AASLD November 13-16, 2020
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THE BEST OF THE LIVER MEETING® 2020

COVID-19 and the Liver

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About the program:

Best of The Liver Meeting 2020 was created by the Scientific Program Committee for the benefit of AASLD members, attendees of the annual conference, and other clinicians involved in the treatment of liver diseases. The program is intended to highlight some of the key oral and poster presentations from the meeting and to provide insights from the authors themselves regarding implications for patient care and ongoing research.

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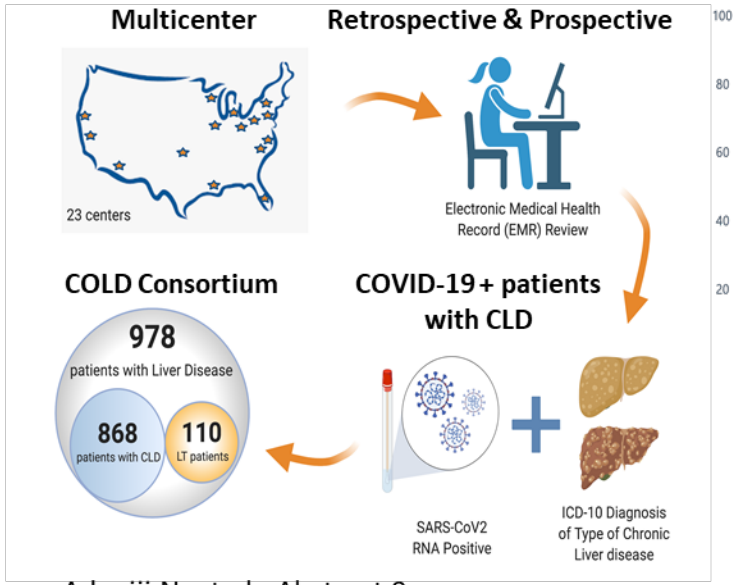
Use of these slides:

Predictors of outcomes of COVID-19 in patients with chronic liver disease (COLD): U.S. multi-center study

Aim

To identify the factors associated with adverse outcomes in patients with chronic liver disease (CLD) who acquire the novel coronavirus-2019 (COVID-19)

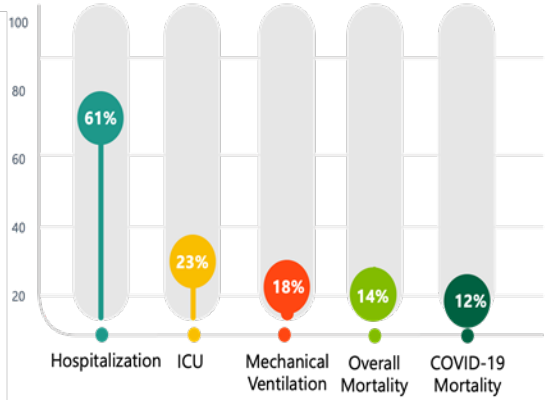
Methods



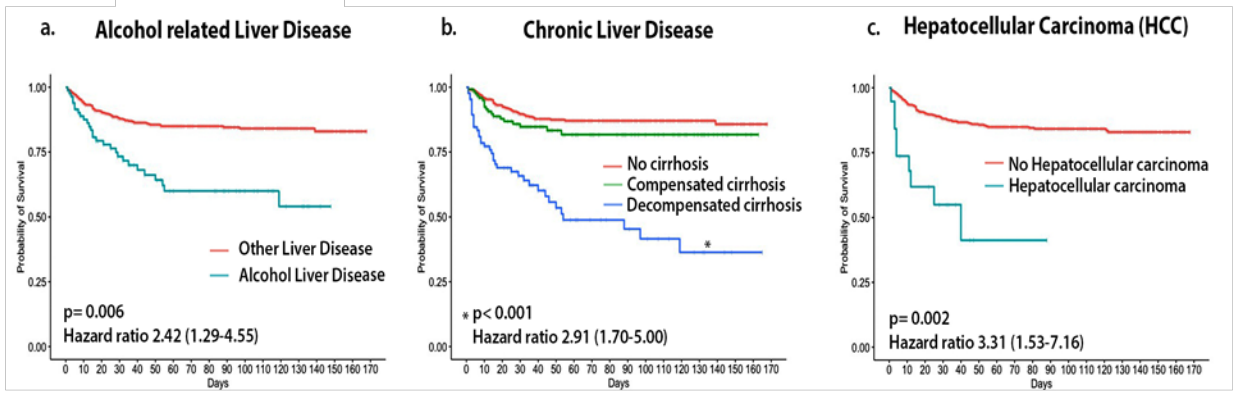
Adeniji N, et al., Abstract 9

Main Findings

- Patients with CLD have high ICU admission (23%), mechanical ventilation (18%), and overall mortality rates (14%).



