HepCure: Latest Updates in Liver Disease

David Bernstein, MD, FAASLD, MACG, FACP, AGAF
Treasurer, Empire Liver Foundation
Disclosures

• OcelotBio- Consultant
Learning Objectives

1. Understand how to use terlipressin to treat HRS-AKI.
2. Understand the common reasons for readmission in patients with cirrhosis.
3. Understand the common indications for liver transplantation in the US.
4. Understand the significance of serum creatinine on the MELD score.
Contents

• HRS-AKI
• Common clinical issues
• NASH
• Primary biliary cholangitis
• Hepatitis B
• AASLD briefs
HRS-AKI and Kidney Disease
Infuse Study: Continuous IV Terlipressin

- Terlipressin approved September 2022 as IV bolus medication
- Used in Europe mostly as continuous infusion
- **Infuse Study**
  - Multi-center, open label study
  - Decompensated cirrhosis and AKI-HRS (per ICA criteria)
  - Continuous terlipressin infusion
  - **Aim:**
    - Assess safety/efficacy of continuous terlipressin infusion in patients with AKI-HRS

Reddy et al. AASLD 2022
Infuse Study: Methods

- Population (N = 46)
  - Inclusion: Cirrhosis, ascites, AKI-HRS
  - Exclusion: MELD ≥ 35, ACLF Grade 3, Serum Creatinine (SCr) > 5.0mg/dL
- Continuous terlipressin infusion following 0.5 mg bolus
  - 2mg - 8mg/day up to 14 days
- Treatment Response
  - Complete Response (CR): ≥ 30% decrease in SCr and EOT SCr ≤ 1.5
  - Partial Response (PR): ≥ 30% decrease in SCr and EOT SCr > 1.5
  - Non-Response (NR): < 30% decrease in SCr
### Infuse Study: Results

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>Complete Response</th>
<th>Partial Response</th>
<th>Non-Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>46</td>
<td>27/46 (59%)</td>
<td>8/46 (17%)</td>
<td>11/46 (24%)</td>
</tr>
<tr>
<td>Age</td>
<td>56.6, 28-78</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transplant Listed/Eligible</td>
<td>36/46 (78%)</td>
<td>20/27 (74%)</td>
<td>7/8 (88%)</td>
<td>9/11 (82%)</td>
</tr>
<tr>
<td>Alcohol-Associated Cirrhosis</td>
<td>24/46 (52%)</td>
<td>16/27 (59%)</td>
<td>3/8 (37.5%)</td>
<td>5/11 (46%)</td>
</tr>
<tr>
<td>NASH/NASH+HepC</td>
<td>11/46 (24%)</td>
<td>5/27 (19%)</td>
<td>3/8 (37.5%)</td>
<td>3/11 (27%)</td>
</tr>
<tr>
<td>Other</td>
<td>11/46 (24%)</td>
<td>6/27 (22%)</td>
<td>2/8 (25%)</td>
<td>3/11 (27%)</td>
</tr>
<tr>
<td>MELD, Baseline</td>
<td>26, 17-34</td>
<td>26, 18-34</td>
<td>27, 17-34</td>
<td>27, 17-34</td>
</tr>
<tr>
<td>MELD, EOT</td>
<td>20, 11-32</td>
<td>19, 11-31</td>
<td>23, 16-31</td>
<td>21, 14-29</td>
</tr>
<tr>
<td>AKI Stage 1B</td>
<td>12/46 (26%)</td>
<td>7/27 (26%)</td>
<td>1/8 (12.5%)</td>
<td>4/11 (36%)</td>
</tr>
<tr>
<td>2</td>
<td>19/46 (41%)</td>
<td>14/27 (52%)</td>
<td>3/8 (37.5%)</td>
<td>2/11 (18%)</td>
</tr>
<tr>
<td>3</td>
<td>15/46 (33%)</td>
<td>6/27 (22%)</td>
<td>4/8 (50%)</td>
<td>5/11 (46%)</td>
</tr>
<tr>
<td>SCr, Baseline</td>
<td>2.7, 1.5-4.9</td>
<td>2.48, 1.5-3.9</td>
<td>3.0, 1.7-4.9</td>
<td>3.2, 2.3-4.4</td>
</tr>
<tr>
<td>SCr, EOT</td>
<td>1.7, 0.8-4.9</td>
<td>1.2, 0.8-1.5</td>
<td>2.6, 1.5-2.5</td>
<td>2.0, 1.7-2.4</td>
</tr>
<tr>
<td>Days of Treatment</td>
<td>8, 1-14</td>
<td>8, 3-14</td>
<td>6, 1-4</td>
<td>10, 3-14</td>
</tr>
<tr>
<td>Total Terlipressin during treatment (mg)</td>
<td>28, 3-87</td>
<td>26, 3-79</td>
<td>44, 5-87</td>
<td>20, 3-67</td>
</tr>
<tr>
<td>Total Albumin during treatment (g)</td>
<td>168, 25-475</td>
<td>192, 50-400</td>
<td>174, 50-475</td>
<td>94, 25-400</td>
</tr>
<tr>
<td>RRT within 30 days of treatment</td>
<td>9/45 (20%)</td>
<td>0/26 (0%)</td>
<td>2/8 (25%)</td>
<td>7/11 (64%)</td>
</tr>
<tr>
<td>Alive at 30 days (% within group)</td>
<td>43/46 (94%)</td>
<td>26/27 (96%)</td>
<td>7/8 (88%)</td>
<td>10/11 (91%)</td>
</tr>
</tbody>
</table>
Results – Response Rate and Etiology

