Differential BMI Changes Following PI- and INSTI-Based ART Initiation by Sex and Race

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Introduction

While older protease inhibitors (PI) were more frequently associated with central fat accumulation, initiation of currently used ART regimens has been associated with increases in body mass index (BMI), particularly in women and with integrase strand transfer inhibitor (INSTI) use.

Objective

To analyze the differential effect of individual PI and INSTI changes in BMI by sex and race in a large urban HIV clinic in the Southern U.S.

Methods

• All patients initiating ART at the Parkland Health and Hospital System in Dallas, TX from 2009 to 2017 were included.
• Exposure to ART was defined as concurrent receipt of two nucleoside reverse transcriptase inhibitors (NRTI) and at least one PI, Non-nucleoside reverse transcriptase inhibitor (NNRTI) or INSTI.
• In regression analysis, we compared yearly change in BMI (kg/m²) following initiation of PI [Boosted or unboosted Atazanavir (ATV), Darunavir (DRV) or Lopinavir (LPV)] or INSTI [Raltegravir (RAL), Evitegravir (EVG) or Dolutegravin (DTG)].
  - Between men and women.
  - Between Blacks, Hispanics and Non-Hispanic Whites.
• We controlled for year of HAART initiation, baseline CD4 count and HIV-1 RNA, and whether patients achieved virologic suppression on HAART.

Study Population:
A total of 4048 patients enrolled with a median follow-up on HAART of 6.7 years. Baseline characteristics are presented in table 1.

Table 1: Baseline Characteristics

<table>
<thead>
<tr>
<th>Race/Ethnicity (N, %)</th>
<th>All (N=4048)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>2141 (52.9%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1144 (28.3%)</td>
</tr>
<tr>
<td>Non Hispanic white</td>
<td>642 (15.9%)</td>
</tr>
<tr>
<td>Men</td>
<td>2775 (68.6%)</td>
</tr>
<tr>
<td>Women</td>
<td>1273 (31.4%)</td>
</tr>
<tr>
<td>Age (Mean, SD)</td>
<td>46.3 ± 11.9</td>
</tr>
<tr>
<td>Baseline BMI (SD)</td>
<td>26.9 (6.3)</td>
</tr>
</tbody>
</table>

Study results

• We observed a differential effect of INSTI and PI-based HAART regimens on BMI changes.
• All PIs were associated with greater BMI gain in women than in men, but with no effect by race/ethnicity. LPV-based ART was associated with relatively smaller BMI gains.
• Among INSTIs, while EVG appeared to be associated with greater BMI gains overall, the effect did not vary by sex or race/ethnicity. DTG and RAL were associated with greater BMI gains in women, and DTG with greater gains in Blacks & Hispanics.
• The mechanisms of this differential effect by sex and race/ethnicity are yet to be determined.

Results

Yearly BMI Changes by HAART Type:
- The BMI slope per year on NNRTI, PI and INSTI were 0.22, 0.24 and 0.32 kg/m², respectively.
- BMI slopes for individual PI- and INSTI-based regimens by sex and race/ethnicity are presented in table 2 and figure 1 (in fully adjusted model controlling for year of HAART initiation, baseline CD4 count and HIV-1 RNA, and whether patients achieved virologic suppression on HAART).

Between Regimen Comparisons of BMI Changes:
- PI vs. INSTI; p=0.025
- PI vs. NNRTI; p=0.18
- NNRTI vs. INSTI; p=0.0004
- ATV vs. DRV: p=0.61
- ATV vs. LPV: p=0.35
- DRV vs. LPV: p=0.46
- RAL vs. EVG: p=0.05
- RAL vs. DTG: p=0.002
- EVG vs. DTG: p=0.99.

Conclusions

We observed a differential effect of INSTI and PI-based HAART regimens on BMI changes.
- All PIs were associated with greater BMI gain in women than in men, but with no effect by race/ethnicity. LPV-based ART was associated with relatively smaller BMI gains.
- Among INSTIs, while EVG appeared to be associated with greater BMI gains overall, the effect did not vary by sex or race/ethnicity. DTG and RAL were associated with greater BMI gains in women, and DTG with greater gains in Blacks & Hispanics.
- The mechanisms of this differential effect by sex and race/ethnicity are yet to be determined.

Table 2: Yearly BMI Changes by Race/Ethnicity and Sex

<table>
<thead>
<tr>
<th>Yearly BMI Change</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATV (n=1278; 2998 PY)</td>
<td>0.29</td>
<td>0.26</td>
</tr>
<tr>
<td>DRV (n=1278; 2998 PY)</td>
<td>0.29</td>
<td>0.26</td>
</tr>
<tr>
<td>LPV/RTV (n=223; 388 PY)</td>
<td>0.13</td>
<td>0.09</td>
</tr>
<tr>
<td>RAL (n=591; 423 PY)</td>
<td>0.16</td>
<td>0.11</td>
</tr>
<tr>
<td>EVG (n=405; 243 PY)</td>
<td>0.25</td>
<td>0.23</td>
</tr>
<tr>
<td>DTG (n=2037; 2473 PY)</td>
<td>0.16</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Figure 1: Comparisons of Yearly BMI Changes on HAART

A. By sex (A) and by race/ethnicity (B)

*Transgender M-F (n=72) not included in analysis.