- Risk factors which predict higher overall mortality amongst patients with CLD and COVID-19 are alcohol liver disease (ALD), decompensated cirrhosis, and hepatocellular carcinoma (HCC).



Implications

Clinicians should employ measures to mitigate the risk of COVID-19 exposure in the most vulnerable CLD patients, discourage excessive alcohol use, prioritize this cohort for vaccination, and include this cohort in prospective studies and drug trials.

SARS-CoV-2 infection in children: an analysis of two different clinical phenotypes caused by the same virus

Objective

To compare clinical features, laboratory data, and degree of acute liver injury in children with each presentation

Methods

Retrospective study of 285 children (≤21 yo) positive for SARS-CoV-2 by PCR or by antibodies in two tertiary care hospitals in New York City

Main Findings

- Patients affected with both MIS-C and COVID-19 were more likely to be overweight.
- MIS-C patients were younger, had more ICU admissions, and higher levels of inflammatory markers.

Conclusions

These data show the severity and frequency of acute liver injury do not significantly differ, despite a seemingly more severe presentation with MIS-C.

Cantor AC, et al., Abstract 11

Variables	ALT < 40	40 < ALT < 150	ALT > 150	*p* value
Multisystem Inflammatory Syndrome in Children (MIS-C)				
Age (y)(mean)	6	10	8.2	<0.05
Obese n (%)	5 (23.8)	8 (26.7)	1 (20.0)	1
ICU admit n (%)	10 (41.7)	20 (64.5)	2 (40)	0.19
Multiorgan Failure n (%)	3 (12.5)	7(22.6)	3 (60)	0.07
Ferritin (mean)	342.7	671	20970.9	<0.01
D-dimer(mean)	5.1	8.2	6.3	0.07
IL-6 (mean)	130.4	497.2	249.2	0.06
COVID-19				
Age (y) (mean)	9.7	12.4	13.2	<0.05
Obese n (%)	15 (20.5)	22 (44)	16 (69.6)	<0.01
ICU admit n (%)	19 (18.4)	18 (30)	10 (43.5)	<0.05
Multiorgan Failure n (%)	3 (2.9)	8 (13.1)	6 (26.1)	<0.01
Death n	4	2	1	N/A
Ferritin (mean)	239.1	1037.4	4672.8	<0.01
CRP (mean)	5.6	14.9	24.3	<0.01
D-dimer (mean)	2.6	6.5	7.3	<0.01
IL-6 (mean)	196.6	193.8	338.3	0.5

APCOLIS score predicts outcome in patients of cirrhosis with SARS-CoV-2 infection: data from ongoing APASL COVID Liver Injury Spectrum (APCOLIS-I) study (NCT04345640)

Aim and Objective

To derive a prognostic model for hospitalized cirrhosis patients with COVID-19

Methods

The retrospective analysis of hospitalized cirrhosis (n=260) with COVID had a 28-day mortality in 54 (20.8%) were analyzed for survival outcome by logistic regression. An equation-based score was obtained with internal validation.

Conclusions

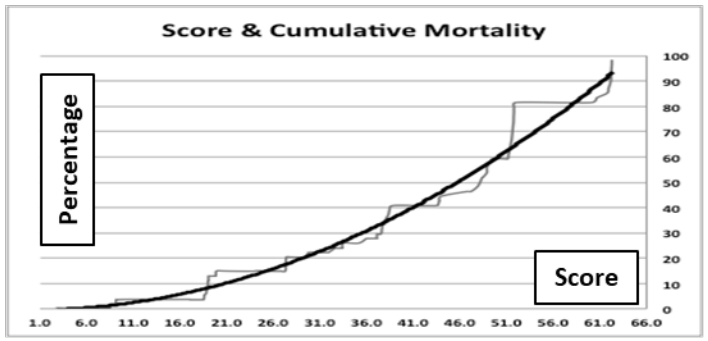
A liver-specific APCOLIS model combining comorbidity, liver-specific ie, hepatic encephalopathy, platelet count and COVID-specific ie, renal failure and respiratory failure had a good prediction of outcome in cirrhosis. Further large series and external validation is needed.