Response Rate

- 59% Complete Response (CR)
- 24% Partial Response (PR)
- 17% Non-Response (NR)

Response to Terlipressin by Etiology of Liver Disease

<table>
<thead>
<tr>
<th>Etiology</th>
<th>CR</th>
<th>PR</th>
<th>NR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol-Associated Cirrhosis</td>
<td>52%</td>
<td>37.5%</td>
<td>20%</td>
</tr>
<tr>
<td>NASH/NASH+HCV</td>
<td>28%</td>
<td>22%</td>
<td>27%</td>
</tr>
<tr>
<td>Other</td>
<td>20%</td>
<td>19%</td>
<td>27%</td>
</tr>
</tbody>
</table>

Abbreviations: All – All Patients; CR – Complete Response; PR – Partial Response; NR – Non-Response
Results – Total Terlipressin Dose and Albumin Dose

Total Terlipressin During Treatment (mg)

Total Albumin During Treatment (g)

Abbreviations: All – All Patients; CR – Complete Response; PR – Partial Response; NR – Non-Response
Infuse Study: Safety Results

- No unexpected drug-related SAEs
- 1 AE of interest (rash)
- Within 30 days post-treatment:
  - 9 cases RRT (7 non-responders)
  - 3 deaths (2 progressive liver failure, 1 progressive renal failure)

Abbreviations: CR – Complete Response; PR – Partial Response; NR – Non-Response; RRT – renal replacement therapy
Infuse: Conclusion

• A high complete response rate of 59% was observed with continuous terlipressin infusion.

• A favorable safety profile in an enriched group of transplant listed/eligible patients with AKI-HRS (MELD < 35, SCr ≤ 5.0mg/dL, ACLF-Grade 0-2) was observed.

• Further enrollment (up to a total of 50 patients) and long term follow up for survival, transplant and kidney-related outcomes is ongoing (up to 12 months).
Early Versus Standard Initiation of Terlipressin For HRS-AKI In ACLF-A Randomized Controlled Trial (ETERLI Study)

Hitesh Singh1, Ankur Jindal2, Manoj K Sharma3 and Shiv K Sarin3, (1)Hepatology, Institute of Liver and Biliary Sciences, (2)Ilbs Hospital, Vasant Kunj, New Del, Ilbs Hospital, Vasant Kunj, New Del, (3) Department of Hepatology, Institute of Liver and Biliary Sciences, New Delhi
**ETERLI Study**

- **Background**
  - Response to terlipressin correlates with AKI-HRD and acute on chronic liver failure stage
- **Methods**
  - Consecutive ACLF patients with stage ii/III AKI despite albumin resuscitation (40 gm) for 12 hours
  - Randomized to receive
    - Terlipressin at 2 mg/24 hrs plus albumin at 12 hours
    - Terlipressin at 2 mg/hour plus albumin after 48 hours SPC therapy + albumin
  - Primary endpoint
    - Reversal of AKI at 7 days
## ETERLI Study: Results

