AASLD November 13-16, 2020
The Liver Meeting®
Digital Experience

THE BEST OF THE LIVER MEETING® 2020

Portal Hypertension/Cirrhosis

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

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.

Scientific Program Committee	
Chair	*Jorge A. Bezerra, MD, FAASLD*
Co-Chair	*Meena B. Bansal, MD, FAASLD*
President-Elect	*Raymond T. Chung, MD, FAASLD*
Senior Councilor	*Laurie D. DeLeve, MD, PhD, FAASLD*
Annual Meeting Education Committee	*Grace L. Su, MD, FAASLD*
Basic Research Committee	*Harmeet Malhi, MD, MBBS, FAASLD*
Clinical Research Committee	*Kymberly Watt, MD*
CME Committee	*Joseph K. Lim, MD, FAASLD*
Hepatology Associates Committee	*Elizabeth K. Goacher, PA-C, MHS, AF-AASLD*
Surgery and Liver Transplantation Committee	*Bijan Eghtesad, MD, FAASLD*
Training and Workforce Committee	*Janice Jou, MD, MHS, FAASLD*

Use of these slides:

Loss of sphingosine 1-phosphate predicts severe intrapulmonary shunting and hepatopulmonary syndrome in patients with cirrhosis

Objective

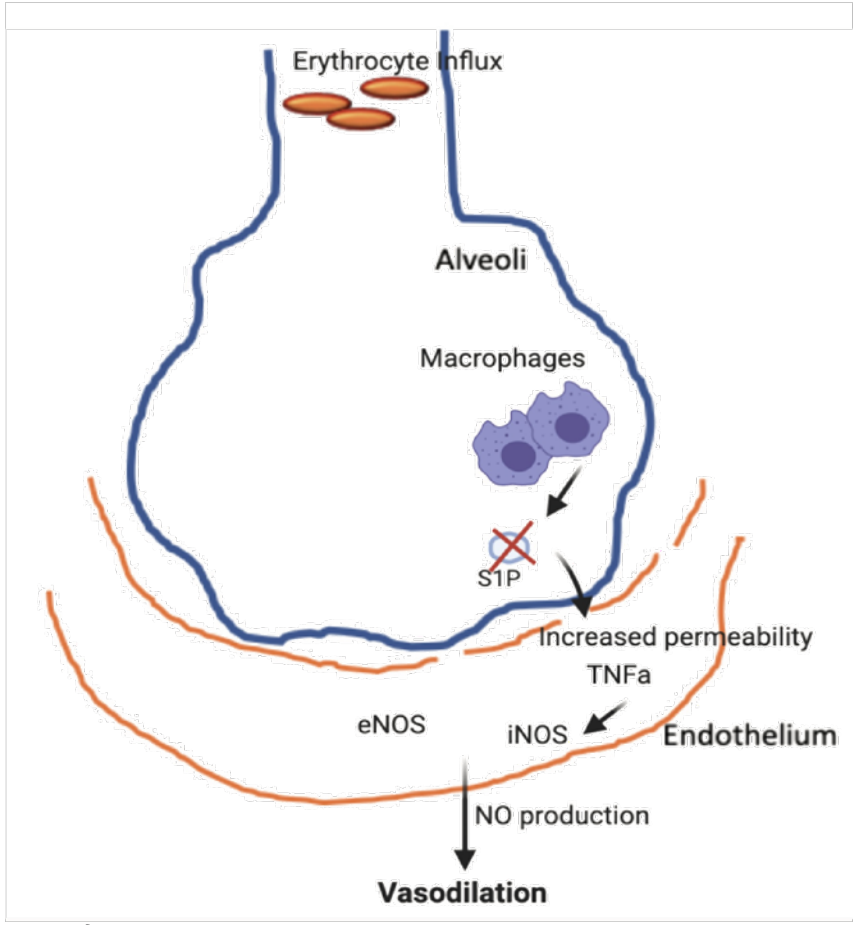
Investigate the role of sphingosine 1-phosphate in severity of hepatopulmonary syndrome in cirrhosis patients and its association with systemic inflammation

Methods

- Group 1: cirrhosis with hepatopulmonary syndrome (n=33)
- Group 2: cirrhosis without hepatopulmonary syndrome (n=32)
- Group 3: healthy controls (n=11)

Main Findings

- Depletion of S1P levels in cirrhosis with HPS is predictive of the severity of intrapulmonary shunting and can be used as a rapid test for diagnosing HPS.
- Low S1P with dysregulated S1PR3 may induce high TNF-α levels that hyperactivate iNOS and eNOS with increased NO production, responsible for intrapulmonary shunting.
- Low enrichment of S1P carrying MV could be suggestive of defective cargos for maintaining vascular tone.