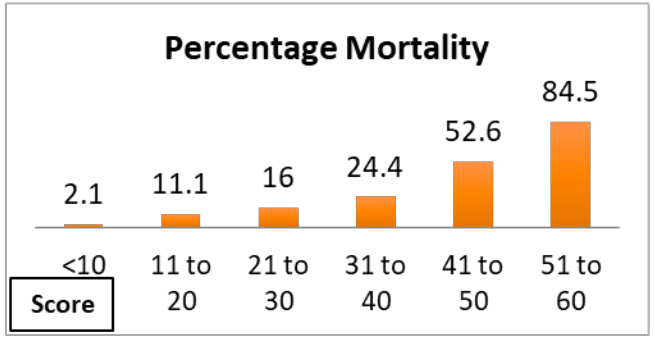
Parameters	Univariate		Multi-variate	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Platelet Count	0.99 (0.98-1.01)	<0.001	0.33 (0.18-0.63)	0.001
CTP Score	1.21 (1.08-1.39)	0.008		
MELD Score	0.96 (0.64-1.02)	0.64		
Presence of Comorbidity	2.80 (1.78-5.30)	0.001	3.61 (1.55-8.44)	0.003
Respiratory Failure	9.76 (4.62-20.61)	<0.001	11.18 (4.46-28.03)	<0.001
Acute Kidney Injury	10.10 (5.01-20.38)	<0.001	6.07 (2.63-14.02)	<0.001
Shock	17.24 (8.2-43.48)	<0.001		
Acute Liver Injury _BL	2.84 (1.54-5.29)	0.001		
Worsening Jaundice	4.98 (2.62-9.43)	<0.001		
Worsening Ascites	3.03 (1.61-5.71)	<0.001		
Acute Variceal Bleed	1.90 (0.84-4.30)	0.01		
Hepatic Encephalopathy	2.49 (1.34-6.24)	0.003	2.91(1.24-6.85)	0.003

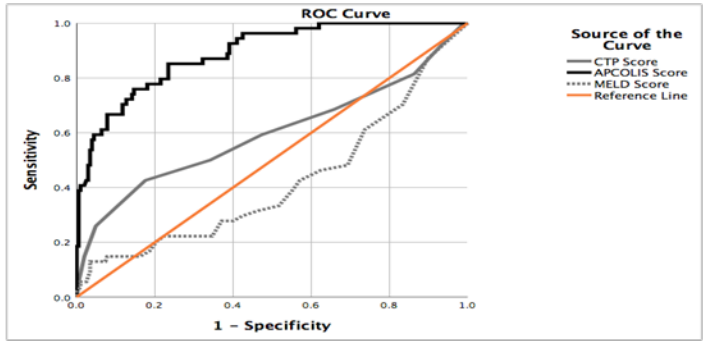
Choudhury A, et al., Abstract 103

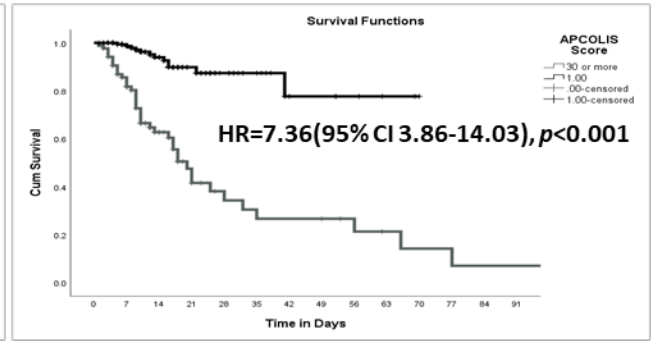
Score = 10{ 1.285*Comorbidity + 1.069*HE + 2.414*Respiratory failure + 1.803*AKI - 0.99*Platelet count} + 0.489

The score ranges from 2 to 63, but was scaled from 10-60









Score	AUROC	Cut off	Sensitivity	Specificity
APCOLIS	0.890	30	77.8	78.6
CTP	0.597	8.5	59.3	52.7
MELD	0.419	<12.5	53.7	62.6

