Acute Decompensation Management of Hepatitis B patients
Case presentation (1)

- 43 years old male
- Present illness: progressive jaundice for 2-3 days.
- Past history: hepatitis B for 10 years
- Family history: father and brother had DM, and hypertension
- Social alcohol consumption, smoking (-)
Case presentation

- Lab data: (2007-9-28) ALT: 2802, AST: 1507, Bili-T: 14.80, bili-D: 8.35, PT: 21.26 (control 10.44 sec), INR: 1.81, HBsAg (+), HCVAb (-), HBeAg (+), Anti-HBeAb (-), Anti-HBc IgM (+), HBV DNA: 1.60 x 10^6 copies/mL, genotype B.
- Echo: chronic liver parenchymal disease score 5
Case presentation (2)

- 60 years old female
- Chief complaint: fatigue and poor appetite for one week
- Past history: hepatitis B for 20 years
- Family history: mother, five sisters and four brothers were hepatitis B carrier
- Alcohol consumption (-), smoking (-), Tattooing (30 years ago), Ear-piercing (30 years ago)
Case presentation (2)

- Lab data: (2010-1-39) ALT: 932, AST: 1076, Bili-T: 1.40, bili-D: 0.4, PT: 15.00 (control 11.34 sec), INR 1.34, HBsAg (+), HCVAb (-), HBeAg (-), Anti-HBeAb (+), HBV DNA > 6.4 x 10^8 copies/mL.
- Echo: chronic liver parenchymal disease score 6
4 Phases of Chronic HBV Infection

Current Understanding of HBV Infection

HBeAg

Anti-HBe

ALT activity

HBV DNA

Phase | Immune Tolerant | Immune Clearance | Inactive Carrier State | Reactivation
--- | --- | --- | --- | ---
Liver | Minimal inflammation and fibrosis | Chronic active inflammation | Mild hepatitis and minimal fibrosis | Active inflammation

Optimal treatment times

Three phases + one variant phase of CHB

- Immune tolerant phase
- Immune clearance phase
- Inactive residual phase
- Reactivation

**HBV DNA**
- 2x10^9 IU/ml
- 2x10^4 IU/ml

**HBeAg-positive**
- Wild type
- Mutant

**Acute Hepatic Decompensation (<5%)**

**Histology**
- Minimal
- Active hepatitis
- Minimal/inactive

**Liver HBcAg**
- Nucleus
- Nucleus/cytoplasm
- Absent

**ALT**

**Age**
- 20
- 35
- 60

**HBV is the driver!**

Liaw & Chu Lancet 2009
Three phases + one variant phase of CHB

- Immune tolerant phase
- Immune clearance phase
- Inactive residual phase
- Reactivation

HBV DNA

- 2x10^9 IU/ml
- 2x10^4

HBeAg-positive

- Pre C/BCP: Wild type
- Wild > Mutant
- Mutant > Wild

Anti-HBe-positive

HBeAg-reversion

HBeAg-negative hepatitis

Cirrhosis

Chronic Hepatic Decompensation (~4%)

- Active hepatitis
- Minimal/inactive
- Active hepatitis

Liver HBcAg

- Nucleus
- Nucleus/cytoplasm
- Absent
- Nucleus/cytoplasm

Histology

- Minimal
- Active hepatitis
- Minimal/inactive
- Active hepatitis

ALT

- Minimal
- Active hepatitis
- Minimal/inactive
- Active hepatitis

Age

- 20
- 35
- 60
- 35 year

HBV is the driver!

