IMPAACT P1101: PHASE I/II STUDY OF RALTEGRAVIR CONTAINING REGIMEN IN HIV/TB CO-TREATED CHILDREN AGED 6 TO <12 YEARS

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STUDY RATIONALE

- HIV/Tb co-infection commonly encountered
- Rifampicin (RIF) induces CYP3A4 and phase II enzymes such as UDP-glucuronosyltransferases, altering the hepatic metabolism of many drugs (including ARVs)
- ARTs are needed that are well tolerated, potent, and have minimal interactions with Rifampicin-containing TB therapy
  
  Current options: Efavirenz, “superboosted’ lopinavir/ritonavir, 3 NRTIs

- RIF enhances glucuronidation and clearance of Raltegravir (RAL)
  
  In adults, doubling the dose of RAL when given in conjunction with RIF partially overcame this PK interaction ➔ adequate RAL plasma $C_{\text{max}}$ and AUC (no safety concerns)*

*Wenning et al AAC 2009
Pharmacokinetics and Virological Responses in ≥ 6-12 yo

**PK Results**

- **GM AUC$_{12h}$**: 38.8 µM-h (CV=38%)  
  Target: 14-45 µM-h

- **GM C$_{12h}$**: 228 nM (CV=78%)  
  Target: ≥ 75 nM (33ng/ml)

**Virological Responses (As Treated Analysis (n =12))**

- 92% (11/12) for Virologic Success
- 83% (10/12) for HIV RNA ≤ 50 copies/mL at Week 8

**Note:** Week 8 Log$_{10}$ HIV-RNA Change from Baseline: Median: -2.78, IQR (-3.41, -2.09).

**Definitions:**

- **Virologic Success:**
  - ≥ 1 log$_{10}$ drop in plasma HIV RNA copies/ml from baseline
  - Or
  - HIV RNA ≤ 400 copies/mL at Week 8