Score>30	D0	D7	D14	D21	D28
At Risk	86	81	71	65	58
Event	0	5	11	13	15

SARS-COV-2 produces serum porphyrin accumulation, dyslipidemia, and severe metabolic dysregulation

Aim

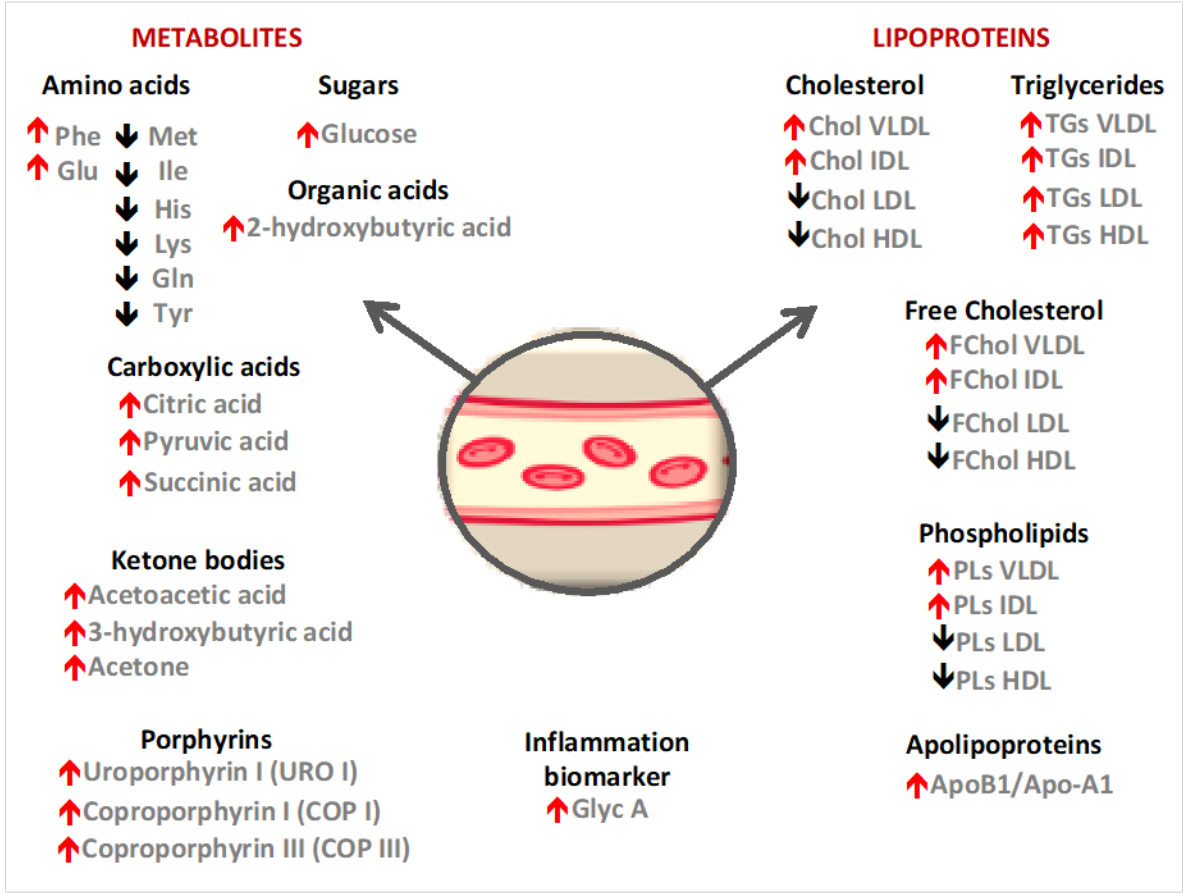
Study the serum metabolomic profile of patients diagnosed with COVID-19

Methods

- Cohorts: 400 acute patients with COVID-19 (PCR+) affected by pneumonia; 60 patients COVID-19 PCR- but with pneumonia; 280 sera from healthy individuals collected during 2018-2019
- 40 metabolites and up to 112 lipoprotein parameters were quantified and identified by NMR-based metabolomics. Porphyrins were separated and quantified by HPLC.

Conclusions

SARS-CoV-2 dysregulates the metabolomic and lipidomic profiles of serum, with impaired mitochondrial function, liver damage, and porphyrin accumulation.