Liaw & Chu Lancet 2009
Spontaneous HBeAg seroconversion

A critical biologic "lock", leaks sometimes

HBeAg+ hepatitis

HBeAg+ hepatitis
HBV-DNA >10^5 cp/ml

HBeAg+ hepatitis
HBV-DNA >10^4-5 cp/ml

HBeAg– hepatitis
HBV-DNA <10^4 cp/ml

Sustained remission

HBsAg loss

Liver cirrhosis

Decompensation

HCC

HBeAg loss and seroconversion

94-100%

0-6%

1.5%

1.5%

* %/year

5-yr Survival in Patients with Chronic Hepatitis B

Survival of 98 patients with HBV related cirrhosis

De Jongh et al. Gastroenterology 1992
Survival and Compensation

De Jongh et al. Gastroenterology 1992

84% vs 14%
HBV Treatment Landscape in 2011

- Peginterferon alfa-2a
- Lamivudine
- Entecavir
- Tenofovir

Timeline:
- 1990: Interferon alfa-2b
- 1998: Lamivudine
- 2002: Entecavir
- 2005: Telbivudine
- 2006: Tenofovir
- 2008:
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST (IU/l)</td>
<td>130±67</td>
<td>72±21</td>
<td>&lt;0.004</td>
</tr>
<tr>
<td>ALT (IU/l)</td>
<td>112±68</td>
<td>58±24</td>
<td>&lt;0.009</td>
</tr>
<tr>
<td>S. albumin (g/dl)</td>
<td>3.33±0.4</td>
<td>3.57±0.4</td>
<td>NS</td>
</tr>
<tr>
<td>PT prolongation (s)</td>
<td>5.13±1.1</td>
<td>4.27±1.4</td>
<td>NS</td>
</tr>
<tr>
<td>S.bilirubin (mg/dl)</td>
<td>1.79±1.1</td>
<td>1.35±1</td>
<td>NS</td>
</tr>
<tr>
<td>Alfa-fetoprotein (ng/ml)</td>
<td>12.5±26</td>
<td>10.8±21</td>
<td>NS</td>
</tr>
<tr>
<td>Child’s stage</td>
<td>14B, 4C</td>
<td>7A, 8B, 3C</td>
<td></td>
</tr>
<tr>
<td>Child-Pugh score</td>
<td>8.3±1.2</td>
<td>6.7±1.8</td>
<td>&lt;0.013</td>
</tr>
</tbody>
</table>

AST: aspartate aminotransferase; ALT: alanine aminotransferase; NS: Not significant; PT: Prothrombin time.

35 patients
Chils’s B/C: 28/72
Rx with lamivudine

5 deaths < 6Ms

23 treated > 6Ms
(mean, 19M)

7 OLT <6Ms

1 no improvement
OLT at 16 M

1 no improvement
OLT at 16 M

22 improved

20 alive 57%

2 deaths
SBP at 17M; HCC at 31M

Villeneuve et al. Hepatology 2000
77 patients enrolled

47 transplanted

(Rx 38M)

30 not transplanted

(Rx: 26 M)

5 treated < 12 weeks

42 > 12 weeks

3 deaths; 2 withdrawals

3 withdrawn at week 1

27 treated > 1 week

22 treated > 52 weeks

Perrillo RP et al. Hepatology 2001
### Table 2. Results of Virologic Testing in 37 Transplanted Patients Completing at Least 52 Weeks of Treatment Posttransplantation

<table>
<thead>
<tr>
<th></th>
<th>Day −1*</th>
<th>Week 52</th>
<th>Week 104</th>
<th>Week 156</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBsAg (+)</td>
<td>34/34 (100)†</td>
<td>12/37 (32)</td>
<td>9/29 (31)</td>
<td>9/22 (41)</td>
</tr>
<tr>
<td>HBeAg (+)</td>
<td>15/34 (44)†</td>
<td>7/37 (19)</td>
<td>6/29 (21)</td>
<td>6/22 (27)</td>
</tr>
<tr>
<td>HBV DNA (+)</td>
<td>6/37 (16)</td>
<td>10/37 (27)</td>
<td>19/29 (66)</td>
<td>11/22 (50)</td>
</tr>
<tr>
<td><strong>HBV DNA (+) at baseline‡</strong>&lt;br&gt;<strong>(n = 20)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBsAg (+)</td>
<td>18/18 (100)</td>
<td>9/20 (40)</td>
<td>9/18 (50)</td>
<td>9/15 (60)</td>
</tr>
<tr>
<td>HBeAg (+)</td>
<td>13/18 (72)</td>
<td>6/20 (30)</td>
<td>6/18 (33)</td>
<td>6/15 (40)</td>
</tr>
<tr>
<td>HBV DNA (+)</td>
<td>5/20 (25)</td>
<td>6/20 (30)</td>
<td>11/18 (61)</td>
<td>9/15 (60)</td>
</tr>
<tr>
<td><strong>HBV DNA (−) at baseline</strong>&lt;br&gt;<strong>(n = 17)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBsAg (+)</td>
<td>16/16 (100)</td>
<td>3/17 (18)</td>
<td>0/11 (0)</td>
<td>0/7 (0)</td>
</tr>
<tr>
<td>HBeAg (+)</td>
<td>2/16 (13)</td>
<td>1/17 (6)</td>
<td>0/11 (0)</td>
<td>0/7 (0)</td>
</tr>
<tr>
<td>HBV DNA (+)</td>
<td>1/17 (6)</td>
<td>4/17 (24)</td>
<td>8/11 (73)</td>
<td>2/7 (29)</td>
</tr>
</tbody>
</table>