Conclusion

Supplementing S1P and its agonists can be a potential therapy for reducing the intrapulmonary shunting in HPS.

Baweja S, et al., Abstract 15

Comparison of intravenous terlipressin infusion and bolus in treatment of ACLF-AKI: an open-label RCT

Hypothesis

Acute increase in portal pressure in ACLF is counteracted better by continuous terlipressin infusion than bolus doses.

Aim/Objective

- Response of AKI (regression/stable/progression)
- 28- and 90-day mortality, cumulative dose of terlipressin, and hospital stay duration

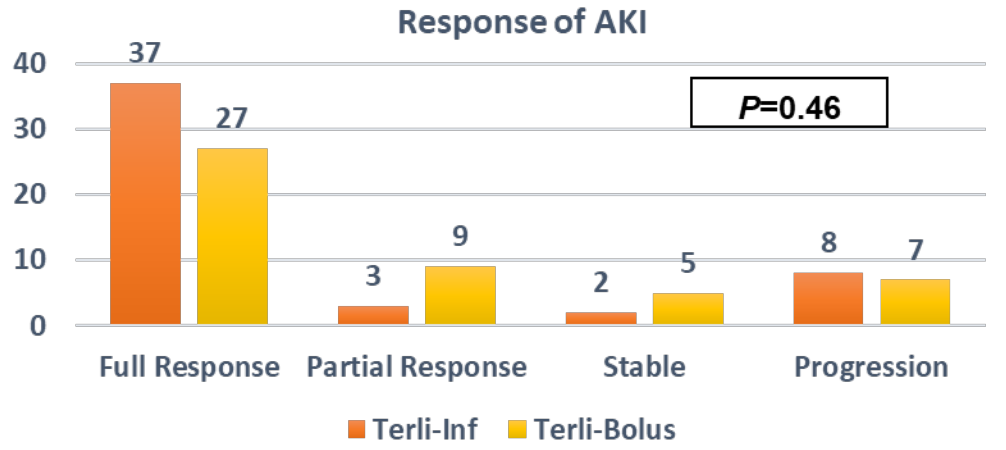
Methods

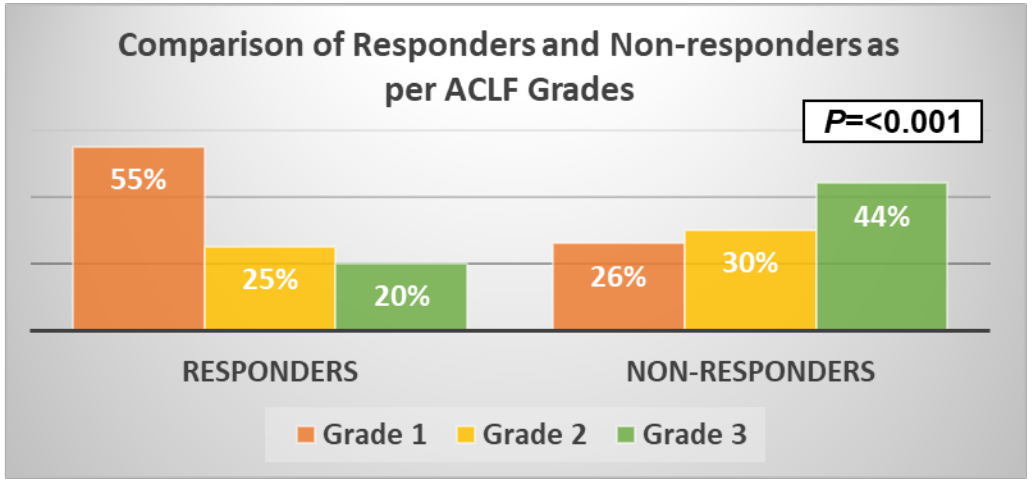
- A prospective, open-label, randomized controlled study
- Patient population-ACLF-AKI (as per CANONIC study and ICA-AKI 2015 criteria) with 50 patients each in Terli-Infusion and Bolus groups

Conclusions

- Terli-Inf had better regression of AKI with lesser cumulative dose of terlipressin and no SAE.
- ACLF grading rather than AKI stage alone is more important for response to therapy and 28- and 90-day survival.

