P231  Lamivudine monotherapy as a safe option for HIV-infected paediatric clients with adherence challenges: new evidence from a large South African cohort
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P232  Potential drug-drug interactions in HIV-perinatally infected adolescents on antiretroviral therapy in Buenos Aires, Argentina
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Lamivudine monotherapy as a safe option for HIV-infected paediatric clients with adherence challenges: new evidence from a large South African cohort

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Background: HIV-infected children in resource-limited settings are a unique population who require antiretroviral therapy (ART) in the context of social (stigma, caregiver dependence) and structural (access, availability) barriers to adherence. Adherence to medical therapy can be challenging and is particularly so--given the requirement for lifelong daily medication, side effects, pill burden, the need for prolonged maintenance of therapy in the absence of symptoms and often in the absence of disclosure to the child patient. Few interventions have been shown to improve childhood and adolescent adherence to antiretroviral therapy.1 In South Africa, for children over 10kg and >3 years old, the recommended first-line regimen is abacavir (or prior to 2010 stavudine) plus lamivudine plus efavirenz, while the second-line regimen is zidovudine plus lamivudine plus ritonavir boosted lopinavir. In South African children who fail second-line regimens, access to a third line regimen is centrally controlled and not readily available. For this reason, clinicians are often reluctant to commence second-line therapy in children whose adherence is predicted to be poor, for fear of selecting resistant viral clones and compromising the success of future ART.2 For these reasons, lamivudine monotherapy (LM) has been employed by a number of clinicians for patients failing ART whose adherence was poor or who lacked other treatment options, in the belief that it offered superior viral suppression in comparison to complete cessation of therapy, which may lead to increased morbidity.

Methods: A retrospective review of all eligible LM events (26 months) from a cohort of two linked health facilities in the Eastern Cape Province was undertaken using initial data extracted from the Paediatric ART Data Management Tool (PADMT). These hospitals are located in one of the more resource-deprived of South Africa’s nine provinces.2 Eligible patient folders were abstracted to determine validity of the digital data and deemed eligible based on the criteria set forth by the research protocol. Ethical review for this study was undertaken and approved by Wolter Sisulu University. Eligible events were disaggregated according to absolute CD4 count at initiation (Group 1: >200 cells/µl, n=64; Group 2: ≤200 cells/µl, n=10). Study endpoints were defined as a decline of absolute CD4 ≤ 200 cells/µl (Group 1), WHO stage 3 or 4 event (Groups 1 & 2), or initiation of 2nd or 3rd line (Groups 1 & 2).

Results: 74 eligible LM events were identified among 71 HIV positive children (58% male; median age at LM 9.7 years and median LM duration 11.5 months). CD4 decreases and measured WHO stage 3 or 4 events did not yield overall significance between groups (Table 1). No deaths were recorded.

Conclusions: Observational studies of unplanned treatment interruptions in children—mainly carried out in resource-rich settings—have generally shown poor immunologic outcomes.3,4 While the rates of stage 3 or 4 events in these studies were not as high as those seen in our population, the different patient populations concerned could account for this. The data to date does not necessarily support a hypothesis that LM leads to equivalent immunologic outcomes as triple ART—therefore, switching from a successful ART regimen to monotherapy simply to reduce pill burden or provide a partial drug holiday would not be a beneficial strategy. LM may, however, be a viable option—particularly in resource-limited settings—for patients who are failing a triple-drug regimen and have no backup option, adolescents who refuse to comply with triple therapy but are willing to take one pill a day and children whose ART failure is due to caregiver inability to manage a more complex regimen.1 In all the above scenarios, LM should only be a limited beneficial strategy. LM may, however, be a viable option—particularly in resource-limited settings—for patients who are failing a triple-drug regimen and have no backup option, adolescents who refuse to comply with triple therapy but are willing to take one pill a day and children whose ART failure is due to caregiver inability to manage a more complex regimen.1 In all the above scenarios, LM should only be a limited

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Table 1. Characteristics for all patients initiated on Lamivudine monotherapy (LM); n=74 (74 initiations in 71 patients)