Embade N, et al., Abstract 105

Liver injury in COVID-19 is associated with endothelial-mediated hypercoagulability driven by IL-6 trans-signaling

Hypothesis

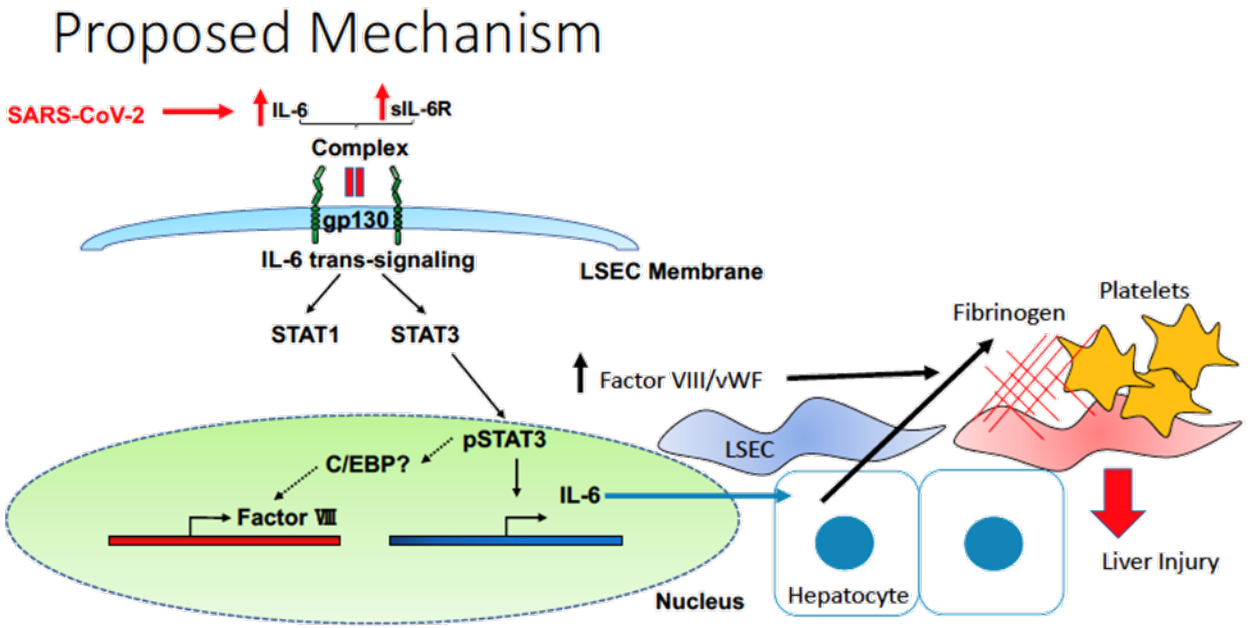
Inflammation secondary to SARS-CoV2 infection produces a procoagulant endotheliopathy in the liver microcirculation, leading to liver injury.

Methods

A cross-sectional study of the coagulation profile and ALT levels of patients with PCR-confirmed COVID-19 disease was performed, along with histological analysis of post-mortem liver samples from COVID-19 patients, and *in vitro* study of IL-6 trans-signaling in primary human liver sinusoidal endothelial cells (LSEC)

Main Findings

COVID patients with elevated ALT exhibited coagulopathy, liver histology in COVID showed high levels of von Willebrand Factor and platelet accumulation, and IL-6 trans-signaling produced a hypercoagulable LSEC phenotype.



Conclusions

Liver injury in COVID-19 is associated with a procoagulant endotheliopathy, which may be driven by IL-6 trans-signaling.

McConnell MJ, et al., Abstract 106

Abnormal liver function tests on admission are associated with increased mortality risk in hospitalized patients with COVID-19

Objective

We aimed to evaluate the prognostic value of abnormal liver tests on admission of hospitalized patients with COVID-19.

Methods

Prospective cohort study including 1611 hospitalized patients with confirmed SARS-CoV-2 from 11 Latin American countries

Main Findings

Abnormal liver tests on admission were present on 45.2% (CI 42.7-47.7) of the cohort (n=726).

Conclusions

The presence of abnormal liver tests on admission is independently associated to mortality in hospitalized patients with COVID-19 infection and may be used as surrogate marker of inflammation.