Gupta T, et al., Abstract 76





VOCAL-Penn improves post-operative mortality prediction compared to Mayo Risk Score or MELD

Aim

To validate performance of the VOCAL-Penn cirrhosis surgical risk score

Methods

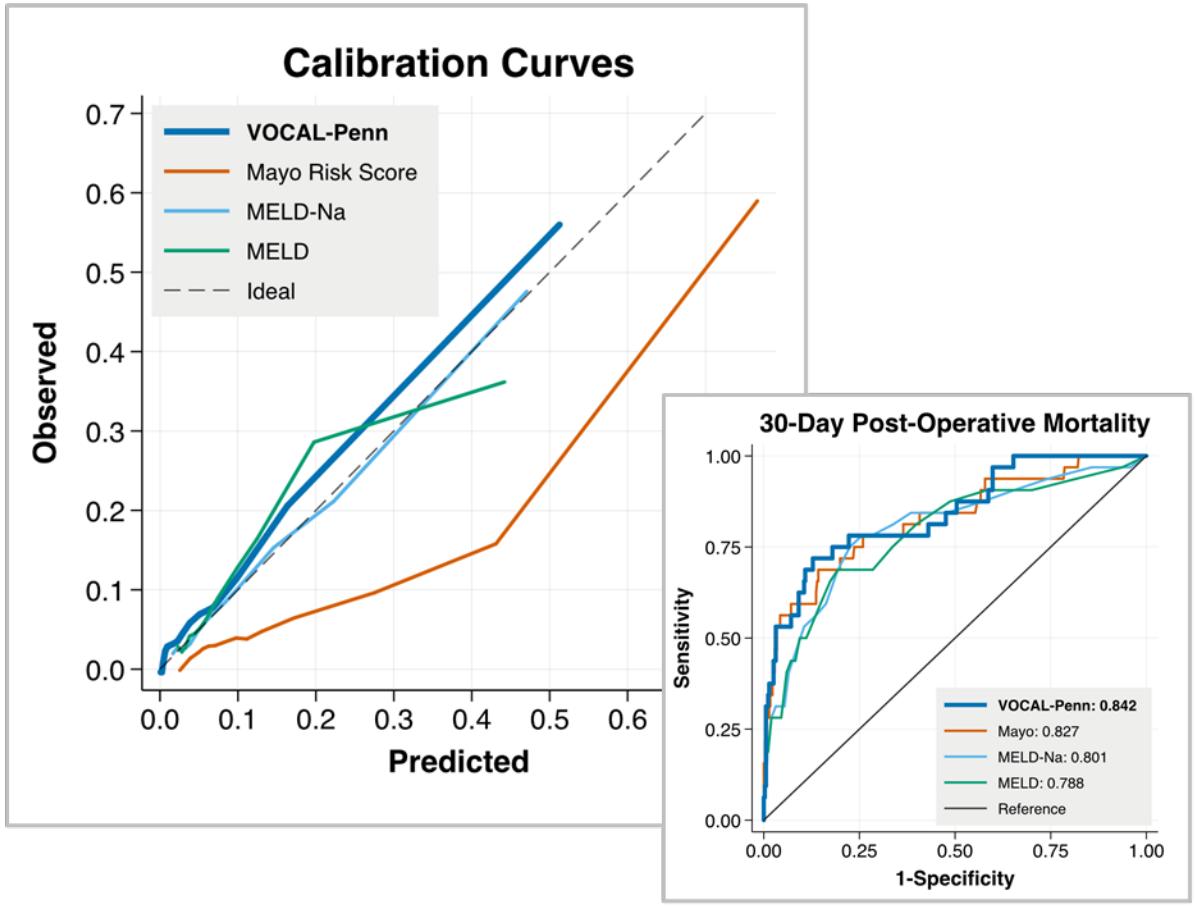
We analyzed model performance in a retrospective cohort of patients with cirrhosis who underwent surgeries at BIDMC.

Main Findings

Among 383 operations, we found improved ROC and calibration of VOCAL-Penn compared to existing models (see Figures).

Conclusions

The VOCAL-Penn score outperforms existing models for post-operative mortality. A calculator is available online: vocalpennscore.com.



Fricker ZP, et al., Abstract 91

Targeted albumin infusions in hospitalized decompensated cirrhosis patients have no effect on markers of systemic inflammation nor ex vivo immune function

Aim

To evaluate if repeated 20% human albumin solutions (HAS) infusions to increase serum albumin level ≥30g/L in the ATTIRE trial (Albumin To prevenT Infection in chronic liveR failure) improved plasma markers of inflammation or immune function

Methods

We blindly analyzed plasma samples from 143 patients at day 1 and 5 of trial (n=71 targeted HAS, n=72 standard care) for cytokines (Luminex multiplex assay), oxidation status of albumin (High Performance Liquid Chromatography), renin, and albumin-radioligand binding. Finally, we examined the effect of plasma on our LPS-stimulated macrophage assay.

