Use of integrase inhibitors in HIV-positive pregnant women: Data from the Frankfurt HIV Cohort

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Background: Integrase inhibitors (INSTI) are highly recommended for the treatment of HIV-positive adults including women of reproductive age. However there are concerns about the use of INSTI in pregnant women. Decreased drug levels of elvitegravir/cobicistat in late pregnancy can potentially result in virologic failure and increase the risk of HIV-mother-to-child-transmission (MTCT). For dolutegravir (DTG) a so called „Red Hand Letter“ has just been sent out in June 2018. Neural tube defects occurred in a small number of neonates whose mothers had been treated with DTG in early pregnancy. In this retrospective study we analysed the maternal and infant outcome of INSTI versus non-INSTIT containing ART during pregnancy in the Frankfurt HIV Cohort.

Method: All women of the Frankfurt HIV Cohort who gave birth between January 2008 and June 2018 were included in this retrospective analysis. Primary objective: virologic response defined as viral load (VL) <50 copies/mL at the time of delivery. Secondary objectives: rate of HIV-mother-to-child-transmissions and the rate of malformations in the ART exposed children. For all parameters we performed a subanalysis of INSTI- and non-INSTIT containing regimen. Table 1 shows characteristics of the INSTI and the non-INSTIT group.

Results: We observed 274 pregnancies resulting in 281 children (5 twins + 1 triplet). INSTI based regimen were used in 52 pregnancies (19%), predominantly raltegravir (n=48); DTG (n=4). 3 of the 4 DTG-based regimen were switched toRAL during pregnancy (pregnancy week 4, 15 and 18). There were 21 conceptions (40%) on INSTI containing ART. Table 2 shows the last lab results before delivery and the number of mother-to-child-transmissions.

Conclusions: We observed 274 pregnancies of HIV positive women, resulting in 281 children. 52 (19%) of the pregnant women received INSTI based ART; 48 raltegravir and 4 dolutegravir. Despite the significant shorter intratero-exposure to ART in the INSTI arm - due to a higher rate of late presenters in this group - there were no differences between the INSTI and non-INSTIT group in terms of virologic response, vertical HIV transmission and the rate of congenital malformations in the exposed neonates.

Table 1: Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>INSTI Group</th>
<th>Non-INSTIT Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years, mean ± SD)</td>
<td>32.0 ± 5.6</td>
<td>32.1 ± 5.6</td>
</tr>
<tr>
<td>Range (years)</td>
<td>19 - 47</td>
<td>20 - 45</td>
</tr>
<tr>
<td>Origin (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>49.6</td>
<td>48.6</td>
</tr>
<tr>
<td>Western Europe</td>
<td>17</td>
<td>26.8</td>
</tr>
<tr>
<td>Asia</td>
<td>5.3</td>
<td>5.9</td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>11.3</td>
<td>10.8</td>
</tr>
<tr>
<td>Latin America</td>
<td>3.3</td>
<td>2.7</td>
</tr>
<tr>
<td>South Europe</td>
<td>6.4</td>
<td>1.9</td>
</tr>
<tr>
<td>North Africa</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Unknown</td>
<td>1.4</td>
<td>2.9</td>
</tr>
<tr>
<td>ART Start (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before pregnancy</td>
<td>62.8</td>
<td>60.5</td>
</tr>
<tr>
<td>1. Trimetor</td>
<td>6.6</td>
<td>6.8</td>
</tr>
<tr>
<td>2. Trimetor</td>
<td>17.2</td>
<td>17.1</td>
</tr>
<tr>
<td>3. Trimetor</td>
<td>6</td>
<td>7.2</td>
</tr>
<tr>
<td>Unknown</td>
<td>5.4</td>
<td>5.4</td>
</tr>
<tr>
<td>CD4 count (median ± SD)</td>
<td>492 ± 262</td>
<td>471.5 ± 241.2</td>
</tr>
<tr>
<td>Range</td>
<td>0 - 1385</td>
<td>13 - 1325</td>
</tr>
<tr>
<td>Viral load (copies/mL, mean ± SD)</td>
<td>58.4</td>
<td>61.5</td>
</tr>
<tr>
<td>Range</td>
<td>50 - 240000</td>
<td>50 - 350000</td>
</tr>
</tbody>
</table>

Table 2: Last lab results before delivery

<table>
<thead>
<tr>
<th>Outcome (last values before childbirth)</th>
<th>INSTI Group</th>
<th>Non-INSTIT Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 count (med ± SD)</td>
<td>521.8 ± 237.1</td>
<td>510.4 ± 232.0</td>
</tr>
<tr>
<td>Range</td>
<td>0 - 1477</td>
<td>0 - 1368</td>
</tr>
<tr>
<td>Viral load &lt;50 copies/mL</td>
<td>81.4</td>
<td>81.1</td>
</tr>
<tr>
<td>Viral load &gt;50 copies/mL</td>
<td>167272.2</td>
<td>167272.2</td>
</tr>
<tr>
<td>Range</td>
<td>50 - 174000</td>
<td>50 - 174000</td>
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<tr>
<td>MTCT</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 3: CD4 count and VL close to delivery and vertical transmissions