Background

- High unplanned pregnancy rates are a public health problem because they negatively influence several indicators of women's and child's health and in HIV infected women may result in vertical transmission.

- Long acting reversible contraceptives (LARCs), such as the etonogestrel releasing implant (ENG) and antiretroviral therapy. Case reports of pregnancy in HIV women under HAART and using ENG implants and efavirenz have been published.

- The ENG implant package insert states that significant interactions have been observed with the co-administration with protease inhibitors or non-nucleoside reverse transcriptase inhibitors.

- We evaluated both the effect of ENG on the PK parameters of 3 highly active antiretroviral (ARV) regimens including: rilpivirine boosted atazanavir (ATV), ritonavir boosted tipranavir (LPV/r) or efavirenz (EFV) and the effect of these ARVs on ENG levels in HIV infected postpartum women.

Methods

- International Maternal Pediatric Adolescent AIDS Clinical Trial Network (IMPAACT) Protocol P1026s is an ongoing, non-blinded, international study of ARV PK in pregnancy and postpartum.

- We enrolled postpartum women who desired to use ENG implants and were taking ATV/r, LPV/r or EFV-based regimens for at least 2 weeks.

- Women on medications known to interfere with absorption, metabolism, or clearance of the drugs being evaluated and those with clinical or laboratory tests that would like to require a change in the medication regimen during the study were excluded.

- ENG implant is an off-white, non-biodegradable, single sterile implant that contains 68 mg of the synthetic progestin etonogestrel. It is expected to provide contraceptive efficacy for up to three years when it should be removed.

- ENG implant was inserted between 2 and 12 weeks postpartum.

- ARV PK sampling was performed before and 6-7 weeks after implant insertion. ENG sample was obtained once at 6-7 weeks after implant insertion.

- Plasma samples collected at 0, 1, 2, 6, 8, 12 hours post-dose for LPV and a 24 hours post-dose sample was obtained in women under ATV or EFV.

- ENG and ARV concentrations were measured using liquid chromatography-mass spectrometry.

- Target minimum AUC for ATV, LPV and EFV were 29.4, 52 and 40 μg/mL, respectively.

- Median (range) ENG concentration of 89.0 (58.9-161.6) ng/mL 6-7 weeks after implant insertion. For the IMPAACT P1026s Protocol Team

Results

Table 1. Participants Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ATV/r (N=12)</th>
<th>LPV/r (N=12)</th>
<th>EFV (N=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Median 35 (28-49)</td>
<td>Median 35 (28-49)</td>
<td>Median 35 (28-49)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>62.5 (38.7-157.9)</td>
<td>26.9 (15.8-41.1)</td>
<td>72.6 (46.7-113.9)</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td>Black Non-Hispanic</td>
<td>Non-Hispanic</td>
<td>Hispanic</td>
</tr>
<tr>
<td>Country</td>
<td>Brazil</td>
<td>Brazil</td>
<td>Argentina</td>
</tr>
</tbody>
</table>

Table 2. ENG Concentration and ARV AUC Comparisons

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ATV/r (N=12)</th>
<th>LPV/r (N=12)</th>
<th>EFV (N=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENG Concentration (ng/mL)</td>
<td>Median 89.0 (58.9-161.6)</td>
<td>Median 89.0 (58.9-161.6)</td>
<td>Median 89.0 (58.9-161.6)</td>
</tr>
</tbody>
</table>

Figure 1: Summary of the Median ATV Exposure

Figure 2: Summary of the Median LPV Exposure

Figure 3: Summary of the Median EFV Exposure

Figure 4: Summary of the Median EFV Concentration

Conclusions

- No significant change in ATV's LPV/r and EFV exposure was seen after ENG insertion.

- EFV use was associated with greater decreased ENG concentration to levels that may impair contraceptive efficacy.

- Women receiving ENG should be counseled about the increased risks of implant failure and advice to use alternative or additional contraceptive method. Implant substitution between three years or ARV regimen change may be considered.

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