ARROW study design and baseline characteristics

**AntiRetroviral Research for Watoto**

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**ARROW STUDY DESIGN**

A 5-year, open-label randomized trial in 1200 HIV-infected children from 3 sites in Uganda (n=800) and one in Zimbabwe (n=400), addressing two strategic management questions:

1. Can children on Anti-Retroviral Therapy (ART) be safely monitored by clinical assessment, without routine laboratory monitoring of toxicity or CD4 count?
   
   **Clinically Driven Monitoring (CDM)**
   
   Clinical & laboratory monitoring 12 weekly, but haematology / biochemistry results only returned to clinician if grade 4 AE or requested for a clinical reason; CD4 results not returned versus
   
   **Laboratory and Clinical Monitoring (LCM)**
   
   Clinical & laboratory monitoring 12 weekly; All results returned

2. Does induction with 4 drugs, followed by 3-drug maintenance, improve outcome in those with high viral loads?

- First use worldwide of scored tablets (which can be dispersed) of ABC, 3TC and Combivir (3TC+ZDV),
- First use of ABC as first-line therapy in African children

**BASELINE CHARACTERISTICS**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children randomised to and including 30 May 2008</td>
<td>870</td>
<td>73%</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>439</td>
<td>51%</td>
</tr>
<tr>
<td>Female</td>
<td>431</td>
<td>49%</td>
</tr>
<tr>
<td>Vertical Exposure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>857</td>
<td>99%</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5 – 2</td>
<td>253</td>
<td>29%</td>
</tr>
<tr>
<td>3 – 6</td>
<td>227</td>
<td>26%</td>
</tr>
<tr>
<td>7 – 12</td>
<td>367</td>
<td>42%</td>
</tr>
<tr>
<td>13 +</td>
<td>23</td>
<td>3%</td>
</tr>
<tr>
<td>WHO stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>17</td>
<td>2%</td>
</tr>
<tr>
<td>II</td>
<td>238</td>
<td>27%</td>
</tr>
<tr>
<td>III</td>
<td>511</td>
<td>59%</td>
</tr>
<tr>
<td>IV</td>
<td>104</td>
<td>12%</td>
</tr>
<tr>
<td>CD4 percent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 – 4 %</td>
<td>156</td>
<td>18%</td>
</tr>
<tr>
<td>5 – 9 %</td>
<td>196</td>
<td>23%</td>
</tr>
<tr>
<td>10 – 14 %</td>
<td>236</td>
<td>27%</td>
</tr>
<tr>
<td>15 + %</td>
<td>271</td>
<td>31%</td>
</tr>
<tr>
<td>Missing</td>
<td>11</td>
<td>1%</td>
</tr>
</tbody>
</table>

**ARROW PARTICIPANTS**

- Are younger than most African cohorts of children starting ART (Median age 6; one third of ARROW children <2 years)
- Are severely immuno-compromised (Median CD4% 11%; two thirds of ARROW children <15%)
- Are markedly wasted and stunted (Approx. 50% z-score <2)
- Are switching to tablets at an early age (Median=3.9 years)

**ON-GOING SUB-STUDIES**

- Adherence, Acceptability and Pharmacokinetics of scored tablets in all children and of syrups versus tablets in young children
- Pharmaco kinetic data on twice versus once daily ABC and 3TC
- Effects of Malnutrition on Pharmacokinetics of ABC, 3TC, ZDV and EFV
- Immunological and Virological responses to ART

**COLLABORATORS and ACKNOWLEDGEMENTS**

We thank all the patients and staff from all the centres participating in the ARROW trial.

**NOTES**

First-line drugs are:

- NNRTI: Nelfinavir (NVP); Efavirenz (EFV)
- NRTI: Abacavir (ABC); Lamivudine (3TC); Zidovudine (ZDV)
- First-line drugs are:
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- NNRTI: Nevirapine (NVP); Efavirenz (EFV)

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