

AASLD Nov. 12-15, 2021

The Liver Meeting[®]



DIGITAL EXPERIENCE

The Best of The Liver Meeting[®]

ALCOHOL ASSOCIATED LIVER DISEASE



About the program:

Best of The Liver Meeting 2021 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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Three-year follow-up of alcohol-related hepatitis patients undergoing healthy donor fecal microbiota transplant (FMT): analysis of clinical outcomes, relapse, gut microbiota, and comparisons with standard care

Aim

To analyze long-term clinical outcomes, alcohol misuse, and prospective analysis of stored fecal microbiota between severe alcohol-related hepatitis (SAH) patients undergoing healthy donor FMT compared to corticosteroid responders

Methods

- SAH patients undergoing FMT (100ml via nasoduodenal tube x 7d) or SOC (prednisolone 40mg x 28d), retrospectively included
- Fecal 16-srRNA sequencing for relative abundances, significant taxa via QIIME® & LEfSe biomarker discovery method at baseline & post therapy (1-2y, 2-3y) between groups

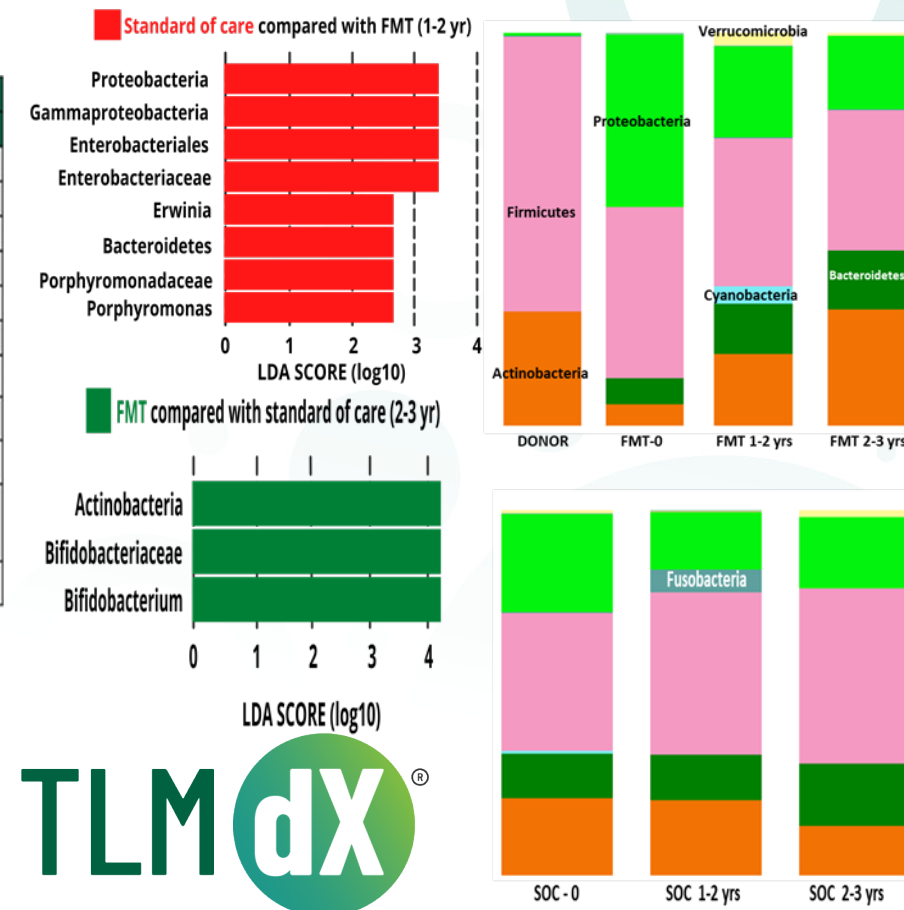
Conclusions

Healthy donor FMT treated SAH patients experienced significantly lesser encephalopathy, critical infections, hospitalizations, alcohol relapse & trend towards improved survival compared to steroids which was associated with significant increase in beneficial *Bifidobacterium* & reduction in *Acinetobacter* in former

Main Findings

- Trend towards improved survival in FMT with higher proportion of patients dying in the SOC arm [hazard ratio (95% CI: 2.14 0.99-4.58), p=0.0504]
- Significant increase in *Bifidobacterium* (1-2y) and reduction of *Acinetobacter* (2-3y) in FMT while higher *Erwinia*, *Porphyromonas* & reduction in *Bifidobacterium* in SOC (1-2y)