<table>
<thead>
<tr>
<th></th>
<th>Early terlipressin (n=35)</th>
<th>SOC (n=35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full AKI response at day 7</td>
<td>24/35 (68.6%)</td>
<td>11/35 (31.4%)</td>
</tr>
<tr>
<td>Full AKI response at day 3</td>
<td>11/35 (31.4%)</td>
<td>4/35 (11.4%)</td>
</tr>
<tr>
<td>Died within 28 days</td>
<td>14/35 (40%)</td>
<td>23/35 (65.7%)</td>
</tr>
<tr>
<td>90-day mortality</td>
<td>57.2%</td>
<td>69.6%</td>
</tr>
</tbody>
</table>
ETERLI: Conclusion

- Early terlipressin improved results of AKI in ACLF stage II/III
- Early terlipressin led to improved hemodynamic parameters with significant short-term mortality benefit
ETERLI: Food for Thought

• Not all patients in the early terli group may have had HRS-AKI
  – Some may have had AKI from another cause and improved with albumin alone
• Terlipressin given off label as a continuous infusion
Rebound in Serum Creatinine Levels After Terlipressin- Based Treatment of Patients With Acute Kidney Injury- Hepatorenal Syndrome (HRS-AKI) is Uncommon over the Short Term In Patients With a Complete Response: Results From the CONFIRM Study

Ethan M Weinberg, Gastroenterology, Hospital of University of Pennsylvania, Florence Wong, Department of Medicine, University of Toronto, R. Todd Frederick, Hepatology and Liver Transplantation, California Pacific Medical Center, Stevan A. Gonzalez, Medicine, Baylor Scott & White All Saints Medical Center, Zachary Fricke, Gastroenterology and Hepatology, University of Pennsylvania; Gastroenterology & Hepatology, Beth Israel Deaconess Medical Center, Douglas A. Simonetto, Mayo Clinic, Manhal Izzy, Department of Medicine, Vanderbilt University Medical Center, S. Chris Pappas, Scientific Affairs, Orphan Therapeutics LLC, Khurram Jamil, Scientific Affairs, Mallinckrodt Pharmaceuticals and K. Rajender Reddy, Division of Gastroenterology, Perelman School of Medicine, University of Pennsylvania, PA
Evaluated CONFIRM patients for SCr rebound up to 14 days after stopping terlipressin
  - Defined rebound as increase to at least 1 stage of AKI
Rebound of Serum Creatinine Following Terlipressin: A Sub-analysis of the CONFIRM Study

Table: Rebound by response level and treatment group in the CONFIRM study, in patients with complete or partial responses

<table>
<thead>
<tr>
<th>Response level, n/N (%)</th>
<th>Terlipressin (n=93)</th>
<th>Placebo (n=27)</th>
<th>P value(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response</td>
<td>4/73 (6)</td>
<td>1/18 (6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Partial response</td>
<td>1/20 (5)</td>
<td>2/9 (22)</td>
<td>0.22</td>
</tr>
<tr>
<td>Complete + partial responses</td>
<td>5/93 (5)</td>
<td>3/27 (11)</td>
<td>0.38</td>
</tr>
</tbody>
</table>

\(^a\) Increase in SCr > 0.3 mg/mL at any time from the end of treatment to the earlier of Day 14 or discharge.

\(^b\) P values using a Fisher’s exact test.
Rebound of Serum Creatinine Following Terlipressin: Conclusions

- Rebound in SCr to AKI stage 1 after resolution of HRS was infrequent
- No significant differences in rebound in PR and CR to either terlipressin or placebo
Pretransplant Terlipressin Treatment For Hepatorenal Syndrome Decreases the Need For Renal Replacement Therapy Both Pre- and Posttransplant: A 12-Month Follow-Up Analysis of the CONFIRM Trial

Ethan M Weinberg, Gastroenterology, Hospital of University of Pennsylvania, Florence Wong, Department of Medicine, University of Toronto, Hugo E. Vargas, Mayo Clinic, Arizona, Michael P. Curry, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA, Khurram Jamil, Scientific Affairs, Mallinckrodt Pharmaceuticals, S. Chris Pappas, Scientific Affairs, Orphan Therapeutics LLC and K. Rajender Reddy, Division of Gastroenterology, Perelman School of Medicine, University of Pennsylvania, PA
# Need for RRT

**Pre- and Post-liver Transplantation**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Terlipressin (n=43)</th>
<th>Placebo (n=27)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RRT Pretransplant</td>
<td>11/43 (26)</td>
<td>16/27 (59)</td>
<td>.005</td>
</tr>
<tr>
<td>RRT by Day 30 Posttransplant</td>
<td>4/43 (9)</td>
<td>5/26 (19)</td>
<td>.282</td>
</tr>
<tr>
<td>RRT by Day 180 Posttransplant</td>
<td>9/43 (21)</td>
<td>11/24 (46)</td>
<td>.033</td>
</tr>
<tr>
<td>RRT by Day 365 Posttransplant</td>
<td>7/40 (18)</td>
<td>10/22 (46)</td>
<td>.018</td>
</tr>
</tbody>
</table>

Data are presented as n/N (%).

n, number of subjects in the treatment group who were alive at each timepoint.