*Day −1 represents day immediately preceding transplantation.
†HBsAg and HBeAg results not available in all patients.
‡Baseline represents value prior to initiation of lamivudine.
**Table 3. Results of Virologic Testing in 27 Nontransplanted Patients**

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n = 27)</th>
<th>Week 52 (n = 22)</th>
<th>Week 104 (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg (+)</td>
<td>27/27 (100)</td>
<td>5/5 (100)*</td>
<td>16/17 (94)</td>
</tr>
<tr>
<td>HBeAg (+)</td>
<td>20/27 (74)</td>
<td>2/6 (33)*</td>
<td>3/17 (18)</td>
</tr>
<tr>
<td>HBV DNA (+)</td>
<td>19/27 (70)</td>
<td>5/22 (23)</td>
<td>5/17 (29)</td>
</tr>
</tbody>
</table>

NOTE. Data does not include 3 patients who completed less than 1 week of lamivudine (see text for details).

*HBsAg and HBeAg results not available in all patients.
162 LAM (+)

147 LAM (-)

91 LT

84 LT

71 non-LT

83 non-LT

18 Deaths

10 Deaths

12 Delisted (16.9%)

7 Delisted (8.4%)

41 Still waiting

46 Still waiting

Fontana RJ et al. Liver Transpl 2002
Median Lamivudine treatment 16 Ms

N=129 88%
N=154 73%
N=25

Fontana RJ et al. Gastroenterology 2002
Multivariate Cox Regression Model of Pretreatment Characteristics and 6-Month Mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>SE of estimate</th>
<th>Risk Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>0.311</td>
<td>5.23 (2.84-9.63)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>0.084</td>
<td>1.69 (1.43-1.99)</td>
<td>0.0001</td>
</tr>
<tr>
<td>HBV DNA (+/-)</td>
<td>0.751</td>
<td>6.13 (1.41-26.76)</td>
<td>0.0158</td>
</tr>
</tbody>
</table>

Fontana RJ et al. Gastroenterology 2002
# Studies of Lamivudine in Decompensated HBV Cirrhosis

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Child B/C</th>
<th>Median Follow-up (months)</th>
<th>%Viral Resistance</th>
<th>%Survival</th>
<th>% Transplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Uncontrolled, open label</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yao FY et al. 2000 (UCSF)</td>
<td>13</td>
<td>0/100</td>
<td>15</td>
<td>7</td>
<td>100</td>
<td>15</td>
</tr>
<tr>
<td>Kapoor D et al. 2001 (India)</td>
<td>18</td>
<td>78/22</td>
<td>18</td>
<td>17</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Villeneuve et al. 2000 (Canada)</td>
<td>35</td>
<td>28/72</td>
<td>19</td>
<td>13</td>
<td>70</td>
<td>20</td>
</tr>
<tr>
<td>Perrillo RP et al. 2001 (North America)</td>
<td>77</td>
<td>NA</td>
<td>26</td>
<td>21</td>
<td>96</td>
<td>61</td>
</tr>
<tr>
<td><strong>Controlled, open label</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yao FY et al. 2001 (UCSF)</td>
<td>23</td>
<td>0/100</td>
<td>13</td>
<td>10</td>
<td>100</td>
<td>35</td>
</tr>
<tr>
<td>Fontana RJ et al. 2002 (North America)</td>
<td>162</td>
<td>NA</td>
<td>10</td>
<td>11</td>
<td>83</td>
<td>56</td>
</tr>
</tbody>
</table>
Severe Acute Exacerbation-Lamivudine vs Entecavir

Table 2. Clinical outcomes of patients with severe acute exacerbation of chronic hepatitis B on entecavir and lamivudine treatment.

