TFV-DP in DBS for pregnant/postpartum adolescent and young women on PrEP in Africa

Peter L. Anderson1, Lynda Stranix-Chibanda2, Sharon Huang3, Sybil Hosek4, Deborah Kacanek5, Teacler Nematadzira6, Frank Taulo7, Violet Korutaro7, Clemensia Nakabito8, Masedole Masenya8, Kathryn Lypen9, Nahida Chakhthoura10, Hans M. Spiegel11, Benjamin H. Chi12, on behalf of the IMPAACT 2009 team

1University of Colorado Anschutz Medical Campus, Aurora, CO, USA 2University of Zimbabwe, Harare, Zimbabwe 3Harvard University, Cambridge, MA, USA 4John H. Stroger Jr. Hospital of Cook County, Chicago, IL, USA 5Malawi College of Medicine-Johns Hopkins University Research Project, Blantyre, Malawi 6Baylor College of Medicine Children’s Foundation, Kampala, Uganda 7Makere University, Kampala, Uganda 8Wits Reproductive Health and HIV Institute, Johannesburg, South Africa 9Pré 365, Durham, NC, USA 10National Institute of Child Health and Human Development, Bethesda, MD, USA 11Hulu Government Solutions, Contractor to DAIDS/NIAID/NIH/HHS, Rockville, USA 12University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

BACKGROUND

• The risk of HIV acquisition more than doubles in pregnant and postpartum women in sub-Saharan Africa, emphasizing the need for programmatic delivery of HIV prevention services including PrEP.

• Intracellular tenofovir-diphosphate (TFV-DP) in red blood cells measured with dried blood spots (DBS) is an established biomarker of cumulative PrEP adherence given its 17 day half-life, analogous to HbA1C for diabetes.

• TFV-DP in DBS informs adherence-efficacy relationships for PrEP. This has been defined for men who have sex with men, but not for pregnant or non-pregnant women.

• Pregnancy causes physiological changes expected to lower TFV-DP in DBS including increased TFV renal clearance and hemodilution.

• IMPAACT 2009 is a two-component observational trial in pregnant and postpartum adolescent girls and young women in sub-Saharan Africa. This communication presents results from the first (PK) component.

OBJECTIVES

The goal of the IMPAACT 2009 PK component was to establish adherence benchmarks for TFV-DP in DBS for pregnant and postpartum adolescents and young women who took PrEP daily under direct observation, and to compare these benchmarks in the pregnant and postpartum groups.

METHODS

• HIV-negative adolescent girls and young women (16-24 years) were recruited in Malawi, South Africa, Uganda, and Zimbabwe.
  - Pregnant: 14-24 wks gestation at enrollment
  - Postpartum: 6-12 wks postpartum at enrollment
  - Daily FTC/TDF was administered for 12 weeks under direct observation (in person or by live video streaming).
  - Five 50μL DBS were collected weekly and stored at -80°C.
  - TFV-DP was assayed in one 50μL spot by validated LC-MS/MS at the University of Cape Town and reported as fmol/3mm punch for consistency with previous studies.
  - Summary statistics were used for observed data at week 12.
  - A one-compartment IV infusion non-linear mixed effects model was fit to concentration time data for individual predictions (modeled data).
  - Observed TFV-DP at week 12 was compared between the pregnant and postpartum groups with the Wilcoxon test.

RESULTS

• 20 pregnant and 20 postpartum women enrolled between March-May 2019
• 3348 of 3360 (99.9%) total doses were directly observed
• All participants met criteria for inclusion in the analysis

Adherence benchmarks using TFV-DP in DBS were established for pregnant/postpartum African adolescents and young women.

TFV-DP in DBS was 31%-37% lower in pregnancy compared with postpartum, in line with expectations. Strict adherence to PrEP is recommended during pregnancy.

Table 1. Baseline Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pregnant (N=20) median (IQR)</th>
<th>Postpartum (N=20) median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>20 (19.5, 22.5)</td>
<td>20 (19, 22)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59 (56, 65)</td>
<td>55 (56, 62)</td>
</tr>
<tr>
<td>HCT (%)</td>
<td>34.9 (33, 37.1)</td>
<td>40.8 (39.1, 41.7)</td>
</tr>
<tr>
<td>CLcr (CG-ideal wt; ml/min)</td>
<td>151 (130, 169)</td>
<td>109 (102, 123)</td>
</tr>
<tr>
<td>Gestational Age (wks)</td>
<td>18 (15, 20)</td>
<td>NA</td>
</tr>
<tr>
<td>Postpartum (wks)</td>
<td>NA</td>
<td>7 (7, 9)</td>
</tr>
</tbody>
</table>

Table 2. TFV-DP at Week 12 Visit

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pregnant (N=20) median (IQR)</th>
<th>Postpartum (N=20)* median (IQR)</th>
<th>Difference (p Wilcoxon)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observed TFV-DP (fmol/µl)</td>
<td>965 (691, 1166)</td>
<td>1406 (1053, 1859)</td>
<td>31% (p=0.0064)</td>
</tr>
<tr>
<td>Modeled TFV-DP (fmol/µl)</td>
<td>890 (704, 1143)</td>
<td>1418 (1179, 2139)</td>
<td>37% (p&lt;0.0001)</td>
</tr>
<tr>
<td>Modeled T-1/2 (days)</td>
<td>14 (10.6, 17.6)</td>
<td>16.5 (13.7, 21.2)</td>
<td>ND</td>
</tr>
</tbody>
</table>

One week 12 value was missing, and their concentration at week 11 was used. Median IQR was 1434 (980, 1600) if only week 12 was used.

- Figures 1 and 2 show TFV-DP concentration time profiles for observed (Figure 1) and modeled (Figure 2) data.
- Figure 3 shows estimated thresholds. These were based on 25th percentiles of observed data that were rounded down to establish the highest adherence group. Lower adherence categories were determined assuming dose-proportionality.

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