ITT, intent-to-treat; RRT, renal replacement therapy.
• Pretransplant terlipressin was associated with decreased need for RRT both pre and post liver transplantation
Timely Albumin Infusion May Improve Survival and Length Of Stay in Patients With Cirrhosis and Acute Kidney Injury

W. Ray Kim, Karthik Raghunathan, Gregory S. Martin, Elisabet Viayna, Rahul Rajkumar and Kunal Lodaya, (1)Stanford University Medical Center, (2) Duke University, (3)Emory University, (4)Scientific & Medical Affairs, Grifols, SA, (5)Boston Strategic Partners, Inc.
Timely Albumin Infusion May Improve Survival and Length of Stay in Patients With Cirrhosis and Acute Kidney Injury

- Evaluated chargemaster dataset (Premier Healthcare Database) for discharge diagnoses of cirrhosis and AKI over 3-year period
- 191,792 encounters identified
  - 62,978 met study entrance criteria
- Timely albumin defined as infusion started ≤ 1 day of hospital admission
Timely Albumin Infusion May Improve Survival and Length of Stay in Patients With Cirrhosis and Acute Kidney Injury

• Timely albumin was associated with a 9% reduction in mortality when compared to the non-timely group
• Timely albumin was associated with:
  – Shorter hospital stay
  – Shorter ICU length of stay
Timely Albumin Infusion May Improve Survival and Length of Stay in Patients With Cirrhosis and Acute Kidney Injury

- Food for thought
  - Concerns of extracting this type of data from a large claims database
  - Incorrect coding?
  - Definition of AKI for coding, etc
Common Clinical Issues
A Prospective Study of Preventable Readmissions and Their Correlates in Hospitalized Patients With Cirrhosis

Eric S. Orman1, Archita Parikh Desai1, Marwan S. Ghabril1, Lauren D. Nephew1, Kavish R. Patidar1, John Holden1, Niharika R Samala1, Minmin Pan2, Sujuan Gao2 and Naga P. Chalasani1, (1)Division of Gastroenterology and Hepatology, Indiana University School of Medicine, (2)Department of Biostatistics, Indiana University School of Medicine
Prospective Study of Preventable Readmissions in Cirrhotic Patients

- Examined 30-day readmissions in a single center from June 2014 to March 2020
- 654 patients of which 246 (38% were readmitted within 30 days)
- 29/246 (12%) were preventable readmissions
Reasons for Readmission (n = 246)

- No difference in preventable vs non-preventable in these groups
- Independent factors of preventable readmissions
  - Non-white race
  - Admission in the prior 30 days

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic encephalopathy</td>
<td>23%</td>
</tr>
<tr>
<td>GI bleeding</td>
<td>13%</td>
</tr>
<tr>
<td>AKI</td>
<td>12%</td>
</tr>
</tbody>
</table>
Preventable Readmissions: Conclusions

• Early hospital readmissions in cirrhotics are common
• Most readmissions are not preventable
• Non-white race and admission in the prior 30 days associated with preventable readmission
Not All MELD Scores are Created Equal: MELD Driven By Creatinine Has Lower Intent to Treat Survival Compared to MELD Driven By Bilirubin or INR

Craig Rosenstengle, Gastroenterology & Hepatology, Baylor University Medical Center, Tsung-Wei Ma, Baylor University Medical Center, Marina Serper, Division of Gastroenterology and Hepatology, University of Pennsylvania, Patrick S. Kamath, Division of Gastroenterology and Hepatology, Mayo Clinic, Pere Gines, Liver Unit, Hospital Clinic and Sumeet K Asrani, Transplant Hepatology, Baylor University Medical Center
MELD Score Components