<table>
<thead>
<tr>
<th>Outcome, n (%)</th>
<th>Entecavir (N = 36)</th>
<th>Lamivudine (N = 117)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death within 30 days</td>
<td>4 (11)</td>
<td>2 (2)</td>
<td>0.028</td>
</tr>
<tr>
<td>Death between 30 days and 48 weeks</td>
<td>3 (8)</td>
<td>3 (3)</td>
<td>0.14</td>
</tr>
<tr>
<td>Mortality among cirrhotic patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death within 30 days</td>
<td>0/5 (0)</td>
<td>1/25 (4)</td>
<td>1.0</td>
</tr>
<tr>
<td>Death between 30 days and 48 weeks</td>
<td>2/5 (40)</td>
<td>1/25 (4)</td>
<td>0.064</td>
</tr>
<tr>
<td>Cause of death (first 48 weeks)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver failure</td>
<td>6 (17)</td>
<td>4 (3)</td>
<td>0.012</td>
</tr>
<tr>
<td>Other malignancies</td>
<td>1 (3)</td>
<td>1 (1)</td>
<td>0.42</td>
</tr>
<tr>
<td>Liver-related complications (first 48 weeks)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>6 (17)</td>
<td>4 (3)</td>
<td>0.012</td>
</tr>
<tr>
<td>Variceal bleeding</td>
<td>3 (8)</td>
<td>3 (3)</td>
<td>0.14</td>
</tr>
<tr>
<td>Ascites</td>
<td>4 (11)</td>
<td>2 (2)</td>
<td>0.028</td>
</tr>
<tr>
<td>Spontaneous bacterial peritonitis</td>
<td>0</td>
<td>1 (1)</td>
<td>1.0</td>
</tr>
<tr>
<td>Hepatorenal syndrome</td>
<td>2 (6)</td>
<td>2 (2)</td>
<td>0.24</td>
</tr>
<tr>
<td>Hospital stay (days)*</td>
<td>7 (1-35)</td>
<td>6 (1-62)</td>
<td>0.95</td>
</tr>
</tbody>
</table>

*Median (range).
Severe Acute Exacerbation-
Lamivudine vs Entecavir

Fig. 1. Kaplan–Meier estimates of time to (A) death and (B) liver-related death in patients on entecavir (solid line) and lamivudine (dotted line) treatment.

Wong VW et al. J hepatol 2011;54:232-246
Severe Acute Exacerbation—Lamivudine vs Entecavir

Table 4: Factors associated with overall and liver-related mortality at week 48.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Univariate Hazard ratio</th>
<th>95% CI</th>
<th>p</th>
<th>Multivariate Hazard ratio</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall mortality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.06</td>
<td>1.02-1.10</td>
<td>0.006</td>
<td>1.03</td>
<td>0.98-1.08</td>
<td>0.31</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.39</td>
<td>0.12-1.29</td>
<td>0.52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline ALT (IU/L)</td>
<td>1.00</td>
<td>1.00-1.10</td>
<td>0.50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline bilirubin (umol/L)</td>
<td>1.00</td>
<td>1.00-1.01</td>
<td>0.036</td>
<td>1.00</td>
<td>1.00-1.01</td>
<td>0.38</td>
</tr>
<tr>
<td>Baseline albumin (g/L)</td>
<td>0.05</td>
<td>0.06-1.05</td>
<td>0.28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline INR</td>
<td>5.9</td>
<td>3.1-11.3</td>
<td>&lt;0.001</td>
<td>3.4</td>
<td>1.8-6.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline HBeAg</td>
<td>0.11</td>
<td>0.014-0.85</td>
<td>0.034</td>
<td>0.18</td>
<td>0.020-1.5</td>
<td>0.12</td>
</tr>
<tr>
<td>Baseline HBV DNA (log copies/ml)</td>
<td>1.02</td>
<td>0.73-1.43</td>
<td>0.89</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>2.1</td>
<td>0.64-7.0</td>
<td>0.22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antiviral therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamivudine</td>
<td>Referent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entecavir</td>
<td>5.0</td>
<td>1.6-15.7</td>
<td>0.006</td>
<td>5.1</td>
<td>1.5-17.2</td>
<td>0.010</td>
</tr>
<tr>
<td>Time from presentation to starting antiviral drugs (days)</td>
<td>0.04</td>
<td>0.07-1.15</td>
<td>0.56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Liver-related mortality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.07</td>
<td>1.02-1.12</td>
<td>0.004</td>
<td>1.05</td>
<td>1.00-1.11</td>
<td>0.058</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.29</td>
<td>0.082-1.03</td>
<td>0.056</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline ALT (IU/L)</td>
<td>1.00</td>
<td>1.00-1.00</td>
<td>0.58</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline bilirubin (umol/L)</td>
<td>1.00</td>
<td>1.00-1.01</td>
<td>0.038</td>
<td>1.00</td>
<td>1.00-1.01</td>
<td>0.56</td>
</tr>
<tr>
<td>Baseline albumin (g/L)</td>
<td>0.91</td>
<td>0.82-1.00</td>
<td>0.057</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline INR</td>
<td>6.4</td>
<td>3.3-12.5</td>
<td>&lt;0.001</td>
<td>4.2</td>
<td>2.1-8.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline HBeAg</td>
<td>0.14</td>
<td>0.017-1.06</td>
<td>0.057</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline HBV DNA (log copies/ml)</td>
<td>1.17</td>
<td>0.78-1.76</td>
<td>0.46</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>2.8</td>
<td>0.79-9.9</td>
<td>0.11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antiviral therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamivudine</td>
<td>Referent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entecavir</td>
<td>5.2</td>
<td>1.5-18.6</td>
<td>0.010</td>
<td>4.0</td>
<td>1.0-15.7</td>
<td>0.044</td>
</tr>
<tr>
<td>Time from presentation to starting antiviral drugs (days)</td>
<td>0.97</td>
<td>0.80-1.17</td>
<td>0.73</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ALT, alanine aminotransferase; CI, confidence interval; HBeAg, hepatitis Be antigen; HBV, hepatitis B virus; INR, international normalized ratio.

Wong VW et al. J hepatol 2011;54:232-246
Entecavir versus lamivudine in the treatment of chronic hepatitis B patients with hepatic decompensation.


Department of Internal Medicine, E-Da Hospital/I-Shou University, Kaohsiung, Taiwan.

Antivir Ther 2011
Abstract

BACKGROUND:
Lamivudine has been widely used in chronic hepatitis B patients with hepatic decompensation, but its use is limited by drug resistance. This outcome research aimed to investigate the comparative efficacy and safety of entecavir versus lamivudine in decompensated patients.

METHODS:
Between November 2004 and February 2010, 126 consecutive treatment-naive patients received either entecavir (n=53) or lamivudine (n=73) for decompensated chronic hepatitis B. All patients presented with both hyperbilirubinaemia and coagulopathy. Primary outcome was mortality within 1 year; secondary outcomes included liver-related mortality, biochemical and virological response, and improvement of hepatic dysfunction.

RESULTS:
Both treatment groups were comparable in baseline characteristics. A total of 19 (35.8%) entecavir and 33 (45.2%) lamivudine receivers expired within 1 year, respectively (P=0.29, log rank test). Age (hazard ratio [HR] 1.04 per year, 95% CI 1.01, 1.06), cirrhosis (HR 2.07, 95% CI 1.02, 4.23), and international normalized ratio for prothrombin time (HR 1.44, 95% CI 1.20, 1.74) were independent baseline predictors for all-cause mortality. Antiviral therapy was also unrelated to liver-specific death. However, more patients taking entecavir tended to attain aminotransferase normalization (76.5% versus 52.5%; P=0.05) and viral DNA undetectability (100% versus 58.3%; P=0.06). Moreover, entecavir was associated with significantly greater reduction of the model for end-stage liver disease scores (median 10.0 versus 4.3; P=0.02). Overall, 3 (7.5%) lamivudine but no entecavir users acquired drug resistance in 1 year (P=0.25).

CONCLUSIONS:
Entecavir as compared with lamivudine is similar in the effect on short-term mortality but is associated with greater clinical improvement among chronic hepatitis survivors who recovered from hepatic decompensation.
Mexico, or India, but cases in the US without associated travel are beginning to be reported. With acute viral hepatitis, as with many other etiologies of ALF, care is mainly supportive. Of note, the nucleoside analog lamivudine (and possibly other nucleos(t)ide analogues), used widely in the treatment of chronic hepatitis B, may be considered in patients with acute hepatitis B, although evidence of efficacy is equivocal. Acute liver failure due to reactivation of
<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbsAg(+)</td>
<td>HbsAg(+)</td>
<td>HbsAg(+)&gt;6M</td>
<td>HbsAg(+)&gt;6M</td>
<td>HbsAg(+)&gt;6M</td>
<td>HbsAg(+)</td>
<td>HbsAg(+)</td>
<td>Anti-HCV(+)</td>
</tr>
<tr>
<td>PT&lt;3s</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HBeAg(+) &gt;3M</td>
<td>HBeAg(+)&gt;3M</td>
<td></td>
</tr>
<tr>
<td>Bil&gt;2mg/dl</td>
<td></td>
<td></td>
<td></td>
<td>ALT&lt;5x</td>
<td>ALT&lt;5x</td>
<td></td>
<td>HBeAg(-)&gt;3M</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HBeAg(-)&gt;3M</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HBeAg(+) &gt;3M</td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Lamivudine**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**Entecavir**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**Telbivudine**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**HBeAg(+) >3M**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**HBeAg(-)>3M**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**Anti-HCV(+)**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**HBeAg(+) >3M**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**Anti-HCV(+)**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**HBeAg(+) >3M**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**Anti-HCV(+)**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**HBeAg(+) >3M**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**Anti-HCV(+)**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**HBeAg(+) >3M**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**Anti-HCV(+)**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**HBeAg(+) >3M**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |

**Anti-HCV(+)**
- 1.  |  |  |  |  |  |  |  |
- 2.  |  |  |  |  |  |  |  |
Thanks for your attention