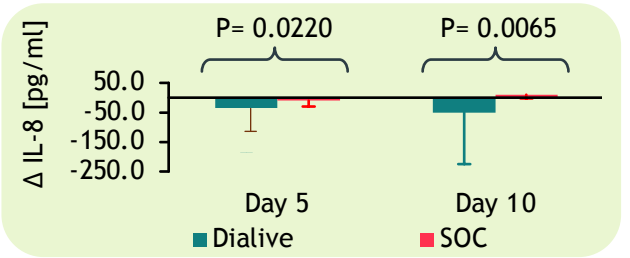
Note: This project has received funding from the European Union's Horizon 2020 research and innovation programme under agreement No. 7733057.

DIALIVE modifies pathophysiological process involved in the pathogenesis of ACLF[1]

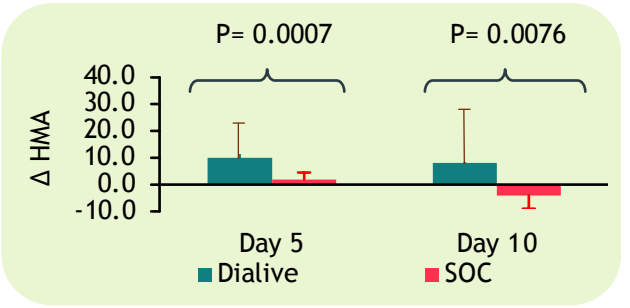
PAMPS

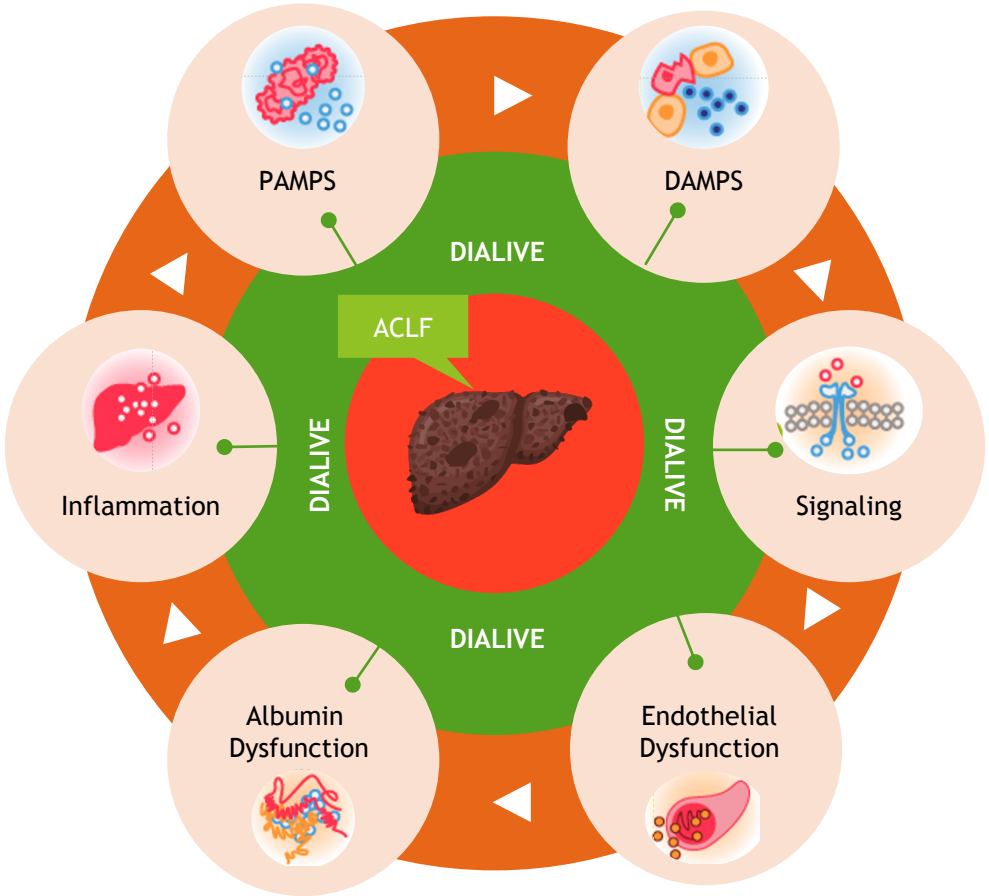


Systemic Inflammation and immune dysfunction



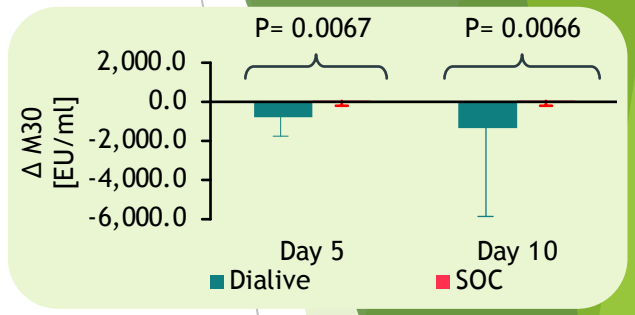
Albumin dysfunction



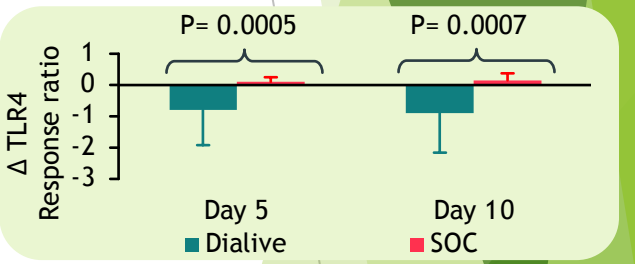


In each case, the figures represent the mean and standard of error mean change in the measure from baseline to day 5 or day 10, as applicable. Population dataset consists of DIALIVE: n=15 at baseline, n =14 at day 5, and n=11 at day 10; SOC: n=15 at baseline, n=15 at day 5, and n=13 at day 10

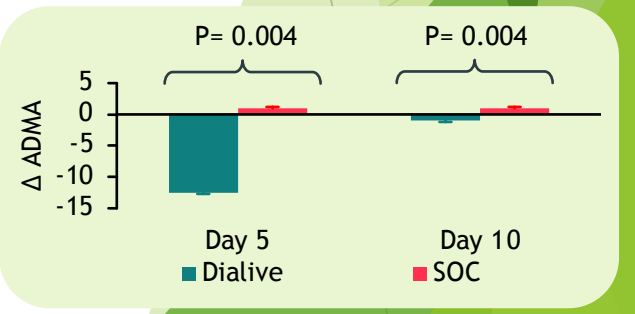
DAMPS



Increased cellular signaling through TLR4 / inflammasome



Endothelial dysfunction



1. The above-presented conclusions were presented at the Dialive Investigators' meeting held on 22 October 2020 and are based on preliminary analyses that may change. Remains subject to finalizing the remaining statistical report and clinical study report and completion of data collection for extended post-hoc study.

Note: This project has received funding from the European Union's Horizon 2020 research and innovation programme under agreement No. 7733057. IL-8 = Interleukin 8. ADMA = asymmetric dimethylarginine. M30 = cellular keratin fragment.

RCT Preliminary Analysis

Objectives	Observations	Implications
Primary objectives: 1. Adverse Events 2. Device Related Events leading to discontinuation	• **Similar to Standard of Care ("SOC")**(1) • One patient with low platelets	• Implement optimization strategy for delivery of DIALIVE treatment • Monitor platelets closely; exclude platelets<30
