LIVING: 48-week data on LPV/r pellets in 990 children in resource-limited settings


for the LIVING Study Team

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12. Drugs for Neglected Diseases initiative (Switzerland, Kenya and USA)
BACKGROUND

- LPV/r-based regimens remain an important treatment for children living with HIV (CLHIV), with established safety and efficacy. Treatment outcome data from large cohorts of CLHIV in resource-poor settings are limited. LIVING (NCT02346487) addresses this data gap across pediatric age groups.

AIM

Test the effectiveness, safety, and acceptability of LPV/r 40/10mg pellets given in combination with ABC/3TC (or AZT/3TC) dispersible tablets to CLHIV under field conditions.
METHODS

• Design: single-arm phase IIIb implementation studies in Kenya, Uganda and Tanzania; open-label, prospective, non-randomized, non-comparative

• Key Eligibility Criteria:
  • CLHIV;
  • ≥ 3 to <25kg;
  • ARV naïve, on liquid LPV/r or failing NNRTI based ART.

• Dosing: twice daily by WHO weight bands

• Clinical/Other assessments: Baseline, Week 2, 4, 12, and 12-weekly thereafter

• Acceptability: via caregiver questionnaire

• Primary endpoint = effectiveness, a composite of
  • Being alive;
  • Being on study drug;
  • Viral load < 1000cp/ml at Week 48.

WHO Weight Band Dosing

<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength</th>
<th>Number of doses by weight band morning &amp; evening</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>3-5.9 kg</td>
</tr>
<tr>
<td>LPV/r</td>
<td>Pellets 40mg/10mg</td>
<td>2</td>
</tr>
<tr>
<td>ABC/3TC</td>
<td>Tablet 60mg/30mg</td>
<td>1</td>
</tr>
<tr>
<td>AZC/3TC</td>
<td>Tablet 60mg/30mg</td>
<td>1</td>
</tr>
</tbody>
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RESULTS

- **Key disposition data:** 990/1003 received study drugs (ITT). 82% received ABC/3TC. 852 had VL at W48 (mITT).
- **At Baseline:** 51% female; age range from 2 to 148 months with 32% aged < 24 months; 91% ART exposed; 19% had VL ≥100,000 cp/ml; 32% with advanced/severe disease.
- **Median treatment duration:** 72.1 weeks (IQR 48.3-96.1).
- **Effectiveness and Efficacy:**

<table>
<thead>
<tr>
<th>Primary endpoint at <strong>W48</strong></th>
<th>ITT population n (% , 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VL&lt;1,000 copies/ml</td>
<td>683/990 (69, 66-72)</td>
</tr>
<tr>
<td>VL≥1,000 copies/ml</td>
<td>169/990 (17, 15-20)</td>
</tr>
<tr>
<td>No VL</td>
<td>138/990 (14, 12-16)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary efficacy endpoints</th>
<th>mITT population n (% , 95% CI)</th>
<th>PP population n (% , 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VL&lt;1,000 copies/ml at <strong>W48</strong></td>
<td>683/852 (80, 77-83)</td>
<td>569/692 (82, 79-85)</td>
</tr>
<tr>
<td>VL&lt;1,000 copies/ml at <strong>W96</strong></td>
<td>296/337 (88, 84-91)</td>
<td>235/265 (89, 84-92)</td>
</tr>
<tr>
<td>Immunological failure by <strong>W48</strong></td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Clinical failure by <strong>W48</strong></td>
<td>49/887 (6, 4-7)</td>
<td>21/686 (3, 2-5)</td>
</tr>
</tbody>
</table>

- **Safety:** 14% children had Gr3/4 AEs. Most frequent: malaria, pneumonia, gastroenteritis, anemia.
- 8% had treatment-related AEs (most frequent diarrhea) with 1 being a SAE. 17 deaths reported during entire study period (one related to AZT).
- **Acceptability:** at last assessment, 93% caregivers described the pellets as easy/very easy to administer and 94% reported their children accepted pellets well.
CONCLUSIONS

• LPV/r pellets plus ABC/3TC or AZT/3TC were effective, well-tolerated, and well-accepted in a large CLHIV cohort, with a significant proportion of children < 24 months and with advanced/severe disease.

• This combination remains a good treatment option for CLHIV, as an alternative 1st line or following failure on Dolutegravir-based ART.

ACKNOWLEDGEMENTS