Bone mineral density/content of postpartum mothers taking treatment including DTG vs EFV, TDF vs TAF in pregnancy and their infants: randomized IMPAACT 2010 trial

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Background

- TDF-containing ART regimens are associated with greater bone loss than regimens without TDF
- The impact of the use of DTG, EFV, TDF and TAF in pregnancy and postpartum on maternal and infant bone is unknown

DTG- Dolutegravir
EFV- Efavirenz
TDF- Tenofovir Disoproxil Fumarate
TAF- Tenofovir Alafenamide

Grant, Current Opinion HIV AIDS. 2016
Study Design

Arm 1: Maternal DTG+FTC/TAF During Pregnancy and Postpartum
- Maternal follow-up for ~12-26 weeks prior to delivery
- Maternal and infant follow-up for 50 weeks after delivery

Arm 2: Maternal DTG+FTC/TDF During Pregnancy and Postpartum
- Maternal follow-up for ~12-26 weeks prior to delivery
- Maternal and infant follow-up for 50 weeks after delivery

Arm 3: Maternal EFV/FTC/TDF During Pregnancy and Postpartum
- Maternal follow-up for ~12-26 weeks prior to delivery
- Maternal and infant follow-up for 50 weeks after delivery

Planned DXA scan evaluations for 213 pairs (~71 per arm) at 7 sites (Uganda, South Africa, Zimbabwe)

Infant DXA at Week 26; Maternal DXA at Week 50

643 pregnant women with HIV at 22 sites in 9 countries

Lockman & Brummel et al, The Lancet, 2021
DXA scanning rationale

- 213 DXA measurements would provide 80% power to detect at least one half a standard deviation difference which the team assessed as clinically relevant.

- Infants had a whole body and lumbar spine scan performed at 26 weeks to ensure the latest practicable timepoint for performing high quality infant DXA scans, whilst minimizing infant radiation exposure.

- Mothers had hip and lumbar spine scans at 50 weeks postpartum to ensure that they were scanned after the longest possible period of ART exposure.

IMPAACT Annual Meeting 2021
Data Analysis

- DXA scans were read by a central reader
- Pairwise comparisons of mean maternal bone mineral density (BMD) Z-scores and infant bone mineral content (BMC) were performed using two-sample t-tests.
## Maternal Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>DTG+FTC/TAF (N = 47)</th>
<th>DTG+FTC/TDF (N = 57)</th>
<th>EFV/FTC/TDF (N = 50)</th>
<th>Total (N = 154)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean years)</td>
<td>25.9</td>
<td>27.9</td>
<td>29.3</td>
<td>27.7</td>
</tr>
<tr>
<td>Black African</td>
<td>47 (100.0%)</td>
<td>57 (100.0%)</td>
<td>50 (100.0%)</td>
<td>154 (100.0%)</td>
</tr>
<tr>
<td>Gestational age (mean weeks)</td>
<td>22.9</td>
<td>22.0</td>
<td>22.0</td>
<td>22.3</td>
</tr>
<tr>
<td>Gestational age &lt;24 weeks</td>
<td>29 (62%)</td>
<td>37 (65%)</td>
<td>32 (64%)</td>
<td>98 (64%)</td>
</tr>
<tr>
<td>BMI (mean g/cm²)</td>
<td>26.7</td>
<td>26.0</td>
<td>25.9</td>
<td>26.2</td>
</tr>
<tr>
<td>Log₁₀ HIV-1 RNA (mean copies/mL)</td>
<td>2.9</td>
<td>2.8</td>
<td>2.9</td>
<td>2.9</td>
</tr>
<tr>
<td>HIV-1 RNA ≥ 1,000 copies/mL</td>
<td>18 (38.3%)</td>
<td>26 (45.6%)</td>
<td>25 (51.0%)</td>
<td>69 (45.1%)</td>
</tr>
</tbody>
</table>

Baseline characteristics were similar between treatment arms.
### Additional Maternal Characteristics

By DXA scan at week 50 postpartum:

<table>
<thead>
<tr>
<th>Study Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) study treatment duration (weeks)</td>
<td>66.0 (8.5)</td>
</tr>
<tr>
<td>Mean (SD) breastfeeding duration (weeks)</td>
<td>43.9 (15.0)</td>
</tr>
<tr>
<td>Number (%) received medroxyprogesterone acetate contraception</td>
<td>95 (62%)</td>
</tr>
<tr>
<td>Bone fractures during follow-up</td>
<td>Zero</td>
</tr>
</tbody>
</table>
Maternal hip or spine BMD Z-scores between treatment groups