Secondary objectives: 1. Change in Albumin Function 2. Change in Endotoxins	• Improved **albumin function** • **Reduced HNA2/HMA** • **Significantly reduced LAL** • EAA>20% at Day 3, 5 and 10 with DIALIVE(2)	• Maybe used as a companion or monitor patients on therapy • Potential CE-mark for (1) endotoxin removal (2) treatment of systemic inflammatory response
Exploratory objectives: 1. Organ Function 2. Biomarkers associated with ACLF	• **Significant improvements in Liver/Brain**; and **prevention of deterioration in Respiration** • Significant improvement in biomarkers • Significant difference in **'time to resolution of ACLF'**	• Application for a potential CE-mark for 'Time to resolution of ACLF' • Possible end-points for pivotal study (1) Survival (2) Time to resolution of ACLF (3) ACLF Free Survival at 28-days • Exclude patients with CLIF-C ACLF>64 (futile)

Note: This project has received funding from the European Union's Horizon 2020 research and innovation programme under agreement No. 7733057. The above-presented conclusions were presented at the Dialive Investigators' meeting held on 22 October 2020 and are based on preliminary analyses that may change. Remains subject to finalizing the remaining statistical report and clinical study report, and completion of data collection for extended post-hoc study.

1. ACLF patients have high rates of Serious Adverse Events (SAE) and mortality: the expected 28-day mortality varies from 25%-75% (Moreau et al. Gastro 2013). In this study, the standard of care arm had three deaths, the treatment arm had four deaths, and after reviewing the details of each case, the independent DSMB concluded "the total number of SAE was broadly similar in DIALIVE and standard treatment groups". 2. Analysis confirmed post investigators meeting.

EAA = Endotoxin Activity Assay. INR = International Normalized Ratio. LAL = Limulus Amoebocyte Lysate. HMA = Human Mercaptalbumin. HNA2 = Human Nonmercaptalbumin2.