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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IMPAACT International Maternal Pediatric Adolescent AIDS Clinical Trials Network

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

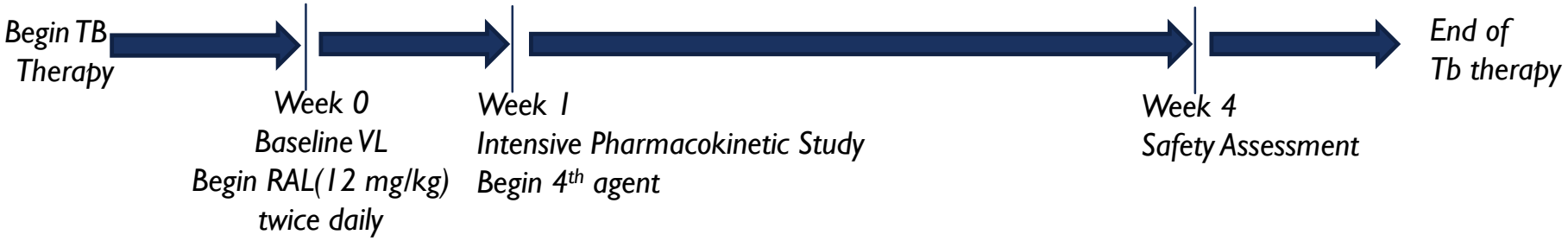
  Current options: Efavirenz, "superboosted" lopinavir/ritonavir, 3 NRTIs

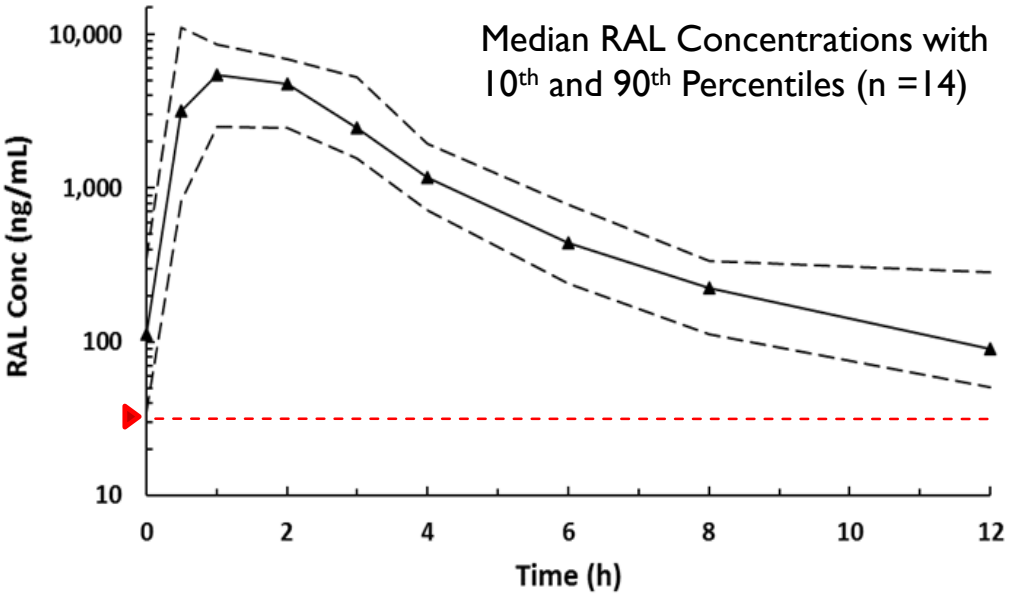
- RIF enhances glucuronidation and clearance of Raltegravir (RAL)

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

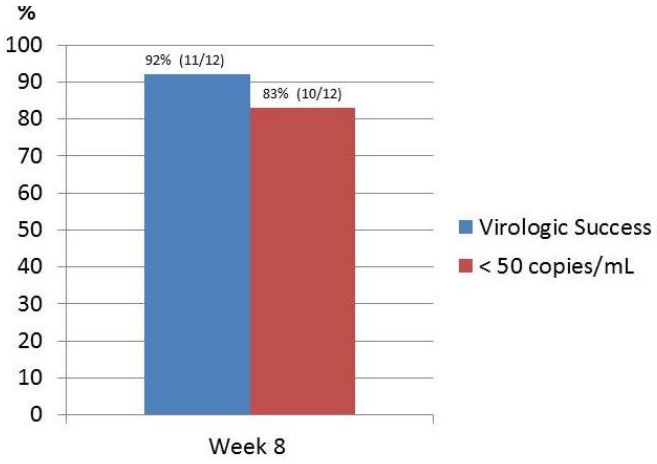
**Wenning et al AAC 2009*

Pharmacokinetics and Virological Responses in ≥ 6-12 yo





Virological Responses
(As Treated Analysis (n =12)



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

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)

Virologic Success:

≥ 1 log_{10} drop in plasma HIV RNA copies/ml from baseline Or

HIV RNA ≤ 400 copies/mL at Week 8