Overview

IMPAAACT Annual Meeting June 18, 2018

P1026s Pharmacokinetic Properties of Antiretroviral Drugs During Pregnancy V 10.0

IMPAAACT 2026 Pharmacokinetic Properties Of HIV, TB, Contraceptive And Related Drugs During Pregnancy And Postpartum V 1.0
As of June 5, 2018, 985 mothers and 492 infants enrolled

Completed pregnancy arms for 17 ARVs, including darunavir, rilpivirine, maraviroc, dolutegravir and elvitegravir

Presented 34 abstracts and published 23 manuscripts
P1026s Design Summary

- Opened 6/1/03, now on version 10.0
- Opportunistic design – enroll pregnant/postpartum women receiving selected ARV’s, TB drugs and/or postpartum contraceptives as part of clinical care
  - Clinical care providers prescribe all drugs, are responsible for clinical management
- Pregnant subjects – ARV’s, TB drugs
  - PK sampling during 2\(^{nd}\) trimester, 3\(^{rd}\) trimester and postpartum
  - Rapid turn around of assay results - to clinician within 2 weeks
  - Adjustment of dosing and repeat PK sampling at caregiver discretion
  - At delivery, collection of maternal plasma and cord blood samples
  - After birth, collection of washout PK samples from neonate
- Postpartum subjects – ARV’s plus contraceptives
  - PK sampling prior to start of contraception (2-12 weeks postpartum), repeated 6-7 weeks later
- Target sample size – 25 evaluable subjects per arm
## IMPAACT P1026s V10: Current Enrollment Status

<table>
<thead>
<tr>
<th>Arm</th>
<th>Number Enrolled</th>
<th>Target Accrual</th>
<th>% Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antepartum/HIV-infected Arms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAF 25 mg with COBI or ritonavir</td>
<td>15</td>
<td>25</td>
<td>60%</td>
</tr>
<tr>
<td>TAF 10 mg with COBI</td>
<td>30</td>
<td>25</td>
<td>100%</td>
</tr>
<tr>
<td>TAF 25 mg w/o COBI or ritonavir</td>
<td>27</td>
<td>25</td>
<td>100%</td>
</tr>
<tr>
<td>ATZ/COBI</td>
<td>5</td>
<td>25</td>
<td>20%</td>
</tr>
<tr>
<td>DRV/COBI</td>
<td>28</td>
<td>25</td>
<td>100%</td>
</tr>
<tr>
<td>DRV/r (800/100)</td>
<td>24</td>
<td>25</td>
<td>96%</td>
</tr>
<tr>
<td>DRV/r (900/100)</td>
<td>2</td>
<td>25</td>
<td>8%</td>
</tr>
<tr>
<td><strong>TB Arms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First line TB drugs with EFV</td>
<td>20</td>
<td>25</td>
<td>80%</td>
</tr>
<tr>
<td>First line TB drugs with LPV/r</td>
<td>1</td>
<td>25</td>
<td>4%</td>
</tr>
<tr>
<td>TB Only</td>
<td>14</td>
<td>25</td>
<td>56%</td>
</tr>
<tr>
<td>Second Line TB drugs (HIV-infected and uninfected)</td>
<td>3</td>
<td>25</td>
<td>12%</td>
</tr>
<tr>
<td><strong>Postpartum Contraception Arms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRV/COBI or ATZ/COBI + oral contraceptives</td>
<td>0</td>
<td>25</td>
<td>0%</td>
</tr>
<tr>
<td>DRV/COBI or ATZ/COBI + etonogestrel</td>
<td>1</td>
<td>25</td>
<td>4%</td>
</tr>
<tr>
<td>EFV + oral contraceptive</td>
<td>27</td>
<td>25</td>
<td>100%</td>
</tr>
</tbody>
</table>
P1026s Dolutegravir Arm

Mother

Infant

- Median (IQR) ratio DTG cord blood to maternal plasma: 1.25 (1.07–1.40)

- Median (IQR) DTG half-life was 32.8 h (25.9–35.9)

- Maternal plasma and cord blood Cobi at delivery BQL in 8 of 15 women
- In other 7 women, median (IQR) Cobi ratio cord blood to maternal plasma: 0.09 (0.05–0.12)
- Cobi BQL in all infant washout samples
Upcoming Changes

• Need arms for new ARV’s and need to revise some existing arms:
  – Bictegravir/FTC/TAF
  – Doravirine
  – Intracellular TAF
  – Cabotegravir injectable
  – TB drugs, including breast milk transfer
  – Interaction between DTG and postpartum contraception
• Protocol needs to become compliant with RAVE and CDISC

• **Solution**: Instead of P1026s v11, a new protocol IMPAACT 2026 is being developed
IMPAAACT 2026

• Component 1: HIV infected pregnant women on oral ARVs
  Bictegravir  Doravirine  TAF (Intracellular)

• Component 2: HIV infected and uninfected pregnant women on LA/ER ARVs
  Cabotegravir

• Component 3: HIV infected pregnant women on first line TB treatment (INH/PZA/EMB/PZA/MFX)
  Dolutegravir  ATZ/r or DRV/r

• Component 4: HIV infected and uninfected pregnant women on second line TB treatment
  Moxifloxacin (MFX)  Levofloxacin (LVX)  Clofazimine (CFZ)
  Linezolid (LZD)  Bedaquiline (BDQ)  Delamanid (DLM)

• Component 5: HIV-infected postpartum women receiving DTG and oral or implant contraceptives

• Component 6: HIV infected and uninfected postpartum women who are breastfeeding while receiving oral ARVs, first or second line TB treatment