<table>
<thead>
<tr>
<th>All LM Initiations</th>
<th>LM Initiation with CD4 &lt;200 (n=64)</th>
<th>LM Initiation with CD4 &gt;200 (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>43 (58)</td>
<td>38 (59)</td>
</tr>
<tr>
<td>Female</td>
<td>31 (42)</td>
<td>26 (41)</td>
</tr>
<tr>
<td>Age at LM initiation, years*</td>
<td>9.7 (5-11.8)</td>
<td>9.0 (6.4-11.2)</td>
</tr>
<tr>
<td>Duration of LM, months*</td>
<td>24.5 (16.5-32.4)</td>
<td>24.5 (13.9-35.0)</td>
</tr>
<tr>
<td>Patients switched to 2nd line*</td>
<td>17 (23)</td>
<td>11 (17)</td>
</tr>
<tr>
<td>Baseline CD4 count, cells/µl</td>
<td>651 (434-879)</td>
<td>717 (532-923)</td>
</tr>
<tr>
<td>Final CD4 count, cells/µl</td>
<td>429 (212-593)</td>
<td>471 (325-632)</td>
</tr>
<tr>
<td>Overall decrease in CD4 count</td>
<td>64 (86)</td>
<td>58 (91)</td>
</tr>
<tr>
<td>&gt;25% decrease in CD4 count</td>
<td>50 (76)</td>
<td>44 (76)</td>
</tr>
<tr>
<td>Stage 3/4 event on holding</td>
<td>6 (8.1)</td>
<td>5 (7.8)</td>
</tr>
</tbody>
</table>

*values given as n (%); bvalues given as median (IQR); c values given as median (95% CI) ¥ final CD4 count prior to switching to 2nd line or final available CD4 count for patients continuing on LM.
Potential drug-drug interactions in HIV-perinatally infected adolescents on antiretroviral therapy in Buenos Aires, Argentina.

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Background
An increasing number of treatment-experienced perinatally HIV-infected adolescents (PHA) are being transitioned from pediatric centers to adult HIV-care. Most of them had been heavily exposed to antiretroviral drugs (ARVs), harbor drug-resistant viruses and require nonantiretroviral medication due to comorbidities. This may predispose for clinically significant drug-drug interactions (CSDDIs). There are no studies concerning CSDDIs in PHA. We aimed to evaluate the prevalence of concomitant medications and CSDDIs in PHA who were transitioned for adult HIV-care to the Infectious Diseases Unit, Cosme Argerich Hospital, Buenos Aires City, Argentina.

Methods
• Descriptive pilot cross-sectional study (March to June 2014).
• PHA under ARVs at the time of the study were assessed for concomitant medication. CSDDIs were screened and categorized using the University of Liverpool Drug Interactions Program (www.hivdruginteractions.org).

Classification of CSDDIs
-red flag interactions These drugs should not be co-administered as they may lead to serious adverse events as a result of increase in plasma drug concentration or to a dramatic decrease in plasma concentration of the ARV.
-green flag interactions No known interactions.

Results
Forty-five patients were included. Female sex: 53%. Median (IQR) age: 20 years (18-22). CDC-stage C was observed in 27 (70%); 50% had ≥ 1 comorbidities including 3 subjects with HCV co-infection. Drug abuse was observed in 6 subjects (13%).

The median of prior ARV regimens was 3 (3-5). Current ARV regimen included: PI: 87%, NNRTI: 27%, INSTI: 20%, enfuvirtide: 7% and CCR5 inhibitor: 4%. Median CD4 T-cell count: 568 cells/mL (279-771). Viral load <50 copies/mL: 80%.
Sixty percent (27/45) had ≥ 1 co-medications (median 1). The most frequent co-medications were NSAIDs (44%), hormonal therapy (19%) and antimicrobials (19%). Use of herbal supplements was observed in 10 (22%).

Overall, 23 (51%) had ≥ 1 CSDDIs: 19/27 (70%) with co-medication (amber flag=18 and red flag=1); and 2/10 (20%) with herbal supplements. ARV-ARV interactions were observed in 4/45 (9%): unboosted atazanavir + tenofovir (n=2), unboosted atazanavir + efavirenz (n=2), and lopinavir/ritonavir + efavirenz (n=1) (all amber flag).

Considering patients with CSDDIs, 6 (26%) had a CSDDI that could reduce ARV levels. Of these, 2 patients had an antiretroviral salvage therapy for multiclass drug-resistant HIV.

Conclusions
In this pilot study, a high prevalence of co-morbidities, co-medications and CSDDIs was observed in PHA. A considerable proportion of patients had CSDDIs with a potential to cause sub-therapeutic ARV levels, what could be a concern in patients harboring drug-resistance viruses. Therefore, clinicians should be aware of co-morbid conditions pharmacologic management in order to avoid CSDDIs with ARVs agents.