Main Findings

- No differences between treatment groups in plasma markers of systemic inflammation, nor immune function in day 1 or 5 samples
- No change in albumin oxidation between day 1 or 5 in both study arms
- An improvement in albumin-binding function at day 5 in both study arms
- No change in mean arterial pressure nor creatinine, although there was a reduction in renin at day 5 in targeted HAS patients.

Conclusions

We found no differences in markers of systemic inflammation nor immune function between targeted HAS and standard care in samples from >140 patients. This was consistent with the null effect seen in the ATTIRE trial.

China L, et al., Abstract 93

	20% HAS treated patients		Standard of care patients	
	Day 1	Day 5	Day 1	Day 5
LPS-induced macrophage cytokine production in the presences of patient plasma (ng/ml) *mean (SD)*				
TNFα	11.07 (3.33)	10.93 (3.01)	10.87 (3.45)	10.93 (3.50)
IL-10	2.20 (1.99)	2.18 (1.87)	2.79 (2.87)	2.76 (2.57)
Plasma cytokines (pg/ml) *median (IQR)*				
TNFα	3.6 (3.9)	3.6 (4.4)	4.2 (3.1)	4.0 (2.7)
IL-6	10.4 (13.8)	9.7 (9.6)	14.5 (23.3)	8.6 (15.2)
IL-8	68.3 (332.1)	45.2 (156.4)	76.9 (200.7)	63.9 (148.9)
IL-10	0 (0.4)	0 (0.6)	0 (0.9)	0 (1.3)
IL-4	0 (0.0)	0 (0.0)	0 (4.2)	0 (4.2)
IL-1β	0 (1.3)	0 (1.3)	0 (1.3)	0 (1.3)
LBP (ng/ml)	1780 (3750)	1495 (1440)	2080 (4700)	1540 (3347)
WCC (x10^9/L)	8.0 (5.2)	8.3 (5.6)	7.6 (5.2)	7.8 (5.0)
CRP (mg/ml)	29.0 (40)	19.0 (29.8)	25.0 (36.3)	24.5 (28.3)

FUNDED BY NIHR | National Institute for Health Research
wellcome

Non-selective beta-blockers reduce the risk of sepsis in cirrhosis

Aim

Examining the role of non-selective beta-blockers (NSBB) for the risk of sepsis in 1198 patients with cirrhosis and ascites

Methods

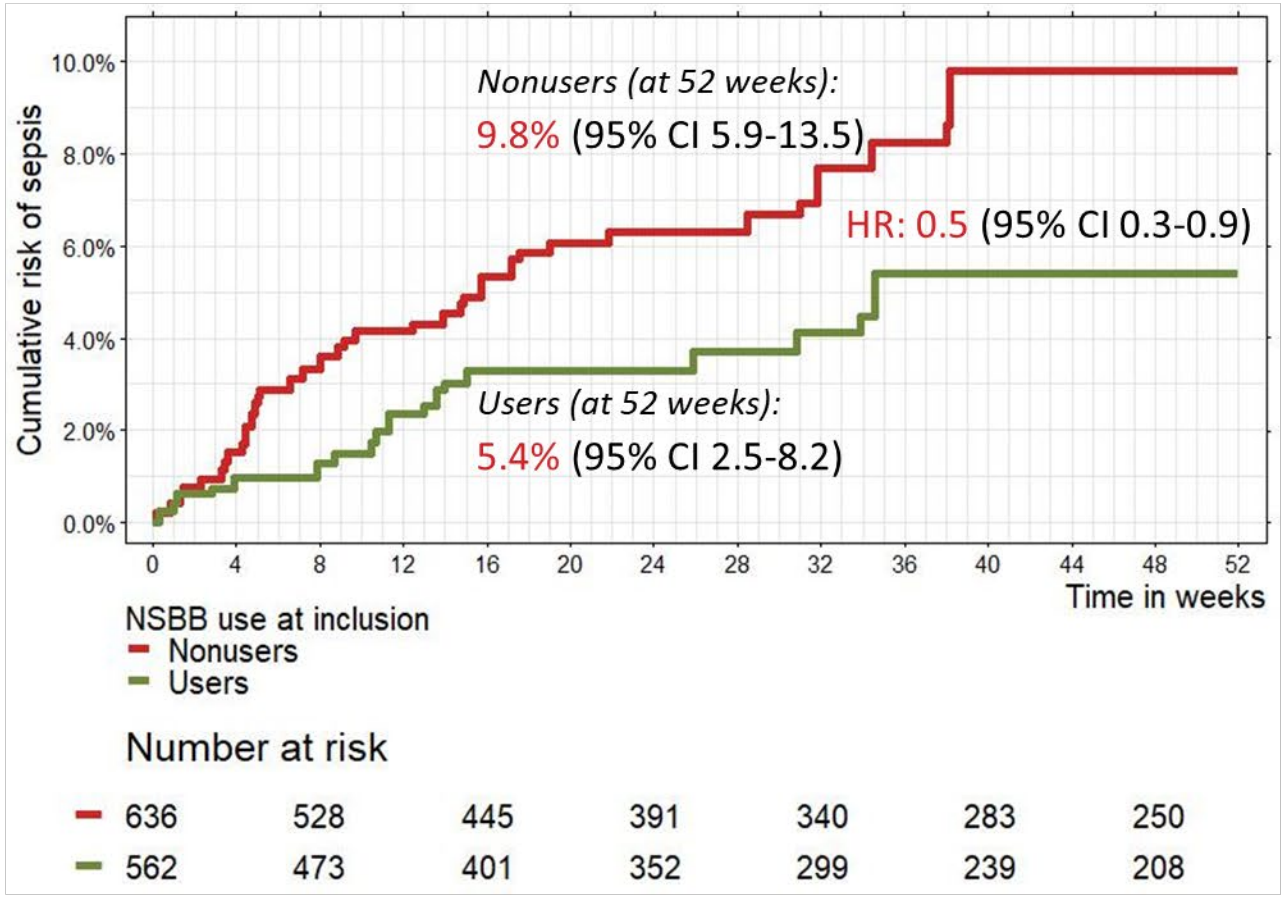
Cumulative risk of sepsis and hazard ratios

