Growth of infants with perinatal exposure to maternal DTG vs EFV and TDF vs TAF: the randomized IMPAACT 2010 trial

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https://www.impaaactnetwork.org/studies/impaaact2010
Impact of contemporary antiretrovirals taken in pregnancy/breastfeeding on infant growth is not fully established

Stunting in infancy impacts cognitive development and adult height

Background

- Impact of contemporary antiretrovirals taken in pregnancy/breastfeeding on infant growth is not fully established
- Stunting in infancy impacts cognitive development and adult height
- We compared growth through 1 year of age in infants randomized to one of 3 maternal ART regimens started in pregnancy in the IMPAACT 2010 trial

Randomized Open-label Trial of the Virologic Efficacy and Safety of Three ART Regimens Started in Pregnancy

643 women with HIV

Key Eligibility Criteria
- Pregnant WLHIV 14-28 weeks gestation
- ART-naïve (up to 14 days ART in current pregnancy allowed)

Participants were enrolled at 22 sites in 9 countries

DTG = dolutegravir
EFV = efavirenz
TDF = tenofovir disoproxil fumarate
TAF = tenofovir alafenamide

Lockman & Brummel et al, The Lancet, 2021
Key Outcomes at Delivery/Birth

- Maternal DTG-containing ART vs EFV/FTC/TDF:
  - Superior virologic efficacy at delivery
  - Closer to expected weight gain in pregnancy
- Maternal DTG+FTC/TAF lowest composite frequency of adverse pregnancy outcome**
- Liveborn infants—similar except for weight
  - Higher proportion low birth weight <2500g EFV/FTC/TDF

**Poster 679 Brummel; Other IMPAACT 2010 posters—Fairlie; Chinula; Boyce
# Additional Infant Characteristics

<table>
<thead>
<tr>
<th></th>
<th>DTG+FTC/TAF (N = 208)</th>
<th>DTG+FTC/TDF (N = 202)</th>
<th>EFV/FTC/TDF (N = 207)</th>
<th>Total (N = 617)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiated breastfeeding, n (%)</td>
<td>161 (77)</td>
<td>158 (78)</td>
<td>160 (77)</td>
<td>479 (78)</td>
</tr>
<tr>
<td>Median (Q1, Q3) breastfeeding duration (weeks)</td>
<td>50 (44, 51)</td>
<td>50 (44, 51)</td>
<td>50 (41, 51)</td>
<td>50 (43, 51)</td>
</tr>
<tr>
<td>ARV prophylaxis, n (%)</td>
<td>203 (98)</td>
<td>200 (99)</td>
<td>196 (95)</td>
<td>599 (97)</td>
</tr>
<tr>
<td>Cotrimoxazole prophylaxis, n (%)</td>
<td>179 (86)</td>
<td>174 (86)</td>
<td>169 (82)</td>
<td>522 (85)</td>
</tr>
<tr>
<td>Acquired HIV, n (%)</td>
<td>2 (1)</td>
<td>1 (0.5)</td>
<td>1 (0.5)</td>
<td>4 (0.6)</td>
</tr>
</tbody>
</table>
Inclusion Flow Chart

643 Pregnant Women Randomized

217 DTG+FTC/TAF
1 withdrew
208 livebirths
8 stillbirths
Anthropometry Available
193 Week 26
179 Week 50

215 DTG+FTC/TDF
2 withdrew
202 livebirths
11 stillbirths
Anthropometry Available
193 Week 26
176 Week 50

211 EFV/FTC/TDF
0 withdrew
207 livebirths
4 stillbirths
Anthropometry Available
188 Week 26
170 Week 50

20 infants died: DTG+FTC/TAF—2 (1%); DTG+FTC/TDF—4 (2%); EFV/FTC/TDF—14 (7%)
Infant Growth Statistical Approach

- Infant growth WHO Z-scores computed at Weeks 26 and 50 for liveborn infants retained on-study with length and weight data available:
  - Length-for-age (LAZ)
  - Weight-for-age (WAZ)
  - Weight-for-length (WHZ)

- WHO standards and software used for Z-score calculations (www.who.int/childgrowth/software/en)
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  - Weight-for-length (WHZ)
- WHO standards and software used for Z-score calculations (www.who.int/childgrowth/software/en)
- Pairwise comparisons of mean z-scores by two-sample t-tests
- Proportion stunting (LAZ <-2) estimated
Length-for-Age Z-scores lower in EFV vs DTG arms, similar TDF- vs TAF-DTG
Weight-for-Age Z-scores lower in EFV vs DTG arms, similar TDF- vs TAF-DTG

Mean WHO Weight-for-Age Z-Score with 95% CI

Mean Differences (95% CI), p-value

-0.0 (-0.3, 0.2) p=0.78
0.3 (0.0, 0.6) p=0.0094
0.3 (0.0, 0.6) p=0.019
Weight-for-Length Z-scores, no apparent differences

**Graph:**
- **DTG+FTC/TAF**
- **DTG+FTC/TDF**
- **EFV/FTC/TDF**

**Mean Differences (95% CI), p-value**
- **DTG+FTC/TAF - DTG+FTC/TDF**
  - 0.3 (-0.1, 0.6) p=0.13
- **DTG+FTC/TDF - EFV/FTC/TDF**
  - -0.3 (-0.6, 0.1) p=0.14
- **DTG+FTC/TAF - EFV/FTC/TDF**
  - 0.0 (-0.3, 0.4) p=0.94

**Study Week:**
- Birth*
- Week 6
- Week 14
- Week 26
- Week 38
- Week 50

*post-hoc analysis
Limitations

- Infant follow-up limited to one year of age
- Included women who started ART in pregnancy (not women conceiving on ART)
- Predominantly breastfeeding populations studied, primarily in Africa
Conclusions

- Infants born to mothers who started EFV/FTC/TDF in pregnancy were significantly smaller throughout infancy than infants whose mothers started DTG+FTC/TAF or DTG+FTC/TDF
- Rates of stunting were high across all arms and higher in EFV arm (1 in 5) than the DTG arms (1 in 7)
- Mechanisms of this difference remain unclear
  - Potential influence of differential maternal weight gain in pregnancy
- Infant growth was similar following exposure to maternal TDF vs. TAF in combination with DTG+FTC
Conclusions

- Extended follow-up required to assess persistence of observed differences
- Infant growth should be factored into the choice of optimal maternal ART regimens during pregnancy and breastfeeding
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