EFFECTIVENESS AND SAFETY OF LPV/R PELLETS-BASED ART IN CHILDREN: 48-WEEK ANALYSIS

Isabelle Andrieux-Meyer1, Olawale Salami2, Raymond Omollo3, Thaddeus Egondi2, Victor Musiime2, Dalton Wamalwa4, Elizabeth Maleche Obimbo4, Adeodata Kekibliwa2, Juliet Mwanga-Arnumpaire4, Patrick Oyar4, Elizabeth A. Bukusi4, Joseph Mbutia3, Moses Waweru2, Monique Wasunna2, Janice Lee3, François Simon3, Marc Laliemant4, for the LIVING STUDY GROUP.

1Drugs for Neglected Diseases Initiative, Geneva, Switzerland; 2Drugs for Neglected Diseases Initiative, Nairobi, Kenya. 3Joint Clinical Research Centre, Kampala, Uganda *University of Nairobi, Nairobi, Kenya. 4Baylor College of Medicine Children’s Foundation, Kampala, Uganda, Epicentre, Mbarara, Uganda, 7Kenya Medical Research Institute, Nairobi, Kenya, 8Gertrudes’ children’s Hospital, Nairobi, Kenya.

Background

Despite the WHO recommendation to use LPV/r-based treatment for all children <3 years, current formulations do not meet the needs of children and caregivers.

A palatable, heat-stable, easy-to-administer pellet formulation of LPV/r has received tentative USFDA approval for use in infants and young children. However, there is a lack of clinical data on its effectiveness and safety in routine care.

Study Objective

The LIVING study aimed to test the effectiveness, safety, pharmacokinetics, and acceptability of LPV/r pellets with ABC/3TC (or AZT/3TC) dispersible tablets under field conditions in HIV infected infants and young children who cannot swallow tablets.

Methods

Study Design

- Single arm phase IIb implementation study
- open-label
- prospective
- non-randomized
- non-comparative
- multicenter, multi-country

Inclusion criteria

- HIV infected children
- ARV naïve, or already on first line liquid lopinavir based treatment, or failing first line, weight ≥3 and <25 kg at the time of enrolment (age is not an inclusion criterion)
- NNRTI based therapy
- Unable to swallow tablets

- Dosing of LPV/r pellets followed WHO weight bands
- Observation of pellets administration performed at clinic

Results

(1) PATIENT DISPOSITION

Enrolled (n = 610)

- ARV experienced 552 (NNRTI = 39; NNRTI+LPV/r = 513; ARV naïve = 58)

Visit Month 3 (n = 467)

Visit Month 6 (n = 377)

Visit Month 12 (n = 220)

(2) BASELINE CHARACTERISTICS

- As of 31/07/17, 610 patients had been enrolled in Kenya and Uganda
- Cohort retention at 48 weeks was 88.7% (5 deaths).
- Baseline and WK 48 VL available in 220 children (49% female; 11% ART naïve, 84% switched from LPV/r and 5% from NVP based ART).
- Median age in months (IQR) was 11 (35.5%)
- Immunodeficiency, wasting, and stunting were present in 70%, 50%, and 35% of naïve respectively, 33%, 17%, and 7.8% of LPV/r and in 40%, 20%, and 14.3% of NVP exposed.

(3) EVOLUTION OF VIRAL SUPPRESSION STRATIFIED BY PRIOR TREATMENT EXPOSURE

HIV RNA VL (log10 copies/ml)