Main Findings

- Lower risk of sepsis in NSBB users vs nonusers at 1 year
- No differences in 1-year risks of sepsis between dose subgroups with all subgroups associated to lower risks (vs nonusers)

Conclusion

NSBB use was associated with a clinically significant reduction in the risk of sepsis in patients with cirrhosis and ascites.



Jensen MD, et al., Abstract 94

Long-term effect of growth hormone therapy in decompensated cirrhosis

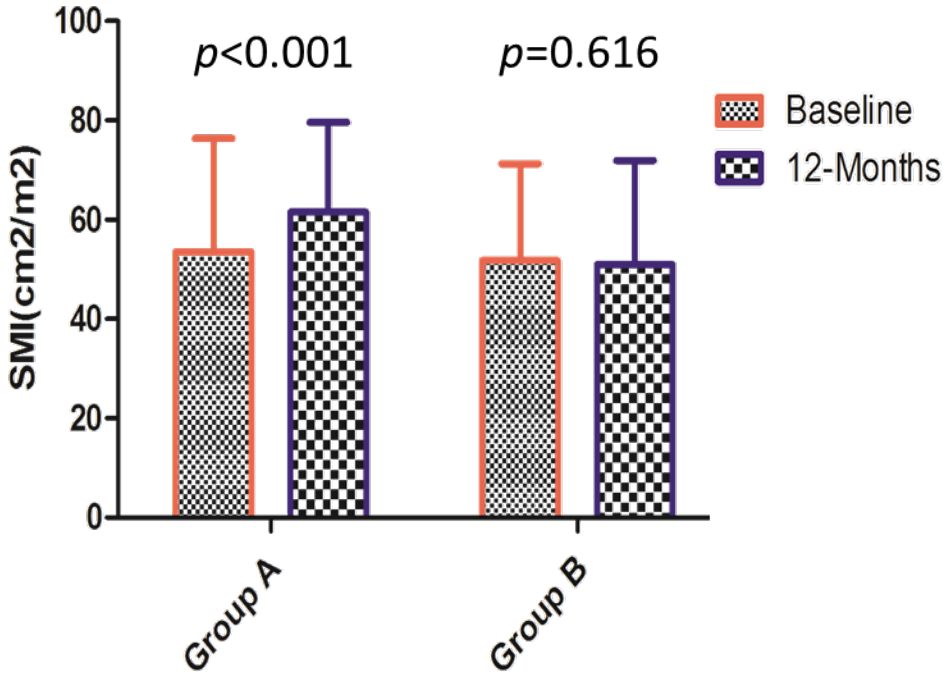
Hypothesis/Aim/Objective

To study the safety and efficacy of growth hormone (GH) therapy and its effect on malnutrition, nitrogen metabolism, and hormonal changes in patients with decompensated cirrhosis (DC)

Methods

- Seventy-one patients with DC were openly randomized to either standard medical therapy (SMT) plus GH (1 IU/day subcutaneously and increased to 2 IU/day by titrating the dose according to IGF-1 levels) (Group A; n=33) or SMT alone (Group B; n=38).
- Nutritional parameters [skeletal muscle index (SMI), body mass index (BMI), mid-arm muscle circumference (MAMC), hand grip strength (HGS), albumin, Liver Frailty Index (LFI)], hormonal changes, and nitrogen balance were studied at baseline, 3, 6, 9, and 12 months.