PARAMETER	GROUP		
	FMT (N=35)	SOC (N=25)	P Value
ON FOLLOW UP			
Ascites	12 (34.3%)	19 (73.1%)	0.003
Hepatic encephalopathy	7 (20%)	18 (69.2%)	<0.001
Acute kidney injury	14 (40%)	17 (65.4%)	0.051
Acute variceal bleeding	15 (42.8%)	14 (53.8%)	0.39
Need for critical care	15 (42.8%)	18 (69.2%)	0.04
Non-critical infections	7 (20%)	17 (65.45%)	<0.001
Critical infections	6 (17.1%)	14 (53.8%)	0.003
Alcohol relapse	10 (28.6%)	14 (53.8%)	0.04
Time to relapse (days) (Median; min – max)	436 (160 – 676)	197 (64 – 412)	0.002
Recurrence of alcohol related hepatitis	6 (60%, N=10)	7 (50%, N=14)	0.63



Efficacy of 6-month lactobacillus therapy in reducing heavy drinking among heavy drinkers diagnosed with moderate alcohol-associated hepatitis

Hypothesis

- Lactobacillus rhamnosus GG (LGG) may reduce drinking in alcohol use disorder (AUD) patients comorbid with moderate alcohol-associated hepatitis (mAH)

Methods

- Double-blind, prospective trial compared the efficacy of LGG vs. placebo in patients with moderate AH (mAH).
- 38 mAH patients grouped by treatment (LGG, N=21; placebo, N=17) were evaluated for their alcohol consumption over 6 months.

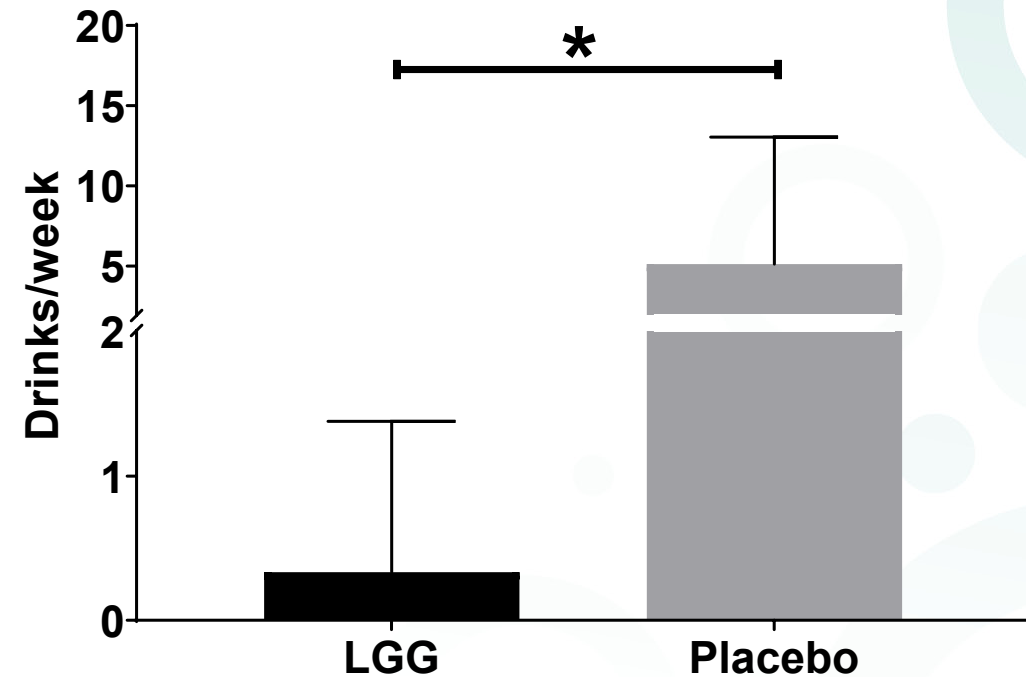
Main Findings

- LGG-treated patients showed a significant reduction in drinking, to the social or abstinence level of <4 drinks/week at the 6-m assessment compared to placebo-treated (Fisher's exact test, $p=0.032$; likelihood ratio=7.227 [moderate-effect]).

Conclusions

- 6-month LGG treatment reduced heavy drinking levels to the social drinking or abstinence levels in this pilot study.

6-month Drinking Report



Vatsalya V, et al., Abstract 127.