**Hip BMD Z-Score**

<table>
<thead>
<tr>
<th>N</th>
<th>Mean</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>47</td>
<td>-0.45</td>
<td>-0.24, 0.33</td>
<td>0.74</td>
</tr>
<tr>
<td>57</td>
<td>-0.50</td>
<td>-0.21, 0.35</td>
<td>0.63</td>
</tr>
<tr>
<td>50</td>
<td>-0.57</td>
<td>-0.18, 0.41</td>
<td>0.43</td>
</tr>
</tbody>
</table>

**Mean Difference (95% CI)**

- Hip: 0.05 (-0.24, 0.33), p = 0.74
- Hip: 0.07 (-0.21, 0.35), p = 0.63
- Hip: 0.12 (-0.18, 0.41), p = 0.43

**Spine BMD Z-Score**

<table>
<thead>
<tr>
<th>N</th>
<th>Mean</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>47</td>
<td>-1.40</td>
<td>-0.24, 0.60</td>
<td>0.26</td>
</tr>
<tr>
<td>57</td>
<td>-1.57</td>
<td>-0.34, 0.47</td>
<td>0.41</td>
</tr>
<tr>
<td>50</td>
<td>-1.64</td>
<td>-0.19, 0.67</td>
<td>0.75</td>
</tr>
</tbody>
</table>

**Mean Difference (95% CI)**

- Spine: 0.24 (-0.19, 0.67), p = 0.26
- Spine: 0.18 (-0.24, 0.60), p = 0.41
- Spine: 0.07 (-0.34, 0.47), p = 0.75

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IMPAACT 2010
Infant Characteristics at birth

<table>
<thead>
<tr>
<th></th>
<th>DTG+FTC/TAF (N = 57)</th>
<th>DTG+FTC/TDF (N = 59)</th>
<th>EFV/FTC/TDF (N = 49)</th>
<th>Total (N = 165)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>27 (47%)</td>
<td>29 (49%)</td>
<td>27 (55%)</td>
<td>83 (50%)</td>
</tr>
<tr>
<td>Gestational age (mean weeks)</td>
<td>40.0</td>
<td>39.5</td>
<td>39.1</td>
<td>39.5</td>
</tr>
<tr>
<td>Weight (mean kg)</td>
<td>3.2</td>
<td>3.1</td>
<td>3.0</td>
<td>3.1</td>
</tr>
</tbody>
</table>

Birth characteristics were similar across arms.
Additional Infant Characteristics

- DXA scans done within the allowable week 26 visit window were 104 (54%) whole body and 157 (83%) spine scans.

### By DXA scan at week 26 of age:

<table>
<thead>
<tr>
<th>Measure</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) age (months)</td>
<td>5.8 (0.6)</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>7.7</td>
</tr>
<tr>
<td>Number (%) still breastfeeding</td>
<td>134/165 (81%)</td>
</tr>
<tr>
<td>Number (%) received cotrimoxazole prophylaxis</td>
<td>153 (93%)</td>
</tr>
</tbody>
</table>
Infant BMC by treatment groups

- **Body BMC**
  - N: 38
  - Mean: 143.4 g
  - Mean: 137.4 g
  - Mean: 133.5 g
  - 6.0 (-8.4, 20.4) p=0.41
  - 3.9 (-11.0, 18.7) p=0.60
  - 9.9 (-4.7, 24.4) p=0.18

- **Body without Head BMC**
  - N: 38
  - Mean: 73.3 g
  - Mean: 70.5 g
  - Mean: 69.0 g
  - 2.8 (-5.8, 11.4) p=0.52
  - 1.5 (-7.0, 10.1) p=0.73
  - 4.3 (-4.0, 12.7) p=0.31

- **Spine BMC**
  - N: 55
  - Mean: 2.9 g
  - Mean: 2.8 g
  - Mean: 2.6 g
  - 0.20 (-0.01, 0.40) p=0.042
  - 0.02 (-0.17, 0.21) p=0.85
  - 0.22 (0.02, 0.42) p=0.028

IMPAACT 2010
Limitations

- The sample size for mothers and their infants was smaller than intended
- DXA scans were only done at a single timepoint for both mothers and infants
Conclusion

Among women randomized to start DTG vs EFV, TDF vs TAF during pregnancy and their babies:

- Maternal BMD were similar across study arms at week 50 postpartum however there was a trend to lower BMD in women receiving TDF vs TAF

- Further analysis is underway to understand the clinically meaningful 1/2 SD lower lumbar spine BMC in infants randomized to EFV arm compared to either of the DTG arms.
Acknowledgements

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