- INR
- Serum creatinine
- Serum bilirubin
- MELD – NA
  - Adds Na to the score
Not All MELD Scores Are Created Equal
MELD scores driven by creatinine
- Patients have lower ITT survival
- Should MELD scores be stratified by driver
NASH
• Consensus analysis: panel of 3 pathologists read digital slides to assess fibrosis
Pemvidutide for NASH

- Long acting GLP1/glucagon dual receptor agonist
- Weekly, subcutaneous injection
- 94 patients randomized to 4 groups received weekly injection for 12 weeks
- Mild and transient GI adverse events
- 2 required discontinuation

Harrison et al. AASLD 2022 Abs 5034
Non-Alcoholic Steatohepatitis (NASH) is Rapidly Becoming the Most Common Indication For Liver Transplantation in the Candidates With Hepatocellular Carcinoma (HCC) in the United States (U.S.)
Proportion of HCC Listings for Liver Transplantation
Primary Biliary Cholangitis
Adequate Biochemical Response to Ursodeoxycholic Acid in Patients With Primary Biliary Cholangitis: Is Normalization of Serum Liver Tests Important?

Christophe Corpechot et al
PBC: Adequate Response to UDCA

- Retrospective cohort study of 1034 adequate responders to UDCA
- **Inclusion criteria**
  - UDCA > 12 months
  - Adequate biochemical response defined by Paris-2 criteria
    - ALP and AST < 1.5 ULN with a normal bilirubin
- **Exclusion criteria**
  - Treatment with OCA, fibrates or corticosteroids
- **Endpoints**
  - Survival without liver transplantation or liver related complications
PBC: Adequate Response to UDCA

Study population:
• 1034 patients
• 91% women
• Mean age 61
• 16% with Fibroscan > 10 kPa
• Mean UDCA treatment duration 7.7 years

Mean follow up 4.5 years
**PBC: Adequate Response to UDCA**  
**Abnormal Liver Tests At Baseline**

<table>
<thead>
<tr>
<th>Test</th>
<th>% abnormal at baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALP</td>
<td>35</td>
</tr>
<tr>
<td>GGT</td>
<td>50</td>
</tr>
<tr>
<td>AST</td>
<td>13</td>
</tr>
<tr>
<td>ALT</td>
<td>15</td>
</tr>
<tr>
<td>Total bilirubin &gt; 0.6 X ULN</td>
<td>25</td>
</tr>
</tbody>
</table>
PBC: Results

Only normalization of ALP was associated with improved survival

<table>
<thead>
<tr>
<th></th>
<th>Normal ALP</th>
<th>Abnormal ALP</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-year survival</td>
<td>95.9%</td>
<td>91.2%</td>
</tr>
<tr>
<td>10-year survival</td>
<td>85.3%</td>
<td>73%</td>
</tr>
</tbody>
</table>
**PBC: Results**

Patients with PBC with a Paris-2 Adequate Biochemical Response to UDCA (n=1034)

- **Survival Without Transplantation or Complication**

  - Normal ALP at entry
  - Elevated ALP at entry

  **Adjusted difference of 10-year survival:** 5.5 mo. (95%CI 0.6 – 10.4), *p* = 0.027
  **Adjusted ratio of 10-year time-lost:** 0.458 (95%CI 0.309 – 0.681), *p* < 0.001

<table>
<thead>
<tr>
<th>Patients at risk</th>
<th>Normal ALP at entry</th>
<th>Elevated ALP at entry</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>673</td>
<td>361</td>
</tr>
<tr>
<td></td>
<td>515</td>
<td>269</td>
</tr>
<tr>
<td></td>
<td>303</td>
<td>176</td>
</tr>
<tr>
<td></td>
<td>189</td>
<td>106</td>
</tr>
<tr>
<td></td>
<td>119</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>54</td>
<td>22</td>
</tr>
</tbody>
</table>
Conclusions

- Normalization of ALP was associated with a modest but significant absolute clinical benefit.
- Normalization of GGT, ALT, AST or total bilirubin to ≤ 0.6 x ULN were not associated with improved survival.
- Adequate responders to UDCA with a persistent ALP elevation should be considered for second line therapy.
Real-World Data on Long Term Efficacy and Safety of Obeticholic Acid For Primary Biliary Cholangitis: First Release From the Italian Recapitulate Study

Antonio De Vincentis1, et al and Umberto Vespasiani-Gentilucci1
AASLD 2022, Late Breaker abstract 5023
Recapitulate Study

- 442 patients
- Median age 57.8 years
- 88% women
- Median disease duration 7 years
- 34% (152) cirrhotic
- OCA therapy for at least 6 months

Results:
- OCA discontinued in 86 patients (19%)
  - Pruritus 41 patients (48%)
  - Hepatic events 18 patients (21%)

Conclusions:
- Confirms long term efficacy and safety of OCA
PBC: Real World OCA Response Data
Recapitulate Study: Independent Predictors of Response

- Pre-treatment ALP level
- Total bilirubin
Hepatitis B
#1: Can we prevent vertical transmission of HBV in highly viremic mothers with HBV vaccination plus oral TDF without HBIG?