Figure 1: SMI at Baseline and at 12 Months in Group A and B



Conclusions

- GH therapy is safe and effective in patients with DC.
- Long-term use of GH improves malnutrition (SMI, BMI, MAMC and HGS, albumin, LFI) and nitrogen balance.

Kumari S, et al., Abstract 123

Survival in adults with ALF and non-APAP ALI using the ^{13}C-methacetin breath test (C-MBT)

Study Aim/Objective

To determine the utility of initial and serial ^{13}C-MBT in predicting 21-day Txp-free survival (TFS) in ALF (n=47) and non-APAP ALI (n=15) adults

Methods

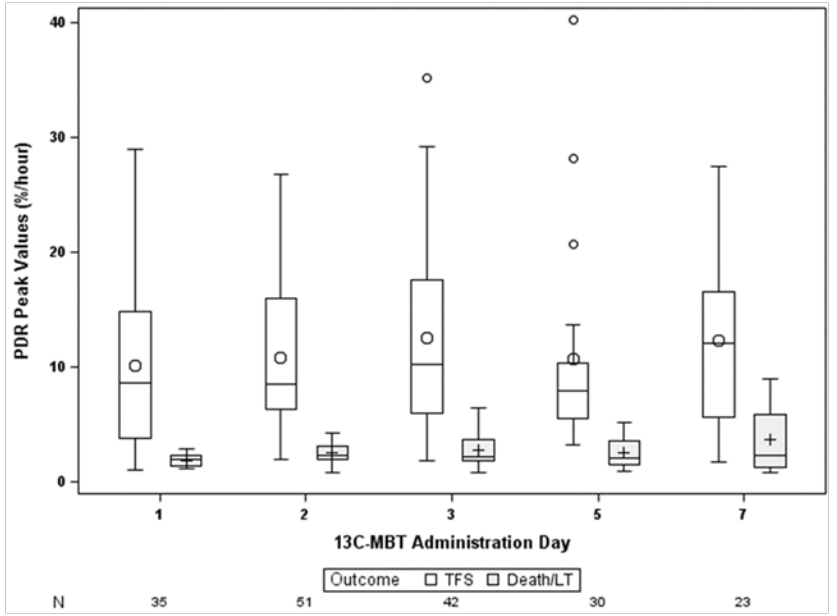
- The ^{13}C-MBT was administered on days 1, 2, 3, 5, and 7.
- The percent dose recovered (PDR) was compared to ALFSG Prognostic Index, MELD, and King's criteria.

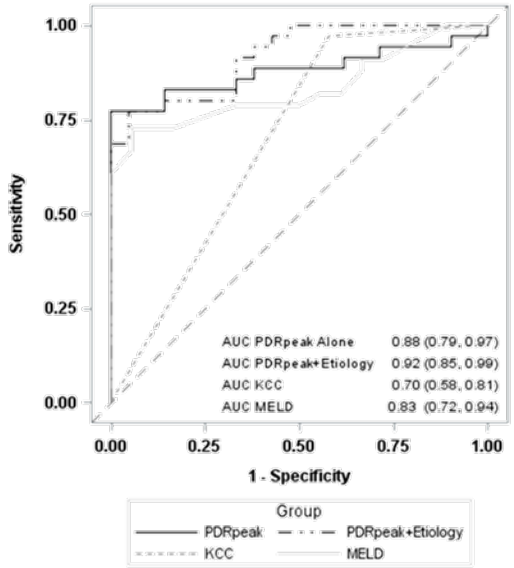
Main Findings

The day ½ PDR_{peak} was significantly higher in those likely to survive vs undergo Txp/death at day 21 (p<0.001).

Conclusions

The ^{13}C-MBT is a promising, non-invasive quantitative hepatic metabolic function test that can identify non-survivors vs survivors with ALF or severe non-APAP ALI.





