The PREDICT study uncovers three clinical courses of acutely decompensated cirrhosis that have distinct pathophysiology

Jonel Trebicka, Javier Fernandez, Maria Papp, Paolo Caraceni, Wim Laleman, Carmine Gambino, Ilaria Giovo, Frank Erhard Uschner, Cesar Jimenez, Rajeshwar Mookerjee, Thierry Gustot, Agustin Albillos, Rafael Bañares, Martin Janicko, Christian Steib, Thomas Reiberger, Juan Acevedo, Pietro Gatti, William Bernal, Stefan Zeuzem, Alexander Zipprich, Salvatore Piano, Thomas Berg, Tony Bruns, Flemming Bendsen, Minneke Coenraad, Manuela Merli, Rudolf Stauber, Heinz Zoller, José Presa Ramos, Cristina Solè, Germán Soriano, Andrea de Gottardi, Henning Gronbaek, Faouzi Saliba, Christian Trautwein, Osman Cavit Özdogan, Sven Francque, Stephen Ryder, Pierre Nahon, Manuel Romero-Gomez, Hans Van Vlierberghe, Claire Francoz, Michael Manns, Elisabet Garcia, Manuel Tufoni, Alex Amoros, Marco Pavesi, Cristina Sanchez, Anna Curto, Carla Pitarch, Antonella Putignano, Esau Moreno, Debbie Shawcross, Ferran Aguilar, Joan Claria, Paola Ponzo, Christian Jansen, Zsuzsanna Vitalis, Giacomo Zaccherini, Boglarka Balogh, Victor Vargas, Sara Montagnese, Carlo Alessandria, Mauro Bernardi, Pere Ginès[4], Rajiv Jalan, Richard Moreau, Paolo Angeli, Vicente Arroyo for the PREDICT STUDY group of the EASL-CLIF CONSORTIUM

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Table S1. Exclusion Criteria

Criteria	n (%)
Pregnancy	0 (0.0)
Age <18 y	0 (0.0)
Patients with acute or subacute liver failure without underlying cirrhosis	1 (0.1)
Patients with cirrhosis who develop decompensation in the postoperative period following partial hepatectomy	0 (0.0)
Evidence of current malignancy except for non-melanocytic skin cancer and hepatocellular carcinoma within Milan criteria	58 (4.0)
Presence or history of severe extra-hepatic diseases, e.g., chronic renal failure requiring hemodialysis, severe heart disease (NYHA > II) severe chronic pulmonary disease (GOLD > III), severe neurological and psychiatric disorders)	19 (1.3)
HIV-positive patients	8 (0.5)
Previous liver or other transplantation	2 (0.1)
Admission/referral of more than 72 hours before inclusion	20 (1.3)
Patients who decline to participate or who cannot provide prior written informed consent and without legal surrogate decision maker and it appears unlikely that the patient will regain consciousness or sufficient ability to provide delayed informed consent	22 (1.5)
Physician’s denial (e.g. the investigator considers that the patient will not follow the protocol scheduled).	18 (1.2)

Table S2. Missing Values Prior to, at the time of, and After Enrollment, in Patients With Pre-ACLF, Unstable Decompensated Cirrhosis (UDC) and Stable Decompensated Cirrhosis (SDC)

Characteristic	**Pre-ACLF** **(n = 218)**	**UDC** **(n = 233)**	**SDC** **(n = 620)**
Data prior to enrollment		*n (%)*	
Age	0 (0)	0 (0)	0 (0)
Female sex	0 (0)	0 (0)	0 (0)
Etiology of cirrhosis			
Alcohol	0 (0)	0 (0)	1 (0.1)
Hepatitis C virus	0 (0)	0 (0)	1 (0.1)
Alcohol and hepatitis C virus	0 (0)	0 (0)	1 (0.1)
Nonalcoholic steatohepatitis	0 (0)	0 (0)	1 (0.1)
Other etiologies	0 (0)	0 (0)	1 (0.1)
Events prior to enrollment			
Ascites	23 (10.6)	48 (20.6)	140 (22.6)
Hepatic encephalopathy	37 (17.0)	61 (26.1)	182 (29.4)
Gastrointestinal hemorrhage	31 (14.2)	63 (27.0)	181 (29.2)
Any hospitalization	31 (14.2)	50 (21.5)	159 (25.6)
Data at enrollment			
Clinical data, organ failures and organ dysfunctions			
Ascites	0 (0)	0 (0)	0 (0)
Hepatic Encephalopathy	0 (0)	0 (0)	0 (0)
Gastrointestinal hemorrhage	0 (0)	0 (0)	0 (0)
No organ failure or dysfunction	0 (0)	0 (0)	0 (0)
Liver failure	0 (0)	0 (0)	0 (0)