Table. Logistic Regression Analysis for the Primary Outcome (Death) Based on Data at Admission, Excluding Patients with Chronic Liver Disease or Cirrhosis (n=137)

Baseline Exposure Variables	Mortality Rate (95% CI)	Adjusted Odds Ratio (95% CI)	*P*
Age, years			
<50	6.1 (4.5-8.1)	-	-
50-65	12.7 (9.7-16.4)	1.6 (1.02-2.5)	0.04
>65	31.6 (26.7-36.6)	5.4 (3.6-8.0)	<.0001
Gender			
Male	16.2 (13.8-18.9)	1.6 (1.1-2.2)	0.007
Female	11.7 (9.3-14.5)	-	
Diabetes Mellitus			
Yes	27.7 (22.1-33.9)	1.8 (1.3-2.6)	0.001
No	11.7 (10.0-13.6)	-	
Pneumonia			
Yes	20.5 (17.7-23.5)	2.2 (1.6-3.2)	<.0001
No	7.3 (5.5-9.5)	-	
Abnormal Liver Tests			
Yes	17.9 (15.0-21.1)	1.5 (1.1-2.0)	0.01
No	11.6 (9.5-14.0)	-	

Note: Calibration (*P*=0.19, Hosmer-Lemeshow test). ROC curve 0.76 (CI 0.73-0.78)

Mendizabal M, et al., Abstract 107. Clinicaltrials.gov: NCT04358380

Acute-on-chronic liver failure related to COVID-19 infection is associated with increased in-hospital mortality

Objective

In a multicenter cohort of COVID-19-infected patients with CLD, we analyzed the incidence and predictors of acute-on-chronic liver failure [ACLF] and its impact on in-hospital mortality.

Methods

We included adults with CLD from among 10,859 patients with confirmed COVID-19 infection. We defined ACLF using the EASL-CLIF Consortium definition. Patient follow-up was through April 30, 2020, or until the date of discharge, transfer, or death.

Main Findings

In-hospital mortality was not different between CLD patients with or without cirrhosis [p=0.24] but was higher in those with cirrhosis and who developed ACLF [adjusted HR 9.06, 95% CI: 2.63-31.12, p<0.001, see Figure A and Table 1]. There was a trend for increased mortality by grade of ACLF [p=0.002, see Figure B].

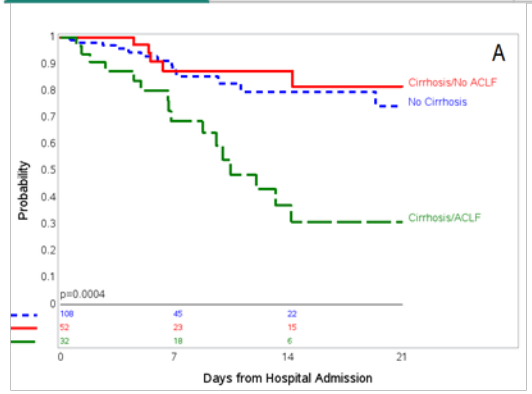
Conclusions

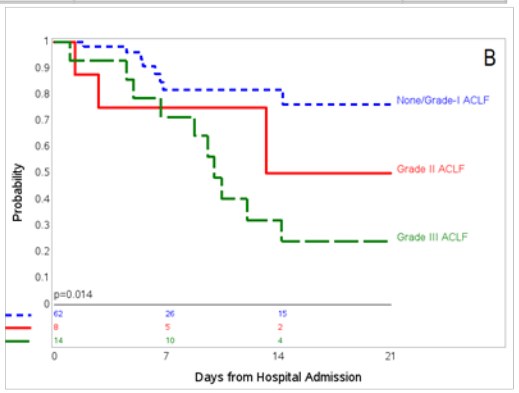
Hospitalized patients with COVID-19 infection and cirrhosis are at risk of developing ACLF, leading to poor survival.

Satapathy SK, et al., Abstract 108

Table 1. Association Between ACLF and In-hospital Mortality Among Cirrhosis Patients Hospitalized with Confirmed COVID-19 Infection

	In-hospital Mortality			
	Unadjusted Analysis		Adjusted Analysis*	
	HR [95% CI]	*P*	HR [95% CI]	*P*
No ACLF	reference		Reference	
Any ACLF	5.05 [1.83-13.86]	0.002	9.06 [2.63-31.12]	<0.001
No ACLF	**reference**		**reference**	
ACLF Grade I	5.64 [1.27-24.83]	0.02	3.09 [0.54-17.34]	0.20
ACLF Grade II	3.29 [0.78-13.81]	0.10	9.99 [1.49-66.95]	0.02
ACLF Grade III	5.84 [1.98-17.16]	<0.001	18.31 [4.50-74.46]	<0.001