## Background

Maternal TDF therapy is recommended for highly viremic mothers with CHB (HBV DNA >200,000 IU/mL) in combination with vaccine + HBIG to HBIG not available in many resource-limited regions with high HBV prevalence.

## Methods

- Multicenter RCT in China: randomized 280 HBeAg+ CHB mothers with DNA >200,000 IU/mL to receive:
  - Control group: TDF 300 mg QD Wk 28 (to delivery) + Vaccine + HBIG
  - Experimental group: TDF 300mg QD Wk 16 (to delivery) + Vaccine

## Primary endpoints: congenital defect rates and MTCT at infant age week 28

## Main Findings

- N=280 (265 mothers completed) – median TDF duration of 23 wk (experimental) vs 11 weeks (control) (p<0.001) and median maternal DNA at delivery was lower in experimental (log 2.4) vs control (log 3.6) (p<0.001)

## Conclusions

Maternal TDF therapy Wk 16 (to delivery) plus vaccine may be associated with similarly low rate of MTCT as SOC TDF Wk 28 (to delivery) + Vaccine + HBIG with public health implications in resource-limited settings.

---

### Table 1. Maternal variables at baseline and infant characteristics at birth

<table>
<thead>
<tr>
<th>Infant Characteristics at Birth</th>
<th>Entire cohort (n=280)</th>
<th>Experimental (n=140)</th>
<th>Comparator (n=140)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at enrollment, median (IQR)</td>
<td>28.22 ± 3.09</td>
<td>28.41 ± 3.15</td>
<td>28.02 ± 3.03</td>
</tr>
<tr>
<td>Gravidity - No.</td>
<td>1.00 (0.00, 2.00)</td>
<td>1.00 (0.00, 2.00)</td>
<td>1.00 (0.00, 2.00)</td>
</tr>
<tr>
<td>HBV DNA - log10 IU/ml</td>
<td>8.23 (7.88, 8.42)</td>
<td>8.23 (7.92, 8.42)</td>
<td>8.23 (8.02, 8.40)</td>
</tr>
<tr>
<td>Alanine aminotransferase - U/l</td>
<td>20.15 (16.00, 28.90)</td>
<td>20.40 (16.00, 31.68)</td>
<td>20.00 (15.05, 28.00)</td>
</tr>
<tr>
<td>eGFR – ml/min</td>
<td>189.55 (165.14, 214.45)</td>
<td>188.01 (165.21, 213.95)</td>
<td>190.73 (166.47, 216.53)</td>
</tr>
</tbody>
</table>

- When comparing variables between the experimental group and comparison group, p values were all >0.05. *LLOQ = 20 IU/mL

---

Figure 1. Mother-to-child transmission rates at the age of 28 weeks

#24: Low level of hepatitis B viremia (HBV DNA <2000 IU/mL) increases the risk of HCC in patients with compensated cirrhosis

**Background**

- Current guidelines diverge on whether antiviral treatment is recommended for patients with CHB patients and compensated cirrhosis with detectable HBV DNA <2000 IU/mL

**Methods**

- Retrospective cohort study of 627 untreated patients with CHB and compensated cirrhosis in Korea between 2007 and 2021
- Primary endpoint: incident HCC
- Comparison of HCC risk of hepatocellular carcinoma (HCC) between patients with low-level viremia (LLV) – HBV DNA 15-2000 IU/mL and undetectable HBV DNA (<15 IU/mL)

**Main Findings**

- Total of 59/627 patients developed HCC with annual incidence of 2.44/100 person-years during study period → 29 in LLV group and 20 in undetectable group
- Higher HCC incidence in LLV (2.56/100 PY) vs. undetectable (2.22/100 PY) group
- Multivariate analysis: LLV associated with higher HCC risk
- Propensity matched cohort: LLV associated with higher HCC risk (aHR 2.16 (p=0.014)