Combination of amoxicillin/clavulanate and prednisolone in severe alcoholic hepatitis: results of the randomized controlled trial Antibiocor

Aim

Antibiotics should be tested in addition to steroids for severe alcoholic hepatitis, to decrease the risk of infection

Methods

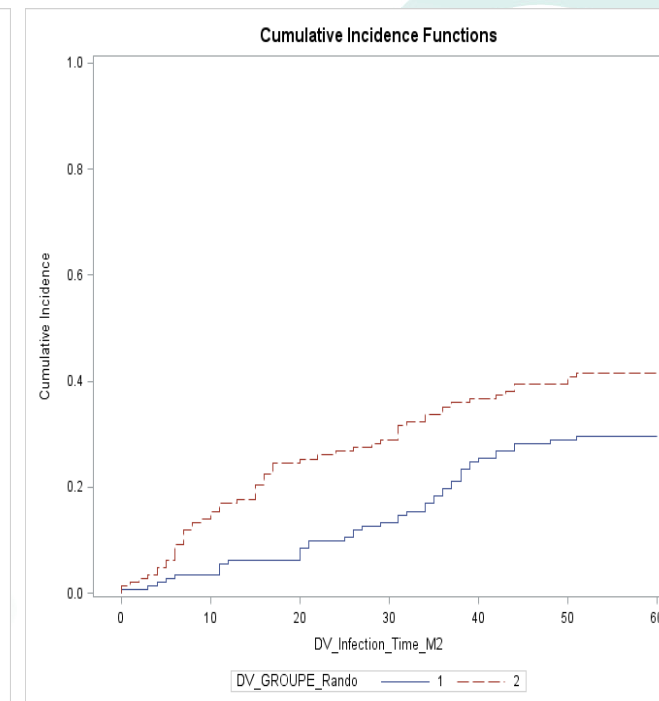
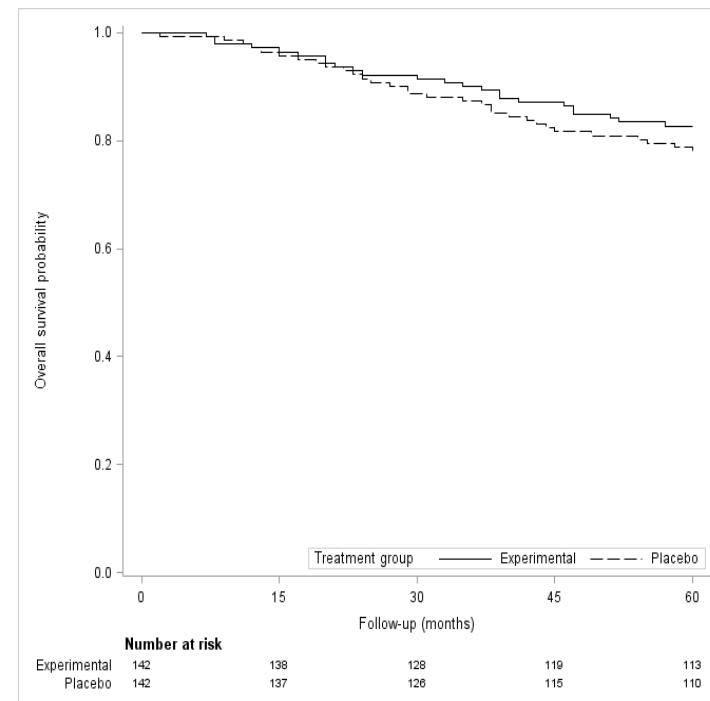
- Double-blind, randomized controlled trial comparing the efficacy of amoxicillin/clavulanate vs. placebo in combination to prednisolone for 30 days in patients with severe alcoholic hepatitis (AH)
- Patient population: Biopsy-proven AH, Maddrey's score ≥ 32 , MELD score ≥ 21

Main Findings

Antibiotics do not improve survival at 2 months but decrease significantly the risk of infection (see figures).

Conclusions

Amoxicillin/clavulanate do not improve short-term survival in combination with prednisolone in patients with severe AH



Figures: Survival curves at 2 months between the two groups (A) and cumulative incidence of infectious events at 2 months (B). Solid and dashed lines represent prednisolone+amoxicillin/clavulanate and prednisolone+placebo respectively.

Louvet A, et al., Abstract 128.