Impact of baseline ALT levels on the safety and efficacy of remdesivir in moderate COVID-19 patients

Objective

To assess safety and clinical outcomes after remdesivir (RDV) treatment vs standard of care (SOC) in patients with normal vs elevated baseline (BL) Alanine Aminotransferase (ALT) levels who had moderate COVID-19 disease

Methods

Prospective randomized open-label trial comparing the efficacy of RDV vs SOC in patients of moderate COVID-19 patients with normal or elevated BL ALT levels

Main Findings

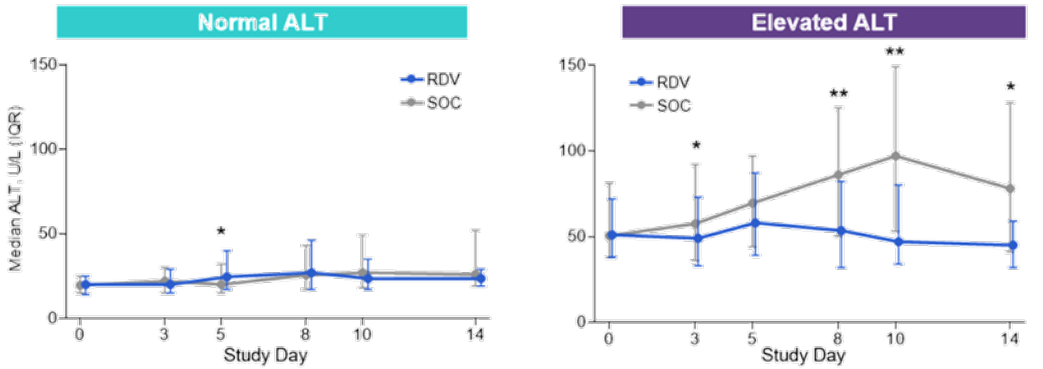
- ALT levels over time were similar with RDV vs SOC in patients with normal BL ALT, but were significantly lower with RDV vs SOC in patients with elevated BL ALT (see Figure 1).
- Clinical improvement and recovery associated with RDV were similar between patients with normal and elevated BL ALT, and there was suggestion of earlier RDV benefit in patients with elevated BL ALT (see Figure 2).

Conclusions

RDV is safe and efficacious vs SOC in moderate COVID-19 patients with normal or elevated BL ALT levels.

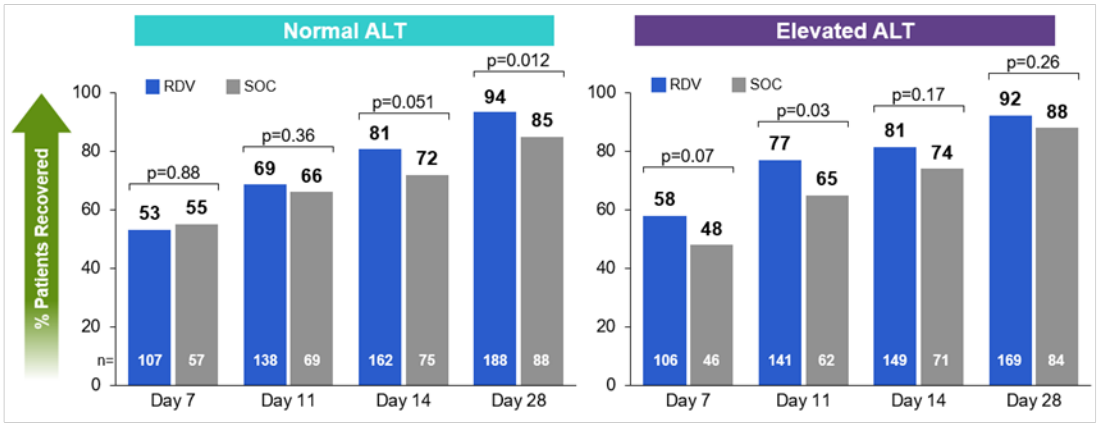
Tsang OTY, et al., Abstract 120

Figure 1. ALT Over Time, RDV vs SOC, by BL ALT



(*p<0.05; **p<0.01)

Figure 2. Recovery by BL ALT



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