<table>
<thead>
<tr>
<th>Patient type</th>
<th>N</th>
<th>Median</th>
<th>IQR</th>
<th>&lt;1.7 (&lt;50cp/ml)</th>
<th>&lt;2.6 (&lt;400 cp/ml)</th>
<th>&lt;3&lt;1000 cp/ml</th>
<th>≥3&gt;1000cp/ml</th>
<th>Data available</th>
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<tbody>
<tr>
<td><strong>Enrollment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Naive</td>
<td>58</td>
<td>5.4</td>
<td>4.8 - 5.8</td>
<td>2 (3.8%)</td>
<td>5 (9.5%)</td>
<td>6 (11.4%)</td>
<td>47 (88.7%)</td>
<td>53</td>
</tr>
<tr>
<td>NNRTI+LPV/r</td>
<td>514</td>
<td>2.2</td>
<td>1.6 - 3.9</td>
<td>142 (29.5%)</td>
<td>279 (57.9%)</td>
<td>306 (63.5%)</td>
<td>177 (36.5%)</td>
<td>483</td>
</tr>
<tr>
<td>NNRTI</td>
<td>38</td>
<td>4.7</td>
<td>4.3 - 5.5</td>
<td>2 (5.3%)</td>
<td>4 (10.6%)</td>
<td>4 (10.6%)</td>
<td>33 (84.9%)</td>
<td>37</td>
</tr>
<tr>
<td>Overall</td>
<td>610</td>
<td>2.5</td>
<td>1.7 - 4.6</td>
<td>146 (25.5%)</td>
<td>288 (50.3%)</td>
<td>316 (55.2%)</td>
<td>257 (44.8%)</td>
<td>573</td>
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<td><strong>Week 24</strong></td>
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</tr>
<tr>
<td>Naive</td>
<td>31</td>
<td>2</td>
<td>1.3 - 3.5</td>
<td>11 (35.5%)</td>
<td>18 (58.1%)</td>
<td>20 (64.6%)</td>
<td>11 (35.4%)</td>
<td>31</td>
</tr>
<tr>
<td>NNRTI+LPV/r</td>
<td>322</td>
<td>1.7</td>
<td>1.3 - 2.5</td>
<td>160 (51.2%)</td>
<td>239 (76.6%)</td>
<td>250 (80.1%)</td>
<td>62 (19.9%)</td>
<td>312</td>
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<tr>
<td>NNRTI</td>
<td>25</td>
<td>1.8</td>
<td>1.3 - 2.5</td>
<td>11 (45.8%)</td>
<td>18 (75%)</td>
<td>20 (83.3%)</td>
<td>4 (16.7%)</td>
<td>24</td>
</tr>
<tr>
<td>Overall</td>
<td>378</td>
<td>1.7</td>
<td>1.3 - 2.6</td>
<td>182 (49.6%)</td>
<td>275 (74.9%)</td>
<td>290 (79%)</td>
<td>77 (21%)</td>
<td>367</td>
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<td><strong>Week 48</strong></td>
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</tr>
<tr>
<td>Naive</td>
<td>23</td>
<td>2.1</td>
<td>1.3 - 3.8</td>
<td>10 (43.5%)</td>
<td>15 (65.2%)</td>
<td>16 (69.6%)</td>
<td>7 (30.4%)</td>
<td>24</td>
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<tr>
<td>NNRTI+LPV/r</td>
<td>188</td>
<td>1.6</td>
<td>1.3 - 2.1</td>
<td>105 (56.8%)</td>
<td>152 (82.1%)</td>
<td>157 (84.9%)</td>
<td>28 (15.1%)</td>
<td>185</td>
</tr>
<tr>
<td>NNRTI</td>
<td>12</td>
<td>1.5</td>
<td>1.3 - 2.5</td>
<td>7 (58.3%)</td>
<td>9 (75%)</td>
<td>10 (83.3%)</td>
<td>2 (16.7%)</td>
<td>12</td>
</tr>
<tr>
<td>Overall</td>
<td>223</td>
<td>1.6</td>
<td>1.3 - 2.3</td>
<td>122 (55.4%)</td>
<td>176 (80%)</td>
<td>183 (83.2%)</td>
<td>37 (16.8%)</td>
<td>220</td>
</tr>
</tbody>
</table>

(4) IMMUNODEFICIENCY, WASTING AND STUNTING

- were present in 6.4%, 9% and 5% of naïve children, 21.7%, 2% and 3% of LPV/r exposed and 40%, 0%, and 14.3% of NVP exposed respectively at Wk48.

(5) ADVERSE EVENTS: 21 children had 67 AEs grade 3/4, 2 leading to treatment stoppage.

Conclusions

LPV/r pellets were well accepted with minimal safety concerns. Naïve patients, those failing NVP, as well as those switching from LPV/r liquid were well suppressed at week 48 and had recuperated immunologically and clinically.

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