Fecal microbial transplant suppresses hepatic and systemic inflammatory responses and gut leakiness in severe alcoholic hepatitis patients

Aims and Objective: We investigated alterations in immune cell subsets, their functions and their association with gut permeability before and after Fecal Microbial Transplant in SAH patients

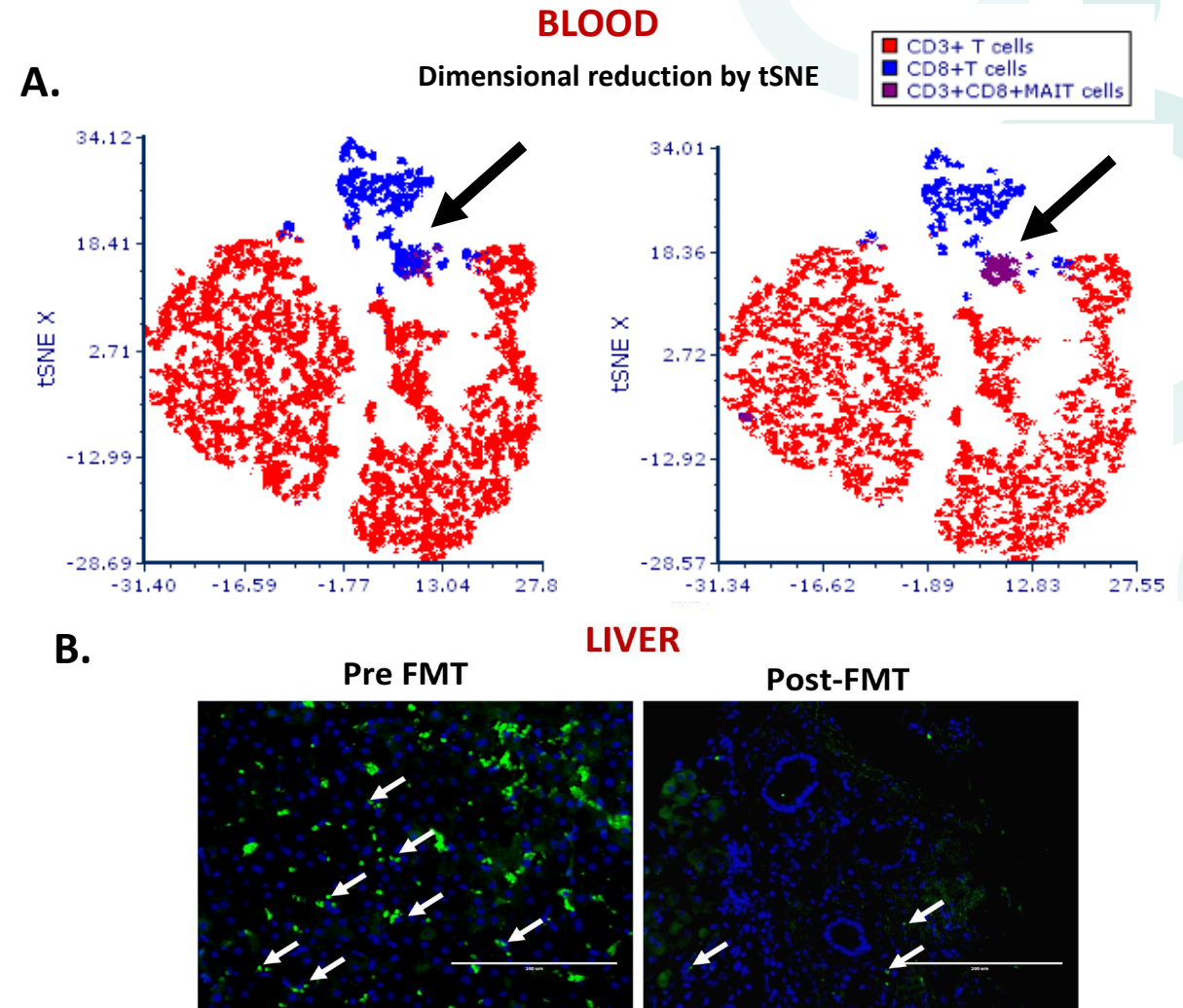
Methods:

- SAH patients, histologically diagnosed, and undergoing FMT (given through nasoduodenal tube for seven days) were studied pre- and post-FMT.
- High-dimensional immune profiling was done by flow cytometry. Duodenal biopsy were obtained pre- and post-FMT, to study intestinal permeability.
- Liver biopsy was studied for intrahepatic MAITs.

Results: In systemic circulation, post-FMT compared to baseline, the T-cell subsets were significantly altered; the frequency of CD3⁺CD8⁺, CD3⁺CD4⁺CD8⁺ and Th17 (CD3⁺CD4⁺RoRg⁺) increased while that of CD3⁺CD19⁺ cells declined. The activation markers CD25⁺ and CD69⁺ were low on MAITs. The intrahepatic MAITs were significantly reduced post-FMT at d28. The intestinal barrier improved.

Conclusions: FMT dampens the intrahepatic and circulatory inflammatory responses in patients with SAH. Gut microbiome modulation by FMT also helps restore the gut barrier function to improve clinical outcomes in SAH patients.

Baweja S, et al., Abstract 181.



Alcohol-associated Liver Disease

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