Day 1 PDR_{peak}
10.2 vs 1.9, p<0.001

21-day Txp-free Survival
Mean age = 43 years
61% Female
42% APAP

Fontana RJ, et al., Abstract 127

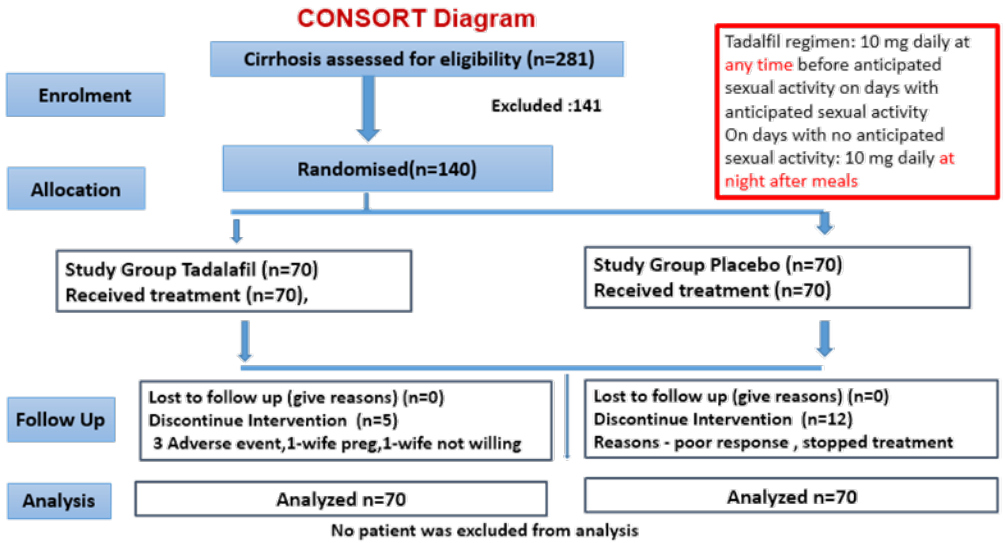
A randomized placebo-controlled trial of tadalafil for erectile dysfunction in patients with cirrhosis

Aim

Efficacy and safety of tadalafil 10 mg vs placebo in erectile dysfunction in patients with Child A and B cirrhosis

Methods

- Double-blind, placebo-controlled, prospective trial of tadalafil for erectile dysfunction in patients with cirrhosis
- Cirrhotic patients with CTP A/B, with ED assessed with International Index of Erectile Function (IIEF) questionnaire and other health-related questionnaires used. Primary outcome was proportion of patients having an increase in more than 5 points in EF score.



Main Findings

Increase in more than 5 points in EF score was seen in 62.82% in tadalafil arm (n=44/70) vs 30% cases in placebo arm (n=21/70) (p<0.001). As compared to placebo, patients taking tadalafil had significant improvements in orgasmic function domain, intercourse satisfaction domain, overall satisfaction domain, anxiety (GAD 7) score, depression (PHQ 9) score, functional impairment (KPS) score, and hepatic venous pressure gradient (HVPG). There were no significant differences in side effect profiles.

Conclusions

Tadalafil significantly improves ED, quality of life, and HVPG in CTP-A and B patients with liver cirrhosis, without any major side effects.

Jagdish RK, et al., Abstract 154

Black patients with cirrhosis have worse outcomes: results from a metropolitan cohort study

Objective

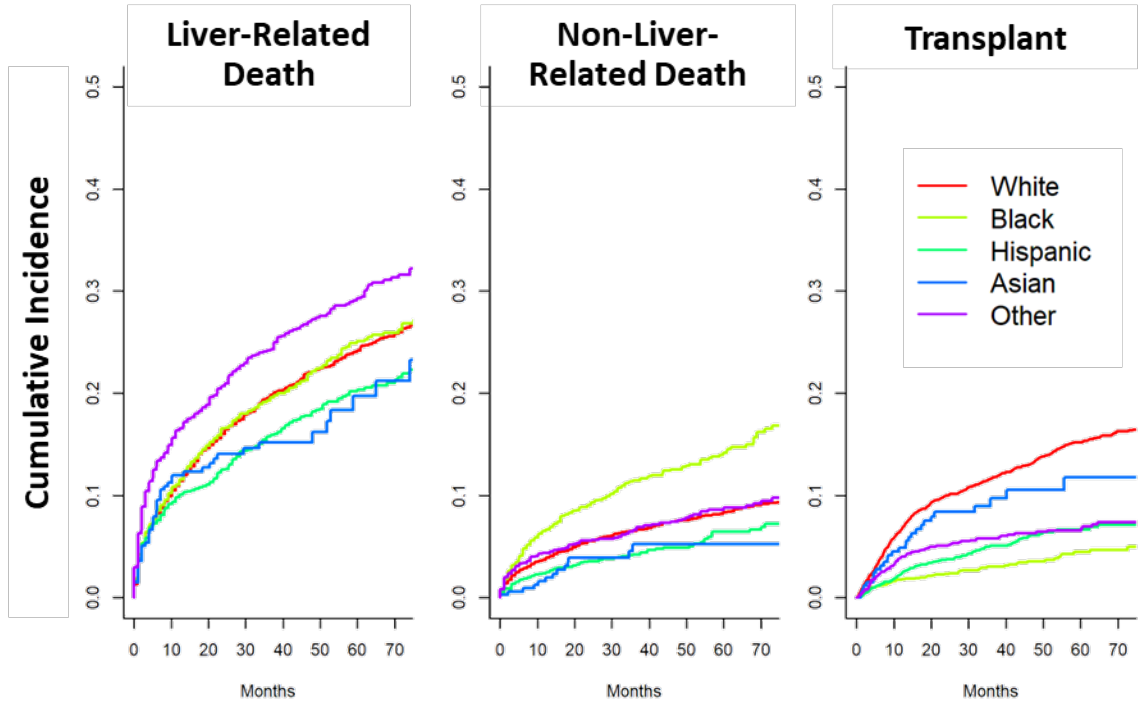
To assess the relationship between race and outcomes in cirrhosis

