Does Early Treatment Provide Long Term Benefit in HIV-1 Infected Infants? Five Year Outcomes in Children Treated Before 3 Months of Age in the PENTA 7 Trial.

**Abstract**

**Background**

Treating HIV-1 infected infants early after birth remains a crucial issue. Guidelines from different countries differ in whether to start immediate or delayed therapy in asymptomatic children <12 months of age. In PENTA 7, 20 infants received ddI+d4T+Nelfinavir before 3 months of age. Clinical and immunological benefit was seen at 18 months. However virological failure and emergence of resistance was a major concern. We describe long-term response to 5 years.

**Trial Design and Methods**

Phase III, non randomised study to assess the toxicity, tolerability and activity of triple therapy ddI+d4T+Nelfinavir in vertically HIV-1 infected children aged less than 3 months.

- Clinical events, CD4 cell counts and percentages, HIV-1 RNA, antiretroviral therapy, weight and height measurements were collected every 3 months between 18 months and 3 years and annually beyond 3 years.

**Results (Follow up, Events, ART, HIV-1 RNA, CD4, growth)**

**BASELINE CHARACTERISTICS**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Female</th>
<th>Male</th>
<th>N</th>
<th>9 : 11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnic origin</td>
<td>White</td>
<td>Black African</td>
<td>Black Caribbean</td>
<td>Other</td>
</tr>
<tr>
<td>Median (range) age in months</td>
<td>2.6 (0.9 – 4.7)</td>
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<tr>
<td>Median (range) weight (kg) at birth</td>
<td>3.0 (0.7 – 3.6)</td>
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<tr>
<td>Median (range) weight (kg) at last entry:</td>
<td>4.8 (1.7 – 5.2)</td>
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</tbody>
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**CHANGES IN HIV-1 RNA**

HIV-1 RNA still continued to decrease by 5 years of follow-up. The mean (range) change in log HIV-1 RNA from baseline was 2.9 (0.9 – 5.1) and half of the children were under 400 copies/ml.

**CHANGES IN CD4 %, CD4 ADJUSTED BY AGE**

By year 5, CD4% values ranged from 22% to 44%. The median increase in CD4 z-score change from baseline was +0.66 (range -5.29 to 3.76, p<0.19).

**DISCUSSION**

Early treatment in HIV-1 infected children is recommended in several guidelines as it can prevent immune deterioration and severe clinical progression. In the PENTA 7 study, infants treated with ddI+d4T-NFV before 3 months of age showed a good clinical and immunological improvement and no major toxicity. Despite a rapid decrease in HIV-1 RNA, viral load was not completely suppressed with the subsequent emergence of resistance mutations. Difficulties in administration of this initial regimen and pharmacokinetic issues of NFV were probably the main reasons for a poor virological response.

By 5 years, no AIDS progression or severe stage B were reported and no clinical lipodystrophy was detected by clinicians. From 19 children alive, I withdrew consent at 3.8 years. Out of the remaining 18, 2 were still on their initial regimen and 4 discontinued drugs permanently (3 for poor compliance and 1 who was completely suppressed due to parents’ request). The majority of children who had switched from the trial therapy are on second line therapy either on PI based regimen (6) or NRTI based (12). Only 2 children are on third line therapy and receive both PI and NNRTI.

No additional resistance mutations were reported after initial switches. Furthermore, all evaluable children had low baseline HIV-1 RNA. The proportion of children with VL< 400 copies/ml (56%) is slightly better than that observed at 18 months (47%). Immunological improvement observed at 3 years was maintained at 5 years with a median CD4% of 31%. Children are growing well and changes in height and weight z-scores are still statistically significant at 5 years.

**Conclusion**

Children treated very early in life in this non comparative study are still experiencing clinical and immunological benefit of HAART at 5 years but the majority of them are not taking the initial regimen. Initial regimen with potent, suitable and palatable drugs may prevent early switches and thus preserve future drug options.

**Participants**

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