Table 3. Maternal Hepatitis Deaths in PROMISE

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median Age (IQR), years</th>
<th>Median BMI</th>
<th>Median CD4 cells/mm³</th>
<th>HBsAg at PROMISE entry</th>
<th>Grade 3 or 4 ALT elevation prior to delivery</th>
<th>EFV Initiation Study Weeks to delivery, median (IQR)</th>
<th>Prior Risk Group</th>
<th>PH-2NR2I</th>
<th>No ARVs</th>
<th>ZDV or ZDV+</th>
<th>AZT or AZT+DDV</th>
<th>NVP/TDF tail</th>
<th>Other</th>
<th>PRF/2 Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH-2NR2I</td>
<td>723 (31%)</td>
<td>22 (16-32)</td>
<td>625 (466-839)</td>
<td>82 (4%)</td>
<td>24 (1%)</td>
<td>114.1 (65-159.4)</td>
<td>1236 (53%)</td>
<td>723</td>
<td>723</td>
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<td>723</td>
<td>103</td>
<td>723</td>
</tr>
<tr>
<td>No ARVs</td>
<td>1432 (62%)</td>
<td>25 (19-33)</td>
<td>58 (33)</td>
<td>105 (6.4%)</td>
<td>122 (1.7%)</td>
<td>53 (32)</td>
<td>136 (5%)</td>
<td>723</td>
<td>723</td>
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<td>723</td>
<td>723</td>
<td>103</td>
<td>723</td>
</tr>
<tr>
<td>ZDV or ZDV+</td>
<td>105 (6.4%)</td>
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<td>723</td>
<td>103</td>
<td>723</td>
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<tr>
<td>NVP/TDF tail</td>
<td>58 (33)</td>
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<td>723</td>
<td>103</td>
<td>723</td>
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<tr>
<td>Other</td>
<td>103 (4%)</td>
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<td>103</td>
<td>723</td>
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<tr>
<td>PRF/2 Ref</td>
<td>103 (4%)</td>
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<td>723</td>
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</tbody>
</table>

*Overall p value is represented here, pair-wise p values for prior ARVs are also presented in parentheses.

- In MV analysis, older age was significantly associated with increased risk of grade 3/4 LEE PP after EFV initiation (HR per 5 years 1.35 CI 1.06-1.71). There was a trend toward increased risk with CD4 in the PROMOTE study.

Conclusions

- **EFV Grade 3 or 4**
  - Grade 3 or 4 hepatitis toxicity rate in PROMISE similar to meta-analysis data of 3.2% and morality of 0.2%.
  - Most women asymptomatic, however serious toxicity resulting in deaths among women on EFV did occur (2 out of 3 months of PROMOTE ending).
  - Older age was the only risk factor noted among this risk with CD4 and grade 3/4 LEE.
  - Monitoring for ALT abnormalities may prevent unnecessary deaths but research needed to identify frequency and WHO high risk groups.
  - **THE PROMOTE study will monitor for hepatitis toxicity in long term follow up of PROMISE participants including during repeat pregnancies.
  - Limitation: Most women in PROMISE did not initiate EFV in pregnancy or early postpartum which is a higher risk period for hepatitis toxicity.

Acknowledgements

- Study participants who participated in the PROMISE (107BF8101-107BF study along with their institutions.
- Members of the site and the Community Advisory Board for their support.
- Study staff and personnel at all the PROMISE sites.
- Pediatric antiretroviral treatment (PPT) regimen of the national and regional programs as additional resource.
- The PROMOTE study will monitor for hepatitis toxicity in long term follow up of PROMISE participants including during repeat pregnancies.
- Limitation: Most women in PROMISE did not initiate EFV in pregnancy or early postpartum which is a higher risk period for hepatitis toxicity.

References

5) Series (2010).