Methods

- Multivariable competing risk analysis of liver-related death and transplant with electronic health records from large metropolitan population, linked to transplant and state death registry
- Adult patients with a diagnosis code for cirrhosis

Main Findings

- Black patients had higher rates of death and lower rates of transplant compared to White patients than would be expected after adjusting for severity of disease and comorbidities.
- No difference was found among patients listed for transplant.



Conclusions

Disparities by race persist among patients with cirrhosis and may be missed among databases of listed patients.

Mazumder NR, et al., Abstract 155

NAFLD and alcohol-related liver disease are current and future drivers of cirrhosis in women

Objective

To describe the current and future burden of cirrhosis in women from the general population

Methods

Retrospective cohort study of 65,217 women with incident cirrhosis 2000-2017 from Ontario, Canada

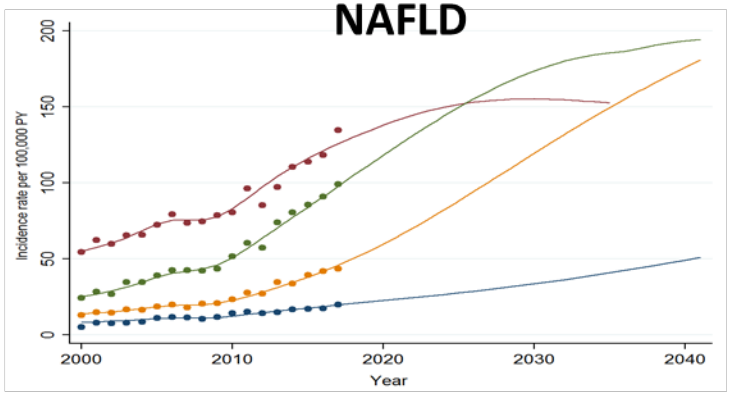
- Cirrhosis incidence described by etiology and birth cohort 2000-2017.
- Cirrhosis incidence projected 2018-2040 using an age-period-cohort model stratified by etiology and birth cohort.

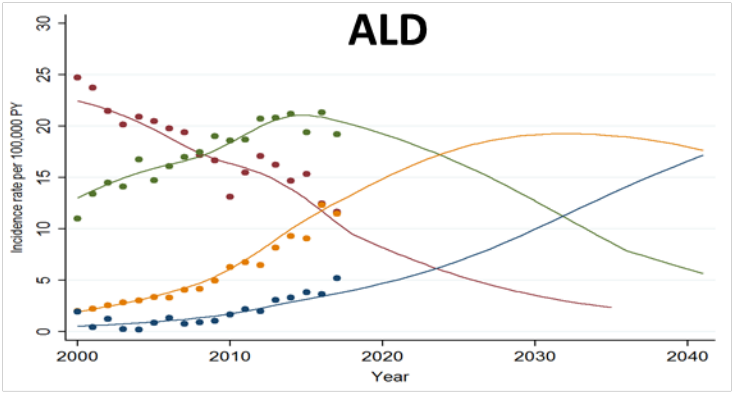
Main Findings

Although the highest increase in cirrhosis incidence 2000-2017 was for women with HCV, the greatest increases from 2018-2040 are anticipated for menopausal females with NAFLD (+246%) and young women with ALD (+320%).

Conclusions

Public health interventions and therapeutics should be specifically targeted to peri-menopausal women with NAFLD and young women with ALD in order to reverse these worrisome trends.





Flemming JA, et al., Abstract 156

AASLD November 13-16, 2020
The Liver Meeting®
Digital Experience

THE BEST OF THE LIVER MEETING® 2020

Portal Hypertension/Cirrhosis

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES