

SUPPLEMENTARY MATERIAL

**Personalised long-term albumin treatment based on three-month ascites response in patients
with decompensated cirrhosis**

Inclusion and exclusion criteria

Inclusion criteria:

- i) patients with diagnosis of cirrhosis based on clinical, laboratory, radiological and/or histological criteria
- ii) prescription of regular human albumin (HA) infusions for at least 1 month
- iii) age greater than 18 years

Exclusion criteria were:

- i) ongoing acute complications of cirrhosis (Hepatorenal syndrome [HRS], spontaneous bacterial peritonitis [SBP] and/or non-SBP-related bacterial infections, grade III/IV hepatic encephalopathy [HE], gastrointestinal bleeding)
- ii) ongoing acute-on-chronic liver failure (ACLF) defined according to the EASL-CLIF criteria (1)
- iii) hepatic surgery in the previous 14 days
- iv) hepatocellular carcinoma (HCC) beyond Milan criteria or other extrahepatic malignancy
- v) previous Liver transplant (LT) or other solid organ transplantation
- vi) previous TIPS
- vii) severe extrahepatic disease that, according to clinical judgement, may be the predominant factor affecting the patient's prognosis

Reference:

(1) European Association for the Study of the Liver (2023). EASL Clinical Practice Guidelines on acute-on-chronic liver failure. *Journal of hepatology*, 79(2), 461–491. <https://doi.org/10.1016/j.jhep.2023.04.021>

Supplementary Table 1. Comparison of baseline characteristics between patients included in the study population (n=252) and those excluded due to long-term albumin (LTA) duration <3 months (n=30).

	Included	Excluded	
	N=252	N=30	
Demographic data			
Age (years)	63 (55-69)	63 (55-74)	0.526
Male sex (n, %)	175 (69)	25 (83)	0.113
Aetiology of cirrhosis			
			0.758
Alcohol (n, %)	99 (39)	11 (37)	
MASLD (n, %)	37 (15)	6 (20)	
Viral (n, %)	33 (13)	4 (13)	
Alcohol + viral (n, %)	27 (11)	3 (10)	
Alcohol + MASLD (n, %)	29 (12)	5 (17)	
Other (n, %)	27 (11)	1 (3)	
Ascites			
Ascites grade			0.940
Ascites grade 2 (n, %)	153 (61)	18 (60)	
Ascites grade 3 (n, %)	99 (39)	12 (40)	
Refractory ascites (n, %)	72 (29)	10 (33)	
Previous paracentesis within 6 months prior to enrolment (n, %)	129 (51)	17 (57)	0.572
- 1-3 paracenteses in last 6 months	73 (29)	6 (20)	
- ≥ 4 paracenteses in last 6 months	56 (22)	7 (23)	
Medical History			
Presence of oesophageal varices (n, %)	189 (75)	27 (90)	0.071
Previous overt HE (n, %)	69 (27)	11 (37)	0.286
Previous gastrointestinal bleeding (n, %)	44 (18)	6 (20)	0.731
Previous spontaneous bacterial peritonitis (n, %)	29 (12)	1 (3)	0.170
Previous hepato-renal syndrome (n, %)	21 (8)	0 (0)	0.099
HCC within Milan criteria (n, %)	26 (10)	3 (10)	0.957
Active alcohol consumption (n, %)	40 (26)	4 (21)	0.653
Concomitant Medications			
Antialdosteronic drugs (mg/day)	200 (100-300)	200 (100-200)	0.299
Furosemide (mg/day)	50 (25-75)	50 (25-100)	0.803

NSBB (n, %)	128 (51)	13 (43)	0.440
Rifaximin for HE prophylaxis	95 (38)	12 (40)	0.806
Comorbidities			
Chronic Heart Disease (n, %)	43 (17)	5 (17)	0.956
Chronic kidney disease (n, %)	39 (16)	2 (7)	0.193
Chronic lung disease (n, %)	25 (10)	2 (7)	0.567
Diabetes (n, %)	84 (33)	12 (40)	0.466
Laboratory and hemodynamic data at inclusion			
WBC (10 ⁹ /L)	5.3 (3.9-7.2)	5.9 (3.9-7.2)	0.779
Sodium (mmol/L)	136 (133-139)	136 (133-138)	0.793
Bilirubin (mg/dL)	2.0 (1.2-3.9)	2.2 (1.0-4.2)	0.925
Creatinine (mg/dL)	0.9 (0.8-1.2)	1.0 (0.8-1.2)	0.690
Albumin (g/L)	31 (27-35)	32 (29-35)	0.245
INR	1.4 (1.2-1.6)	1.4 (1.2-1.6)	0.956
Prognostic scores			
Child-Pugh score	9 (7-10)	9 (8-11)	0.242
MELD score	14 (11-18)	14 (11-18)	0.730
MELD-Na score	18 (15-21)	17 (14-22)	0.674

Data are reported by median and interquartile range or absolute frequency and percentage (%) as appropriate.

Abbreviation. HCC: hepatocellular carcinoma; HE: hepatic encephalopathy; INR: international normalised ratio; MASLD: metabolic dysfunction-associated steatotic liver disease; MELD: model for end-stage liver disease; MELD-Na: model for end-stage liver disease incorporating serum sodium; NSBB: non-selective beta blockers; WBC: white blood cells.

Supplementary Table 2: *Reasons for discontinuation of long-term albumin treatment (LTA) in patients excluded from the current analyses due to treatment duration of less than 3 months.*

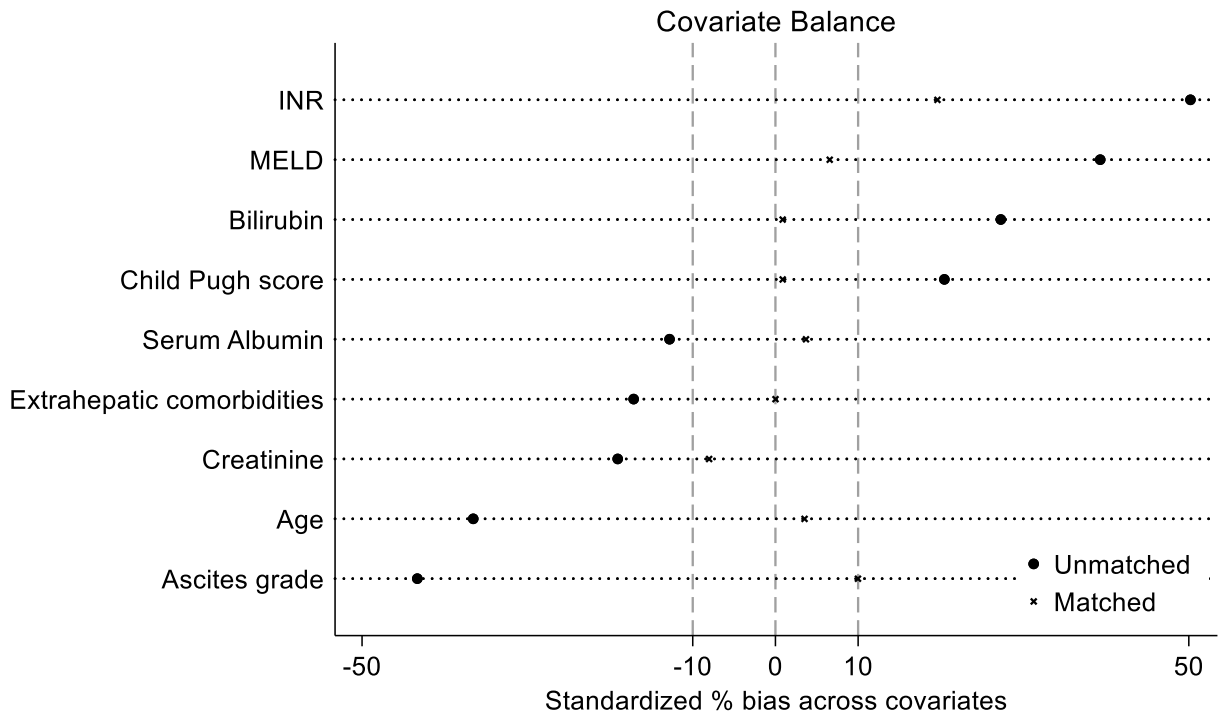
Reasons for LTA discontinuation	n
Stop for clinical improvement (n, %)	9 (30)
Liver Transplant (n, %)	3 (10)
TIPS placement (n, %)	4 (13)
Death (n, %)	8 (27)
Other (n, %)	6 (20)
TOTAL	30

Supplementary Table 3: Comparison of baseline characteristics between Responders and Partial/Non-Responders in the Propensity Score Matched cohort (n=170).

	Partial/non-responders	Responders	p
	N=85	N=85	
Age (years)	60.0 ± 9.5	60.3 ± 10.3	0.814
Any extrahepatic comorbidities (n, %)	39 (46)	39 (46)	1.000
Ascites grade 2 (n, %) / grade 3 (n, %)	66 (78) / 19 (22)	62 (73) / 23 (27)	0.477
Bilirubin (mg/dL)	2.81 (1.34 - 4.36)	2.46 (1.50 - 4.50)	0.903
Albumin (g/L)	30.0 (27.0 - 34.0)	30.9 (27.0 - 35.0)	0.935
INR	1.40 (1.23 - 1.60)	1.49 (1.32 - 1.64)	0.111
Creatinine (mg/dL)	0.92 (0.73 - 1.20)	0.87 (0.71 - 1.12)	0.300
Child-Pugh score	8.9 ± 1.7	8.9 ± 1.7	0.957
MELD score	15.4 ± 4.6	15.7 ± 4.7	0.670

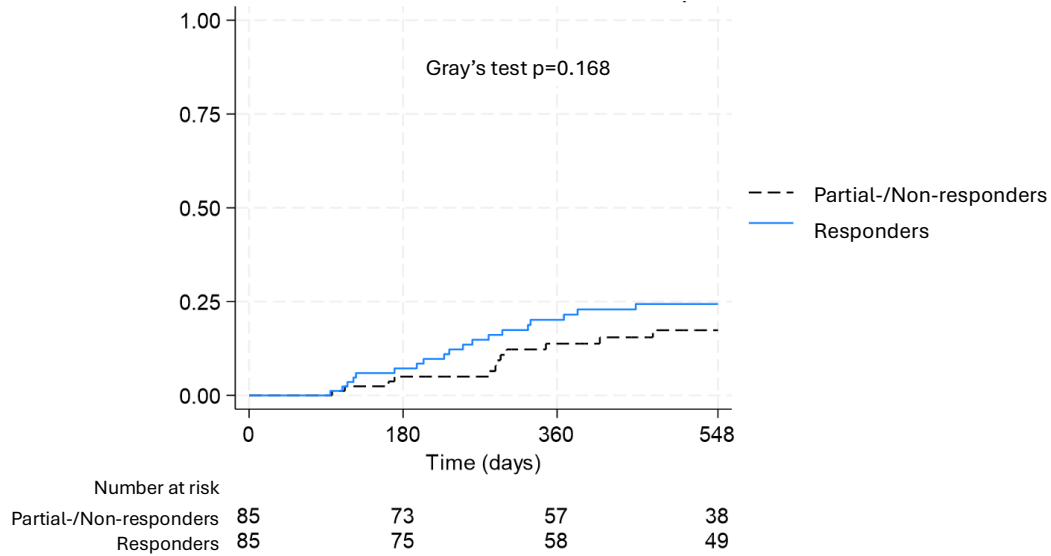
Data are presented as mean ± standard deviation (SD), median (interquartile range [IQR]), or number (%), as appropriate. P-values were calculated using Student's t-test or Mann-Whitney U test for continuous variables and Chi-square test for categorical variables. In the Propensity Score Matching (PSM) analysis responders were matched 1:1 with Partial/Non-Responders based on age, MELD score, ascites grade, and extrahepatic comorbidities using a caliper width of 0.2. *Abbreviations:* MELD, Model for End-Stage Liver Disease; INR, International Normalized Ratio.

Supplementary Figure 1: Assessment of covariate balance before and after Propensity Score Matching. The dot plot displays the standardized percentage bias (Standardized % Bias) for baseline characteristics between Responders and Partial/Non-Responders in the original unmatched cohort (Unmatched, solid dots) and in the propensity score-matched cohort (Matched, crosses). The vertical dashed line at zero represents perfect balance. After matching, all covariates show a significant reduction in bias



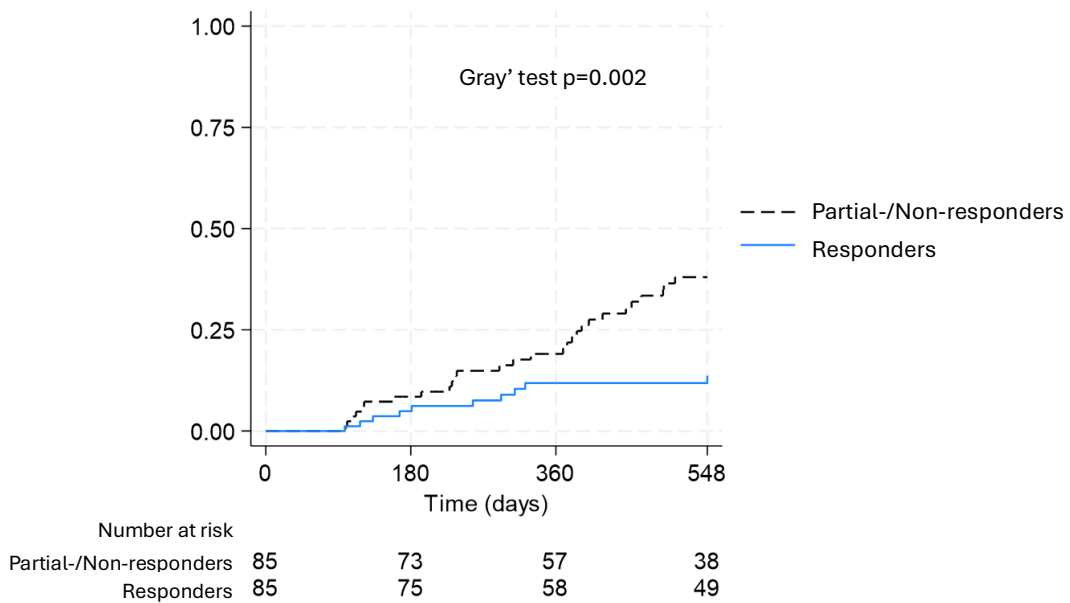
Supplementary Figure 2

Panel A: Cumulative incidence function (CIF) of liver transplantation at 18 months in the Propensity Score Matched cohort (n=170).



Death was considered as a competing event. The p-value was calculated using Gray's test. Blue line: Responders; Dashed black line: Partial/Non-Responders.

Panel B: Cumulative incidence function (CIF) of mortality at 18 months in the Propensity Score Matched cohort (n=170).



Liver transplantation (LT) was considered as a competing event. The p-value was calculated using Gray's test. Blue line: Responders; Dashed black line: Partial/Non-Responders.