We present the first evaluation of the pharmacokinetics, safety, and efficacy of a single-tablet regimen containing bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) in children aged 6 to <12 years with HIV-1 infection.

**Title:** Pharmacokinetics, safety, and efficacy of bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) single-tablet regimen in HIV-1-infected children (6 to <12 years)

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Background: Bictegravir (BIC, B), a novel, unboosted integrase strand transfer inhibitor (INSTI) with a high barrier to resistance and low potential for drug interactions, has been coformulated with the recommended NRTI backbone of emtricitabine (F, FTC) and tenofovir alafenamide (TAF) (B/F/TAF) into a once-daily (OD), single-tablet regimen (STR). We report pharmacokinetics (PK), safety and efficacy in children who switched from a stable antiretroviral regimen to B/F/TAF.

Methods: We conducted a prospective, single-arm, open-label, 2-part, 48-week (W) clinical trial to evaluate switching to the adult formulation of B/F/TAF (50/200/25 mg) OD in virologically suppressed children (6 to < 12 years) weighing 25 kg. Intensive PK was evaluated at W2 or W4. PK parameters were compared to B/F/TAF-treated adults to confirm BIC dose. Adverse events (AE), laboratory tests, HIV-1 RNA, were assessed. We report follow up data through W12.

Results: 25 children enrolled; median (range) age 10 (6-11) yrs, median (range) weight 28.4 (25.0-39.0) kg, 52% female, 64% Black, median CD4 count 928 cells/µL. BIC AUC was similar, C<sub>sub</sub> 77% higher, and C<sub>tau</sub> 22% lower in children 25 kg than adults. BIC C<sub>sub</sub> was well above protein-adjusted effective concentration for wild-type virus (162 ng/mL) in all children. FTC and TAF exposures were within safe and efficacious ranges of adults (table).

Conclusions: B/F/TAF maintained virologic suppression and was well tolerated in children through at least 12 weeks. Similar to adults, protein-adjusted concentration of all B/F/TAF components of B/F/TAF were achieved. Efficacy and safety in children are consistent with phase 3 B/F/TAF results in adults and adolescents, showing high proportions with viral suppression, excellent tolerability, and no resistance. B/F/TAF may be an important unboosted INSTI, STR option for HIV-infected children due to its small tablet size, high barrier to resistance and lack of food requirement.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Children</th>
<th>Adults</th>
<th>%GLSM Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC&lt;sub&gt;tau&lt;/sub&gt;, ng*h/mL</td>
<td>17565 (36.9)</td>
<td>102001 (26.9)</td>
<td>2610 (35.2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;tau&lt;/sub&gt;, ng/mL</td>
<td>227 (323)</td>
<td>78.3 (69.9, 96.7)</td>
<td>116 (104, 130)</td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt;, ng/mL</td>
<td>257 (226)</td>
<td>78.3 (69.9, 96.7)</td>
<td>116 (104, 130)</td>
</tr>
</tbody>
</table>

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