**Conclusions**

- Among patients with compensated cirrhosis, low level viremia is associated with increased HCC risk compared with patients with undetectable HBV DNA – implications for guidance on antiviral therapy in this clinical context.
#25: Functional cure with PEG-IFN in NUC-suppressed HBeAg negative CHB: Everest Project (4-year data update)

**Background**
- Functional cure is rarely achieved in patients treated with NA
- Add-on or switch to peg-IFN in NUC-suppressed e-neg CHB may improve HBsAg loss

**Methods**
- Everest Project: large real-world multicenter study in China which examines role of peg-IFN for 48 or 96 weeks in NUC-suppressed e-neg CHB (defined as: HBV DNA <100 IU/mL, HBeAg negative, HBsAg ≤1500 IU/mL)

**Main Findings**
- N=20,693 enrolled → 3472 have achieved HBsAg loss to date
- HBsAg loss rate: 9.5 to 33.2% at weeks 12-48
- Multivariate analysis: low baseline HBsAg, HBsAg decline > 1 log10 IU/mL at week 24, and ALT elevation at week 12 are predictors of functional cure at week 48 (p<0.0001)

**Conclusions**
- Functional cure is achieved in significant proportion of patients with NUC-suppressed e-neg CHB treated with peg-IFN

---

**Figure. HBsAg loss rate at different time points in PP analysis.**

#36: Antiviral therapy reduces HCC risk in patients with CHB in the indeterminate phase (REAL-B study)

Objective
- HCC risk in CHB may be higher in the indeterminate phase compared to the inactive phase, but it is unclear if antiviral therapy reduces HCC risk in this population. Examination of association between antiviral therapy and HCC risk in the indeterminate phase.

Methods:
- Retrospective cohort study of 14 sites (US/Europe/Asia) with consecutive, treatment-naïve, adult patients with CHB in the indeterminate phase → exclude pts with FIB-4>3.25 or cirrhosis.

Main Findings
- N=855 patients: age 46.4 yr, 21% HBeAg pos, mean DNA log 4.4
- Mean follow-up of 6.2 years: lower HCC incidence among treated than untreated patients at 10 years (4% vs 15%), and 15 years (11% vs. 34%)
- Multivariable Cox proportional hazards model adjusted for age, sex, HBeAg, HBV DNA, ALT, diabetes, and platelet count → antiviral therapy was an independent predictor of lower HCC risk (adjusted HR 0.30, 95% CI 0.1 – 0.8, P=0.001).

Conclusions:
- Antiviral therapy may reduce HCC risk by 70% among CHB patients in the indeterminate phase → implications for treatment decision for patients in the grey zone.

15-year HCC incidence: 34% (untreated) vs. 11% (treated), P=0.02

Antiviral treatment is independently associated with 70% HCC risk reduction

Huang D, et al., Abstract 36.
#45: Global progress towards HBV and HCV elimination, updated through 2021

**Objectives**

**Methods**
- Years of elimination (by target) were extracted from models maintained by the CDA Foundation; results from a policy assessment survey were used to score national viral hepatitis elimination policies.

**Main Findings**
- Considering 2020 and 2022 survey data, top scores (9 or 10) for political will were observed in 17 countries (30%) for HBV and 25 countries (42%) for HCV. Top scores for financing of the national program were observed in 30 countries (51%) for HBV and 33 countries (54%) for HCV.
- Fourteen countries were on track to achieve all absolute or relative targets for HCV, while no countries on track to achieve all targets for HBV by 2030. More than 80 countries were on track to achieve the HBsAg prevalence target for children ≤5 years of age by 2030.

**Conclusions**
- As countries progress toward eliminating HCV and HBV, more work is needed to enhance political will and financing of national elimination programs; in particular, expanded screening and treatment for HBV is needed.

Blach S, et al., Abstract 45.
AASLD Briefs: Treatment Of Severe ETOH Hepatitis

A. Overall 90-day Survival

p = 0.0025

Gawrieh et al. AASLD 2022 Abs. 5007
• Asymptomatic hepatitis A infection in plasma donors with high viral RNA titers
  – FDA identified asymptomatic plasma donors with elevated ALT and HAVRNA among plasma donors who donate weekly (Costa et al. AASLD 2022 Abs 5024)
• Fibroscans placed in primary care offices increase referrals to hepatologists (Mantry et al. AASLD 2022 Abs 5060)
Thanks for your attention!