Liver dysfunction	0 (0)	0 (0)	0 (0)
Circulatory dysfunction	0 (0)	0 (0)	0 (0)
Renal dysfunction	0 (0)	0 (0)	0 (0)
Coagulation failure	0 (0)	0 (0)	0 (0)
Coagulation dysfunction	0 (0)	0 (0)	0 (0)
Brain failure	0 (0)	0 (0)	0 (0)
Brain dysfunction	0 (0)	0 (0)	0 (0)
Respiratory dysfunction	0 (0)	0 (0)	0 (0)
Main reason of hospitalization			
Ascites	1 (0.5)	0 (0)	0 (0)
Hepatic Encephalopathy	1 (0.5)	0 (0)	0 (0)
Gastrointestinal hemorrhage	1 (0.5)	0 (0)	0 (0)
Bacterial infection	1 (0.5)	0 (0)	0 (0)
Others	1 (0.5)	0 (0)	0 (0)
Biomarkers of systemic inflammation			
White-cell count	0 (0)	0 (0)	1 (0.2)
Serum C-reactive protein	18 (20.2)	31 (13.3)	68 (11.0)
Measurements estimating organ function			
Serum bilirubin	0 (0)	0 (0)	1 (0.2)
Serum albumin	10 (4.6)	21 (9.0)	45 (7.3)
INR	0 (0)	1 (0.4)	1 (0.2)
Serum creatinine	0 (0)	0 (0)	0 (0)
Plasma sodium	0 (0)	0 (0)	0 (0)
Severity scores			
Child-Pugh score	13 (6.0)	23 (9.9)	59 (9.5)
Model for End-Stage Liver Disease	0 (0)	1 (0.4)	3 (0.5)

(MELD) score			
MELD-Na score	0 (0)	1 (0.4)	3 (0.5)
Chronic Liver Failure-Consortium acute decompensation score	0 (0)	1 (0.4)	4 (0.6)
Data after enrollment			
Mortality rates			
90-day mortality rate	0 (0)	0 (0)	0 (0)
1-year mortality rate	0 (0)	0 (0)	0 (0)
Main causes of death			
ACLF	0 (0)	0 (0)	0 (0)
Hypovolemic shock	0 (0)	0 (0)	0 (0)
Other causes of death	0 (0)	0 (0)	0 (0)
Unknown	0 (0)	0 (0)	0 (0)
Liver transplantation within 12 months after enrollment	0 (0)	0 (0)	0 (0)
Indicators of severe portal hypertension			
Transjugular intrahepatic portosystemic shunting (TIPS)	0 (0)	0 (0)	1 (0.2)
TIPS for gastrointestinal hemorrhage	0 (0)	0 (0)	1 (0.2)
Any episode of gastrointestinal hemorrhage	0 (0)	0 (0)	0 (0)

Table S3. Association between main baseline risk factors at enrollment and 3-month ACLF development in the derivation set

Variable	No ACLF Development (n = 494)	ACLF Development (n = 145)	*p* value
Age, y, mean ± SD	58.6 ± 11.15	61.7 ± 10.17	0.003
Ascites 3 months prior to enrollment, n (%)	204 (52.6)	81 (63.8)	0.028
Gastrointestinal hemorrhage 3 months prior enrollment, n (%)	51 (14.0)	7 (6.0)	0.021
Bacterial infection 3 months prior enrollment, n (%)	55 (15.6)	33 (26.8)	0.006
Ascites at enrollment, n (%)	332 (67.2)	113 (77.9)	0.014
Gastrointestinal hemorrhage at enrollment, n (%)	77 (15.6)	9 (6.2)	0.004
Bacterial infection at enrollment, n (%)	135 (27.3)	53 (36.6)	0.032
White-cell count, x10^9/L	5.8 (4.2-8.7)	6.8 (4.9-9.3)	0.007
Serum C-reactive protein, mg/L	15.1 (6.4-32.7)	21.6 (11.6-39.3)	<0.001
International Normalized Ratio, median (IQR)	1.4 (1.2-1.7)	1.5 (1.3-1.8)	<0.001
Serum albumin, g/dL, median (IQR)	2.9 (2.6-3.3)	2.7 (2.3-3.2)	<0.001

Total bilirubin, mg/dL, median (IQR)	2.2 (1.3-4.6)	3.6 (1.9-9.5)	<0.001
Serum creatinine, mg/dL, median (IQR)	0.8 (0.7-1.1)	1.1 (0.8-1.5)	<0.001
Plasma sodium, mEq/L, mean ± SD	135.7 ± 4.8	133.7 ± 6.0	<0.001

NOTE: p values were obtained using the Student's t-test, chi-square test, or Wilcoxon signed rank test where appropriate.

Table S4. Factors Independently predicting the development of ACLF in the derivation cohort.

Factor	Subdistribution Hazard Ratio For ACLF (95% Confidence Interval)	*p* Value
Age, yr	1.03 (1.01-1.05)	<0.001
Ascites at enrollment	1.57 (1.09-2.27)	0.016
Blood white-cell count, x10^9/L	1.30 (0.97-1.73)	0.078
Albumin, g/dL	0.63 (0.48-0.84)	0.001
Total bilirubin, mg/dL	1.78 (1.45-2.17)	<0.001
Creatinine, mg/dL	5.61 (3.27-9.62)	<0.001

NOTE: The subdistribution hazard ratios were obtained using the Fine and Gray model.